A Phase 2, Randomized, Double-Blind, Placebo- Controlled Study of the Efficacy and Safety of CF102 in the Second-Line Treatment of Advanced Hepatocellular Carcinoma in Subjects with Child-Pugh Class B Cirrhosis

STATISTICAL ANALYSIS PLAN
Version 7.0
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CONFIDENTIAL

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
A_3AR	Adenosine A3 receptor (A_3AR)
AASLD	American Association for the Study of Liver Diseases
AE(s)	Adverse event(s)
AFP	α-fetoprotein (alpha-fetoprotein)
ALT	Alanine Aminotransferase (also referred to as SGPT, ALAT)
ANC	Absolute neutrophil count
ANCOVA	Analysis of Covariance
AST	Aspartate Aminotransferase (also referred to as SGOT, ASAT)
BID	Twice a day
BMI	Body mass index
BUN	Blood Urea Nitrogen
CBC	Complete blood count
CF102	Sponsor defined name for the study medication
CFB	Change From Baseline
cm	Centimeter(s)
CP	Child-Pugh
CPB	Child-Pugh Class B (cirrhosis)
CR	Complete Response
CRF	Case Report Form
CS	Clinically Significant
CT	Computed Tomography
CTCAE	Common Terminology Criteria for Adverse Events
DB	Double Blind
DC	Disease Control (CR + PR + SD)
DCR	Disease Control (CR + PR + SD) Rate; also referred to as DC Rate
ECG	Electrocardiogram
ECOG	Eastern Collaborative Oncology Group
EHS	Extrahepatic Spread
EOS	End Of Study (end of dosing)
HBV	Hepatitis B Virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C Virus
HR	Heart rate
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ID	Identification
IMP	Investigational medicinal product
INR	International normalized ratio
ITT	Intent-to-treat
kg	Kilogram(s)
KM	Kaplan-Meier
LD	Longest diameter
LDH	Lactate dehydrogenase

Abbreviation	Definition
LOCF	Last observation carried forward
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram(s)
mmHg	Millimeter of Mercury
MRI	Magnetic resonance imaging
NAB	Normal Approximation to the Binomial Distribution
NCI	National Cancer Institute
NCS	Not clinically significant
NYHA	New York Heart Association
OL	Open Label
OR	Objective response (CR + PR)
ORR	Objective response (CR + PR) Rate; also referred to as OR Rate
OS	Overall Survival
PBMC	Peripheral blood mononuclear cells
PD	Progressive disease
PE	Physical examination
PFS	Progression-Free Survival
PK	Pharmacokinetic(s)
PO	per os; oral(ly)
PR	Partial response
PS	Performance status
PT	Prothrombin Time (laboratory parameter); Preferred Term (MedDRA)
PTT	Partial Thromboplastin Time
PVT	Portal Vein Thrombosis
QTc	Corrected QT
QTcF	Corrected QT (Fridericia)
RECIST	Response Evaluation Criteria in Solid Tumors
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Stable disease (also Standard Deviation in tables)
SE	Standard Error
SGOT	Serum Glutamic Oxaloacetic Transaminase (also referred to as AST)
SGPT	Serum Glutamic Pyruvic Transaminase (also referred to as ALT)
SOC	System Organ Class (MedDRA)
TEAE	Treatment-emergent adverse event
TTP	Time To Progression
ULN	Upper limit of normal
WBC	White blood cell count

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1. INTRODUCTION AND BACKGROUND

This Statistical Analysis Plan (SAP; Version 7.0) is to be used in conjunction with the protocol (Amendment 5, dated 6 November 2018) and the corresponding case report forms (CRFs). Table shells and mock listings corresponding to the contents of this document will be prepared and included with the final version. This document, with table shells and mock listings, will be reviewed prior to unblinding, and revised if necessary. The contents of this document were developed prior to unblinding, except as noted.

CF102 is a selective, high affinity agonist for the human adenosine A_3 receptor (A_3AR) and is being developed as a non-cytotoxic agent for the treatment for hepatocellular carcinoma (HCC). A_3ARs are expressed primarily in normal lung, liver, kidney and heart tissues, with very little expression in the brain or in skeletal muscle. A_3ARs are over-expressed by human HCC cells, but not those from healthy donors. A_3AR expression is also elevated in PBMC isolated from patients with hepatitis C viral (HCV) infections. Further details are given in the protocol.

2. TRIAL DESIGN

2.1 STUDY OBJECTIVES

The primary objective of this trial is to:

- Evaluate the efficacy of orally administered CF102 25 mg BID as compared to placebo, as determined by Overall Survival (OS), when used as second-line therapy in subjects with advanced hepatocellular carcinoma (HCC) and Child-Pugh Class B (CPB) cirrhosis.

The secondary objectives of this trial are to:

- Evaluate other indicators of efficacy of CF102 25 mg BID as compared to placebo, including time to progression (TTP), progression-free survival (PFS), objective response (OR) rate, and disease control (DC) rate in this population;
- Explore exposure-response relationships using sparse pharmacokinetic (PK) sampling;
- Characterize the safety profile of CF102 25 mg BID in subjects with advanced HCC and CPB cirrhosis;
- Characterize the effects of CF102 25 mg BID on laboratory parameters associated with viral hepatitis, hepatic dysfunction, and cirrhosis; and
- Explore the relationship between the white blood cell (WBC) adenosine A_3 receptor (A_3AR) expression and clinical response.

The planned analyses of PK results will be presented in a separate document.

2.2 STUDY DESIGN

This is a multicenter, randomized, double-blind, placebo-controlled clinical trial in subjects with advanced HCC and CPB cirrhosis who did not tolerate prior sorafenib therapy or experienced disease progression on prior sorafenib therapy. The trial will evaluate the efficacy and safety of CF102 25 mg BID as compared to placebo.

Tumor imaging will be performed every 8 weeks. Treatment will continue until the subject experiences unacceptable drug-related intolerability. Subjects will return for a follow-up visit 28 days after completion of the last dose of study drug, and every attempt will be made to obtain survival data on all randomized subjects. Subjects who discontinue will be followed indefinitely for survival status. Enrollment will continue until 75 deaths have been recorded. All randomized subjects will continue to be followed for survival status after 75 deaths have been recorded.

Once the requisite number of events has occurred and the blind is broken for analysis of the trial results, any surviving subjects who remain on blinded drug will be offered the opportunity to continue dosing with open-label CF102 25 mg BID indefinitely, following the protocol-specified schedule of events (Table 1-2), referred to below as the Open-Label (OL) period. The period prior to breaking the blind is referred to as the Double-Blind (DB) period. Bottles of study drug dispensed to subjects at the start of each treatment cycle during the OL period will contain a sufficient supply of CF102 for one cycle (28 days) of continuous dosing.

2.3 STUDY DRUG DOSAGE AND ADMINISTRATION

Subjects will be randomly assigned in a 2:1 ratio to treatment with either CF102 25 mg or matching placebo. CF102 or placebo will be self-administered orally twice daily (BID) on an empty stomach (1 hour before or 2 hours after meals) beginning on Day 1 of the trial and thereafter at approximately the same times each day of the 28-day cycle.

During the OL period, CF102 will be administrated in continuous 28-day cycles beginning on Day 1 of Cycle 1 of the OL period.

2.4 DOSE MODIFICATION

Any safety-related modification of study drug dosing (i.e., dose reduction or interruption of scheduled dosing) and the reason for such action must be clearly noted on the Adverse Events page of the CRF, and the Medical Monitor informed.

In the case of any Grade 3 toxicity by CTCAE v4.0 judged by the Principal Investigator to be at least “possibly” drug-related, the dose of study drug will be interrupted for up to 7 days. If toxicity does not resolve to Grade $\leq$ 1 within 7 days, the subject will be discontinued from treatment. If toxicity resolves to Grade $\leq$ 1 within 7 days, dosing will be resumed at the decreased dose of 1 capsule per day.

In the case of any Grade 4 toxicity judged by the Principal Investigator to be at least “possibly” drug-related, the dose of study drug will be withdrawn permanently.

Only 1 dose reduction will be allowed. If a Grade 3 or 4 toxicity judged by the Principal Investigator to be at least “possibly” drug-related occurs upon rechallenge at the reduced dose, study drug dosing will be withdrawn permanently.

3. SAMPLE SIZE, RANDOMIZATION AND BLINDING

3.1 SAMPLE SIZE

Approximately 78 subjects will be enrolled during an accrual period estimated to be approximately 102 weeks (24 months) in duration and randomized to either CF102 or placebo using a 2:1 randomization. The post-accrual treatment period will continue until a total of 75 subjects have died. Assuming a hazard ratio of 0.5, 75 deaths will provide 80% power for the logrank test at level 0.05 (EAST 6, Cytel, 2014).

3.2 RANDOMIZATION AND BLINDING

On Day 1, each subject will be randomly assigned to receive either CF102 25 mg BID or placebo BID, using a 2:1 randomization. The subject ID number identifies the subject and consists of the site number followed by the subject number for that site. The randomization number identifies the treatment.

The trial will be double-blind; the subject, Investigator/staff, and Sponsor will not have access to or knowledge of any subject's treatment assignment. Upon completion of the DB period, the blind will be broken and all analyses will be performed. Any surviving subjects who remain on blinded drug will be offered the opportunity to continue dosing with open-label CF102 25 mg BID indefinitely (OL Period).

4. SELECTION AND WITHDRAWAL

4.1 INCLUSION CRITERIA

Inclusion Criteria (DB Period)

Subjects must meet all of the following inclusion criteria to be eligible for the trial:

1. Males and females at least 18 years of age.
2. Diagnosis of HCC:
   - For subjects without underlying cirrhosis at the time of diagnosis, diagnosis of HCC documented by cytology and/or histology.
   - For subjects with underlying cirrhosis at the time of diagnosis, diagnosis of HCC established according to the American Association for the Study of Liver Diseases Practice Guideline algorithm (Appendix E of the protocol).
3. HCC is advanced, i.e., treatment-refractory or metastatic, and no standard therapies are expected to be curative.
4. Receipt of prior sorafenib therapy for at least 3 weeks and withdrawal from treatment due either to intolerability or to radiographic evidence of disease progression. If treatment was withdrawn due to intolerability manifested as a Grade 3 or 4 event by National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE v4.0), less than 3 weeks of continuous prior administration prior to withdrawal is acceptable (see also Exclusion Criterion #3).
5. Prior sorafenib treatment was discontinued for at least 2 weeks prior to the Baseline Visit.

6. Eastern Cooperative Oncology Group (ECOG) performance status (PS) of ≤2 (Appendix D).
7. Cirrhosis classified as Child-Pugh Class B (Appendix A).
8. The following laboratory values must be documented ≤ 3 days prior to the first dose of study drug:
   - Absolute neutrophil count (ANC) ≥ 1.5×10^9/L
   - Platelet count ≥ 75×10^9/L
   - Serum creatinine ≤ 2.0 mg/dL
   - Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 5 × the upper limit of normal (ULN)
   - Total bilirubin ≤ 3.0 mg/dL
   - Serum albumin ≥ 2.8 g/dL
   - Prothrombin time (PT) no greater than 6 seconds longer than control.
9. Life expectancy of ≥ 6 weeks.
10. For women of childbearing potential, negative serum pregnancy test result.
11. Provide written informed consent to participate.
12. Willing to comply with scheduled visits, treatment plans, laboratory assessments, and other trial-related procedures.

Inclusion Criteria (OL Period)

1. The subject signed the ICF for the Open Label treatment.
2. The subject received double blind treatment with CF102/placebo and is still taking the investigational medication when Amendment 5 is approved.

4.2 EXCLUSION CRITERIA

Subjects meeting any of the following criteria are ineligible for the trial:

1. Receipt of no, or of >1, prior systemic drug therapies for HCC.
2. Receipt of systemic cancer therapy, immunomodulatory drug therapy, immunosuppressive therapy, or corticosteroids > 20 mg/day prednisone or equivalent within 14 days prior to the Baseline Visit or concurrently during the trial.
3. Presence of an acute or chronic toxicity of prior chemotherapy that has not resolved to ≤ Grade 1, as determined by CTCAE v 4.0.
4. Locoregional treatment within 4 weeks prior to the Baseline Visit.
5. Major surgery or radiation therapy within 4 weeks prior to the Baseline Visit.
6. Use of any investigational agent within 4 weeks prior to the Baseline Visit.
7. Child-Pugh Class A or C cirrhosis or hepatic encephalopathy.
8. Occurrence of esophageal or other gastrointestinal hemorrhage requiring transfusion within 4 weeks prior to the Baseline Visit.
9. Uncontrolled or clinically unstable thyroid disease, per judgment of the Principal Investigator.
10. Active bacterial, viral, or fungal infection requiring systemic therapy, or operative or radiological intervention.
11. Known human immunodeficiency virus- or acquired immunodeficiency syndrome- related illness.

12. Liver transplant.
13. Active malignancy other than HCC.
14. Uncontrolled arterial hypertension or congestive heart failure (New York Heart Association Classification 3 or 4) (Appendix E).
15. Angina, myocardial infarction, cerebrovascular accident, coronary/peripheral artery bypass graft surgery, transient ischemic attack, or pulmonary embolism within 3 months prior to initiation of study drug.
16. History of or ongoing cardiac dysrhythmias requiring treatment, atrial fibrillation of any grade, or persistent prolongation of the QTc (Fridericia) interval to >450 msec for males or >470 msec for females.
17. Pregnant or lactating female.
18. Women of childbearing potential, unless they agree to use dual contraceptive methods which, in the Investigator's opinion, are effective and adequate for the subject's circumstances while on study drug.
19. Men who partner with a woman of childbearing potential, unless they agree to use effective, dual contraceptive methods (i.e., a condom, with female partner using oral, injectable, or barrier method) while on study drug and for 3 months afterward.
20. Any severe, acute, or chronic medical or psychiatric condition, or laboratory abnormality that may increase the risk associated with trial participation or study drug administration; may interfere with the informed consent process and/or with compliance with the requirements of the trial; or may interfere with the interpretation of trial results and, in the Investigator's opinion, would make the subject inappropriate for entry into this trial.

4.3 DISCONTINUATION FROM DOSING

Discontinuation from dosing means that the EOS visit is to be performed upon termination and indefinite monthly survival follow-up will be performed.

Subjects should be discontinued from dosing for the following reasons:

- Grade 3 toxicity considered by the Investigator to be at least "possibly" drug-related that does not resolve to Grade ≤ 1 within 7 days following interruption of treatment.
- Need for > 1 dose reduction.
- Grade 4 toxicity considered by the Investigator to be at least "possibly" drug-related.
- Treatment interruption or delay for more than 14 days after the next scheduled dose due to an event unrelated to toxicity (e.g., intercurrent illness, scheduled surgery, etc.).
- Subject withdrawal of consent for trial participation at any time, for any reason, and without prejudice.
- Withdrawal of a subject by the Investigator, at his/her discretion, for any reason that the Investigator believes continuation of study drug therapy would not be in the subject's best interest. The reason for the subject's discontinuation must be recorded on the case report form (CRF).

- An intercurrent illness which, in the Investigator's opinion, would prevent completion of trial-related evaluations.
- Pregnancy.
- Subject noncompliance with trial or follow-up procedures.
- Termination of the trial by the Sponsor.

If a subject is withdrawn from treatment, the Investigator will make every effort to complete all final evaluations and laboratory tests required by the protocol. The reason(s) for discontinuation of dosing must be clearly documented on the CRF. Subjects who discontinue from dosing will be followed indefinitely for survival status.

4.4 WITHDRAWAL FROM THE TRIAL

A subject will be considered to be withdrawn from the trial for the following reasons:

- Withdrawal of consent (in which every effort will be made to follow the subject for survival information);
- Termination of the trial by the Sponsor;
- Patient Death;
- Other.

5. CLINICAL PROCEDURES AND ASSESSMENTS

The schedule of clinical procedures and assessments conducted during the study is presented in the following table. Further details are given in the protocol.

TABLE 1–1: SCHEDULE OF EVENTS FOR DOUBLE BLIND (DB) PERIOD

		Cycle 1		Subsequent Cycles		End of Study/ End of Dosing (EOS)[l]	Follow-Up (28 ± 3 Days Post- EOS)
Trial Procedures	**Pre-Study (-28 days)**	**Day 1 Baseline**	**Days 8 and 15 ± 2 days**	**Day 1 ± 2 days**	**Day 15 ± 2 days**	**Day 1 + 2 days**	
Medical history	X						
Physical examination	X[a]	X[a,c]	X[b]	X[b]	X[b]	X[b]	X[a]
Inclusion/exclusion criteria	X	X					
Informed consent	X						
Body weight	X	X[c]		X		X	X
Vital signs[d]	X	X	X	X	X	X	X
Clinical laboratory testing[e]	X	X[c]	X	X	X	X	X
T3. T4, TSH	X	X		X		X	X
ECG[f]	X	X	X	X	X	X	X
Pregnancy test (serum)[g]	X	X[c]		X		X	X
ECOG PS[g]	X	X[c]		X		X	
α-fetoprotein (AFP)		X		X		X	X
WBC A3AR sample		X		X[h]			
PK samples		X[k]	X[k]	X[k]			
Hepatitis B/C virus serology	X						
Hepatitis B/C viral load (if seropositive)		X		X[i]		X[i]	
Tumor imaging for RECIST	X[j]			X[j]		X	
Concomitant medications	X	X	X	X	X	X	X
Adverse events		X	X	X	X	X	X
Dispense study drug supplies		X		X			
Review treatment compliance		X	X	X	X	X	

[a] Complete PE performed at the Pre-Study (and/or the Baseline Visit if performed > 3 days prior to first dose) and End of Study/End of Dosing (EOS) visits.
[b] Symptom-directed examination.
[c] If Pre-Study assessment was performed ≤ 3 days prior to the Baseline Visit, assessments do not need to be repeated prior to initiation of dosing.
[d] Temperature, pulse, respiration, blood pressure at: Pre-Study; pre-dose at all visits; at 1, 2, 3, 4h (± 5 min), 6 and 8h (± 10 min) post-dose on Cycle 1 Day 1; and at Follow-up.
[e] See list of parameters in Appendix C.
[f] ECG at Pre-Study; pre-dose at all visits; and at 2, 4, and 8h (± 10 min) post-dose on Cycle 1 Day 1; and at Follow-up.
[g] Performed at Pre-Study, prior to the first dose, at the end of each cycle, and at Follow-up.
[h] Day 1 of odd-numbered cycles, unless waived by the Sponsor (selected sites only).
[i] For subjects with measurable viral load at the Baseline Visit; on Day 1 of odd-numbered cycles only and at EOS.
[j] CT scan or MRI at Pre-Study, the end of Cycle 2, and at the end of subsequent even-numbered cycles. For trial eligibility purposes, a scan performed ≤ 21 days prior to the Pre- Study Visit may be used (allowed time window is of -7/+1 day with respect to day 28 of each even numbered cycles; if performed at +1 day after day 28, CT/MRI scan must be performed before administration of the morning dose of that day)
[k] Sparse sampling on Day 1 of Cycles 1 and 2 only. Pre-dose trough samples on Cycle 1 Days 8 and 15 only. See Table 10-1 of the protocol for PK sampling time points.
[l] End of Study visit timeframe is of 2 days since the last administered dose of IMP/matching Placebo.

TABLE 1–2: SCHEDULE OF EVENTS FOR OPEN LABEL (OL) PERIOD

Trial Procedures	OL Cycle 1		Subsequent OL Cycle		OL End of Study/End of Dosing (EOS) [j]	OL Follow-up (28 ± 3 Days Post EOS)
	Day 1 Baseline	Days 8 and 15 ± 2 Days	Day 1 ± 2 Days	Day 15 ± 2 Days	Day 1 ± 2 Days	
Physical examination	X[b]	X[b]	X[b]	X[b]	X[a]	X[b]
Eligibility criteria for OL	X					
Informed consent for OL	X					
Body weight	X		X		X	X
Vital signs [c]	X	X	X	X	X	X
Clinical laboratory testing [d]	X	X	X	X	X	X
T3, T4, TSH	X		X		X	X
ECG [e]	X	X	X	X	X	X
Pregnancy test (serum) [f]	X		X		X	X
ECOG PS [f]	X		X		X	
α-fetoprotein (AFP)	X		X		X	X
WBC A_3AR sample	X		X[g]			
Hepatitis B/C viral load (if seropositive)	X		X [h]		X [h]	
Tumor imaging for RECIST			X [i]		X	
Concomitant medications	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X
Dispense study drug supplies	X		X			
Review treatment compliance	X	X	X	X	X	

a. Complete PE performed at Open Label (OL) End of Study/OL End of Dosing (EOS) visits.

b. Symptom-directed physical examination.
c. Temperature, pulse, respiration, blood pressure performed at the following times: pre-dose at all visits; at 1, 2, 3, 4h (± 5 min), 6h and 8h (± 10 min) post-dose on OL Cycle 1 Day 1 and at OL Follow-up.
d. See list of parameters in Appendix C.
e. ECG at pre-dose at all visits; and at 2, 4, and 6h (± 10 min) post-dose on OL Cycle 1 Days 1 and 8; and at OL Follow-up.
f. Performed pre-dose on Day 1 of each OL cycle, and at OL Follow-up.
g. Day 1 of odd-numbered cycles, unless waived by the Sponsor (selected sites only).
h. For subjects with measurable viral load at the Baseline Visit; on Day 1 of OL odd-numbered cycles only and at OL EOS.
i. CT scan or MRI at the end of OL even-numbered cycles. If performed at +1 day after day 28, CT/MRI scan must be performed before administration of the morning dose of that day).
j. End of Study OL visit timeframe is of 2 days since the last administered dose of IMP.

6. STUDY ENDPOINTS

Baseline typically refers to Day 1 of Cycle 1 and Screening refers to the Pre-Study Visit. For some variables, Baseline is Cycle 1 Day 1 unless the assessment was performed at Screening which was ≤ 3 days prior to Cycle 1 Day 1, in which case the assessment was not to be repeated (footnotes 'a' and 'c' of Table 1-1). In the protocol and footnotes above, some assessments are given as performed at Day 28 or 29 of a cycle; consistent with the table above and the CRFs, these assessments are described below as being performed at Day 1 of the following cycle.

Tumor assessments performed at the End of Study/ End of Dosing (EOS) Visit, the Follow-up Visit, and Unscheduled Visits will be assigned to the next cycle for calculation of summary statistics.

The subjects who are still on blinded treatment when Amendment 5 is approved will be switched to open-label treatment at their next scheduled visit. The first day of open-label study drug dosing will be considered Day 1 (OL) of the trial. During this visit, the OL Cycle 1 Day 1 for OL procedures will be performed (Table 1-2). During the OL period, clinic visits will take place within ± 2 working days of the scheduled day; during these visits, assessments will be performed prior to administration of the study drug dose for that day.

6.1 EFFICACY ASSESSMENTS

Tumor response will be assessed at the Pre-Study Visit, Day 1 of odd-numbered cycles, and at the follow-up visit using Response Evaluation Criteria In Solid Tumors (RECIST v1.1) from Eisenhauer et al. (2009), presented in Appendix A of the protocol, and further described below in Appendix B. In general, target lesions will be assessed as Complete Response (CR), Partial Response (PR), Stable Disease (SD), or Progressive Disease (PD) and non-target lesions will be assessed as Complete Response (CR), Incomplete Response/Stable Disease (SD), or Progressive Disease (PD). Tumor responses from target lesions and from non-target lesions will be used to determine Overall Response as described in Appendix B. If the Overall Response is CR or PR, tumor assessments are to be repeated within 4 weeks. Overall Response will be tabulated by cycle and treatment; the responses for target lesions and non-target lesions will be included in listings, but will not be tabulated. If Overall Response of PD is observed at any time, the patient will not automatically be discontinued. Further imaging or target lesion measurements will not be required and all other trial visits and procedures will continue.

If assessments are made after the Overall Response of PD is recorded, then the Overall Response at all subsequent cycles will be PD and will be included at every cycle for which the Overall Response is recorded through Cycle 11 (see Section 7.2).

6.1.1 TIME TO EVENT ENDPOINTS

The primary efficacy endpoint is Overall Survival (OS), the time from Baseline to death due to any cause, calculated as date of death- date of Cycle 1 Day 1+1. Secondary time-to-event endpoints are:

- TTP: the time from Baseline to the first Overall Response of PD, calculated as date of first PD - date of Cycle 1 Day 1+1, and
- PFS: the time from Baseline to the first Overall Response of PD or death due to any cause if the subject dies without experiencing PD, calculated as date of first PD or death - date of Cycle 1 Day 1+1.

6.1.2 TUMOR RESPONSE

The secondary endpoints which are based directly on tumor response are:

- ORR (OR Rate): proportion of subjects who have CR or PR,
- DCR (DC Rate): proportion of subjects who have CR, PR, or SD, and
- Best Overall Response during the duration of the study.
  (The best overall response for each subject is the best response recorded from the start of the study treatment until the end of study, in the order of CR, PR, SD, or PD from best to worst.)

6.1.3 EXPLORATORY EFFICACY

Laboratory parameters associated with hepatic dysfunction and cirrhosis (ALT, AST, bilirubin, and albumin levels, prothrombin time (PT), and International Normalized Ratio (INR)) will be assessed every cycle and will be considered exploratory efficacy variables.

The effect of CF102 on α-fetoprotein (alpha-fetoprotein; AFP) will be assessed. AFP levels will be assessed at Baseline and on Day 1 of each subsequent cycle.

Liver chemistry tests and viral load will be presented as exploratory efficacy variables, as will WBC A_3AR expression. Viral load for Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) will be assessed at Baseline, at Day 1 of each subsequent odd cycle, at the end of dosing, and at the Follow-up visit for subjects with positive serology at Screening.

6.2 SAFETY EVALUATIONS

Safety parameters assessed throughout the trial include adverse events, ECOG performance status, vital signs, weight, physical examinations, laboratory parameters including thyroid functions, ECG, and concomitant medications. Any clinically significant change from baseline in a laboratory parameter will be reported as an AE. Liver chemistry tests and viral load will be presented as exploratory efficacy variables.

At each visit, all AEs will be recorded in the appropriate section of the CRF and will be evaluated by the Investigator. The minimum information required for each AE includes the following:

- Type of event
- Duration (start and end dates)
- Severity
- Seriousness
- Relationship to study drug (Unrelated, Possibly Related, Probably Related, or Related)
- Action taken
- Outcome.

In most cases, the CTCAE v4.0 criteria will preferably be used to grade severity; however, if an AE is not listed in the CTCAE, the following grading scale may be used: Mild (Grade 1), Moderate (Grade 2), Severe (Grade 3), Life-Threatening (Grade 4), or Fatal (Grade 5).

7. STATISTICAL CONSIDERATIONS AND DATA ANALYSIS

Tables and data listings will be prepared using SAS Version 9.0 or higher. A subject's Baseline value for a specified variable will be the measurement for that variable taken on Day 1 of Cycle 1, unless the pre-study assessment was performed within 3 days prior to baseline. In the latter case, assessments do not need to be repeated prior to initiation of dosing for Physical Examination, Body Weight, Clinical Laboratory testing, Pregnancy Test, and ECOG PS, as noted in the Schedule of Procedures in Section 5 and the Baseline value will be the value at Screening.

For any variable with Change From Baseline (CFB) calculated, CFB will be calculated as

CFB = Value at Post-Baseline visit – Value at Baseline.

If the final pre-treatment assessment was performed at Screening, prior to Baseline, then CFB is defined as the difference between the value at the post-Baseline visit and the value at Screening.

Simple descriptive statistics for continuous data are: n (number of non-missing observations), mean, standard deviation, maximum, median, and minimum. Categorical data will be summarized by the number and percentage of subjects in each category. The data will be summarized upon completion of the final subject. All data collected for the OL period will be listed and select variables will be summarized. Listings and summaries for the OL period will be presented separately and a separate SAP will be prepared. The following pertains to the analyses and summaries for the DB period.

7.1 ANALYSIS POPULATIONS

Analyses will be conducted using the populations described below.

The **Safety Population** consists of all subjects who received at least one dose of study medication. Analyses of safety assessments will be performed using the Safety Population.

The **Intent-To-Treat (ITT) Population** is defined as all subjects in the Safety Population with any post-Baseline assessment recorded. Exclusion of subjects from the ITT Population will be determined prior to unblinding. All efficacy analyses will be performed using the ITT Population.

The **Per Protocol (PP) Population** is defined as all subjects in the ITT Population with no major protocol deviations, including major violations of inclusion and exclusion criteria and violation of RECIST requirements regarding the number of target lesions at Screening (Appendix B). Exclusion of subjects from the PP Population will be determined prior to unblinding. Tumor response (Sections 6.1.2 and 7.6.4) will be analyzed for the PP Population.

7.2 GENERAL ANALYSIS

The following standards will be applied for analyses unless otherwise specified. Simple descriptive statistics for continuous data are: n (number of non-missing observations), mean, standard deviation, maximum, median, and minimum. Categorical data will be summarized by the number and percentage of subjects in each category. Summaries of efficacy variables will be presented by visit through end of Cycle 11. Best Overall Response will be summarized once for the entire study. All data will be listed for the Safety Population, sorted by investigator number, subject number and, where appropriate, by visit, including data from visits after Cycle 11. The choice of Cycle 11 as the final time for tabulation will be finalized prior to unblinding. Tumor assessments performed at the EOS Visit, the Follow-up Visit, and Unscheduled Visits will be assigned to the next cycle and will be analyzed with that cycle. Tumor responses recorded on the CRF will be listed. Other data from Unscheduled Visits will not be summarized, except for AEs.

7.3 SUBJECT DISPOSITION

The total number of subjects will be presented with the number and percentage of subjects in each analysis population by treatment and overall. The number and percentage of subjects who completed the study, who discontinued, and primary reason for discontinuation will be summarized by treatment for the Safety Population.

7.4 DEMOGRAPHICS AND MEDICAL HISTORY

7.4.1 DEMOGRAPHICS

Demographic parameters, including age, sex, and origin, will be summarized for the Safety Population by treatment and overall. Age will be computed as (the number of days from Date of Birth to Date of Screening Visit)/365.25. After unblinding, it was decided to include the frequency distribution of Child-Pugh (CP) Score at Screening (7, 8, or 9) in the table of demographics and baseline characteristics. The CP Score for Subject 311-003 was recorded as 6, but this was corrected to 7 after unblinding.

7.4.2 HCC DISEASE HISTORY AND PRIOR THERAPIES

HCC disease history includes

- date of initial HCC diagnosis and staging,
- date of most recent relapse and/or re-staging,
- method used for diagnosis (histology / cytology or American Association for the Study of Liver Diseases (AASLD) Practice Guideline algorithm),
- history of viral hepatitis, including date of diagnosis,
- hepatitis B and hepatitis C virus serology (positive or negative), with the last date of testing, and
- known complication(s) of cirrhosis and/or portal hypertension.

History of viral hepatitis is recorded as “Yes, Hepatitis B”; “Yes, Hepatitis C”; “No”; or “Not known”, with the date of diagnosis recorded for the first two responses, both of which are possible. The summary statistics will include the counts and percentages for each of the four possible responses by treatment for the Safety Population.

Known complication(s) of cirrhosis and/or portal hypertension are reported on the CRF as “Ascites”, “Esophageal varices with bleeding”, or “Other (specify)”. If none of these responses are selected, then the response should be reported as “None”.

Prior therapies include

- modality,
- start and stop dates of treatments,
- numbers of cycles, and
- best response to each treatment.

The number of subjects reporting the use of a modality at least once will be summarized by treatment for the Safety Population. Other variables pertaining to HCC disease history and prior therapies will be listed for the Safety Population.

A table of the number of target hepatic lesions and the number of target non-hepatic lesions (Appendix B) at Screening for the Safety Population will be presented.

A table of the incidence of Extrahepatic Spread (EHS), Portal Vein Thrombosis (PVT) at Baseline, including either EHS or PVT (“Yes” or “No”), will be provided.

7.4.3 MEDICAL HISTORY

Medical history, excluding past HCC, cirrhosis, and viral hepatitis-related history, will be summarized using frequencies and percentages of subjects with a finding or procedure for each body system (or "None") by treatment for the Safety Population by treatment and overall. "Other" will be listed but will not be included in the summaries.

7.5 MEDICATION AND TREATMENT ANALYSIS

7.5.1 COMPLIANCE AND EXPOSURE

Compliance will be calculated as the number of total capsules dispensed (over the duration of the study) minus the total number of capsules returned, and then that quantity is divided by twice the duration of treatment in days. The duration of treatment is date of final dose minus date of Baseline + 1. If the date of final dose is missing or if the subject is still receiving treatment, the date of final dose will be imputed as described in Section 8. Descriptive statistics for compliance and the duration of treatment will be provided for the Safety Population by treatment. The summary statistics pooled across treatments will also be computed for duration of treatment, to be used in efficacy evaluations as described in Sections 7.6.1- 7.6.3.

7.5.2 CONCOMITANT MEDICATIONS

Concomitant and prior medications taken within 30 days prior to Screening Visit will be summarized by ATC Level 3.

7.6 EFFICACY

Efficacy will be assessed using the response based upon overall survival, time to progression, RECIST, and hepatitis viral load. Liver chemistry tests and viral load will be presented as exploratory efficacy variables, as will AFP and WBC A_3AR expression. Summaries of efficacy variables by visit will be presented using visits through end of Cycle 11. Analyses of time to event (OS, TTP, and PFS) and Best Overall Response will not be restricted to visits through Cycle 11. All efficacy data will be listed. Binary response variables will not be analyzed using SAS PROC FREQ, which uses equal variances for the differences, as opposed to the unequal variances given below.

7.6.1 OVERALL SURVIVAL (OS)

Overall survival (OS) is the time from Baseline to death due to any cause. OS will be summarized in months, which will be obtained by dividing OS in days by 30 days/month. Subjects who are alive at last contact will be considered censored at the date of last contact. Summary statistics (25^{th} percentile, median, and 75^{th} percentile) will be determined using the Kaplan-Meier (KM) estimate of the survival function. These summary statistics will be listed to one decimal place, rounded down such as the SAS FLOOR function. The KM curve for OS will be presented. The value of the KM curve for OS at the median duration of therapy (Section 7.5.1) will be presented. The between-treatment comparison will be performed using the logrank test as the primary analysis. Between-treatment comparisons with respect to OS will be also performed using the proportional hazards model with AFP at Baseline and A_3AR level at Baseline as covariates individually as secondary analyses, including the hazard ratio and the 95% confidence interval for the hazard ratios for both treatment and the covariate. Additional details are given in Section 9.

7.6.2 TIME TO PROGRESSION (TTP)

Time to Progression (TTP) is the time from Baseline to the first Overall Response of Progressive Disease (PD), computed as in Section 6.1.1. TTP will be summarized in months, which will be obtained by dividing TTP in days by 30 days/month. Subjects who do not have an Overall Response of PD by the time of last contact will be considered censored at the date of last contact; subjects who died without experiencing PD will be censored at the day of death. Summary statistics (25^{th} percentile, median, and 75^{th} percentile) will be determined using the KM estimate of the survival function for TTP. These summary statistics will be listed to one decimal place, rounded down such as the SAS FLOOR function. The KM curve for TTP will be presented. The value of the KM curve for TTP at the median duration of therapy (Section 7.5.1) will be presented. The between-treatment comparison will be performed using the logrank test. Additional details are given in Section 9.

7.6.3 PROGRESSION-FREE SURVIVAL (PFS)

Progression-free Survival (PFS) is the time from Baseline to the first Overall Response of Progressive Disease (PD) or death due to any cause if the subject dies without experiencing PD, computed as in Section 6.1.1. PFS will be summarized in months, which will be obtained by dividing PFS in days by 30 days/month. Subjects who are alive without experiencing an Overall Response of PD at the time of last contact will be considered censored at the date of last contact. Summary statistics (25^{th} percentile, median, and 75^{th} percentile) will be determined using the KM estimate of the survival function for PFS. These summary statistics will be listed to one decimal place, rounded down such as the SAS FLOOR function. The KM curve for PFS will be presented. The value of the KM curve for PFS at the median duration of therapy (Section 7.5.1) will be presented. The between-treatment comparison will be performed using the logrank test. Additional details are given in Section 9.

7.6.4 TUMOR RESPONSE

The Objective Response Rate (ORR) is the percentage of subjects who achieved either CR or PR. ORR will be summarized using counts and percentages for the ITT Population by treatment and cycle. The between-treatment comparison will be performed using the normal approximation to the binomial distribution (NAB) with unequal variances, as follows.

For each cycle, let p_{CF} and p_0 denote the proportions of subjects who experienced CR or PR based on n_{CF} and n_0 subjects for CF102 and Placebo, respectively, and let

$$Z=(p_{CF}-p_0)/(p_{CF}(1-p_{CF})/n_{CF} + p_0(1-p_0)/n_0)^{1/2}.$$

Then the corresponding p-value is p=2*(1-PROBNORM(ABS(Z))).

The Disease Control Rate (DCR) is the percentage of subjects who achieved either CR, PR, or SD. DCR will be summarized using counts and percentages for the ITT Population by treatment and cycle. The between-treatment comparison will be performed using the (NAB), similar to that for ORR.

For each subject, the Best Overall Response during the duration of the study will be determined and will be summarized using counts and percentages for the ITT Population by treatment. The between-treatment comparison will be performed using the NAB, for both the percentage of subjects who achieved either CR or PR (similar to ORR) and the percentage of subjects who achieved either CR, PR, or SD (similar to DCR).

7.6.5 BIOMARKERS

The biomarker α-fetoprotein (AFP) will be assessed at Baseline, at Day 1 of each cycle, and at the follow-up visit. Summary statistics for AFP levels and CFB in AFP levels will be provided for the ITT Population by treatment and visit. Between-treatment comparisons will be performed by visit using Analysis of Covariance (ANCOVA) with CFB as the dependent variable and Baseline as the covariate. Summary statistics for AFP and CFB in AFP will be provided for each level of Overall Response for the ITT Population by treatment. Distribution of Overall Response will be presented for subjects with AFP levels <20, 20-200, or >200 ng/mL and for subjects with AFP levels above or at most the pooled median by treatment and cycle; the percentages will be calculated using number of subjects within each category defined by AFP levels as the denominator for each treatment.

WBC A_3AR expression will be assessed at Baseline and at Day 1 of each odd-numbered cycle. Summary statistics for WBC A_3AR expression and CFB in WBC A_3AR expression will be provided for the ITT Population by treatment and visit. Summary statistics for CFB in WBC A_3AR expression will be provided for each level of Overall Response for the ITT Population by treatment. To assess the relationship between Overall Response and changes in WBC A_3AR at each visit, the distribution of Overall Response will be presented for subjects with WBC A_3AR less than the pooled median and for subjects with WBC A_3AR at least the pooled median at each post-baseline visit.

7.6.6 CHEMISTRY AND COAGULATION PARAMETERS

The following laboratory parameters will be examined as exploratory efficacy variables:

- alanine aminotransferase (ALT)
- albumin
- aspartate aminotransferase (AST)
- bilirubin (direct and total)
- International Normalized Ratio (INR)
- prothrombin time (PT).

The above variables and CFB for each variable will be summarized by treatment and visit for the ITT Population. Between-treatment comparisons will be performed by visit using ANCOVA with CFB as the dependent variable and the Baseline value of the variable as the covariate. These variables will be listed for the Safety Population with the other laboratory parameters.

7.6.7 HEPATITIS VIRAL LOAD

Viral load for Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) for subjects with positive serology at Screening will be summarized using summary statistics for log-transformed values using the base 10 logarithm, which will be presented by treatment and visit for the ITT Population. Between-treatment comparisons will be performed by visit using ANCOVA with CFB for log-transformed values as the dependent variable and Baseline as the covariate. These variables (viral load (IU/mL) and log-transformed viral load) will be listed for the Safety Population. Any viral load recorded for subjects who do not have positive serology at Screening will not be included in tables but will be included in listings only.

7.6.8 SUBGROUP ANALYSES

After unblinding, it was decided to perform various subgroup analyses of OS. The subgroup analyses will be performed by the following assessments at Screening or Baseline:

CP Score at Screening (7, 8, 7+8, or 9),
Sex,
ECOG PS at Screening (0 or 1+2),
AFP (≤400 ng/mL or >400 ng/mL) at Baseline,
Prior Locoregional therapy (HCC Prior Therapies of Radiation or Chemoembolization =Yes, Otherwise =No),
EHS (Yes or No), PVT (Yes or No), and Either EHS or PVT (Yes or No),
History of HBV (Known history of HBV=Yes or No),
History of HCV (Known history of HCV=Yes or No),
Diagnostic Procedure (Cytology/histology or AASLD), and
Country (based on the first digit of the site number, given as Bulgaria=1, Serbia=2, Israel=3, Romania=5, or United States=7).

The subgroup analyses will be performed as univariate analyses within each level of the corresponding subgrouping variable. For each subgrouping variable, the between-treatment comparisons will be performed using the logrank test (Section 7.6.1). Each analysis will include the hazard ratio with the corresponding 95% confidence interval from proportional hazards model with no additional covariates and the p-value (Chi-Square), as described in Section 9. The subgroup analyses do not include a plot of each KM curve, except for the analyses by CP Score at Screening (CP=7, CP=8, or CP=7 or 8), and do not include the value of the KM curve at the median duration of therapy, provided in the analyses for the ITT Population.

History of viral hepatitis is recorded as “Yes, Hepatitis B”; “Yes, Hepatitis C”; “No”; or “Not known”, with the date of diagnosis recorded for the first two responses, both of which are possible. If both of these responses are recorded, then the response for both History of HBV and History of HCV will be considered “Yes”. Subjects with responses of “Not known” will be excluded from the subgroup analyses using history of viral hepatitis.

Subgroup analyses for other time-to-event variables or tumor response variables may be presented as further exploratory analyses after review.

7.7 SAFETY ANALYSES

Safety data consist of adverse events (AEs), laboratory tests including thyroid functions, vital signs and weight, and physical examinations. Summaries of safety data will be conducted on all subjects in the Safety Population. Missing safety data will not be imputed. Summaries of all safety variables by visit will be presented for visits at which there are at least 4 subjects in either treatment group. Summaries of AEs, deaths, SAEs, and Discontinuation due to AE will not be restricted to visits with at least 4 subjects in either treatment group. All safety data will be listed.

7.7.1 ADVERSE EVENTS

The original reported (verbatim) terms used by the Investigator to identify adverse events in the CRFs will be entered into the database and coded by Preferred Term using the Medical Dictionary for Regulatory Activities (MedDRA) coding dictionary (MedDRA MSSO, Reston, Virginia USA). Adverse events will then be grouped by MedDRA Preferred Term (PT) into frequency tables according to System Organ Classification (SOC).

An adverse event that started during the treatment period (on or after the day of the baseline visit) or that was present at Baseline and increased in severity during the treatment period will be considered a treatment-emergent adverse event (TEAE). Events ending prior to the day of the baseline visit and events present at Baseline that do not increase in severity during treatment will be considered as Baseline adverse events and will not be included in the presentation of TEAEs. If the date of a new AE does not allow for determination of whether the AE is treatment emergent, it will be assumed to be a TEAE.

The number and percentage of subjects experiencing TEAEs will be presented for the Safety Population for each body system and preferred term by treatment, and for each severity and relationship to study medication. When an adverse event occurs more than once, the maximum severity grade and relationship will be counted. For severity, only “Mild” and “Moderate” will be included for all SOCs and PTs; “Severe”, “Life-Threatening”, or “Fatal” will be included for SOCs and PTs only when such are recorded for severity. Similarly, only “Possibly Related” and “Not Related” will be included for all SOCs and PTs; “Definitely Related” and “Probably Related” will be included for SOCs and PTs when such are recorded for relationship.

Serious adverse events and discontinuations due to an adverse event will be provided in separate listings for the Safety Population. Each serious adverse event (SAE) will be listed for subjects in the Safety Population.

7.7.2 LABORATORY TESTS

Laboratory tests (hematology, clinical chemistry, coagulation, urinalysis, and thyroid functions) will be performed at the timepoints specified in Appendix C, which also contains a complete list of all clinical laboratory tests. Clinical laboratory evaluations and CFB for each laboratory value will be listed and summarized using descriptive statistics by treatment and visit for visits with at least 4 subjects in either treatment group for the Safety Population. If a laboratory test is repeated during a visit, only the first values will be included in the summary; all values will be included in the listings. Clinically significant (CS) out-of-range laboratory values should be recorded as AEs. ALT (Alanine Aminotransferase; SGPT) and AST (Aspartate Aminotransferase; SGOT) are referred to as ALAT (SGPT) and ASAT (SGOT), respectively, in the listing of Blood Chemistry parameters. Urinalysis laboratory values will be listed only and CFB will not be computed. Laboratory assessments that are considered exploratory efficacy variables (Section 7.6.7) will be presented both as efficacy variables and laboratory variables, through Cycle 11 when considered exploratory efficacy variables and for all visits when considered safety variables.

7.7.3 ECOG PERFORMANCE STATUS

ECOG Performance Status (PS) is an assessment using a five-point scale, with 0= Normal activity,…, 5=100 % bedridden; details are given in Appendix D. ECOG PS will be recorded at Pre-study visit, Day 1 of Cycle 1 (Baseline), Day 1 of each subsequent cycle, and at Follow-up. ECOG PS and categories of CFB in ECOG PS (decreased, no change, increased) will be presented for the Safety Population by treatment and cycle for cycles with at least 4 subjects in either treatment group.

7.7.4 VITAL SIGNS AND WEIGHT

Vital signs will be recorded at Days 1 and 15 of each cycle, Day 8 of Cycle 1, Hours 1, 2, 3, 4, 6 and 8 on Cycle 1 Day 1, and at Follow-up. Systolic blood pressure (mmHg), diastolic blood pressure (mmHg), respiratory rate (breaths/min), pulse (beats/min), oral temperature (degrees C), and CFB for each of these vital signs will be listed and summarized using descriptive statistics for the Safety Population by treatment and visit for visits with at least 4 subjects in either treatment group. Height (cm) will be recorded at the Pre-Study Visit only and will be included in listings only. Body weight (kg) will be recorded at Days 1 and 15 of each cycle, Day 8 of Cycle 1, and at Follow-up; BMI (kg/m^2) will be computed for each of these visits using the height recorded at the Pre-Study Visit.

7.7.5 ECG PARAMETERS

A resting 12-lead electrocardiogram (ECG) will be performed at the Pre-Study visit, Days 1 and 15 of all cycles, Day 8 of Cycle 1, and at 2, 4, and 6 hours post-dose on Day 1 of Cycle 1, and at Follow-up. ECG interval data (Heart Rate [HR], PR, QRS, QT) and the corresponding CFBs will be listed and summarized using descriptive statistics for the Safety Population by treatment and visit for visits with at least 4 subjects in either treatment group. QTc will be computed using Fridericia's correction, $QTcF=QT*(HR/60)^{1/3}$. QT will not be summarized and will be included in the listing only. ST Segment (normal or abnormal), Cardiac Rhythm (normal or abnormal), and Overall Impression (normal, abnormal- NCS, or abnormal- CS) will be summarized using counts and percentages for the Safety Population by treatment and visit.

7.7.6 PHYSICAL EXAMINATIONS

A physical examination (PE) will be performed at every visit. A complete PE will be performed at the Pre-Study, Cycle 1 Day 1 (the Baseline Visit if the Pre-Study visit not performed within 3 days prior), and End of Study/End of Dosing (EOS) visits, including a thorough review of all body systems (general appearance, head/neck, ears/nose/throat, skin, chest/lungs, heart, abdomen, genitourinary, extremities, musculoskeletal, lymph nodes, neurological and other, specify) as well as measurement of weight (kg) and height (cm). At all other visits, a symptom-directed PE, including weight (kg), will be performed. If the Pre-Study visit is within 3 days of Cycle 1 Day 1, then no responses should be reported for Cycle 1 Day 1.

At the Pre-Study visit, each body system, including "Other" (specify) if appropriate, will be assessed (Normal, Abnormal, or Not Done). At each visit after the Pre-Study visit, assessments will be recorded for any body systems with clinically significant (CS) changes from the PE conducted at the previous assessment (Normal, Abnormal, or Not Done), with details. The CRF indicates that these assessments should be recorded if the body system with a clinically significant change from the PE conducted at the previous assessment is "Abnormal", with a description of the abnormality; these assessments should be recorded for any CS change from the previous PE, not just "Abnormal", including a CS change from "Abnormal" to "Normal".

Assessments at the Pre-Study visit will be summarized by body system (Normal or Abnormal). Any subject with more than one assessment of "Other" will be counted once. Assessments recorded as "Not Done" will not be included in the table. Any description of an abnormality will be included in the corresponding listing. At each visit after the Pre-Study visit, the number of subjects with at least one CS change from the PE conducted at the previous assessment will be summarized for the Safety Population by treatment and visit for visits with at least 4 subjects in either treatment group. Any body systems with a CS change from the PE conducted at the previous assessment will be included in the corresponding listing with the result and description.

8. MISSING DATA

Missing dates will be imputed only when the date is required to calculate the duration of an event for summary. As such, the only missing date that would need to be imputed is the date of final dose, required for calculation of duration of treatment. In such situations, the month and year would be recorded. For subjects who have completed dosing, the missing date of final dose will be imputed as the 15-th of the month; for subjects who are still receiving treatment, the missing date of final dose will be imputed as the date of the last completed visit.

Missing data from intermediate visits for AFP, WBC A3AR, viral load, and laboratory assessments when considered exploratory efficacy variables will be imputed using Last Observation Carried Forward (LOCF). Missing data for the latter laboratory variables will not be imputed when examined with laboratory assessments as safety variables. Due to the nature of the study, there is no imputation due to discontinuation.

The protocol specifies that certain assessments will not be repeated at Baseline (Cycle 1 Day 1) if assessed at the Pre-Study visit <= 3 days prior to Cycle 1 Day 1, resulting in missing values for Baseline; in such cases, the missing value at Baseline will be imputed by the value from the Pre-Study visit.

9. DIFFERENCES AND CHANGES FROM THE PROTOCOL

The protocol states that disease history includes duration of prior sorafenib therapy, reason(s) for discontinuation of sorafenib, and if applicable, nature of intolerability to sorafenib. The duration is not directly collected, but can be computed from the start and stop dates, as provided for all prior HCC therapies. The reasons(s) for discontinuation, including nature of intolerability, were not collected for prior HCC therapies, including sorafenib.

The protocol states that the listing of “dosing interruptions and dose reductions” will be provided. This listing is not provided, as these data were not specifically recorded, but are available as the “Action Taken” for AEs.

In the protocol, ITT Population is defined as “all subjects in the Safety Population who have any post-Baseline efficacy data, including Liver Chemistry Tests and/or INR on Day 8 of Cycle 1, or death or discontinuation due to disease progression at any time.” According to SAP, ITT Population “is defined as all subjects in the Safety Population with any post-Baseline assessment recorded”. The difference has no impact, especially since no subjects were excluded from the ITT Population.

Summaries of all safety variables by visit will be presented for visits at which there are at least 4 subjects in either treatment group. AEs, deaths, SAEs, and Discontinuation due to AE are not subject to this constraint. This restriction was not given in the protocol.

Summaries and analyses of efficacy variables by visit will be presented using visits through end of Cycle 11. Analyses of time to event (OS, TTP, and PFS) and Best Overall Response will not be restricted to visits through Cycle 11. This restriction was not given in the protocol.

Analyses of time to event (OS, TTP, and PFS) originally included summary statistics (25th percentile, median, and 75th percentile) from the KM estimate of the survival function and the value of the KM curve at the median duration of therapy. The between-treatment comparisons were performed using the logrank test. After unblinding, it was decided to include the hazard ratio with the corresponding 95% confidence interval from proportional hazards model with no additional covariates and the p-value (Chi-Square). The subgroup analyses of OS (Section 7.6.8) were not presented in the protocol.

After unblinding, it was decided to present incidence of EHS and PVT at Baseline (Section 7.4.2), which are not given in the protocol.

Any changes not presented in this or any subsequent version of the SAP will be described in the clinical study report.

10. APPENDICES

10.1 APPENDIX A – CHILD-PUGH CLASSIFICATION OF SEVERITY OF LIVER DISEASE

Child-Pugh classification of severity of liver disease is defined using the degree of ascites, plasma concentrations of bilirubin and albumin, prothrombin time, and the degree of encephalopathy.

Class A (well-compensated disease): total score of 5-6.

Class B (significant functional compromise): total score of 7-9.

Class C (decompensated disease): total score of 10-15.

Parameter	**Points Assigned**		
	1	**2**	**3**
Ascites	Absent	Slight	Moderate
Bilirubin, mg/dL	<2	2-3	>3
Albumin, g/dL	>3.5	2.8-3.5	<2.8
Prothrombin time * Seconds over control * INR	 1-3 <1.7	 4-6 1.7-2.3	 >6 >2.3
Encephalopathy	None	Grade 1-2	Grade 3-4

Parameter	**1**	**2**	**3**
Total bilirubin (μmol/L)	<34	34-50	>50
Albumin (g/L)	>35	28-35	<28

10.2 APPENDIX B – DETERMINATION OF OVERALL RESPONSE

Tumor status will be assessed at the Pre-Study Visit, Day 1 of odd-numbered cycles, and at the follow-up visit using Response Evaluation Criteria In Solid Tumors (RECIST), as presented in Appendix A of the protocol. The protocol states that tumor status will be assessed "at baseline and every 8 weeks thereafter (i.e., at the end of even-numbered cycles) by computed tomography (CT) scan or magnetic resonance imaging (MRI)"; however, the "baseline" assessment is performed at the Pre-Study Visit and the assessments of tumor status are recorded on CRF for Day 1 of odd-numbered cycles.

Details regarding the calculation of Overall Response, and related variables, are presented here. The following details are from RECIST v1.1 (Eisenhauer et al. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *European J Cancer*. 45(2009): 228-247), the subsequent modification (Santoro et al. Tivantinib for second-line treatment of advanced hepatocellular carcinoma: a randomized, placebo-controlled phase 2 study. *Lancet Oncol*. 2013; 14: 55-63), and the protocol.

At Screening, target lesions are assessed: Up to 5 liver lesions and up to 2 lesions from other organs that can be accurately measured in at least one dimension with longest diameter ≥ 20 mm using conventional techniques (CT scan or MRI) or ≥ 10 mm with spiral CT scan. The LD for each target lesion should be compared to these minima, and any discrepancies noted for investigation and possible query. Lesions with LD less than these values and lesions from various sites which are "truly non-measurable" (Eisenhauer et al, 2009) are assessed as non-target lesions.

Target Lesions

The lesions identified at Screening as "Target Lesions" will be measured and the longest diameter (LD) of each target lesion is recorded, as well as the sum of the longest diameters. The sum of the longest diameters is recorded on CRF but should be re-computed for accuracy; any discrepancy between this calculated value and the recorded sum will be noted for investigation and possible query, except in the case of minor round-off discrepancies. In the latter case, the recorded value will be presented in the listings, but the calculated value will be used for all subsequent calculations. At each visit after Screening, the LDs for target lesions identified at Screening will be assessed; any new lesions will be recorded as such with "Non- Target Lesions" and discussed below.

Listing 16.2.6.1.1 (Tumor Evaluations: Target Lesions) is the listing of assessment (LD) for each target lesion by subject and visit. Listing 16.2.6.1.2 (Summary of Target Lesions) is the listing of "Sum of Longest Diameters (mm), Smallest Sum On Study (mm), Percent Change from Smallest, Screening Sum on study, and Percent Change From Screening" by subject and visit for target lesions. These variables are recorded on CRF, but should be determined from the individual assessments reported in Listing 16.2.6.1.1 as a check on accuracy. Inconsistencies, other than minor round-off, should be investigated. Percent Change from Smallest and Percent Change From Screening will be listed to one decimal place.

Based on results given in Listing 16.2.6.1.2, Response for Target Lesions can be determined as Complete Response (CR), Partial Response (PR), Stable Disease (SD), or Progressive Disease (PD) according to the following algorithm (from CRF).

Pick the one response that applies from most recent assessment for Target Lesions:

Complete Response (CR)	Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.
Partial Response (PR)	At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters.
Progressive Disease (PD)	At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. Note: the appearance of one or more new lesions is also considered progression.
Stable Disease (SD)	Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study.

Note that CR and PR are assessed relative to the baseline sum of diameters, whereas PD is assessed relative to the smallest sum of diameters. Note that "smallest sum on study" at any visit refers to sums prior to, and including, the visit of interest, including the baseline sum of diameters.

Prior to unblinding, it was decided that subjects who can be assigned both PR and PD for target lesions at a cycle will be assigned PR. This will occur at a cycle whenever 1.2*(Smallest Sum of LDs) ≤ Sum of LDs at Cycle ≤ 0.7* (Sum of LDs at Screening). For Subject 530-006 at Cycle 13, the Investigator recorded the response as PD and chose not to change the recorded response; both responses are provided in listings.

Non-Target Lesions

Listing 16.2.6.2 (Tumor Evaluations: Non-Target Lesions) is listing of status (Present, Absent, New, Progressive) for each non-target lesion by subject and visit. Based on results given in Listing 16.2.6.2, Response for Non-Target Lesions can be determined as Complete Response (CR), Non-CR/ Non-PD, or Progressive Disease (PD) according to the following algorithm (from CRF). The assessment also allows for "not evaluated".

Pick the one response that applies from most recent assessment for Non-Target Lesions:

Complete Response (CR):	Disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (< 10 mm short axis). Note: If tumor markers are initially above the upper normal limit, they must normalize for a patient to be considered in complete clinical response.
Non-CR/ Non-PD:	Persistence of one or more non-target lesions(s) or/and maintenance of tumor marker level above the normal limits.
Progressive Disease (PD):	Appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions. Unequivocal progression should not normally trump target lesion status. It must be representative of overall disease status change, not a single lesion increase.

Listing 16.2.6.3 (Tumor Response) includes Response for Target Lesions (based on results in Listing 16.2.6.1.2 and the above algorithm), Response for Non-Target Lesions (based on results in Listing 16.2.6.2 and the above algorithm), Overall Response, and Best Response. Overall Response is based on the Response for Target Lesions and the Response for Non-Target Lesions, according to the following algorithms, depending on whether subject has measurable disease or non-target lesions only.

Overall Response - For Patients with Measurable Disease (i.e., Target Disease)			
Target Lesions	**Non-Target Lesions**	**New Lesions**	**Overall Response**
CR	CR	No	CR
CR	Non-CR/Non-PD	No	PR
CR	Not evaluated	No	PR
PR	Non-CR/Non-PD/not evaluated	No	*PR*
SD	Non-CR/Non-PD/not evaluated	No	*SD*
PD	Any	Yes or No	PD
Any	PD *	Yes or No	PD
Any	Any	Yes	PD
*In exceptional circumstances, unequivocal progression in non-target lesions may be accepted as disease progression			

Note that this differs from the CRF; the corrections are given by the italicized entries.
If Response for Non-Target Lesions='CR' or if there are no non-target lesions, then the Overall Response will be equal to the Response for Target Lesions.

Overall Response -For Patients with Non-Measurable Disease (i.e., Non-Target Disease)		
Non-Target Lesion	**New Lesions**	**Overall Response**
CR	No	CR
Non-CR/non-PD	No	Non-CR/non-PD *
Not all evaluated	No	Not evaluated
Unequivocal PD	Yes or No	PD
Any	Yes	PD
* 'Non-CR/non-PD' is preferred over 'stable disease' for non-target disease since SD is increasingly used as an endpoint for assessment of efficacy in some trials so to assign this category when no lesions can be measured is not advised.		

Using the above tables, the overall response, given in Listing 16.2.6.3 is:

Complete Response (CR),
Partial Response (PR),
Progressive Disease (PD),
Stable Disease (SD),
Non-CR/non-PD, or
Unable to evaluate (NE) (with Comment).

Analyses are based on these variables from Listing 16.2.6.3. Although these variables are recorded on the CRF, the algorithms should be programmed as a check on accuracy. Inconsistencies would be investigated.

Other variables to be analyzed are

ORR (OR Rate) = proportion of subjects who have CR or PR,
DCR (DC Rate) = proportion of subjects who have CR, PR, or SD.

Theses variables, ORR and DCR, are analyzed by visit and are also included in Listing 16.2.6.3.

10.3 APPENDIX C – CLINICAL LABORATORY TESTS

Except for the "OTHER" category, the following laboratory tests will be performed at Pre-Study Visit; Days 1 (i.e., the Baseline Visit if not performed ≤ 3 days prior), 8, and 15 of Cycle 1; Days 1 and 15 of subsequent cycles; EOS; and Follow-Up.

HEMATOLOGY TESTS	CHEMISTRY TESTS
• hematocrit • hemoglobin • platelet count • red blood cell count • white blood cell count and differential (absolute and percentage); neutrophils, lymphocytes, monocytes, eosinophils, basophils, and reticulocyte count	• alanine aminotransferase (ALT)* • albumin* • alkaline phosphatase • aspartate aminotransferase (AST)* • bicarbonate • bilirubin (direct and total)* • blood urea nitrogen (BUN) • calcium • chloride • creatinine • glucose • lactate dehydrogenase (LDH) • phosphorus • potassium • sodium • total protein • uric acid
URINALYSIS	
• glucose • ketones • occult blood • pH • protein • specific gravity • and, when indicated by dipstick abnormality, microscopic sediment evaluation	
COAGULATION PARAMETERS	**OTHER**
• International Normalized Ratio (INR)* • partial thromboplastin time (PTT) • prothrombin time (PT)*	• alpha-fetoprotein (AFP): at baseline and Day 1 of each subsequent cycle* • thyroid functions (T3, T4, TSH) at Pre-Study, Baseline, Day 1 of subsequent cycles, EOS, and Follow-up • serum pregnancy test: females of childbearing potential • hepatitis B and C viral load measurement every odd numbered cycle (where applicable)*

*Exploratory efficacy variables

10.4 APPENDIX D – ECOG PERFORMANCE STATUS

Level	ECOG Performance Status
0	Normal activity
1	Symptoms but ambulatory
2	In bed < 50% of time
3	In bed > 50 % of time
4	100 % bedridden

10.5 APPENDIX E – CARDIAC FUNCTION CLASSIFICATION

	Cardiac Functional Classification
NYHA Class	**Symptoms**
I	Cardiac disease, but no symptoms and no limitation in ordinary physical activity, e.g. shortness of breath when walking, climbing stairs etc.
II	Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.
III	Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g. walking short distances (20–100 m). Comfortable only at rest.
IV	Severe limitations. Experiences symptoms even while *at rest*. Mostly bedbound patients.

A Phase 2, Randomized, Double-Blind, Placebo- Controlled Study of the Efficacy and Safety of CF102 in the Second-Line Treatment of Advanced Hepatocellular Carcinoma in Subjects with Child-Pugh Class B Cirrhosis

Mock Tables and Listings
Version 7.0
29 August 2019

CONFIDENTIAL

Table of Contents

1. INTRODUCTION

This document is to be used in conjunction with the current Statistical Analysis Plan (SAP), protocol (Amendment 5, dated 6 November 2018), and corresponding CRFs.

The following pertains to the double-blind period only. Shells for the open-label period will be presented with a separate SAP.

Hyper-links are identified in this document as blue underlined text.

2. REPORTING CONVENTIONS

All output will be generated by SAS and exported into a Microsoft Word document in RTF format. All output will be in landscape orientation. Left and right margins will be 1 inch from the side; the top and bottom margins will be 1.12 inches. Font size will be Arial 8 pt.

The header containing the sponsor name (Can-Fite BioPharma, Ltd.) and protocol number (CF102-201HCC) will appear on the top left corner of each page of the output. The page number, in the format of “Page x of y”, will appear on the top right corner of the output, where y = last page of corresponding output. Horizontal lines will appear after the title, after the column headers and after the main body of the output.

The header and the titles section will be separated by one line. After the header, there will be a blank line. The titles will be presented as:

Line1: Table or Figure [number]
Line2a: [title]
Line2b: [subtitle, if applicable]
Line3: [xxx] Population

Footnotes will be placed after the main body of the table, under the horizontal line. Footnotes that need to reference a specific phrase will use a numeric convention (Example: 1, 2, 3). The last footnote will identify the listing or statistical appendix cross-reference as follows: Source: Listing 16.2.x. The sources for each table are identified in Section 3.1, Table Titles.

Table Format Specification

Maximum and minimum values will be reported with the same number of decimal places as collected. Means and medians will be reported to one additional decimal place. Standard deviations and standard errors will be reported to two decimal places more than the collected data. Percents will be reported with one decimal place. P-values will be rounded to three decimal places (e.g., “0.xxx”). If a p-value <0.001, then the p-value will be reported as “<0.001”.

If the frequency is 0 or 1 for a category for calculation of a standard deviation or standard error, then enter ‘(NE)’ for calculation of the standard deviation or standard error and add a footnote (penultimate preceding Source) of ‘NE= Not Estimable’.

If the frequency for “Total” <2 for a categorical variable for either treatment group, or frequency is “Total” for any category, i.e. a percent of 100 for that category, for both treatment groups, then enter ‘NA’ for the p-value with a footnote (penultimate preceding “Source”) of ‘NA = Not Applicable’.

Data in the tables are formatted as follows:

- Text fields in the body of the tables and listings will be left-justified.
- All numeric values between -1 and 1 are outputted with zero to the left of the decimal point (e.g. 0.12, 0.3).
- Unless otherwise specified, percentage values are output with one digit to the right of the decimal point (e.g., 12.3, 4.5). Percentages that are > 0.0 and < 0.1 (not 0.0) are reported as “< 0.1”.
- When no data are available for a table, an empty page with the title will be produced with suitable text. Example: THERE WERE NO SERIOUS ADVERSE EVENTS.

For many variables assessed at Pre-Study Visit, Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1) or if value at Cycle 1 Day 1 is missing. These are variables are identified with a footnote indicating this.

Dates will be presented as recorded. All listings will include the Safety Population and will be sorted by site, subject, and cycle (if appropriate). Treatments are to be formatted as CF102 and Placebo in listings.

3. OUTPUT TITLES

3.1. Table Titles

Table examples related to the following titles are located in the next section. Please footnote all information in the ‘Listing Source’ column for the corresponding table.

Number	Title of Table	Analysis Population	Listing Source
	DISPOSITION, DEMOGRAPHIC AND TREATMENT DATA		
14.1.1	Analysis Populations	Safety	16.2.1.1, 16.2.1.2
14.1.2	Study Completion and Primary Reason for Withdrawal	Safety	16.2.1.1
14.1.3	Demographic and Baseline Characteristics	Safety	16.2.3.1
14.1.4.1	HCC History and Diagnosis	Safety	16.2.3.2, 16.2.3.3.1, 16.2.3.5
14.1.4.2	Number of Target Lesions at Screening	Safety	16.2.6.1.1
14.1.4.3	Extrahepatic Spread (EHS) and Portal Vein Thrombosis (PVT)	Safety	16.2.3.3.2
14.1.5	Medical History (Excluding Past HCC, Cirrhosis, and Viral Hepatitis-Related History)	Safety	16.2.3.6
14.1.6	HCC Prior Therapies	Safety	16.2.3.4
14.1.7	Treatment Compliance and Duration of Treatment	Safety	16.2.4.1
	EFFICACY		
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	Figure 14.2.1: Kaplan-Meier curve for OS	ITT	16.2.5.1
	Figure 14.2.2: Kaplan-Meier curve for TTP	ITT	16.2.5.1
	Figure 14.2.3: Kaplan-Meier curve for PFS	ITT	16.2.5.1
14.2.2.1.1	Overall Response Using RECIST Criteria	ITT	16.2.6.3.1
14.2.2.1.2	Overall Response Using RECIST Criteria	PP	16.2.6.3.1, 16.2.1.2
14.2.2.2.1	Best Overall Response	ITT	16.2.6.3.1
14.2.2.2.2	Best Overall Response	PP	16.2.6.3.1, 16.2.1.2
14.2.3.1	WBC A3AR expression	ITT	16.2.6.4
14.2.3.2	WBC A3AR expression by Overall Response	ITT	16.2.6.3.1, 16.2.6.4
14.2.3.3	Overall Response by CFB for WBC A3AR expression	ITT	16.2.6.3.1, 16.2.6.4
14.2.4.1	Alpha-fetoprotein (AFP)	ITT	16.2.6.4
14.2.4.2	Alpha-fetoprotein (AFP) by Overall Response	ITT	16.2.6.3.1, 16.2.6.4
14.2.4.3	Overall Response by Categorical Alpha-fetoproterin (AFP)	ITT	16.2.6.3.1, 16.2.6.4
14.2.4.4	Overall Response by CFB for Alpha-fetoproterin (AFP)	ITT	16.2.6.3.1, 16.2.6.4

Number	Title of Table	Analysis Population	Listing Source
	EXPLORATORY EFFICACY		
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14.2.5.2	Aspartate aminotransferase (AST)	ITT	16.2.8.2
14.2.5.3	Albumin	ITT	16.2.8.2
14.2.5.4	Bilirubin (direct)	ITT	16.2.8.2
14.2.5.5	Bilirubin (total)	ITT	16.2.8.2
14.2.5.6	International Normalized Ratio (INR)	ITT	16.2.8.3
14.2.5.7	Prothrombin time (PT)	ITT	16.2.8.3
14.2.6	Hepatitis Viral Load	ITT	16.2.3.3.1, 16.2.6.5.1, 16.2.6.5.2
	SUBGOUP ANALYSES - EFFICACY		
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	Figure 14.2.7.1: Kaplan-Meier curve for OS, CP Score at Screening = 7	ITT	16.2.3.1, 16.2.5.1
	Figure 14.2.7.2: Kaplan-Meier curve for OS, CP Score at Screening = 8	ITT	16.2.3.1, 16.2.5.1
	Figure 14.2.7.3: Kaplan-Meier curve for OS, CP Score at Screening = 7 or 8	ITT	16.2.3.1, 16.2.5.1
14.2.7.2	Overall Survival (OS; months) by Sex	ITT	16.2.3.1, 16.2.5.1
14.2.7.3	Overall Survival (OS; months) by ECOG PS at Screening	ITT	16.2.9.3, 16.2.5.1
14.2.7.4	Overall Survival (OS; months) by Alpha-fetoprotein (AFP) at Baseline	ITT	16.2.6.4, 16.2.5.1
14.2.7.5	Overall Survival (OS; months) by Prior Locoregional Therapy	ITT	16.2.3.4, 16.2.5.1
14.2.7.6	Overall Survival (OS; months) by Either EHS or PVT	ITT	16.2.3.3.2, 16.2.5.1
14.2.7.7	Overall Survival (OS; months) by History of HBV	ITT	16.2.3.3.1, 16.2.5.1
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	THE PREVIOUS SHOULD BE IN THE SAME ORDER AS IN TEXT		
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Number	Title of Table	Analysis Population	Listing Source
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14.3.6.3	Clinical Laboratory Evaluations: Coagulation	Safety	16.2.8.3
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	Other Safety		
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14.3.8	Vital Signs And Weight	Safety	16.2.9.1, 16.2.9.2
14.3.9.1	Electrocardiogram (ECG) Parameters	Safety	16.2.10.1
14.3.9.2	Categorical Electrocardiogram (ECG) Parameters	Safety	16.2.10.2
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14.3.10.2	Physical Examination	Safety	16.2.11.2
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3.2. Listing Titles

4. EXAMPLES

4.1. Table Examples

Table 14.1.1

Analysis Populations

	CF102 (N=xx)	Placebo (N=xx)	Total (N=xx)
Safety Population	xx	xx	xx
Bulgaria	xx (xx.x)	xx (xx.x)	xx (xx.x)
Serbia	xx (xx.x)	xx (xx.x)	xx (xx.x)
Israel	xx (xx.x)	xx (xx.x)	xx (xx.x)
Romania	xx (xx.x)	xx (xx.x)	xx (xx.x)
United States	xx (xx.x)	xx (xx.x)	xx (xx.x)
Exclusions from ITT Population			
No Post-Baseline Tumor Assessment	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
ITT Population	xx (xx.x)	xx (xx.x)	xx (xx.x)
Bulgaria	xx (xx.x)	xx (xx.x)	xx (xx.x)
Serbia	xx (xx.x)	xx (xx.x)	xx (xx.x)
Israel	xx (xx.x)	xx (xx.x)	xx (xx.x)
Romania	xx (xx.x)	xx (xx.x)	xx (xx.x)
United States	xx (xx.x)	xx (xx.x)	xx (xx.x)
Exclusions from PP Population			
Reason 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
PP Population	xx (xx.x)	xx (xx.x)	xx (xx.x)
Bulgaria	xx (xx.x)	xx (xx.x)	xx (xx.x)
Serbia	xx (xx.x)	xx (xx.x)	xx (xx.x)
Israel	xx (xx.x)	xx (xx.x)	xx (xx.x)
Romania	xx (xx.x)	xx (xx.x)	xx (xx.x)
United States	xx (xx.x)	xx (xx.x)	xx (xx.x)

Percentages are calculated using the number of subjects in the Safety Population for each treatment (or Total) as the denominator.
ITT= Intent-to-Treat
PP=Per Protocol
Country is based on the first digit of the site number (1=Bulgaria, 2=Serbia, 3=Israel, 5=Romania, or 7=United States).
Source: Listings 16.2.1.1, 16.2.1.2

Programming Notes: Any reasons for exclusion from ITT Population (other than "No Post-Baseline Tumor Assessment") and reasons for exclusion from PP Population, and identification of subjects excluded, will be finalized prior to unblinding.

Table 14.1.2

Study Completion and Primary Reason for Withdrawal
Safety Population

Status, n(%)	CF102 (N=xx)	Placebo (N=xx)	Total (N=xx)
Primary Reason for Withdrawal from Dosing			
Grade 3 toxicity considered by the Investigator to be at least "possibly" drug-related that does not resolve to Grade ⩽ 1 within 7 days following interruption of treatment	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 4 toxicity considered by the Investigator to be at least "possibly" drug-related	xx (xx.x)	xx (xx.x)	xx (xx.x)
Need for > 1 dose reduction	xx (xx.x)	xx (xx.x)	xx (xx.x)
Treatment interruption or delay for more than 14 days after the next scheduled dose due to an event unrelated to toxicity	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject withdrawal of consent for trial participation at any time, for any reason, and without prejudice	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal of a subject by the Investigator, at his/her discretion, for any reason that the Investigator believes continuation of study drug therapy would not be in the subject's best interest.	xx (xx.x)	xx (xx.x)	xx (xx.x)
An intercurrent illness which, in the Investigator's opinion, would prevent completion of trial-related evaluations	xx (xx.x)	xx (xx.x)	xx (xx.x)
Pregnancy	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject noncompliance with trial or follow-up procedures	xx (xx.x)	xx (xx.x)	xx (xx.x)
Termination of the trial by the Sponsor	xx (xx.x)	xx (xx.x)	xx (xx.x)
Total	xx (xx.x)	xx (xx.x)	xx (xx.x)
Primary Reason for Withdrawal from Trial			
Withdrawal of consent	xx (xx.x)	xx (xx.x)	xx (xx.x)
Termination of the trial by the Sponsor	xx (xx.x)	xx (xx.x)	xx (xx.x)
Death	xx (xx.x)	xx (xx.x)	xx (xx.x)
Total	xx (xx.x)	xx (xx.x)	xx (xx.x)

Percentages are calculated using the number of subjects in the Safety Population for each treatment (or Total) as the denominator.
Source: Listing 16.2.1.1

Programming Note: Subjects should have response to either Primary Reason for Withdrawal from Dosing or Primary Reason for Withdrawal from Trial, but not BOTH.

Table 14.1.3

Demographic and Baseline Characteristics
Safety Population

Parameter (1)	Statistic	CF102	Placebo	Total

		(N=xx)	(N=xx)	(N=xx)
Age (years)	n	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx
Sex, n (%)	Male	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Female	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx	xx	xx
Origin, n (%)	White/Caucasian	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Black/African	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Oriental	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx	xx	xx
Child-Pugh Score, n (%)	7	xx (xx.x)	xx (xx.x)	xx (xx.x)
	8	xx (xx.x)	xx (xx.x)	xx (xx.x)
	9	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx	xx	xx

(1) Age is age at Screening.
Percentages are calculated using the number of subjects in the Safety Population for each treatment (or Total) as the denominator.
Source: Listing 16.2.3.1

Table 14.1.4.1

HCC History and Diagnosis
Safety Population

Parameter		CF102 (N=xx)	Placebo (N=xx)	Total (N=xx)
History of Viral Hepatitis, n (%) (1)	Yes – Hepatitis B	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Yes – Hepatitis C	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Not Known	xx (xx.x)	xx (xx.x)	xx (xx.x)
Hepatitis B Serology, n (%)	Negative	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Positive	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx	xx	xx
Hepatitis C Serology, n (%)	Negative	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Positive	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx	xx	xx
Complications, n (%) (1)	None	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Ascites	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Esophageal varices with bleeding	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Other	xx (xx.x)	xx (xx.x)	xx (xx.x)
Diagnostic Procedure, n (%) (2)	Cytology/histology	xx (xx.x)	xx (xx.x)	xx (xx.x)
	AASLD	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx	xx	xx

Percentages are calculated using the number of subjects in the Safety Population for each treatment (or Total) as the denominator.
(1) Percentages may sum to more than 100% because more than one response is possible.
(2) AASLD=American Association for the Study of Liver Diseases
Source: Listings 16.2.3.2, 16.2.3.3.1, 16.2.3.5

Programming Note: Check that no subject has "None" for Complications with another response.

Table 14.1.4.2

Number of Target Lesions at Screening
Safety Population

	Non- Liver Site Code (1)	Number of Non- Liver Lesions	Number of Liver Lesions							
			0	1	2	3	4	5	7	Total
CF102 (N=xx)	None				xx	xx	xx	xx		xx
	01	1			xx	xx	xx	xx		xx
		2	xx	xx	xx	xx		xx		xx
	02	1		xx	xx	xx		xx		xx
		2		xx	xx	xx	xx	xx		xx
	10	1			xx	xx	xx	xx		xx
	99	1		xx	xx	xx	xx	xx		xx
		2	xx	xx	xx	xx	xx	xx		xx
		3		xx	xx	xx	xx	xx		xx
	Total (2)		xx	xx	xx	xx	xx	xx		xx
Placebo (N=xx)	None			xx			xx	xx		xx
	02	0		xx	xx	xx	xx	xx	xx	xx
		1		xx	xx	xx	xx	xx		xx
	04	1		xx			xx	xx		xx
		2		xx	xx	xx	xx	xx		xx
	99	1		xx	xx			xx		xx
		2		xx	xx	xx	xx	xx		xx
		3	xx	xx	xx	xx				xx
	Total (2)		xx	xx	xx	xx	xx	xx		xx
Total (N=xx)	None			xx	xx	xx	xx	xx		xx
	01	1			xx	xx	xx	xx		xx
		2	xx	xx	xx	xx		xx		xx
	02	0		xx	xx	xx	xx	xx	xx	xx
		1	xx	xx	xx	xx	xx	xx		xx
		2	xx	xx	xx	xx	xx	xx		xx
	04	1		xx			xx	xx		xx
		2		xx	xx	xx	xx	xx		xx
	10	1			xx	xx	xx	xx		xx
	99	1		xx	xx	xx	xx	xx		xx
		2	xx	xx	xx	xx	xx	xx		xx
		3	xx	xx	xx	xx	xx	xx		xx
	Total (2)		xx	xx	xx	xx	xx	xx		xx

(1) Site Codes: 01 = Abdominal Wall, 02 = Adrenal, 03 = Bladder, 04 = Bone, 05 = Breast, 06 = CNS, 07 = Colon, 08 = Liver, 09 = Lung, 10 = Lymph Nodes, 11 = Pancreas, 12 = Pelvis, 13 = Pleura, 14 = Rectum, 15 = Retroperitoneal Cavity, 16 = Retroperitoneum, 17 = Small Intestine, 18 = Uterus, 99 = Other
(2) Number of non-liver lesions may not sum to Total due to subjects with more than one non-liver site.
Source: Listing 16.2.6.1.1

Programming Notes: Do not skip numbers for liver lesions for 1 through 5. There should be no subjects with 0 liver lesions or more than 5 liver lesions; if these are observed, include them as above, but otherwise only 1 through 5. Include only non-zero counts. For non-liver lesions, exclude rows with no entries. If any subjects have only liver lesions, include "None" row as non-liver site code. The values will be the counts of lesions at "Screening" from Listing 16.2.6.1.1.

Table 14.1.4.3

Extrahepatic Spread (EHS) and Portal Vein Thrombosis (PVT)
Safety Population

Parameter, n (%)		CF102 (N=xx)	Placebo (N=xx)	Total (N=xx)
Extrahepatic Spread (EHS)	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx	xx	xx
Portal Vein Thrombosis (PVT)	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx	xx	xx
Either EHS or PVT	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx	xx	xx
Both EHS and PVT	Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
	No	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx	xx	xx

Percentages are calculated using the number of subjects for each treatment (or Total) as the denominator.

Source: Listing 16.2.3.3.2

Programming Note: "Either EHS or PVT"= "Yes" if EHS= "Yes" or PVT= "Yes" and otherwise "Either EHS or PVT"= "No". "Both EHS and PVT"= "Yes" if EHS= "Yes" and PVT= "Yes" and otherwise "Both EHS and PVT"= "No".

Table 14.1.5

Medical History (Excluding Past HCC, Cirrhosis, and Viral Hepatitis-Related History)
Safety Population

Body System, n (%)	CF102 (N=xx)	Placebo (N=xx)	Total (N=xx)
None	xx (xx.x)	xx (xx.x)	xx (xx.x)
Allergy/Immunological	xx (xx.x)	xx (xx.x)	xx (xx.x)
Cardiovascular	xx (xx.x)	xx (xx.x)	xx (xx.x)
Dermatological	xx (xx.x)	xx (xx.x)	xx (xx.x)
ENT	xx (xx.x)	xx (xx.x)	xx (xx.x)
Gastrointestinal/ Hepatobiliary	xx (xx.x)	xx (xx.x)	xx (xx.x)
Hematological/ Lymphatic	xx (xx.x)	xx (xx.x)	xx (xx.x)
Metabolic/Endocrine	xx (xx.x)	xx (xx.x)	xx (xx.x)
Musculoskeletal	xx (xx.x)	xx (xx.x)	xx (xx.x)
Neoplastic	xx (xx.x)	xx (xx.x)	xx (xx.x)
Neurological/ Psychiatric	xx (xx.x)	xx (xx.x)	xx (xx.x)
Pulmonary	xx (xx.x)	xx (xx.x)	xx (xx.x)
Renal/Urological	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reproductive	xx (xx.x)	xx (xx.x)	xx (xx.x)

Counts represent the number of subjects with a finding or procedure recorded for each body system or None.
Percentages are calculated using the number of subjects in the Safety Population for each treatment (or Total) as the denominator.
Source: Listing 16.2.3.6

Programming Notes: Present body systems alphabetically after "None".
Check that no subject has "None" for Body System with another response.

Table 14.1.6

HCC Prior Therapies
Safety Population

Prior Therapy, n (%)	CF102 (N=xx)	Placebo (N=xx)	Total (N=xx)
01 = Surgery			
Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	xx (xx.x)	xx (xx.x)	xx (xx.x)
Total	xx	xx	xx
02 = Radiation			
Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	xx (xx.x)	xx (xx.x)	xx (xx.x)
Total	xx	xx	xx

The entries are the number (and percentage) of subjects reporting the use of a modality at least once.
Percentages are calculated using the number of subjects in the Safety Population for each treatment (or Total) as the denominator.
Source: Listing 16.2.3.4

Programming Note: Continue for Modality Codes: 03 = Chemotherapy, 04 = Immunotherapy, 05 = Hormonal therapy, 06 = Targeted Therapy (sorafenib), 07 = Chemoembolization, 08 = Anti-viral therapy, 09 = Other.

Table 14.1.7

Treatment Compliance and Duration of Treatment
Safety Population

	CF102 (N=xx)	Placebo (N=xx)	Total (N=xx)
Compliance Rate, % (1)			
n	xx	xx	xx
Mean (SD)	xx.xx (xx.xxx)	xx.xx (xx.xxx)	xx.xx (xx.xxx)
Median	xx.xx	xx.xx	xx.xx
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Duration of Treatment (days)			
n	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx

(1) A subject's compliance rate during the study is 100% * (total number of capsules dispensed minus the total number of capsules returned) divided by twice the subject's duration of treatment.

Source: Listing 16.2.4.1

Table 14.2.1

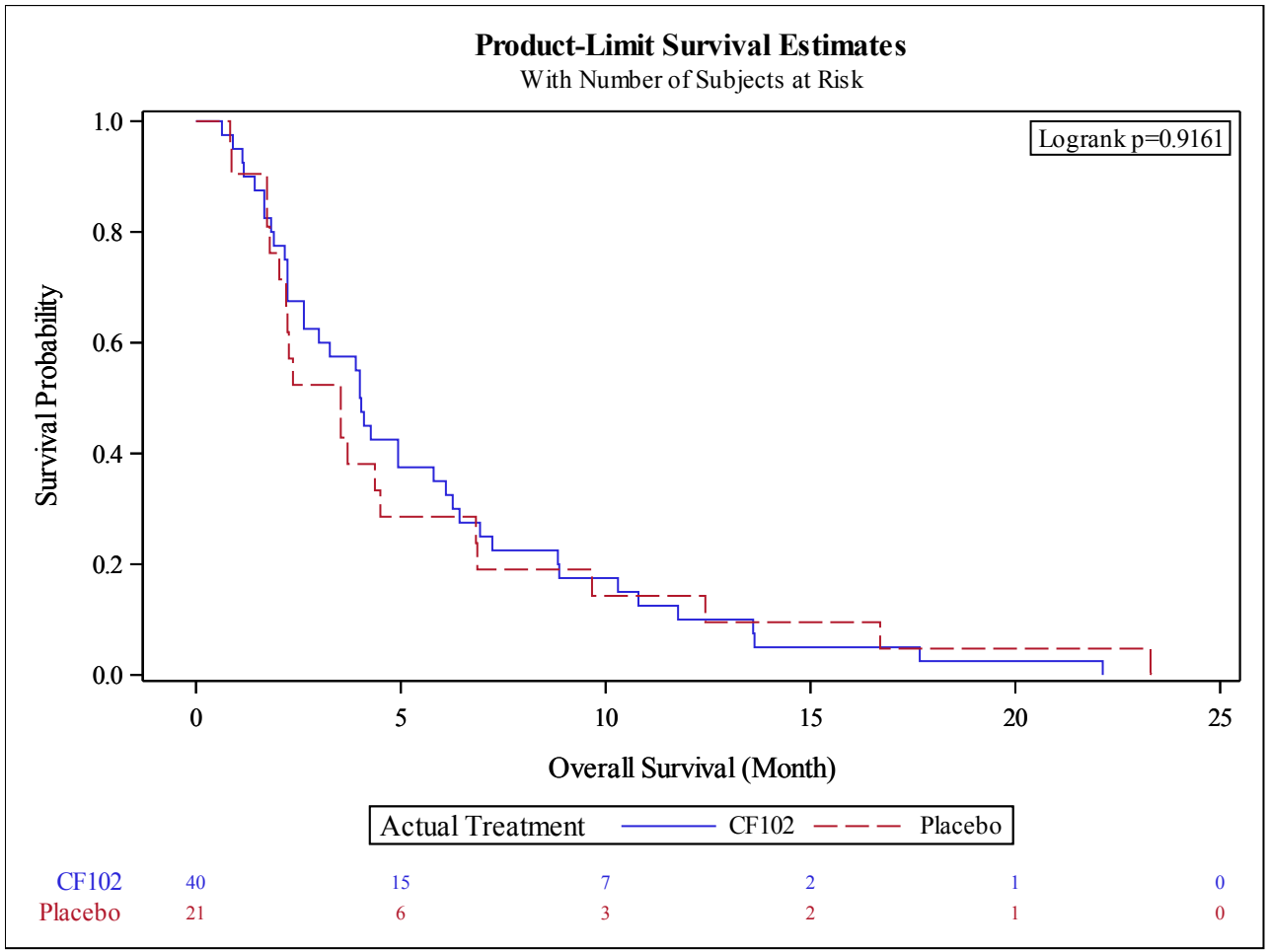
Time to Event (months)
ITT Population

Parameter	Statistic	CF102 (N=xx)	Placebo (N=xx)
Overall Survival (OS)	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Value of KM at Median Duration (%)	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	Covariate= Baseline AFP		
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
	Covariate= Baseline WBC A3AR		
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
Time To Progression (TTP)	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Value of KM at Median Duration (%)	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
Progression-free Survival (PFS)	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Value of KM at Median Duration (%)	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	

P-value (LR) =P-value using the logrank test. KM=Kaplan-Meier
Baseline=Cycle 1 Day 1
Percentages are calculated using the number of subjects in the ITT Population for each treatment as the denominator.
For Median Duration, see Table 14.1.7.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment and the specified covariate in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listing 16.2.5.1

Figure 14.2.1

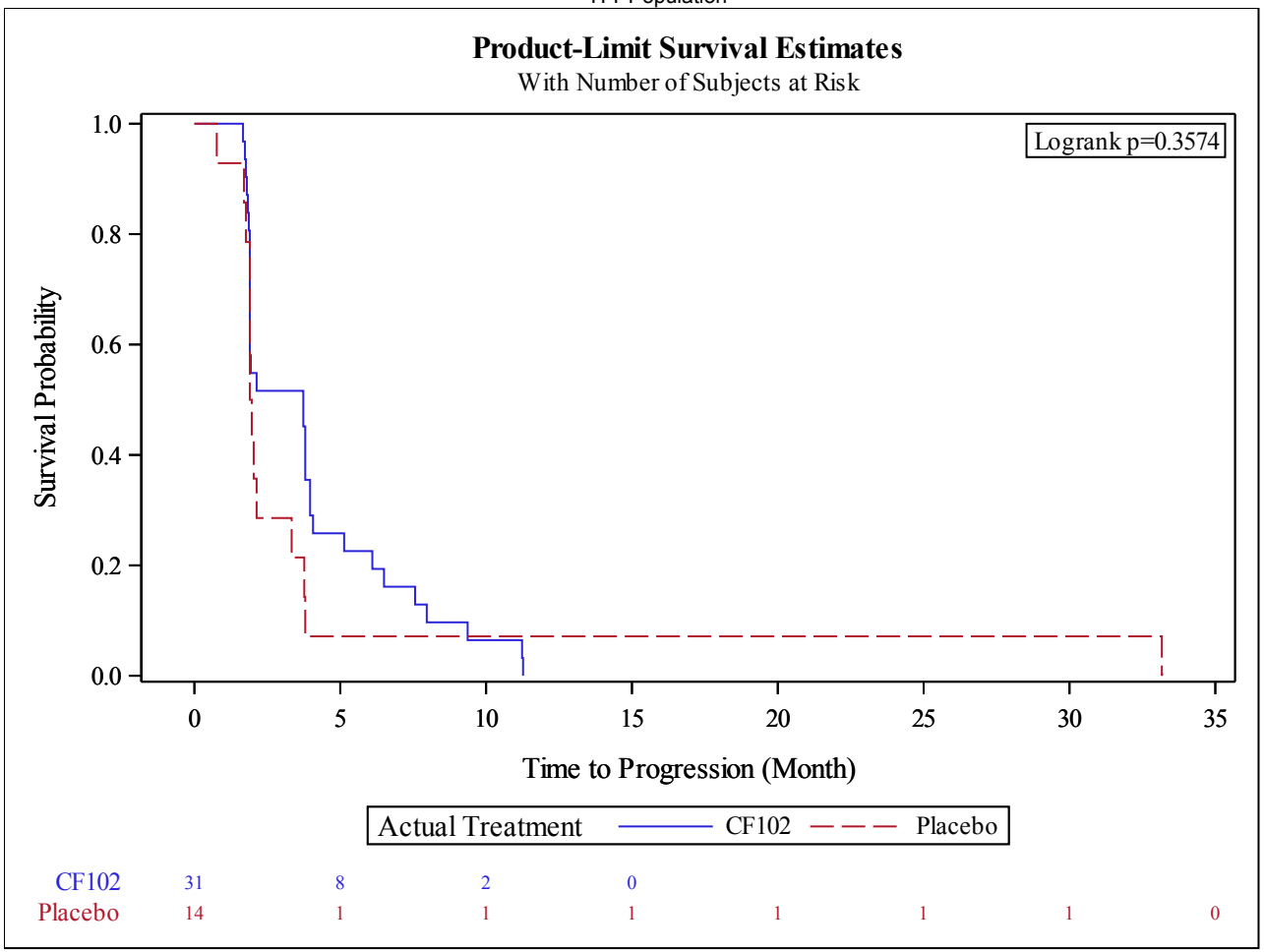
Kaplan-Meier curve for OS
ITT Population



Source: Listing 16.2.5.1

Figure 14.2.2

Kaplan-Meier curve for TTP
ITT Population

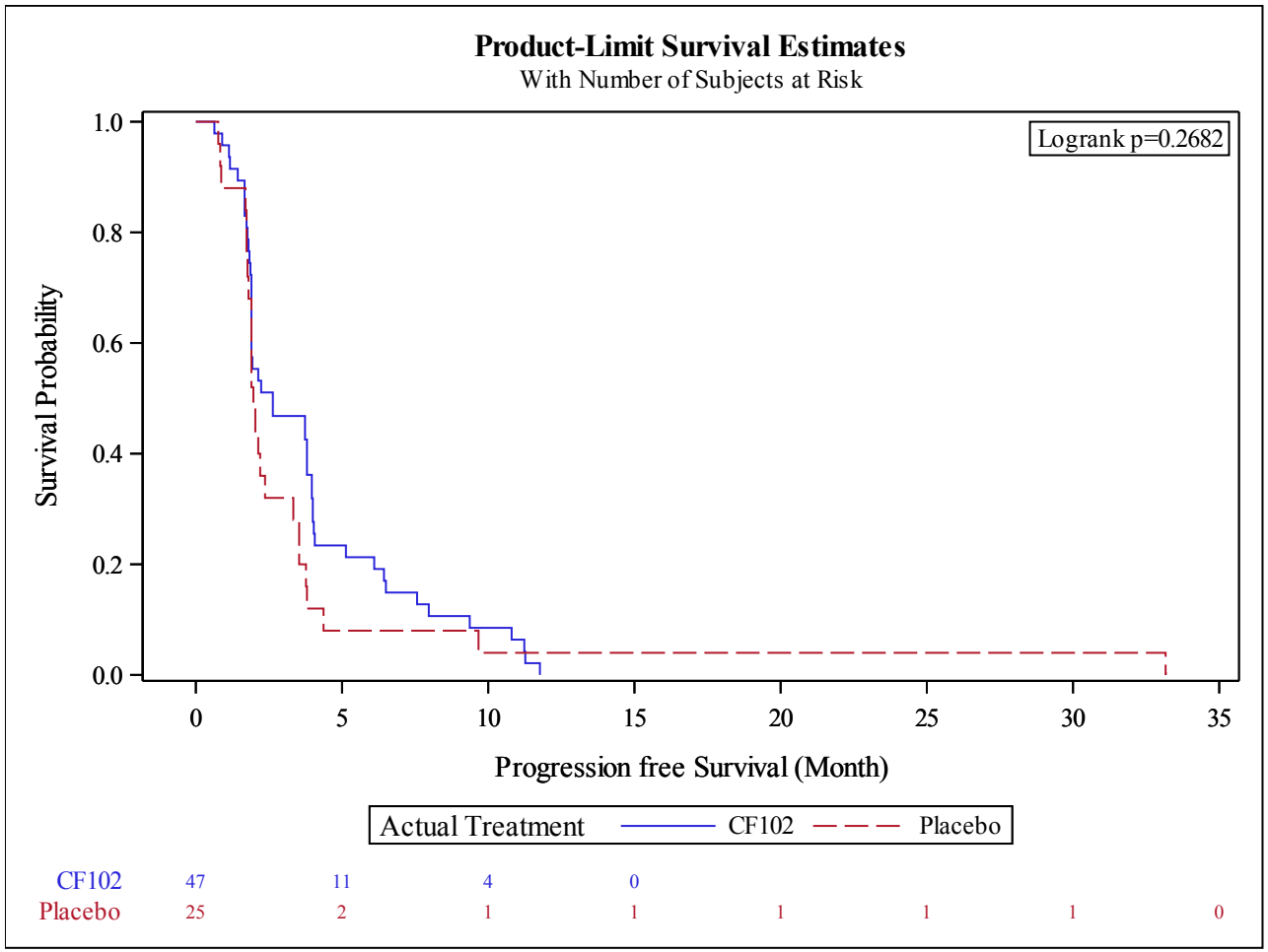


Source: Listing 16.2.5.1

Programming Note: Include number of patients at any month in the figure.

Figure 14.2.3

Kaplan-Meier curve for PFS
ITT Population



Source: Listing 16.2.5.1

Programming Note: Include number of patients at any month in the figure.

Table 14.2.2.1.1

Overall Response Using RECIST Criteria
ITT Population

Visit	Response, n (%)	CF102 (N=xx)	Placebo (N=xx)
Cycle 3 Day 1	CR	xx (xx.x)	xx (xx.x)
	PR	xx (xx.x)	xx (xx.x)
	SD	xx (xx.x)	xx (xx.x)
	PD	xx (xx.x)	xx (xx.x)
	Total	xx	xx
	ORR	xx (xx.x)	xx (xx.x)
	P-value	0.xxxx	
	DCR	xx (xx.x)	xx (xx.x)
	P-value	0.xxxx	
Cycle 5 Day 1	CR	xx (xx.x)	xx (xx.x)
	PR	xx (xx.x)	xx (xx.x)
	SD	xx (xx.x)	xx (xx.x)
	PD	xx (xx.x)	xx (xx.x)
	Total	xx	xx
	ORR	xx (xx.x)	xx (xx.x)
	P-value	0.xxxx	
	DCR	xx (xx.x)	xx (xx.x)
	P-value	0.xxxx	

Includes only assessments through Cycle 11.
CR=Complete Response, PR =Partial Response, SD =Stable Disease, PD=Progressive Disease
ORR=Objective Response Rate= proportion of subjects who have response of CR or PR
DCR=Disease Control Rate= proportion of subjects who have response of CR, PR, or SD
Percentages are calculated using the number of subjects in the ITT Population for each treatment as the denominator.
P-values determined using the normal approximation to the binomial distribution using observed responses.
ITT= Intent-to-Treat
NA = Not Applicable
Source: Listing 16.2.6.3.1

Programming Notes: Continue for all cycles through Cycle 11.
Use same structure for Table 14.2.2.1.2 (PP Population) with PP instead of ITT in the two appropriate footnotes and the last footnote changed to "Source: Listings 16.2.6.3.1, 16.2.1.2".

Table 14.2.2.2.1

Best Overall Response
ITT Population

Best Overall Response, n (%)	CF102 (N=xx)	Placebo (N=xx)
CR	xx (xx.x)	xx (xx.x)
PR	xx (xx.x)	xx (xx.x)
SD	xx (xx.x)	xx (xx.x)
PD	xx (xx.x)	xx (xx.x)
Total	xx	xx
ORR	xx (xx.x)	xx (xx.x)
P-value	0.xxxx	
DCR	xx (xx.x)	xx (xx.x)
P-value	0.xxxx	

CR=Complete Response, PR =Partial Response, SD =Stable Disease, PD=Progressive Disease
ORR=Objective Response Rate= proportion of subjects who have response of CR or PR
DCR=Disease Control Rate= proportion of subjects who have response of CR, PR, or SD
Percentages are calculated using the number of subjects in the ITT Population for each treatment as the denominator.
P-values determined using the normal approximation to the binomial distribution using observed responses.
Best Overall Response is determined for the entire duration of the study and is counted once per subject, although it may occur more than once.
ITT= Intent-to-Treat
NA = Not Applicable
Source: Listing 16.2.6.3.1

Programming Notes: Best Overall Response is determined for the entire duration of the study.
Use same structure for Table 14.2.2.2.2 (PP Population) with PP instead of ITT in the two appropriate footnotes and the last footnote changed to "Source: Listings 16.2.6.3.1, 16.2.1.2".

Table 14.2.3.1

WBC A3AR expression
ITT Population

Visit	Statistic	CF102 (N=xx)	Placebo (N=xx)
Baseline	n	xx	xx
	Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
	Median	xxx.x	xxx.x
	Min, Max	xxx, xxx	xxx, xxx
Cycle 3 Day 1	n	xx	xx
	Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
	Median	xxx.x	xxx.x
	Min, Max	xxx, xxx	xxx, xxx
CFB at Cycle 3 Day 1	n	xx	xx
	Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
	Median	xxx.x	xxx.x
	Min, Max	xxx, xxx	xxx, xxx
Cycle 5 Day 1	n	xx	xx
	Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
	Median	xxx.x	xxx.x
	Min, Max	xxx, xxx	xxx, xxx
CFB at Cycle 5 Day 1	n	xx	xx
	Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
	Median	xxx.x	xxx.x
	Min, Max	xxx, xxx	xxx, xxx

CFB=Change from Baseline
Baseline=Cycle 1 Day 1
Missing data for intermediate visits are imputed using LOCF.

Source: Listing 16.2.6.4

Programming Note: Continue for all visits (Day 1 for each odd-numbered cycle through Cycle 11), including CFB.

Table 14.2.3.2

WBC A3AR expression at Baseline by Overall Response
ITT Population

Visit	Overall Response	Statistic	CF102 (N=xx)	Placebo (N=xx)
Cycle 3 Day 1	CR	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	PR	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	SD	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	PD	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
CFB at Cycle 3 Day 1	CR	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	PR	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	SD	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	PD	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx

Baseline=Cycle 1 Day 1
Missing data for intermediate visits are imputed using LOCF.

Source: Listings 16.2.6.3.1, 16.2.6.4

Programming Note: Continue for all visits (Day 1 for each odd-numbered cycle through Cycle 11), including CFB.

Table 14.2.3.3

Overall Response by CFB for WBC A3AR expression
ITT Population

Visit	CFB for WBC A3AR expression	Overall Response (n, %)	CF102 (N=xx)	Placebo (N=xx)
Cycle 3 Day 1	< xxx.x (M)	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
	>= xxx.x (M)	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
Cycle 5 Day 1	< xxx.x (M)	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
	>= xxx.x (M)	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx

CFB=Change from Baseline
Baseline=Cycle 1 Day 1
Percentages are calculated using the number of subjects in the ITT Population for each treatment as the denominator.
M=pooled median of CFB for WBC A3AR expression at the specified visit
Missing data for intermediate visits are imputed using LOCF.

Source: Listings 16.2.6.3.1, 16.2.6.4

Programming Notes: Continue for all visits (Day 1 for each odd-numbered cycle through Cycle 11). Specify the value of the median M (xxx.x) at each visit, followed by "(M)".

Table 14.2.4.1

Alpha-fetoproterin (AFP)
ITT Population

Visit	Statistic	CF102 (N=xx)	Placebo (N=xx)
Cycle 1 Day 1	n	xx	xx
	Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
	Median	xxx.x	xxx.x
	Min, Max	xxx, xxx	xxx, xxx
Cycle 2 Day 1	n	xx	xx
	Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
	Median	xxx.x	xxx.x
	Min, Max	xxx, xxx	xxx, xxx
CFB at Cycle 2 Day 1	n	xx	xx
	Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
	Median	xxx.x	xxx.x
	Min, Max	xxx, xxx	xxx, xxx
	P-value (1)	0.xxxx	
Cycle 3 Day 1	n	xx	xx
	Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
	Median	xxx.x	xxx.x
	Min, Max	xxx, xxx	xxx, xxx
CFB at Cycle 3 Day 1	n	xx	xx
	Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
	Median	xxx.x	xxx.x
	Min, Max	xxx, xxx	xxx, xxx
	P-value (1)	0.xxxx	

(1) P-value determined using ANCOVA with Baseline and Treatment in the model.
CFB=Change from Baseline
Baseline=Cycle 1 Day 1
Missing data for intermediate visits are imputed using LOCF.
Source: Listing 16.2.6.4

Programming Notes: Continue for all visits (Day 1 of each cycle through Cycle 11), including CFB. P-values are included with each CFB. AFP is collected with lab data.
Exclude any data for days other than Day 1.

Table 14.2.4.2

Alpha-fetoproterin (AFP) by Overall Response
ITT Population

Visit	Overall Response	Statistic	CF102 (N=xx)	Placebo (N=xx)
Cycle 3 Day 1	CR	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	PR	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	SD	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	PD	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
CFB at Cycle 3 Day 1				
Cycle 5 Day 1				

CFB=Change from Baseline
Baseline=Cycle 1 Day 1
Missing data for intermediate visits are imputed using LOCF.

Source: Listings 16.2.6.3.1, 16.2.6.4

Programming Notes: Continue for all visits (Day 1 for each odd-numbered cycle through Cycle 11), including CFB. AFP is collected with lab data.

Table 14.2.4.3

Overall Response by Categorical Alpha-fetoproterin (AFP)
ITT Population

Visit	AFP (ng/mL)	Overall Response (n, %)	CF102 (N=xx)	Placebo (N=xx)
Cycle 3 Day 1	<20	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
	20-200	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
	>200	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
Cycle 5 Day 1	<20	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
	20-200	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
	>200	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx

Percentages are calculated using the number of subjects in the ITT Population in each category defined by AFP for each treatment as the denominator.
Missing data for intermediate visits are imputed using LOCF.

Source: Listings 16.2.6.3.1, 16.2.6.4

Programming Notes: Continue for all visits (Day 1 for each odd-numbered cycle).
AFP is collected with lab data.

Table 14.2.4.4

Overall Response by CFB for Alpha-fetoproterin (AFP)
ITT Population

Visit	CFB for AFP	Overall Response (n, %)	CF102 (N=xx)	Placebo (N=xx)
Cycle 3 Day 1	<xxx.x (M)	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
	>= xxx.x (M)	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
Cycle 5 Day 1	< xxx.x (M)	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx
	>= xxx.x (M)	CR	xx (xx.x)	xx (xx.x)
		PR	xx (xx.x)	xx (xx.x)
		SD	xx (xx.x)	xx (xx.x)
		PD	xx (xx.x)	xx (xx.x)
		Total	xx	xx

CFB=Change from Baseline
Baseline=Cycle 1 Day 1
M=pooled median of CFB for AFP at the specified visit
Percentages are calculated using the number of subjects in the ITT Population in each category defined by AFP for each treatment as the denominator.
Missing data for intermediate visits are imputed using LOCF.

Source: Listings 16.2.6.3.1, 16.2.6.4

Programming Notes: Continue for all visits (Day 1 for all odd-numbered cycles through Cycle 11). Specify the value of the median M (xxx.x) at each visit, followed by "(M)". AFP is collected with lab data.

Table 14.2.5.1

Alanine aminotransferase (ALT)
ITT Population

Visit	Statistic	CF102 (N=xx)	Placebo (N=xx)
Pre-Study	n	xx	xx
	Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
	Median	xxx.xx	xxx.xxx
	Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
Cycle 1 Day 1	n	xx	xx
	Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
	Median	xxx.xx	xxx.xxx
	Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
Cycle 1 Day 8	n	xx	xx
	Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
	Median	xxx.xx	xxx.xxx
	Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
CFB to Cycle 1 Day 8	n	xx	xx
	Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
	Median	xxx.xx	xxx.xxx
	Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	P-value (1)	0.xxxx	
Cycle 1 Day 15	n	xx	xx
	Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
	Median	xxx.xx	xxx.xxx
	Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
CFB to Cycle 1 Day 15	n	xx	xx
	Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
	Median	xxx.xx	xxx.xxx
	Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	P-value (1)	0.xxxx	

(1) P-value determined using ANCOVA with Baseline and Treatment in the model.
CFB=Change From Baseline
Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)
Missing data for intermediate visits are imputed using LOCF.
Source: Listing 16.2.8.2

Programming Notes: Continue for remaining visits (Days 1 and 15 through Cycle 11), including CFB. P-values are included with each CFB. The following tables will use the above format: Table 14.2.5.2: Aspartate aminotransferase (AST), Table 14.2.5.3: Albumin, Table 14.2.5.4: Bilirubin (direct), Table 14.2.5.5: Bilirubin (total), Table 14.2.5.6: Prothrombin time (PT) with Source Listing 16.2.8.3, and Table 14.2.5.7: International Normalized Ratio (INR) with Source Listing 16.2.8.3

Table 14.2.6

Hepatitis Viral Load
ITT Population

Parameter	Visit	Statistic	CF102 (N=xx)	Placebo (N=xx)
log(HBV Load)	Cycle 1 Day 1	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	Cycle 3 Day 1	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	CFB to Cycle 3 Day 1	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
		P-value (1)	0.xxxx	
log(HCV Load)	Cycle 1 Day 1	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	Cycle 3 Day 1	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	CFB to Cycle 3 Day 1	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
		P-value (1)	0.xxxx	

(1) P-value determined using ANCOVA with Baseline and Treatment in the model.
Includes only subjects with positive serology at Screening (Listing 16.2.3.3.1)
HBV =Hepatitis B Viral; HCV =Hepatitis C Viral.
log (Value) is the base 10 logarithm of the value.
CFB= Change From Baseline
Baseline=Cycle 1 Day 1
Missing data for intermediate visits are imputed using LOCF.
Source: Listings 16.2.3.3.1, 16.2.6.5.1, 16.2.6.5.2

Programming Notes: Include only subjects with positive serology at Screening; other subjects should not have data recorded.
If subjects without positive serology have viral load recorded, include the values in Listings 16.2.6.5.1 and 16.2.6.5.2, but not in the table.
Continue for all visits (Day 1 of odd-numbered cycles through Cycle 11), including CFB. P-values are included with each CFB.

Table 14.2.7.1

Overall Survival (OS; months) by Child-Pugh (CP) Score at Screening
ITT Population

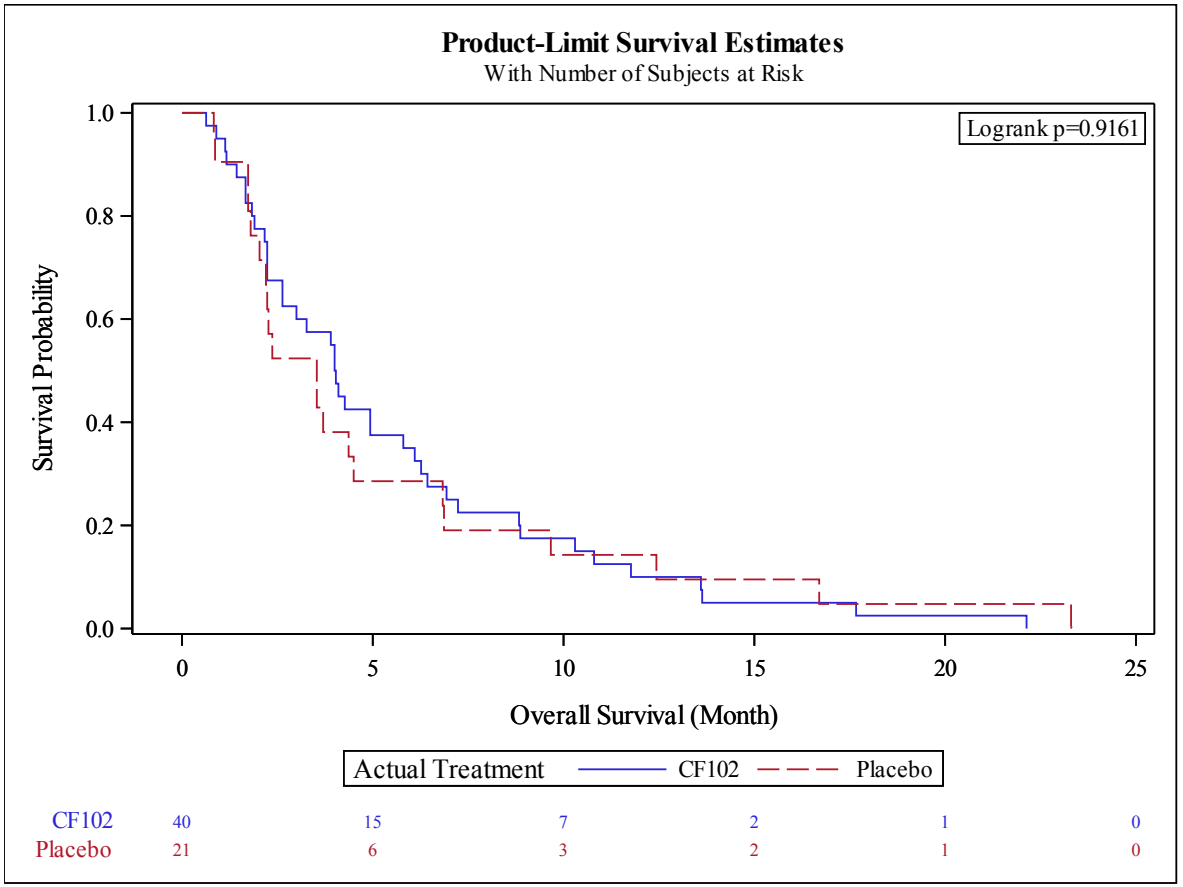
CP Score	Statistic	CF102 (N=xx)	Placebo (N=xx)
CP= 7	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
CP=8	n	xx	xx
CP=7 or 8	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
CP=9	n	xx	0
	25th Percentile	xx.x	
	Median	xx.x	
	75th Percentile	xx.x	
	Number (%) observed events	xx (xx.x)	
	Number (%) censored	xx (xx.x)	

P-value (LR) =P-value using the logrank test.
Percentages are calculated using the number of subjects in the ITT Population in the specified subgroup category for each treatment as the denominator.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment as the only factor in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listings 16.2.3.1, 16.2.5.1

Programming Notes: Continue for CP=8.
For CP=9, do not include P-value (LR), HR, 95% CI for HR, and P-value (PH) and only enter 0 for 'n' for Placebo.

Figure 14.2.7.1

Kaplan-Meier curve for OS
CP Score at Screening = 7
ITT Population



Source: Listings 16.2.3.1, 16.2.5.1

Programming Note: Use same structure for Figures 14.2.7.2 (OS, CP=8) and 14.2.7.3 (OS, CP= 7 or 8).

Table 14.2.7.2

Overall Survival (OS; months) by Sex
ITT Population

Sex	Statistic	CF102 (N=xx)	Placebo (N=xx)
Male	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
Female	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	

P-value (LR) =P-value using the logrank test.
Percentages are calculated using the number of subjects in the ITT Population in the specified subgroup category for each treatment as the denominator.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment as the only factor in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listings 16.2.3.1, 16.2.5.1

Table 14.2.7.3

Overall Survival (OS; months) by ECOG PS at Baseline
ITT Population

ECOG PS	Statistic	CF102 (N=xx)	Placebo (N=xx)
0	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
1 or 2	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	

P-value (LR) =P-value using the logrank test.
Percentages are calculated using the number of subjects in the ITT Population in the specified subgroup category for each treatment as the denominator.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment as the only factor in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listings 16.2.9.3, 16.2.5.1

Table 14.2.7.4

Overall Survival (OS; months) by Alpha-fetoprotein (AFP) at Baseline
ITT Population

AFP	Statistic	CF102 (N=xx)	Placebo (N=xx)
<=400 ng/mL	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
>400 ng/mL	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	

P-value (LR) =P-value using the logrank test.
Percentages are calculated using the number of subjects in the ITT Population in the specified subgroup category for each treatment as the denominator.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment as the only factor in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listings 16.2.6.4, 16.2.5.1

Table 14.2.7.5

Overall Survival (OS; months) by Prior Locoregional Therapy
ITT Population

Prior Locoregional Therapy	Statistic	CF102 (N=xx)	Placebo (N=xx)
Yes	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
No	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	

Locoregional Therapy = HCC Prior Therapies of Radiation or Chemoembolization
P-value (LR) =P-value using the logrank test.
Percentages are calculated using the number of subjects in the ITT Population in the specified subgroup category for each treatment as the denominator.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment as the only factor in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listings 16.2.3.4, 16.2.5.1

Table 14.2.7.6

Overall Survival (OS; months) by EHS, PVT, and Either EHS or PVT
ITT Population

Parameter	Response	Statistic	CF102 (N=xx)	Placebo (N=xx)
EHS	Yes	n	xx	xx
		25th Percentile	xx.x	xx.x
		Median	xx.x	xx.x
		75th Percentile	xx.x	xx.x
		Number (%) observed events	xx (xx.x)	xx (xx.x)
		Number (%) censored	xx (xx.x)	xx (xx.x)
		P-value (LR)	0.xxx	
		HR	x.xx	
		95% CI for HR	(x.xx, x.xx)	
		P-value (PH)	0.xxx	
	No	n	xx	xx
		25th Percentile	xx.x	xx.x
		Median	xx.x	xx.x
		75th Percentile	xx.x	xx.x
		Number (%) observed events	xx (xx.x)	xx (xx.x)
		Number (%) censored	xx (xx.x)	xx (xx.x)
		P-value (LR)	0.xxx	
		HR	x.xx	
		95% CI for HR	(x.xx, x.xx)	
		P-value (PH)	0.xxx	
PVT	Yes	n	xx	xx
		25th Percentile	xx.x	xx.x
Either EHS or PVT	Yes	n	xx	xx
		25th Percentile	xx.x	xx.x

EHS= Extrahepatic Spread; PVT= Portal Vein Thrombosis
P-value (LR) =P-value using the logrank test.
Percentages are calculated using the number of subjects in the ITT Population in the specified subgroup category for each treatment as the denominator.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment as the only factor in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listings 16.2.3.3.2, 16.2.5.1

Programming Note: Continue PVT= Yes and Either EHS or PVT= Yes, and add PVT= No and Either EHS or PVT= No.

Table 14.2.7.7

Overall Survival (OS; months) by History of HBV
ITT Population

History of HBV	Statistic	CF102 (N=xx)	Placebo (N=xx)
Yes	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
No	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	

HBV =Hepatitis B Virus
P-value (LR) =P-value using the logrank test.
Percentages calculated using the number of subjects in the ITT Population in the specified subgroup category as the denominator.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment as the only factor in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listings 16.2.3.3.1, 16.2.5.1

Table 14.2.7.8

Overall Survival (OS; months) by History of HCV
ITT Population

History of HCV	Statistic	CF102 (N=xx)	Placebo (N=xx)
Yes	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
No	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	

HCV =Hepatitis C Virus
P-value (LR) =P-value using the logrank test.
Percentages calculated using the number of subjects in the ITT Population in the specified subgroup category as the denominator.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment as the only factor in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listings 16.2.3.3.1, 16.2.5.1

Table 14.2.7.9

Overall Survival (OS; months) by Diagnostic Procedure
ITT Population

Diagnostic Procedure	Statistic	CF102 (N=xx)	Placebo (N=xx)
Cytology/histology	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
AASLD	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	

Diagnostic Procedure= Cytology/histology or American Association for the Study of Liver Diseases (AASLD)
P-value (LR) =P-value using the logrank test.
Percentages are calculated using the number of subjects in the ITT Population in the specified subgroup category for each treatment as the denominator.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment as the only factor in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listings 16.2.3.2, 16.2.5.1

Table 14.2.7.10

Overall Survival (OS; months) by Country
ITT Population

Country	Statistic	CF102 (N=xx)	Placebo (N=xx)
Bulgaria	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	
Israel	n	xx	xx
	25th Percentile	xx.x	xx.x
	Median	xx.x	xx.x
	75th Percentile	xx.x	xx.x
	Number (%) observed events	xx (xx.x)	xx (xx.x)
	Number (%) censored	xx (xx.x)	xx (xx.x)
	P-value (LR)	0.xxx	
	HR	x.xx	
	95% CI for HR	(x.xx, x.xx)	
	P-value (PH)	0.xxx	

P-value (LR) =P-value using the logrank test.
Percentages are calculated using the number of subjects in the ITT Population in the specified subgroup category for each treatment as the denominator.
HR=Hazard Ratio for Treatment from Proportional Hazards Model with Treatment as the only factor in the model and P-value (PH) is the corresponding p-value (Chi-Square).
Source: Listings 16.2.1.1, 16.2.5.1

Programming Note: Continue for each country (Bulgaria, Israel, Romania, Serbia, or United States) alphabetically.

Table 14.3.1

Incidence of Treatment-Emergent Adverse Events
Safety Population

MedDRA System Organ Class	MedDRA Preferred Term, n (%)	CF102 (N=xx)	Placebo (N=xx)
Any	Any	xx (xx.x)	xx (xx.x)
Body as a Whole	Any	xx (xx.x)	xx (xx.x)
	Fever	xx (xx.x)	xx (xx.x)

All AEs in this table are treatment emergent.
Percentages are calculated using the number of subjects in the Safety Population for each treatment as the denominator.
MedDRA version: 21.0
Source: Listing 16.2.7

Programming Note: Continue for all SOCs and Preferred Terms.

Table 14.3.2

Incidence of Treatment-Emergent Adverse Events by Relationship
Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	Relationship, n (%)	CF102 (N=xx)	Placebo (N=xx)
Any	Any	Definitely Related	xx (xx.x)	xx (xx.x)
		Probably Related	xx (xx.x)	xx (xx.x)
		Possibly Related	xx (xx.x)	xx (xx.x)
		Not Related	xx (xx.x)	xx (xx.x)
Body as a Whole	Any	Definitely Related	xx (xx.x)	xx (xx.x)
		Probably Related	xx (xx.x)	xx (xx.x)
		Possibly Related	xx (xx.x)	xx (xx.x)
		Not Related	xx (xx.x)	xx (xx.x)
	Fever	Definitely Related	xx (xx.x)	xx (xx.x)
		Probably Related	xx (xx.x)	xx (xx.x)
		Possibly Related	xx (xx.x)	xx (xx.x)
		Not Related	xx (xx.x)	xx (xx.x)

All AEs in this table are treatment emergent.
Relationship is the most related AE for each MedDRA System Organ Class and Preferred Term for each subject.
Percentages are calculated using the number of subjects in the Safety Population for each treatment as the denominator.
MedDRA version: 21.0
Source: Listing 16.2.7

Programming Notes: Continue for all SOCs and Preferred Terms. Include "Possibly Related" and "Not Related" for all SOCs and PTs; include "Definitely Related" and "Probably Related" for SOCs and PTs when such are recorded for relationship.

Table 14.3.3

Incidence of Treatment Emergent Adverse Events By Severity
Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	Severity, n (%)	CF102 (N=xx)	Placebo (N=xx)
Any	Any	Mild	xxx (xx.x)	xxx (xx.x)
		Moderate	xxx (xx.x)	xxx (xx.x)
		Severe	xxx (xx.x)	xxx (xx.x)
Body as a Whole	Any	Mild	xxx (xx.x)	xxx (xx.x)
		Moderate	xxx (xx.x)	xxx (xx.x)
		Severe	xxx (xx.x)	xxx (xx.x)
	Fever	Mild	xxx (xx.x)	xxx (xx.x)
		Moderate	xxx (xx.x)	xxx (xx.x)
		Severe	xxx (xx.x)	xxx (xx.x)

All AEs in this table are treatment emergent.
Severity is the most severe AE, i.e. largest severity grade, for each MedDRA System Organ Class and Preferred Term for each subject.
Percentages are calculated using the number of subjects in the Safety Population for each treatment as the denominator.
MedDRA version: 21.0
Source: Listing 16.2.7

Programming Notes: Continue for all SOCs and Preferred Terms.AE severity is recorded using grade. Display as Mild, Moderate, Severe, Life-Threatening, or Fatal for Grade 1, Grade 2, Grade 3, Grade 4, or Grade 5, respectively. Include Mild or Moderate for all SOCs and PTs and include Severe, Life-Threatening, or Fatal only for those SOCs and PTs when such are recorded for severity (i.e. with severity of Grades 3, 4 or 5, respectively).

Table 14.3.4.1

Listing of Deaths
Safety Population

Site/ Subject	Treatment	Last Visit	Date of Final Dose	Date of Death	Primary Cause of Death	Autopsy Performed?	Date of Autopsy
xxx/xxxx	xxxxxxxx	xx	DD/MM/YY	DD/MM/YY	xxxxxxxxxxxx	xxxx	DD/MM/YY
xxx/xxxx	xxxxxxxx	xx	DD/MM/YY	DD/MM/YY	xxxxxxxxxxxx	xxxx	DD/MM/YY

Includes subjects who discontinued from dosing or discontinued from the study for termination reason of death.
All deaths are given in Listing 16.2.5.1.
Source: Listings 16.2.1.1, 16.2.5.1, 16.2.7

Table 14.3.4.2

Listing of Serious Adverse Events
Safety Population

Site/ Subject	Treatment	System Organ Class / Preferred Term/ Verbatim Term	Start Date	Stop Date (1)	Relative Start Day	Relative Stop Day	Severity (2)	Freq. (3)	Relation (4)	Action Taken (5)	Outcome (6)	Serious?
xxx/xxxx	xxxxx	xxxxxx / xxxxxx/ xxxxxxx	DD/MM/YY	DD/MM/YY	xx	xx	x	x	x	x	x	x
xxx/xxxx	xxxxx	xxxxxx / xxxxxx/ xxxxxxx	DD/MM/YY	DD/MM/YY	xx	xx	x	x	x	x	x	x

Relative Start / Stop Dates = Days from Baseline to Start / Stop
(1) O=AE ongoing
(2) Severity: 1= Mild, 2= Moderate, 3= Severe but not immediately life-threatening, 4= Life-threatening consequences, 5=Death
(3) Frequency: 1= Single episode 2= Intermittent 3= Continuous
(4) Relationship: 1= Definitely related 2= Probably related 3= Possibly related 4= Not related
(5) Action Taken: 0= None 1= Medication TX 2= Non-medication TX 3= Hospitalization 4= Study drug delayed, 5= Study drug discontinued
(6) Outcome: 1= Resolved 2= Resolved with sequelae 3= Unresolved 4= Death
MedDRA version: 21.0

Source: Listing 16.2.7

Programming Note: Sort by site, subject and start date.

Table 14.3.5

Listing of Discontinuations Due to Adverse Events
Safety Population

Site/ Subject	Treatment	Date of Final Dose	Date of Withdrawal from Trial or Dosing	Primary Reason	Specify
xxx/xxxx	xxxxxxxx	DD/MM/YY	DD/MM/YY	xxxxxxxxxxxxxxxxxx	xxx

Includes only subjects with AE recorded as reason for withdrawal from dosing or trial
Source: Listings 16.2.1.1, 16.2.7

Table 14.3.6.1

Clinical Laboratory Evaluations: Hematology
Safety Population

Parameter (Units)	Visit	Statistic	CF102 (N=xx)	Placebo (N=xx)
XXXXXXXXX	Pre-Study	n	xx	xx
(UNITS)		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	Cycle 1 Day 1	n	xxx	xxx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	Cycle 1 Day 8	n	xxx	xxx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	CFB to Cycle 1 Day 8	n	xxx	xxx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	xxxxx	n	xxx	xxx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	CFB to xxxxx	n	xxx	xxx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x

CFB=Change From Baseline
Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)
Includes visits with at least 4 subjects in either treatment group
Source: Listing 16.2.8.1

Programming Notes: Continue for all parameters and all visits (Days 1, 8, and 15 for Cycle 1, and Days 1 and 15 for subsequent cycles), including CFB. Include visits with at least 4 subjects in either treatment group. The following tables will use the above format:
Table 14.3.6.2 Clinical Laboratory Evaluations: Blood Chemistry (Safety Population) with Source: Listing 16.2.8.2 and
Table 14.3.6.3 Clinical Laboratory Evaluations: Coagulation (Safety Population) with Source: Listing 16.2.8.3.

Table 14.3.6.4

Clinical Laboratory Evaluations: Thyroid Function
Safety Population

Parameter (Units)	Visit	Statistic	CF102 (N=xx)	Placebo (N=xx)
T3 (Unit)	Pre-Study	n	xx	xx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	Cycle 1	n	xxx	xxx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	Cycle 2	n	xxx	xxx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	CFB to Cycle 2	n	xxx	xxx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	xxxxx	n	xxx	xxx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	CFB to xxxxx	n	xxx	xxx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x

CFB=Change From Baseline
Baseline=Cycle 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)
Includes visits with at least 4 subjects in either treatment group
Source: Listing 16.2.8.5

Programming Note: Continue for T4 (Unit) and TSH (Unit) and all cycles with at least 4 subjects in either treatment group.

Table 14.3.7.1

ECOG Performance Status
Safety Population

Visit	ECOG PS, n (%)	CF102 (N=xx)	Placebo (N=xx)
Pre-Study	0	xx (xx.x)	xx (xx.x)
	1	xx (xx.x)	xx (xx.x)
	2	xx (xx.x)	xx (xx.x)
	3	xx (xx.x)	xx (xx.x)
	4	xx (xx.x)	xx (xx.x)
	Total	xx	xx
Cycle 1 Day 1	0	xx (xx.x)	xx (xx.x)
	1	xx (xx.x)	xx (xx.x)
	2	xx (xx.x)	xx (xx.x)
	3	xx (xx.x)	xx (xx.x)
	4	xx (xx.x)	xx (xx.x)
	Total	xx	xx
Cycle 2 Day 1	0	xx (xx.x)	xx (xx.x)
	1	xx (xx.x)	xx (xx.x)
	2	xx (xx.x)	xx (xx.x)
	3	xx (xx.x)	xx (xx.x)
	4	xx (xx.x)	xx (xx.x)
	Total	xx	xx
Cycle 3 Day 1	0	xx (xx.x)	xx (xx.x)
	1	xx (xx.x)	xx (xx.x)
	2	xx (xx.x)	xx (xx.x)
	3	xx (xx.x)	xx (xx.x)
	4	xx (xx.x)	xx (xx.x)
	Total	xx	xx

0=Normal activity, 1=Symptoms but ambulatory, 2= In bed <50% of time, 3=In bed >50% of time, 4=100% bedridden
Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)
Percentages are calculated using the number of subjects in the Safety Population for each treatment as the denominator.
Includes visits with at least 4 subjects in either treatment group
Source: Listing 16.2.9.3

Programming Notes: Continue for all cycles with at least 4 subjects in either treatment group. Include '4' only for cycles with a non-zero frequency for at least one treatment.

Table 14.3.7.2

Change from Baseline in ECOG Performance Status
Safety Population

Visit	CFB in ECOG PS, n (%)	CF102 (N=xx)	Placebo (N=xx)
Cycle 2 Day 1	Decrease	xx (xx.x)	xx (xx.x)
	No Change	xx (xx.x)	xx (xx.x)
	Increase	xx (xx.x)	xx (xx.x)
	Total	xx	xx
Cycle 3 Day 1	Decrease	xx (xx.x)	xx (xx.x)
	No Change	xx (xx.x)	xx (xx.x)
	Increase	xx (xx.x)	xx (xx.x)
	Total	xx	xx

CFB=Change from Baseline
Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)
Percentages are calculated using the number of subjects in the Safety Population for each treatment as the denominator.
Includes visits with at least 4 subjects in either treatment group
Source: Listing 16.2.9.3

Programming Note: Continue for all visits (Day 1 for all cycles) with at least 4 subjects in either treatment group.

Table 14.3.8

Vital Signs And Weight
Safety Population

Parameter (Units)	Visit	Statistic	CF102 (N=xx)	Placebo (N=xx)
Systolic BP (mmHg)	Pre-Study	n	xx	xx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	Baseline	n	xx	xx
		Mean(SD)	xxx.xx (xxx.xxx)	xxx.xx (xxx.xxx)
		Median	xxx.xx	xxx.xxx
		Min, Max	xxx.x, xxx.x	xxx.x, xxx.x
	Cycle 1 Day 1 Hour 1	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	CFB to Cycle 1 Day 1 Hour 1	n	xx	xx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx

BP=Blood Pressure
BMI=Body mass index
CFB= Change From Baseline
Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)
Includes visits with at least 4 subjects in either treatment group
Source: Listings 16.2.9.1, 16,2.9.2

Programming Notes: Continue for Diastolic BP (mmHg), Pulse (beats/min), Temperature (deg C), Respiratory Rate (/min), Weight (kg), and BMI (kg/m2) and visits (Days 1 and 15 of each cycle, Day 8 of Cycle 1, and Hours 1, 2, 3, 4, 6 and 8 on Cycle 1 Day 1) with CFB. Weight (kg) is not recorded at Hours 1, 2, 3, 4, 6 and 8 on Cycle 1 Day 1. Include visits with at least 4 subjects in either treatment group.

Table 14.3.9.1

Electrocardiogram (ECG) Parameters
Safety Population

Parameter	Visit	Statistic	CF102 (N=xx)	Placebo (N=xx)
Heart Rate (bpm)	Pre-Study	n	xxx	xxx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	Baseline	n	xxx	xxx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	Cycle 1 Day 1 Hour 2	n	xxx	xxx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	CFB to Cycle 1 Day 1 Hour 2	n	xxx	xxx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
QTcF (msec) (1)	Pre-Study	n	xxx	xxx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	Baseline	n	xxx	xxx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	Cycle 1 Day 1 Hour 2	n	xxx	xxx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx
	CFB to Cycle 1 Day 1 Hour 2	n	xxx	xxx
		Mean (SD)	xxx.x (xxx.xx)	xxx.x (xxx.xx)
		Median	xxx.x	xxx.x
		Min, Max	xxx, xxx	xxx, xxx

(1) QTcF= QT Correction- Fridericia
CFB= Change From Baseline
Baseline=Cycle 1 Day 1 Hour 0 (or Pre-Study if value at Cycle 1 Day 1 is missing)
Includes visits with at least 4 subjects in either treatment group
Source: Listing 16.2.10.1

Programming Notes: Continue for QRS Complex (msec), PR Interval (msec), and QTcF (msec) in that order and all visits (pre-Study, pre-dose at all visits, and at 2, 4, and 6 hours post-dose on Days 1 and 8 of Cycle 1) with CFB. Compute $QTcF=QT*(HR/60)^{1/3}$. *Include visits with at least 4 subjects in either treatment group.*

Table 14.3.9.2

Categorical Electrocardiogram (ECG) Parameters
Safety Population

Parameter	Visit	Response, n (%)	CF102 (N=xx)	Placebo (N=xx)
Overall Impression	Pre-Study	Normal	xxx (xx.x)	xxx (xx.x)
		NCS	xxx (xx.x)	xxx (xx.x)
		CS	xxx (xx.x)	xxx (xx.x)
		Total	xx	xx
	Baseline	Normal	xxx (xx.x)	xxx (xx.x)
		NCS	xxx (xx.x)	xxx (xx.x)
		CS	xxx (xx.x)	xxx (xx.x)
		Total	xx	xx
	Cycle 1 Day 1 Hour 2	Normal	xxx (xx.x)	xxx (xx.x)
		NCS	xxx (xx.x)	xxx (xx.x)
		CS	xxx (xx.x)	xxx (xx.x)
		Total	xx	xx
	Cycle 1 Day 1 Hour 4	Normal	xxx (xx.x)	xxx (xx.x)
		NCS	xxx (xx.x)	xxx (xx.x)
		CS	xxx (xx.x)	xxx (xx.x)
		Total	xx	xx
	Cycle 1 Day 1 Hour 6	Normal	xxx (xx.x)	xxx (xx.x)
		NCS	xxx (xx.x)	xxx (xx.x)
		CS	xxx (xx.x)	xxx (xx.x)
		Total	xx	xx
	Cycle 1 Day 8 Pre-Dose	Normal	xxx (xx.x)	xxx (xx.x)
		NCS	xxx (xx.x)	xxx (xx.x)
		CS	xxx (xx.x)	xxx (xx.x)
		Total	xx	xx
	Cycle 1 Day 8 Hour 2	Normal	xxx (xx.x)	xxx (xx.x)
		NCS	xxx (xx.x)	xxx (xx.x)
		CS	xxx (xx.x)	xxx (xx.x)
		Total	xx	xx

NCS= Abnormal-not clinically significant (NCS)
CS= Abnormal-clinically significant (CS)
Baseline=Cycle 1 Day 1 Hour 0 (or Pre-Study if value at Cycle 1 Day 1 is missing)
Percentages are calculated using the number of subjects in the Safety Population for each treatment as the denominator.
Includes visits with at least 4 subjects in either treatment group
Source: Listing 16.2.10.2.

Programming Notes: Continue for ST Segment and Cardiac Rhythm (Normal, Abnormal, and Total) and all visits (Pre-Study visit, Days 1 and 15 of all cycles, Day 8 of Cycle 1, and at 2, 4, and 6 hours post-dose on Day 1 of Cycle 1, and at Follow-up). Include visits with at least 4 subjects in either treatment group.

Table 14.3.10.1

Physical Examination at Pre-Study Visit
Safety Population

Body System	Response, n (%)	CF102 (N=xx)	Placebo (N=xx)
General Appearance	Normal	xxx (xx.x)	xxx (xx.x)
	Abnormal	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Head and Neck	Normal	xxx (xx.x)	xxx (xx.x)
	Abnormal	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Eyes, Ears, Nose, Throat	Normal	xxx (xx.x)	xxx (xx.x)
	Abnormal	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Skin	Normal	xxx (xx.x)	xxx (xx.x)
	Abnormal	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Chest / Lungs / Breast	Normal	xxx (xx.x)	xxx (xx.x)
	Abnormal	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Heart	Normal	xxx (xx.x)	xxx (xx.x)
	Abnormal	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Neurological	Normal	xxx (xx.x)	xxx (xx.x)
	Abnormal	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Other (1)	Normal	xxx (xx.x)	xxx (xx.x)
	Abnormal	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx

(1) Subjects with more than one assessment of “Other” are counted once.
Percentages are calculated using the number of subjects in the Safety Population for each treatment as the denominator.
Abnormalities are provided in the listing.
Source: Listing 16.2.11 .1

Programming Notes: Include other body systems. Subjects with more than one assessment of “Other” are counted once. Do not include “Not Assessed”.

Table 14.3.10.2

Physical Examination
Safety Population

Visit	Clin. Sig. Changes (1), n (%)	CF102 (N=xx)	Placebo (N=xx)
Cycle 1 Day 1	Yes	xxx (xx.x)	xxx (xx.x)
	No	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Cycle 1 Day 8	Yes	xxx (xx.x)	xxx (xx.x)
	No	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Cycle 1 Day 15	Yes	xxx (xx.x)	xxx (xx.x)
	No	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Cycle 2 Day 1	Yes	xxx (xx.x)	xxx (xx.x)
	No	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx
Cycle 2 Day 15	Yes	xxx (xx.x)	xxx (xx.x)
	No	xxx (xx.x)	xxx (xx.x)
	Total	xxx	xxx

(1) Are there any clinically significant changes from the physical examination conducted at the previous assessment?
Percentages are calculated using the number of subjects in the Safety Population for each treatment as the denominator.
Abnormalities associated with clinically significant changes are provided in the listing.
Includes visits with at least 4 subjects in either treatment group
Source: Listing 16.2.11.2

Programming Note: Continue for all visits (Days 1, 8, and 15 of Cycle 1 and Days 1 and 15 of subsequent cycles) with at least 4 subjects in either treatment group.

Table 14.3.11

Prior and Concomitant Medications
Safety Population

ATC Level 3 Class, n (%)	CF102 (N=xx)	Placebo (N=xx)
None	xx (xx.x)	xx (xx.x)
Class 1	xx (xx.x)	xx (xx.x)
Class 2	xx (xx.x)	xx (xx.x)

Includes medications taken within 30 days prior to Screening Visit.
Percentages are calculated using the number of subjects in the Safety Population for each treatment as the denominator.
Sum of percentages may exceed 100% because subjects could take Concomitant Medications within more than one ATC Level 3 Class.
Source: Listing 16.2.12

Programming Note: Continue for all observed Therapeutic Classes
Individual medications are not tabulated; only the ATC Level 3 Class.
Check that no subject has "None" for Complications with another response.

4.2. Listing Examples

Listing 16.2.1.1

Completed and Discontinued Subjects with Primary Reason for Withdrawal

Site/ Subject	Country	Treatment	Date of Final Dose	Complete 6 Months?	Withdrawn from dosing or from trial?	Date of Early Termination	Primary Reason for Withdrawal from Dosing	Primary Reason for Withdrawal from Trial	Specify / Comment
xxx/xxxx	xxxxxxx	xxxxxxx	DD/MM/YY	No	Yes	DD/MM/YY	xxxxxxxx		
xxx/xxxx	xxxxxxx	xxxxxxx	DD/MM/YY	Yes	Yes	DD/MM/YY		xxxxxxxx	
xxx/xxxx	xxxxxxx	xxxxxxx	DD/MM/YY	Yes	No				
xxx/xxxx	xxxxxxx	xxxxxxx	DD/MM/YY	No	Yes	DD/MM/YY		xxxxxxxx	xxxxxxxx

Country is based on the first digit of the site number (1=Bulgaria, 2=Serbia, 3=Israel, 5=Romania, or 7=United States).
Further information regarding deaths is given in Table 14.3.4.1.

Programming Notes: For Primary Reason for Withdrawal from Dosing, use:
"Grade 3", "Grade 4", "> 1 dose reduction", "Delay > 14 days", "Withdrawal of consent", "Withdrawal of subject by Investigator", "Intercurrent illness", "Pregnancy", "Noncompliance", or "Termination of the trial by Sponsor".

For Primary Reason for Withdrawal from Trial, use: "Withdrawal of consent", "Termination of the trial by Sponsor", "Death", or "Other".
The response to "Specify / Comment" is the text description for
Primary Reason for Withdrawal from Dosing = "Grade 3", "Grade 4", or "Withdrawal of subject by Investigator", or
Primary Reason for Withdrawal from Trial = 'Other', or 'Comments' at the end of the "Termination" module.

Subjects should have response to either Primary Reason for Withdrawal from Dosing or Primary Reason for Withdrawal from Trial, but not BOTH.
Sort listing by site and subject. Present country as Bulgaria, Serbia, Israel, Romania, or United States.

Listing 16.2.1.2

Subjects Excluded from Analysis Populations

Site/ Subject	Treatment	Excluded from ITT Population?	Excluded from PP Population?	Reason for Exclusion
xxx/xxxx	xxxxxxx	No	Yes	xxxxxxx
xxx/xxxx	xxxxxxx	Yes	Yes	xxxxxxx

Includes only subjects excluded from the ITT or PP Population.
All subjects excluded from the ITT Population are also excluded from the PP Population.
ITT= Intent-to-Treat
PP=Per Protocol

Programming Notes: Include only subjects excluded from ITT or PP Population.
All subjects excluded from the ITT Population are also excluded from the PP Population.

Listing 16.2.2.1

Inclusion Criteria

Site/ Subject	Treatment	Consent Date	Date of Screening Visit	IN1	IN2	IN3	IN4	IN5	IN6	IN7	IN8	IN9	IN10	IN11	IN12
xxx/xxxx	xxxxx	DD/MM/YYYY	DD/MM/YY	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
xxx/xxxx	xxxxx	DD/MM/YYYY	DD/MM/YY	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

See last page for list of criteria.

Programming Note: Place the criteria definitions on the last page(s).

Listing 16.2.2.1

Inclusion Criteria

Inclusion Criteria Questions

IN1= Males and females at least 18 years of age.
IN2= Diagnosis of HCC:

- For patients without underlying cirrhosis at the time of diagnosis, diagnosis of HCC documented by cytology and/or histology.
- For patients with underlying cirrhosis at the time of diagnosis, diagnosis of HCC established according to the American Association for the Study of Liver Diseases Practice Guideline algorithm.

IN3= HCC is advanced, ie, treatment-refractory or metastatic, and no standard therapies are expected to be curative.
IN4= Receipt of prior sorafenib therapy for at least 3 weeks and withdrawal from treatment due either to:
a) Intolerability; If treatment was withdrawn due to intolerability manifested as a Grade 3 or 4 event by National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE v4.0), less than 3 weeks of continuous prior administration prior to withdrawal is acceptable (see also Exclusion Criterion #3). Or;
b) Radiographic evidence of disease progression.
IN5= Prior sorafenib treatment was discontinued for at least 2 weeks prior to the Baseline Visit.
IN6= Eastern Collaborative Oncology Group (ECOG) performance status (PS) of ≤ 2.
IN7= Cirrhosis classified as Child-Pugh Class B.
IN8= The following laboratory values must be documented within 3 days prior to the first dose of study drug:

- Absolute neutrophil count (ANC) ≥ 1.5 x 10^9/L
- Platelet count ≥ 75 x 10^9/L
- Serum creatinine ≤2.0 mg/dL
- Aspartic aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 5 × upper limit of normal (ULN)
- Total bilirubin ≤ 3.0 mg/dL.
- Serum albumin ≥ 2.8 g/dL.
- Prothrombin time (PT) no greater than 6 seconds longer than control.

IN9= Life expectancy of ≥ 6 weeks.
IN10= For women of childbearing potential, negative serum pregnancy test result.
IN11= Provide written informed consent to participate.
IN12= Willing to comply with scheduled visits, treatment plans, laboratory assessments, and other trial related procedures.

Listing 16.2.2.2

Exclusion Criteria

Site/ Subject	Treatment	EX1	EX2	EX3	EX4	EX5	EX6	EX7	EX8	EX9	EX10	EX11	EX12	EX13	EX14	EX15	EX16	EX17	EX18	EX19
xxx/xxxxx	xxxxx	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
xxx/xxxxx	xxxxx	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

See last page for list of criteria.

Programming Note: Place the criteria definitions on the last page(s).

Listing 16.2.2.2

Exclusion Criteria

Exclusion Criteria Questions:

EX1= Receipt of no, or of >1, prior systemic drug therapies for HCC.
EX2= Any systemic cancer therapy, immunomodulatory drug therapy, immunosuppressive therapy, or corticosteroids > 20 mg/day prednisone or equivalent, within 14 days prior to the Baseline Visit or concurrently during the trial.
EX3= Presence of an acute or chronic toxicity of prior chemotherapy that has not resolved to ≤ Grade 1, as determined by CTCAE v 4.0.
EX4= Locoregional treatment within 4 weeks prior to the Baseline Visit.
EX5= Major surgery or radiation therapy within 4 weeks prior to the Baseline Visit.
EX6= Use of any investigational agent within 4 weeks prior to the Baseline Visit.
EX7= Child-Pugh Class A or C cirrhosis, or hepatic encephalopathy.
EX8= Occurrence of esophageal or other gastrointestinal hemorrhage requiring transfusion within 4 weeks prior to the Baseline Visit.
EX9= Uncontrolled or clinically unstable thyroid disease, per judgment of the Principal Investigator.
EX10= Active bacterial, viral, or fungal infection requiring systemic therapy or operative or radiological intervention.
EX11= Known human immunodeficiency virus- or acquired immunodeficiency syndrome-related illness.
EX12= Liver transplant.
EX13= Active malignancy other than HCC.
EX14= Uncontrolled arterial hypertension or congestive heart failure (New York Heart Association Classification 3 or 4).
EX15= Angina, myocardial infarction, cerebrovascular accident, coronary/peripheral artery bypass graft surgery, transient ischemic attack, or pulmonary embolism within 3 months prior to initiation of study drug.
EX16= History of or ongoing cardiac dysrhythmias requiring treatment, atrial fibrillation of any grade, or persistent prolongation of the QTc (Fridericia) interval to > 450 msec for males or > 470 msec for females.
EX17= Pregnant or lactating female.
EX18= Women of childbearing potential, unless they agree to use dual contraceptive methods which, in the opinion of the Investigator, are effective and adequate for the subject's circumstances while on study drug.
EX19= Men who partner with a woman of childbearing potential, unless they agree to use effective, dual contraceptive methods (i.e., a condom, with female partner using oral, injectable, or barrier method) while on study drug and for 3 months afterward.
EX20= Any severe, acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or study drug administration, may interfere with the informed consent process and/or with compliance with the requirements of the study, or may interfere with the interpretation of study results and, in the investigator's opinion, would make the subject inappropriate for entry into this study.

Listing 16.2.3.1

Demographic and Baseline Characteristics

Site/ Subject	Treatment	Age	Date of Birth	Origin	Sex	CP Score (1)
xxx/xxxx	xxxxx	xx	DD/MM/YY	xxxxx	xxxxx	x
xxx/xxxx	xxxxx	xx	DD/MM/YY	xxxxx	xxxxx	x

(1) CP Score= Child- Pugh Score at Screening

Programming Note: Compute Age as (the number of days from Date of Birth to Date of Screening Visit)/365.25

Listing 16.2.3.2

HCC Diagnosis

Site/ Subject	Treatment	Diagnosis Date	Most recent relapse and/or re-staging date	Diagnosis Established by (1)	If Diagnosis Established by Cytology/histology, specify histopathological diagnosis
xxx/xxxx	xxxxx	DD/MM/YY	DD/MM/YY	xxxxxx	xxxxxxxxxxxx
xxx/xxxx	xxxxx	DD/MM/YY	DD/MM/YY	xxxxxx	
xxx/xxxx	xxxxx	DD/MM/YY	DD/MM/YY	xxxxxx	xxxxxxxxxxxx

(1) AASLD=American Association for the Study of Liver Diseases

Programming Note: If diagnosis was established by American Association for the Study of Liver Diseases, present as AASLD.

Listing 16.2.3.3.1

HCC History

Site/ Subject	Treatment	Date of Screening Visit	Known History of Viral Hepatitis?	Date of Diagnosis of Hepatitis B	Date of Diagnosis of Hepatitis C	Hepatitis B Virus Serology	Date of Last Hepatitis B Testing	Hepatitis C Virus Serology	Date of Last Hepatitis C Testing	Complications (1)
xxx/xxxx	xxxxx	DD/MM/YY	Yes	DD/MM/YY	DD/MM/YY	xxxxxxxxxx	DD/MM/YY	xxxxxxxxxx	DD/MM/YY	xxxxx
xxx/xxxx	xxxxx	DD/MM/YY	No			xxxxxxxxxx	DD/MM/YY	xxxxxxxxxx	DD/MM/YY	xxxxx
xxx/xxxx	xxxxx	DD/MM/YY	Yes	DD/MM/YY	DD/MM/YY	xxxxxxxxxx		xxxxxxxxxx	DD/MM/YY	xxxxx
xxx/xxxx	xxxxx	DD/MM/YY	Yes	DD/MM/YY		xxxxxxxxxx	DD/MM/YY	xxxxxxxxxx	DD/MM/YY	xxxxx xxxxx
xxx/xxxx	xxxxx	DD/MM/YY	Yes	DD/MM/YY	DD/MM/YY	xxxxxxxxxx	DD/MM/YY	xxxxxxxxxx	DD/MM/YY	None
xxx/xxxx	xxxxx	DD/MM/YY	Yes		DD/MM/YY	xxxxxxxxxx	DD/MM/YY	xxxxxxxxxx	DD/MM/YY	xxxxx

(1) Known complication(s) of cirrhosis and/or portal hypertension

Programming Notes: If date of last testing is missing, then the field should be blank. "Serology" should not be blank. If none of the specified responses, including Other, are selected for Complications, then the response should be reported as "None". If "Other, specify" is reported for complication, then report the specified details as the complication. If more than 1 complication is reported, then multiple lines per subject should be used. Date of Screening Visit must match that given in Listing 16.2.2.1.

Listing 16.2.3.3.2

Extrahepatic Spread (EHS) and Portal Vein Thrombosis (PVT)

Site/ Subject	Treatment	EHS	PVT	Either EHS or PVT	Both EHS and PVT
xxx/xxxx	xxxxx	xxx	xxx	xxx	xx
xxx/xxxx	xxxxx	xxx	xxx	xxx	xx

EHS = Extrahepatic Spread, PVT = Portal Vein Thrombosis

Programming Notes: Record each response as "Yes", "No", or "Unknown". Include only subjects with one of these responses recorded.

Listing 16.2.3.4

HCC Prior Therapies

Site/ Subject	Treatment	Modality Code (1)	Modality Details	Intent (2)	Best response to treatment	If Intent="Other", Specify	Start Date	Stop Date
xxx/xxxx	xxxxx	xx	xxxxxxxxxxxxxxx	xx	xx		DD/MM/YY	DD/MM/YY
xxx/xxxx	xxxxx	xx	xxxxxxxxxxxxxxx	xx	xx	xxxxxxxxx	DD/MM/YY	DD/MM/YY

(1) Modality Codes: 01 = Surgery, 02 = Radiation, 03 = Chemotherapy, 04 = Immunotherapy, 05 = Hormonal therapy, 06 = Targeted Therapy (sorafenib), 07 = Chemoembolization, 08 = Anti-viral therapy, 09 = Other
(2) Intent Codes: 01 = Curative / Palliative, 02 = Adjuvant, 03 = Neo adjuvant, 04 = Diagnostic, 05 = Therapy of Viral Hepatitis, 06 = Therapy for Complication of Portal Hypertension, 09 = Other (specify)
(3) Best Response Codes: 01 = CR – Complete Response; 02 = PR – Partial Response; 03 = PD – Progressive Disease; 04 = SD – Stable Disease; 09 = Unknown

Programming Note: There may be multiple lines per subject.

Listing 16.2.3.5

Cirrhosis / Virus Complications and Treatment

Site/ Subject	Treatment	Modality Code (1)	Modality Details	Intent (2)	Start Date	Stop Date
xxx/xxxx	xxxxx	xx	xxxxxxxxxxxxxxx	xxxxxx	DD/MM/YY	DD/MM/YY
xxx/xxxx	xxxxx	xx	xxxxxxxxxxxxxxx	xxxxxx	DD/MM/YY	DD/MM/YY

(1) Modality Codes: 01 = Surgery, 02 = Radiation, 03 = Chemotherapy, 04 = Immunotherapy, 05 = Hormonal therapy, 06 = Targeted Therapy (sorafenib), 07 = Chemoembolization, 08 = Anti-viral therapy, 09 = Other

(2) Intent Codes: 01 = Curative / Palliative, 02 = Adjuvant, 03 = Neo adjuvant, 04 = Diagnostic, 05 = Therapy of Viral Hepatitis, 06 = Therapy for Complication of Portal Hypertension, 09 = Other (specify)

Programming Note: There may be multiple lines per subject.

Listing 16.2.3.6

Medical History (Excluding Past HCC, Cirrhosis, and Viral Hepatitis-Related History)

Site/ Subject	Treatment	Past findings or surgery? (1)	Body System	Finding or Procedure	Start Date	Stop Date
xxx/xxxx	xxxxx	Yes	xxxxxxxxx	xxxxxxxxxxx	DD/MM/YY	DD/MM/YY
			xxxxxxxxx	xxxxxxxxxxx	DD/MM/YY	DD/MM/YY
xxx/xxxx	xxxxx	Yes	xxxxxxxxx	xxxxxxxxxxx	DD/MM/YY	DD/MM/YY
xxx/xxxx	xxxxx	No				
xxx/xxxx	xxxxx	Yes	xxxxxxxxx	xxxxxxxxxxx	DD/MM/YY	DD/MM/YY

(1) Has the patient had any past medical findings or surgical procedures?

Programming Note: There may be multiple lines per subject.

Listing 16.2.4.1

Study Drug Accountability and Treatment Compliance

Site/ Subject	Treatment	Total Number of Capsules Dispensed	Total Number of Capsules Returned	Date of Final Dose (1)	Date of Baseline Visit	Treatment Duration (Days)	Compliance (%)
xxx/xxxxx	xxxxx	xxx	xxx	DD/MM/YY	DD/MM/YY	xxx	xx.x
xxx/xxxxx	xxxxx	xxx	xxx	DD/MM/YY	DD/MM/YY	xxx	xx.x

(1) Date of Last Recorded Visit for subjects who are ongoing.
The numbers of capsules dispensed and returned by visit are in the next listing.

Programming Notes: Treatment Duration= date of final dose minus date of Baseline + 1.
Compliance (%) =100(total number of capsules dispensed over study - total number of capsules returned over study)/ (2*treatment duration).*
*Total number of capsules dispensed over study = 65*sum of the Number of Bottles Dispensed from next listing.*
*Total number of capsules returned over study = 65*sum of the Number of Unopened Bottles Returned from above table*
+ sum of Number of capsules returned (open bottle) from next listing.

Listing 16.2.4.2

Study Drug Accountability by Visit

Site/ Subject	Treatment	Visit	Date	Treatment Number	Number of Bottles Dispensed	Comments	Number of unopened bottles returned	Number of capsules returned (open bottle)	Comments
xxx/xxxxx	xxxxx	Cycle 1	xx/xxx/xxxxx	xxxx	xxx	xxxxxx			
		Cycle 2	xx/xxx/xxxxx	xxxx	xxx	xxxxxx	xxx	xxx	xxxxxxxx
		Cycle 3	xx/xxx/xxxxx	xxxx	xxx	xxxxxx	xxx	xxx	xxxxxxxx
xxx/xxxxx	xxxxx	Cycle 1	xx/xxx/xxxxx	xxxx	xxx	xxxxxx			
		Cycle 2	xx/xxx/xxxxx	xxxx	xxx	xxxxxx	xxx	xxx	xxxxxxxx
		Cycle 3	xx/xxx/xxxxx	xxxx	xxx	xxxxxx	xxx	xxx	xxxxxxxx
		Cycle 4	xx/xxx/xxxxx	xxxx	xxx	xxxxxx	xxx	xxx	xxxxxxxx

Programming Note: Continue for all cycles.

Listing 16.2.5.1

Time to Event

Site/ Subject	Treatment	Date of First Dose	Progressive Disease?	Death?	Date of Death	Date of First Progression	Date of Last Contact	OS (months)	TTP (months)	PFS (months)
xxx/xxxxx	xxxx	DD/MM/YY	Yes	Yes	DD/MM/YY	DD/MM/YY	DD/MM/YY	xx.x	xx.x	xx.x
xxx/xxxxx	xxxx	DD/MM/YY	Yes	No		DD/MM/YY	DD/MM/YY	xx.x *	xx.x	xx.x
xxx/xxxxx	xxxx	DD/MM/YY	No	No			DD/MM/YY	xx.x *	xx.x *	xx.x *
xxx/xxxxx	xxxx	DD/MM/YY	No	Yes	DD/MM/YY		DD/MM/YY	xx.x	xx.x *	xx.x

OS= Overall Survival (Time to Death due to any cause); TTP=Time to Progression; PFS= Progression-Free Survival (Time to Progression or Death)
* indicates censored value.

Programming Notes: If an event did not occur, leave the date of the event blank.
Date of Last Contact is the last date known to be alive in next listing.
*Add * for censored values, defined as follows.*
OS is time to death due to any cause and is censored at date of last contact if death is not reported.
TTP is time to progression and is censored at date of last contact (including death) if progression is not reported.
PFS is time to progression or death and is censored at date of last contact if neither progression nor death is reported.

Listing 16.2.5.2

Survival Follow-up Contact Dates

Site/ Subject	Treatment	Follow-up Date	Is the Subject Alive?	Last date known to be alive	If not alive, date of death
xxx/xxxxx	xxxx	DD/MM/YY	xx	DD/MM/YY	DD/MM/YY
		DD/MM/YY	xx	DD/MM/YY	DD/MM/YY
		DD/MM/YY	xx	DD/MM/YY	DD/MM/YY
xxx/xxxxx	xxxx	DD/MM/YY	xx	DD/MM/YY	DD/MM/YY
		DD/MM/YY	xx	DD/MM/YY	DD/MM/YY
		DD/MM/YY	xx	DD/MM/YY	DD/MM/YY

Includes all subjects who discontinue from dosing.

Programming Notes: Continue for all follow-up dates.
The CRF Page is to be completed for all subjects who discontinue from dosing.

Listing 16.2.6.1.1

Tumor Evaluations: Target Lesions

Site/ Subject	Treatment	Cycle	Lesion#	Site Code (1)	Description	Assessment Date	Method Code (2)	Longest Diameter (LD)
xxx/xxxx	xxxxx	Screening	xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
			xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
			xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
			xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
		Cycle 3	xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
			xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
			xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
			xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
		Cycle 5	xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
			xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
			xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
			xx	xx	xxxxxx	DD/MM/YY	xxx	xxx

(1) Site Codes:
01 = Abdominal Wall, 02 = Adrenal, 03 = Bladder, 04 = Bone, 05 = Breast, 06 = CNS, 07 = Colon, 08 = Liver, 09 = Lung, 10 = Lymph Nodes, 11 = Pancreas, 12 = Pelvis, 13 = Pleura, 14 = Rectum, 15 = Retroperitoneal Cavity, 16 = Retroperitoneum, 17 = Small Intestine, 18 = Uterus, 99 = Other, specify

(2) Method Codes:
B = Bone Scan, C = Conventional CT scan, D = Direct Measure by Physical Exam, E = Endoscopy, L = Laparoscopy, M = Magnetic Resonance Imaging, S = Spiral CT scan, U = Ultrasound, X = X-Ray, O = Other, specify

Programming Notes: Continue for all odd-numbered cycles.
Sort listing by lesion within cycle. There is one line for each target lesion.

Column "None?" has been deleted
It was intended only for cases with assessments made and there were no target lesions detected.
This would require "CR" for Target Lesions with disappearance of all Target Lesions; there were no such cases.

Listing 16.2.6.1.2

Summary of Target Lesions

Site/ Subject	Treatment	Cycle	Sum of Longest Diameters (mm)	Smallest Sum On Study (mm)	Percent Change from Smallest:	Screening Sum on study	Percent Change From Screening
xxx/xxxx	xxxxx	Screening	xx	xx	xxx	xxx	xxx
		Cycle 3	xx	xx	xxx	xxx	xxx
		Cycle 5	xx	xx	xxx	xxx	xxx
xxx/xxxx	xxxxx	Screening	xx	xx	xxx	xxx	xxx
		Cycle 3	xx	xx	xxx	xxx	xxx
		Cycle 5	xx	xx	xxx	xxx	xxx
xxx/xxxx	xxxxx	Screening	xx	xx	xxx	xxx	xxx
		Cycle 3	xx	xx	xxx	xxx	xxx
		Cycle 5	xx	xx	xxx	xxx	xxx
		Cycle 7	xx	xx	xxx	xxx	xxx

"Smallest sum on study" at any visit refers to sums prior to, and including, the visit of interest, including the baseline sum of diameters.

Programming Notes: Continue for all odd-numbered cycles. There is one line for each cycle.
Column "None?" has been deleted
It was intended only for cases with assessments made and there were no target lesions detected.
This would require "CR" for Target Lesions with disappearance of all Target Lesions; there were no such cases.

Listing 16.2.6.2

Tumor Evaluations: Non-Target Lesions

Site/ Subject	Treatment	Cycle	None?	Lesion#	Site Code (1)	Description	Assessment Date	Method Code (2)	Status
xxx/xxxx	xxxxx	Screening		xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
		Cycle 3		xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
		Cycle 5		xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
		Cycle 7	None				DD/MM/YY		
		Cycle 9		xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx
				xx	xx	xxxxxx	DD/MM/YY	xxx	xxx

'None?' = 'None' if no non-target lesions were recorded
(1) Site Codes:
01 = Abdominal Wall, 02 = Adrenal, 03 = Bladder, 04 = Bone, 05 = Breast, 06 = CNS, 07 = Colon, 08 = Liver, 09 = Lung, 10 = Lymph Nodes, 11 = Pancreas, 12 = Pelvis, 13 = Pleura, 14 = Rectum, 15 = Retroperitoneal Cavity, 16 = Retroperitoneum, 17 = Small Intestine, 18 = Uterus, 99 = Other, specify

(2) Method Codes:
B = Bone Scan, C = Conventional CT scan, D = Direct Measure by Physical Exam, E = Endoscopy, L = Laparoscopy, M = Magnetic Resonance Imaging, S = Spiral CT scan, U = Ultrasound, X = X-Ray, O = Other, specify

Programming Notes: Continue for all odd-numbered cycles.
Sort by lesion within cycle. There is one line for each non-target lesion.

Listing 16.2.6.3.1

Tumor Response

Site/ Subject	Treatment	Cycle	Assessment Date	Response: Target Lesions (1)	Response: Non-Target Lesions (2)	Comment	Overall Response (3)	OR (4)	DC (5)	Best Response (6)
xxx/xxxxx	xxxx	Cycle 3	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	xxx
xxx/xxxxx	xxxx	Cycle 3	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 5	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	xxx
530/006	xxxx	Cycle 3	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 5	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 7	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	xxx
		Cycle 9	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 11	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 13 (7)	DD/MM/YY	PR	xxx		PR	xxx	xxx	
		Cycle 15	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 29	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	

(1) CR= Complete Response, PR= Partial Response, SD= Stable Disease, PD= Progressive Disease
(2) CR= Complete Response, PD= Progressive Disease, Non-CR/non-PD= Neither CR nor PD, NE= Not evaluated/ Unable to evaluate
(3) CR= Complete Response, PR= Partial Response, SD= Stable Disease, PD= Progressive Disease, Non-CR/non-PD= Neither CR nor PD, NE= Not evaluated/ Unable to evaluate
(4) OR= Objective Response= Overall Response of CR or PR (Yes or No)
(5) DC= Disease Control = Overall Response of CR, PR, or SD (Yes or No)
(6) Best Response = Best overall response recorded from the start of the study treatment until the end of study, in the order of CR, PR, SD, or PD from best to worst
(7) Subject 530/006 ay Cycle 13 had Response: Target Lesions that met RECIST criteria for both PR and PD, included above as PR.

Programming Notes: Continue for all odd-numbered cycles.
Use "Comment" for "Response: Non-Target Lesions" = "Unable to evaluate (NE)".
Record "Best Response" only at visit(s) at which it occurs.

Listing 16.2.6.3.2

Tumor Response (Investigator Assessments)

Site/ Subject	Treatment	Cycle	Assessment Date	Response: Target Lesions (1)	Response: Non-Target Lesions (2)	Comment	Overall Response (3)	OR (4)	DC (5)	Best Response (6)
xxx/xxxxx	xxxx	Cycle 3	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	xxx
xxx/xxxxx	xxxx	Cycle 3	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 5	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	xxx
530/006	xxxx	Cycle 3	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 5	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 7	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	xxx
		Cycle 9	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 11	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 13 (7)	DD/MM/YY	PR	xxx		PD	xxx	xxx	
		Cycle 15	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	
		Cycle 29	DD/MM/YY	xxx	xxx		xxx	xxx	xxx	

(1) CR= Complete Response, PR= Partial Response, SD= Stable Disease, PD= Progressive Disease
(2) CR= Complete Response, PD= Progressive Disease, Non-CR/non-PD= Neither CR nor PD, NE= Not evaluated/ Unable to evaluate
(3) CR= Complete Response, PR= Partial Response, SD= Stable Disease, PD= Progressive Disease, Non-CR/non-PD= Neither CR nor PD, NE= Not evaluated/ Unable to evaluate
(4) OR= Objective Response= Overall Response of CR or PR (Yes or No)
(5) DC= Disease Control = Overall Response of CR, PR, or SD (Yes or No)
(6) Best Response = Best overall response recorded from the start of the study treatment until the end of study, in the order of CR, PR, SD, or PD from best to worst
(7) Subject 530/006 ay Cycle 13 had Response: Target Lesions that met RECIST criteria for both PR and PD, included above as PD.

Programming Notes: Continue for all odd-numbered cycles.
Use "Comment" for "Response: Non-Target Lesions" = "Unable to evaluate (NE)".
Record "Best Response" only at visit(s) at which it occurs.
Include Tumor Responses as recorded on CRF, including EOS Visit, the Follow-up Visit, and Unscheduled Visits.

Listing 16.2.6.4

Biomarkers: AFP and WBC A3AR

Site/ Subject	Treatment	Cycle	Date	alpha-fetoproterin (AFP) (1)	CFB in AFP	WBC A3AR Expression Level	CFB in WBC A3AR Expression Level
xxx/xxxxx	xxxx	Baseline	DD/MM/YY	xxx		xxx	
		Cycle 2	DD/MM/YY	xxx	xxx		
		Cycle 3	DD/MM/YY	xxx	xxx	xxx	xxx
		Cycle 4	DD/MM/YY	xxx	xxx		
		Cycle 5	DD/MM/YY	xxx	xxx	xxx	xxx
xxx/xxxxx	xxxx	Baseline	DD/MM/YY	xxx		xxx	
		Cycle 2	DD/MM/YY	xxx	xxx		
		Cycle 3	DD/MM/YY	xxx	xxx	xxx	xxx
		Cycle 4	DD/MM/YY	xxx	xxx		
		Cycle 5	DD/MM/YY	xxx	xxx	xxx	xxx

CFB=Change from Baseline
(1) H=Abnormal High, L=Abnormal Low
Normal ranges are given at the end of the listing.
Baseline=Cycle 1 Day 1

Programming Note: Continue for all cycles.

Listing 16.2.6.4

Biomarkers: AFP and WBC A3AR
Normal Ranges

Parameter	Low	High
AFP		xx
Normal range for WBC A3AR not specified		

Listing 16.2.6.5.1

Hepatitis B Viral Load

Site/ Subject	Treatment	Visit	Date	Screening Serology	Sample Taken? (1)	Viral Load (IU/mL)	Log (Viral Load)	CFB in Log (Viral Load)
xxx/xxxxx	xxxx	Baseline	DD/MM/YY	xxxxxxxx	xxx	xxxxxx	xxxx.xx	
		Cycle 3	DD/MM/YY		xxx	xxxxxx	xxxx.xx	xxxx.xx
		Cycle 5	DD/MM/YY		xxx	xxxxxx	xxxx.xx	xxxx.xx
		Cycle 7	DD/MM/YY		xxx	xxxxxx	xxxx.xx	xxxx.xx

(1) Yes, No, or NA
Should include only subjects with positive serology at Screening, per protocol. Others are included if viral load was recorded (Listing 16.2.3.3).
CFB=Change from Baseline
Baseline=Cycle 1 Day 1
Log (Value) is the base 10 logarithm of the value.

Programming Notes: Continue for all odd-numbered cycles. Include Screening Serology as "Positive" or "Negative".

Listing 16.2.6.5.2

Hepatitis C Viral Load

Site/ Subject	Treatment	Visit	Date	Screening Serology	Sample Taken? (1)	Viral Load (IU/mL)	Log (Viral Load)	CFB in Log (Viral Load)
xxx/xxxxx	xxxx	Baseline	DD/MM/YY	xxxxxxxx	xxx	xxxxxx	xxxx.xx	
		Cycle 3	DD/MM/YY		xxx	xxxxxx	xxxx.xx	xxxx.xx
		Cycle 5	DD/MM/YY		xxx	xxxxxx	xxxx.xx	xxxx.xx
		Cycle 7	DD/MM/YY		xxx	xxxxxx	xxxx.xx	xxxx.xx

(1) Yes, No, or NA
Should include only subjects with positive serology at Screening, per protocol. Others are included if viral load was recorded (Listing 16.2.3.3).
CFB=Change from Baseline
Baseline=Cycle 1 Day 1
Log (Value) is the base 10 logarithm of the value.

Programming Notes: Continue for all odd-numbered cycles. Include Screening Serology as "Positive" or "Negative".

Listing 16.2.7

Adverse Events

Site/ Subject	Treatment	System Organ Class / Preferred Term/ Verbatim Term	Start Date	Stop Date (1)	Duration (2)	Severity Grade (3)	Frequency (4)	Relation (5)	Action Taken (6)	Outcome (7)	Serious?
xxx/xxxx	xxxxx	xxxxxx / xxxxxx/ xxxxxxx	DD/MM/YY	DD/MM/YY	x	x	x	x	x	x	xx
xxx/xxxx	xxxxx	xxxxxx / xxxxxx/ xxxxxxx	DD/MM/YY	DD/MM/YY	x	x	x	x	x	x	xx

(1) O=AE ongoing
(2) Duration (days)= Stop Date – Start Date + 1; Duration =Date of Last Dose – Start Date + 1 if AE is ongoing
(3) Severity Grade: 1=Mild, 2=Moderate, 3=Severe or medically significant but not immediately life-threatening, 4=Life-threatening consequences, or 5=Death related to AE.
(4) Frequency: 1= Single episode 2= Intermittent 3= Continuous
(5) Relationship: 1= Definitely related 2= Probably related 3= Possibly related 4= Not related
(6) Action Taken: 0= None 1= Medication TX 2= Non-medication TX 3= Hospitalization 4= Study drug delayed, 5= Study drug discontinued
(7) Outcome: 1= Resolved 2= Resolved with sequelae 3= Unresolved 4= Death
Sorted by Start Date, then alphabetically by SOC and Preferred Term within subject.

Programming Note: Sort by Start Date, then alphabetically by SOC and Preferred Term within subject for AEs starting on the same date.

Listing 16.2.8.1

Clinical Laboratory Evaluations: Hematology

Site/ Subject	Treatment	Visit	Day	Date	Laboratory Parameter (Units)	Value (1)	CFB
xxx/xxxx	xxxxx	Pre-Study		MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
		Baseline		MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
		Cycle 1	8	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
		Cycle 1	15	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
		Cycle 2	1	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
		Cycle 2	15	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
		Cycle 3	1	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx

(1) H=Abnormal High, L=Abnormal Low
Normal ranges are given at the end of the listing.
CFB=Change from Baseline
Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)

Programming Note: Continue for all cycles, Days 1 and 15.

Listing 16.2.8.1

Clinical Laboratory Evaluations: Hematology
Normal Ranges

Parameter	Gender	Age (Years)	Low - High
BASOPHILS (%)	–	18 - 65+	0 - 2
BASOPHILS ABSOLUTE (GI/L)	–	18 - 65+	0 - 0.2
EOSINOPHILS (%)	–	18 - 65+	0 - 7
EOSINOPHILS ABSOLUTE (GI/L)	–	18 - 65+	0.05 - 0.55
HEMATOCRIT (1)	Male	18 - 64	0.41 - 0.50
	Male	65+	0.36 - 0.49
	Female	18 - 64	0.35 - 0.46
	Female	65+	0.33 - 0.46
HEMOGLOBIN (G/L)	Male	18 - 64	138 - 172
	Male	65+	118 - 168
	Female	18 - 64	120 – 156
	Female	65+	111 - 155
LYMPHOCYTES (%)	–	18 - 65+	16 - 46
LYMPHOCYTES ABSOLUTE (GI/L)	–	18 - 65+	0.85 - 4.10
MONOCYTES (%)	–	18 - 65+	0 - 12
MONOCYTES ABSOLUTE (GI/L)	–	18 - 65+	0.2 - 1.1
PLATELET COUNT (GI/L)	–	18 - 65+	130 - 400
RED CELL COUNT (TI/L)	Male	18 - 64	4.4 - 5.8
	Male	65+	3.7 - 5.5
	Female	18 - 64	3.9 - 5.2
	Female	65+	3.6 - 5.1
RETICULOCYTES (%)	–	18 - 65+	0.5 - 2.3
RETICULOCYTES, ABS (10e9/L)	–	18 - 65+	25 - 85
TOTAL NEUTROPHILS (%)	–	18 - 65+	40 - 75
TOTAL NEUTROPHILS AB (GI/L)	–	18 - 65+	1.8 – 8.0
WHITE CELL COUNT (GI/L)	–	18 - 65+	3.8 - 10.8

Ranges are given for adults (age at least 18 years).
Age (Years) = “18 - 65+” indicates that there is no restriction on normal due to age in adults.

Listing 16.2.8.2

Clinical Laboratory Evaluations: Blood Chemistry

Site/ Subject	Treatment	Visit	Day	Date	Laboratory Parameter (Units)	Value (1)	CFB
xxx/xxxx	xxxxx	Pre-Study		MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
		Baseline		MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	
		Cycle 1	8	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
		Cycle 1	15	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
		Cycle 2	1	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
		Cycle 2	15	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
		Cycle 3	1	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx	xxx

(1) H=Abnormal High, L=Abnormal Low
Normal ranges are given at the end of the listing.
CFB=Change from Baseline
Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)

Programming Note: Continue for all cycles, Days 1 and 15.

]

Listing 16.2.8.2

Clinical Laboratory Evaluations: Blood Chemistry
Normal Ranges

Parameter	Gender	Age (Years)	Low - High
ALAT (SGPT) (U/L)	–	18 - 65+	0 - 48
ALBUMIN (G/L)	–	18 - 65+	32 - 50
ALKALINE PHOSPHATASE (U/L)	–	20+	20 - 125
ASAT (SGOT) (U/L)	–	18 - 64	0 - 42
	–	65+	0 - 55
BILIRUBIN, DIRECT (UMOL/L)	–	18 - 65+	0 - 6
BILIRUBIN, TOTAL (UMOL/L)	–	18 - 65+	0 - 22
CALCIUM (MMOL/L)	–	18 - 65+	2.12 - 2.56
CARBON DIOXIDE (CO2) (MMOL/L)	–	18 - 65+	20 - 32
CHLORIDE (MMOL/L)	–	18 - 65+	95 - 108
GLUCOSE (MMOL/L)	–	18 - 49	3.9 - 6.4
	–	50+	3.9 - 6.9
LACTIC DEHYDROGENASE (U/L)	–	18 - 64	0 - 250
	–	65+	0 - 270
PHOSPHORUS INORGANIC (MMOL/L)	–	18 - 64	0.80 - 1.45
	–	65+	0.7 - 1.4
POTASSIUM (MMOL/L)	–	18 - 65+	3.5 - 5.3
PROTEIN, TOTAL SERUM (G/L)	–	18 - 64	60 - 85
	–	65+	58 - 81
SODIUM (MMOL/L)	–	18 - 65+	135 - 146
UREA NITROGEN (MMOL/L)	–	18 - 64	2.5 - 9
	–	65+	2.5 - 10.5
URIC ACID (UMOL/L)	Male	18 - 65+	240 - 510
	Female	18 - 65+	150 - 450

Ranges are given for adults (age at least 18 years).
Age (Years) = “18 - 65+” indicates that there is no restriction on normal due to age in adults.

Listing 16.2.8.2

Clinical Laboratory Evaluations: Blood Chemistry
Normal Ranges (CREATININE ENZ)

Parameter	Gender	Age (Years)	Low - High
CREATININE ENZ, SER (UMOL/L)	Male	20 - 29	70.7 - 114.9
	Male	30 - 39	69.8 - 117.6
	Male	40 - 49	69.0 - 118.5
	Male	50 - 59	67.2 - 129.1
	Male	60 - 69	67.2 - 129.1
	Male	70+	59.2 - 136.1
	Female	30 - 39	51.3 - 93.7
	Female	40 - 49	52.2 - 94.6
	Female	50 - 59	53.0 - 97.2
	Female	60 - 69	53.0 - 104.3
	Female	70+	55.7 - 107.8

Ranges are given for adults (age at least 18 years).
Age (Years) = “18 - 65+” indicates that there is no restriction on normal due to age in adults.

Listing 16.2.8.3

Clinical Laboratory Evaluations: Coagulation

					PTT		INR		PT	
Site/ Subject	Treatment	Visit	Day	Date	Value (1)	CFB	Value (1)	CFB	Value (1)	CFB
xxx/xxxx	xxxxx	Pre-Study		MM/DD/YYYY	xxx		xxx		xxx	
		Baseline		MM/DD/YYYY	xxx		xxx		xxx	
		Cycle 1	8	MM/DD/YYYY	xxx	xxx	xxx	xxx	xxx	xxx
			15	MM/DD/YYYY	xxx	xxx	xxx	xxx	xxx	xxx
		Cycle 2	1	MM/DD/YYYY	xxx	xxx	xxx	xxx	xxx	xxx
			15	MM/DD/YYYY	xxx	xxx	xxx	xxx	xxx	xxx
		Cycle 3	1	MM/DD/YYYY	xxx	xxx	xxx	xxx	xxx	xxx
			15	MM/DD/YYYY	xxx	xxx	xxx	xxx	xxx	xxx

PTT= Partial Thromboplastin Time; INR= International Normalized Ratio; PT= Prothrombin Time
(1) H=Abnormal High, L=Abnormal Low
Normal ranges are given at the end of the listing.
CFB=Change from Baseline
Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)

Programming Note: Continue for all cycles, Days 1 and 15.

Listing 16.2.8.3

Clinical Laboratory Evaluations: Coagulation
Normal Ranges

Parameter	Gender	Age (Years)	Low - High
PTT	–	18 - 65+	22 - 34
INR	–	18 - 65+	0.9 - 1.1
PT	–	18 - 65+	9 - 11.5

Ranges are given for adults (age at least 18 years).
Age (Years) = “18 - 65+” indicates that there is no restriction on normal due to age in adults.

Listing 16.2.8.4

Clinical Laboratory Evaluations: Urinalysis

Site/ Subject	Treatment	Visit	Day	Date	Laboratory Parameter (Units)	Value
xxx/xxxx	xxxxx	Pre-Study		MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
		Baseline		MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
		Cycle 1	8	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
		Cycle 1	15	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
		Cycle 2	1	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
		Cycle 2	15	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
		Cycle 3	1	MM/DD/YYYY	XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx
					XXXXXXXXXXXXXXXXXXXX (XXX)	xxx

Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)

Programming Notes: Continue for all cycles, Days 1 and 15. CFB is not computed for any urinalysis parameter.

Listing 16.2.8.5

Clinical Laboratory Evaluations: Thyroid Function

				T3 (Unit)		T4 (Unit)		TSH (Unit)	
Site/ Subject	Treatment	Visit	Date	Value (1)	CFB	Value (1)	CFB	Value (1)	CFB
xxx/xxxx	xxxxx	Pre-Study	MM/DD/YYYY	xxx		xxx		xxx	
		Cycle 1	MM/DD/YYYY	xxx		xxx		xxx	
		Cycle 2	MM/DD/YYYY	xxx	xxx	xxx	xxx	xxx	xxx
		Cycle 3	MM/DD/YYYY	xxx	xxx	xxx	xxx	xxx	xxx
xxx/xxxx	xxxxx	Pre-Study	MM/DD/YYYY	xxx		xxx		xxx	
		Cycle 1	MM/DD/YYYY	xxx		xxx		xxx	
		Cycle 2	MM/DD/YYYY	xxx	xxx	xxx	xxx	xxx	xxx
		Cycle 3	MM/DD/YYYY	xxx	xxx	xxx	xxx	xxx	xxx

(1) H=Abnormal High, L =Abnormal Low
Normal ranges are given at the end of the listing.
CFB=Change from Baseline
Baseline=Cycle 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)

Programming Notes: Continue for all cycles. Include units.
Column for "Day" deleted since Thyroid Function assessed only at Day 1.

Listing 16.2.8.5

Clinical Laboratory Evaluations: Thyroid Function
Normal Ranges

Parameter	Gender	Age (Years)	Low - High
T3	–	18 - 65+	3.5 - 6.5
T4	–	18 - 65+	10.3 - 23.2
TSH	–	20+	0.4 - 4.5

Ranges are given for adults (age at least 18 years).
Age (Years) = “18 - 65+” indicates that there is no restriction on normal due to age in adults.

Listing 16.2.8.6

Pregnancy Test

Site/ Subject	Treatment	Visit	Test Date	Result	Not Done?	Not Applicable?	Menopausal date/ Other Specify
xxx/xxxxx	xxxxx	Pre-Study	DD/MM/YY	xxxx			
		Cycle 1	DD/MM/YY	xxxx			
		Cycle 2	DD/MM/YY		xxxx		
		Cycle 3	DD/MM/YY	xxxx			
xxx/xxxxx	xxxxx	Pre-Study	DD/MM/YY			xxxx	
		Cycle 1	DD/MM/YY			xxxx	
		Cycle 2	DD/MM/YY			xxxx	
		Cycle 3	DD/MM/YY			xxxx	

Programming Note: Continue for all cycles. For "Not Applicable?", enter reason if not applicable.

Listing 16.2.9.1

Vital Signs

				Systolic BP (mmHg)		Diastolic BP (mmHg)		Temperature (degrees C)			Respiratory Rate (/min)		Pulse (beats/min)	
Site/ Subject	Treatment	Visit	Time	Value	CFB	Value	CFB	Value	CFB	Method	Value	CFB	Value	CFB
xxx/xxxxx	xxxx	Pre-Study		xxx		xxx		xxx		x	xxx		xxx	
		Cycle 1	Day 1	xxx		xxx		xxx		x	xxx		xxx	
			Day 1 Hour 1	xxx	xxx	xxx	xxx	xxx	xxx	x	xxx	xxx	xxx	xxx
			Day 1 Hour 2	xxx	xxx	xxx	xxx	xxx	xxx	x	xxx	xxx	xxx	xxx
			Day 8	xxx	xxx	xxx	xxx	xxx	xxx	x	xxx	xxx	xxx	xxx
			Day 15	xxx	xxx	xxx	xxx	xxx	xxx	x	xxx	xxx	xxx	xxx
		Cycle 2	Day 1	xxx	xxx	xxx	xxx	xxx	xxx	x	xxx	xxx	xxx	xxx
			Day 15	xxx	xxx	xxx	xxx	xxx	xxx	x	xxx	xxx	xxx	xxx
		Cycle 3	Day 1	xxx	xxx	xxx	xxx	xxx	xxx	x	xxx	xxx	xxx	xxx
			Day 15	xxx	xxx	xxx	xxx	xxx	xxx	x	xxx	xxx	xxx	xxx

CFB=Change from Baseline
Baseline=Cycle 1 Day 1 (or Pre-Study if value at Cycle 1 Day 1 is missing)
Method= 'O' for oral, 'A' for Axillary

Programming Note: Continue for all visits (Days 1 and 15 of each cycle, Day 8 of Cycle 1, and Hours 1, 2, 3, 4, 6 and 8 on Cycle 1 Day 1) with CFB.

Listing 16.2.9.2

Weight, Height, and BMI

					Weight (kg)		BMI (kg/m^2)	
Site/ Subject	Treatment	Visit	Time	Height (cm)	Value	CFB	Value	CFB
xxx/xxxxx	xxxx	Pre-Study		xxx	xxx		xxx	
		Cycle 1	Day 1		xxx		xxx	
			Day 8		xxx	xxx	xxx	xxx
			Day 15		xxx	xxx	xxx	xxx
		Cycle 2	Day 1		xxx	xxx	xxx	xxx
			Day 15		xxx	xxx	xxx	xxx
		Cycle 3	Day 1		xxx	xxx	xxx	xxx
			Day 15		xxx	xxx	xxx	xxx
xxx/xxxxx	xxxx	Pre-Study		xxx	xxx		xxx	
		Cycle 1	Day 1		xxx		xxx	
			Day 8		xxx	xxx	xxx	xxx
			Day 15		xxx	xxx	xxx	xxx
		Cycle 2	Day 1		xxx	xxx	xxx	xxx
			Day 15		xxx	xxx	xxx	xxx
		Cycle 3	Day 1		xxx	xxx	xxx	xxx
			Day 15		xxx	xxx	xxx	xxx

CFB=Change from Baseline
Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)
BMI=Body mass index.
BMI is computed using Height recorded at Pre-Study.

Programming Note: Continue for all cycles.

Listing 16.2.9.3

ECOG Performance Status

Site/ Subject	Treatment	Visit	Assessment Date	ECOG PS	CFB ECOG PS
xxx/xxxxx	xxxx	Pre-Study	DD/MM/YY	xxx	
		Cycle 1	DD/MM/YY	xxx	
		Cycle 2	DD/MM/YY	xxx	xxx
		Cycle 3	DD/MM/YY	xxx	xxx
		Cycle 4	DD/MM/YY	xxx	xxx
xxx/xxxxx	xxxx	Pre-Study	DD/MM/YY	xxx	
		Cycle 1	DD/MM/YY	xxx	
		Cycle 2	DD/MM/YY	xxx	xxx
		Cycle 3	DD/MM/YY	xxx	xxx
		Cycle 4	DD/MM/YY	xxx	xxx

CFB=Change from Baseline
Baseline=Cycle 1 Day 1 (or Pre-Study if <= 3 days prior to Cycle 1 Day 1 or if value at Cycle 1 Day 1 is missing)
PS = Performance Status
0=Normal activity, 1=Symptoms but ambulatory, 2= In bed <50% of time, 3=In bed >50% of time, 4=100% bedridden

Programming Notes: Continue for all cycles. Record CFB as Decrease, No Change, or Increase.

Listing 16.2.10.1

Electrocardiogram (ECG) – Continuous Variables

						Heart Rate (bpm)		Interval (msec)							
								PR		QRS		QT		QTcF (1)	
Site/ Subject	Treatment	Visit	Day	Hour	Time	Value	CFB	Value	CFB	Value	CFB	Value	CFB	Value	CFB
xxx/xxxxx	xxxxxxx	Pre-Study			xx:xx	xx		xx		xx		xx		xx	
		Cycle 1	1	0	xx:xx	xx		xx		xx		xx		xx	
				2	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
				4	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
				6	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
			8	0	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
				2	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
				4	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
				6	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
			15	0	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
		Cycle 2	1	0	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
			15	0	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
		Cycle 3	1	0	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
			15	0	xx:xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Hour 0=Pre-Dose
CFB=Change from Baseline
Baseline=Cycle 1 Day 1 Hour 0 (or Pre-Study if the value at Cycle 1 Day 1 is missing)
(1) QTcF=QT Correction: Fridericia.

Programming Notes: Continue for QRS Complex (msec), PR Interval (msec), and QTcF (msec) in that order and all visits (Pre-Study, Pre-dose on Days 1 and 15 of all cycles, Pre-dose on Day 8 of Cycle 1, and at 2, 4, and 6 hours post-dose on Days 1 and 8 of Cycle 1) with CFB. Compute QTcF=QT(HR/60)$^{1/3}$.*

Listing 16.2.10.2

Electrocardiogram (ECG) – Categorical Variables

Site/ Subject	Treatment	Visit	Day	Hour	Time	Overall Impression (1)	ST Segment	Cardiac Rhythm
xxx/xxxxx	xxxx	Pre-Study				xx	xx	xx
		Cycle 1	1	0	xx:xx	xx	xx	xx
				2	xx:xx	xx	xx	xx
				4	xx:xx	xx	xx	xx
				6	xx:xx	xx	xx	xx
			8	0	xx:xx	xx	xx	xx
				2	xx:xx	xx	xx	xx
				4	xx:xx	xx	xx	xx
				6	xx:xx	xx	xx	xx
			15	0	xx:xx	xx	xx	xx
		Cycle 2	1	0	xx:xx	xx	xx	xx
			15	0	xx:xx	xx	xx	xx
		Cycle 3	1	0	xx:xx	xx	xx	xx
			15	0	xx:xx	xx	xx	xx

(1) 1=Normal, 2=Abnormal Not Clinically Significant, 3= Abnormal Clinically Significant
Hour 0 = Pre-Dose

Programming Note: Continue for all visits (Pre-Study, Pre-dose on Days 1 and 15 of all cycles, Pre-dose on Day 8 of Cycle 1, and at 2, 4, and 6 hours post-dose on Days 1 and 8 of Cycle 1).

Listing 16.2.11.1

Physical Examination at Pre-Study Visit

Site/ Subject	Treatment	Body System	Result	Description If 'Abnormal'
xxx/xxxxx	xxxxx	General Appearance	Normal	
		Head and Neck	Normal	
		Eyes, Ears, Nose, Throat	Abnormal	xxxxx
		Skin	Normal	
		Chest / Lungs / Breast	Normal	
		Heart	Normal	
		Abdomen	Abnormal	xxxxx
		Genitourinary	Normal	
		Extremities	Normal	
		Musculoskeletal	Normal	
		Lymph Nodes	Abnormal	xxxxx
		Neurological	Normal	
		Other	Normal	xxxxx
xxx/xxxxx	xxxxx	General Appearance	Normal	
		Head and Neck	Normal	
		Eyes, Ears, Nose, Throat	Normal	
		Skin	Normal	
		Chest / Lungs / Breast	Normal	
		Heart	Not Done	
		Abdomen	Normal	
		Genitourinary	Normal	
		Extremities	Normal	
		Musculoskeletal	Normal	
		Lymph Nodes	Abnormal	xxxxx
		Neurological	Normal	
		Other	Not Done	

Programming Note: Record result as 'Normal', 'Abnormal', or 'Not Done'

Listing 16.2.11.2

Physical Examination

Site/ Subject	Treatment	Visit	Screening <= 3 days from Baseline?	Clin, Sig, Changes (1)	Body System	Result	Description If different From Previous Assessment
xxx/xxxxx	xxxxx	Cycle 1 Day 1	No	No			
		Cycle 1 Day 8		No			
		Cycle 1 Day 15		No			
		Cycle 2 Day 1		Yes	Eyes, Ears, Nose, Throat	Abnormal	xxxxx
				Yes	xxxxxxxxxxxxxx	xxxxxxx	xxxxxxxxxxxxx
		Cycle 2 Day 15		No			
		Cycle 3 Day 1		Yes	Lymph Nodes	xxxxxxx	xxxxx
		Cycle 3 Day 15		No			
		Cycle 4 Day 1		No			
xxx/xxxxx	xxxxx	Cycle 1 Day 1	Yes				
		Cycle 1 Day 8		No			
		Cycle 1 Day 15		No			
		Cycle 2 Day 1		Yes			

(1) Are there any clinically significant changes from the physical examination conducted at the previous assessment?
Baseline=Cycle 1 Day 1

Programming Notes: Continue for other cycles. If there are 'No' clinically significant changes from the physical examination conducted at the previous assessment, then the assessments for individual body systems should not be completed.
If "Clin, Sig, Changes" = 'Yes', then results should be recorded for at least one body systems with a "Result" differing from the previous assessment list. If "Screening <= 3 days from Baseline?" is Yes, there should be no responses for Cycle 1 Day 1.

Listing 16.2.12

Prior and Concomitant Medications

Site/ Subject	Treatment	Medication	ATC Level 3	Reason for Use	AE no. (1)	Dose & Units	Regimen	Route (2)	Start Date Stop Date (3)
xxx/xxxxx	xxxxx	xxxx	xxxx	xxxxx	x	xxxx	xxxx	xx	DD/MM/YY DD/MM/YY
xxx/xxxxx	xxxxx	xxxx	xxxx	xxxxx	x	xxxx	xxxx	xx	DD/MM/YY DD/MM/YY
xxx/xxxxx	xxxxx	xxxx	xxxx	xxxxx	x	xxxx	xxxx	xx	DD/MM/YY O

Includes medications taken within 30 days prior to Screening Visit.
(1) Blank if Not Applicable
(2) 1=PO; 2=IV; 3=SC; 5=IM; 11=T; 12=OU,OS,OD; 13=AU,AS,AD; 14=IN; 15=PV; 16=PR; 24=SL; 30=BUC; 37=IA; 71=NG; 136=INH; 358=TD; 135=Other; 139= Unknown
(3) O=Ongoing

Programming Note: Sort by start date for each subject.

Listing 16.2.13

Investigator Comments

Site/ Subject	Treatment	Date Event Occurred or Study Visit	CRF Page(s)	Description of Event/Comment
xxx/xxxxx	xxxxx	DD/MM/YY	xx	xxxxxxxxxxx
xxx/xxxxx	xxxxx	DD/MM/YY	xx	xxxxxxxxxxx
xxx/xxxxx	xxxxx	DD/MM/YY	xx	xxxxxxxxxxx

Programming Notes: Sort by date/visit.
Include only subjects for whom the "None" box is not checked, i.e. only subjects with comments.