Official Title: Statistical Analysis Plan

An open-label, randomized, controlled, multicenter, phase II study evaluating safety and efficacy of intratumorally administered Intuvax pre-nephrectomy followed by Sunitinib post-nephrectomy, compared to Sunitinib post-nephrectomy in metastatic renal cell carcinoma patients

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CONFIDENTIAL

STATISTICAL ANALYSIS PLAN

An open-label, randomized, controlled, multicenter, phase II study evaluating safety and efficacy of intratumorally administered Intuvax pre-nephrectomy followed by Sunitinib post-nephrectomy, compared to Sunitinib post-nephrectomy in metastatic renal cell carcinoma patients

Sponsor Study Code: IM-201

[redacted]

Sponsor	Immunicum AB
Product/Compound/Device	Intuvax (preactivated allogeneic dendritic cells)
Phase of the study	II
Author	[redacted]
Company	[redacted]
Address	[redacted]
Telephone number	[redacted]
Version	Final 1.0 **Date** 2019-06-19

SIGNATURES

Sponsor Study Code: IM-201

Author

Name, highest [redacted]

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ABBREVIATIONS

AE	Adverse Event
CDM	Clinical Data Manager
CR	Complete Response
CRF	Case Report Form
CSP	Clinical Study Protocol
CSR	Clinical Study Report
DCR	Disease Control Rate
ECOG	Eastern Cooperative Oncology Group
FAS	Full Analysis Set
IMP	Investigational Medicinal Product
MedDRA	Medical Dictionary for Regulatory Activities
mRCC	Metastatic Renal Cell Carcinoma
OS	Overall Survival
ORR	Object ve Response Rate
PD	Progress ve D sease
PFS	Progress on Free Surv va
PPS	Per Protocol Set
PR	Part a Response
[redacted]	[redacted]
RECIST	Response Evaluation Criteria In Solid Tumors
SAP	Statistical Analysis Plan
SD	Stab e D sease
SOC	System Organ C ass
TTF	Time to Treatment Failure
TTP	Time to Tumor Progression
WHO	World Health Organization

1 INTRODUCTION

This Statistical Analysis Plan (SAP) is based on Clinical Study Protocol (CSP) Version 9.0 dated 12 February 2019 (and Version 9.1 dated 19 February 2019 for France). It should be noted that, prior to procol version 4.0, the trial design was different for intermediate risk patients, which leads to some specific considerations to be taken for subjects included in the trial corresponding to these versions.

2 STUDY OBJECTIVES

The primary objectives are:

- To evaluate median overall Survival (OS) from randomization in metastatic renal cell carcinoma (mRCC) patients overall and by subgroup, i.e. in high-risk and in intermediate-risk patients separately, receiving two (2) vaccine doses of Intuvax pre-nephrectomy, followed by sunitinib initiated five (5) to eight (8) weeks post-nephrectomy and in non-vaccinated mRCC patients receiving sunitinib initiated five (5) to eight (8) weeks post nephrectomy
- To evaluate 18-month survival rate from randomization in mRCC patients overall and by subgroup, i.e. in high-risk and in intermediate-risk patients separately, receiving two (2) vaccine doses of Intuvax pre-nephrectomy followed by sunitinib post-nephrectomy and in non-vaccinated patients receiving sunitinib post-nephrectomy

The secondary objectives are:

- To evaluate safety and tolerability in high- and intermediate-risk mRCC patients receiving two (2) vaccine doses of Intuvax pre-nephrectomy followed by sunitinib post-nephrectomy and in non-vaccinated patients receiving sunitinib post nephrectomy
- To evaluate progression free survival (PFS) according to Response Evaluation Criteria In Solid Tumors (RECIST) 1.1 criteria from Sunitinib Start Visit in intermediate- and high-risk mRCC patients after receiving two (2) vaccine doses of Intuvax pre-nephrectomy followed by sunitinib post-nephrectomy and in non-vaccinated patients receiving sunitinib post nephrectomy
- To evaluate response and its duration according to RECIST 1.1 criteria from Sunitinib Start Visit in intermediate- and high-risk mRCC patients receiving two (2) vaccine doses of Intuvax pre nephrectomy followed by sunitinib post-nephrectomy and in non-vaccinated patients receiving sunitinib post-nephrectomy
- To evaluate time to tumor progression (TTP) from Sunitinib Start Visit in intermediate- and high-risk mRCC patients receiving two (2) vaccine doses of Intuvax pre-nephrectomy followed by sunitinib post-nephrectomy and in non-vaccinated patients receiving sunitinib post-nephrectomy
- To evaluate the number of infiltrating CD8+ T-cells in available diagnostic pre-biopsy (sample from either primary tumor or metastasis acceptable) and in the resected primary renal tumor in intermediate- and high-risk mRCC patients receiving two (2) vaccine doses of Intuvax pre-nephrectomy and in non-vaccinated patients

[redacted]

[redacted]

3 EFFICACY AND SAFETY ENDPOINTS

3.1 Primary Efficacy Endpoints

- OS from randomization overall in mRCC patients and by each subgroup, i.e. in high-risk and in intermediate-risk mRCC patients and
- 18-month survival rate from randomization overall in mRCC patients and by each subgroup, i.e. in high-risk and in intermediate-risk mRCC patients.

3.2 Secondary Efficacy Endpoints

- PFS from start of sunitinib according to RECIST 1.1
- Proportion of Objective Response Rate (ORR) from start of sunitinib treatment and duration of response in each subgroup
- Time to tumor progression (TTP) from start of sunitinib treatment
- Relative number of tumor infiltrating CD8+ T-cells in the resected primary tumor compared to number of infiltrating CD8+ T-cells in available diagnostic pre-biopsy (sample from either primary tumor or metastasis acceptable)

3.3 [redacted]

[redacted]

- [redacted]

3.4 Safety Endpoints

- Frequency and proportion of AEs including clinical significant changes in laboratory tests and vital signs from Screening
- Physical Examination
- Vital Signs
- Laboratory Safety Assessments blood (hematology, clinical chemistry, and coagulation) and urine including pregnancy
- Other Safety Measurements (auto- and alloimmunization)

4 OVERALL STUDY DESIGN

4.1 Overview of Study Design

The study is an open-label, randomized, controlled, two (2) armed, multicenter, phase II study. Intermediate- and high-risk mRCC patients according to Heng criteria are eligible for participation. Pateients are stratified and randomised based on Heng-risk.

High-risk mRCC patients are included according to the following criteria:

Patients fulfilling three (3) to six (6) of the following prognostic factors:
- Hemoglobin (Hb) less than the lower limit of normal (LLN)
- Corrected Calcium (Ca) greater than upper limit of normal (ULN)
- Karnofsky performance status less than 80%
- Time for diagnosis to treatment less than one (1) year
- Neutrophils greater than ULN
- Platelets greater than ULN

Intermediate-risk mRCC patient according to criteria

One (1) or two (2) of the following prognostic factors:
- Hb less than the lower limit of normal (LLN)
- Corrected Ca greater than upper limit of normal (ULN)
- Karnofsky performance status less than 80%

- Time for diagnosis to treatment less than one (1) year
- Neutrophils greater than ULN
- Platelets greater than ULN

The patients are randomized in a consecutive order to one (1) of the following two (2) treatment arms when eligibility has been confirmed;

(i) Two (2) doses of Intuvax (10x106 DCs) administered intratumorally into the primary tumor 14 ±3 days apart followed by nephrectomy at least three (3) days after the second vaccine dose and sunitinib treatment initiated five (5) to eight (8) weeks after nephrectomy, administered dose in accordance with the SmPC/USPI.

(ii) Sunitinib treatment initiated five (5) to eight (8) weeks after nephrectomy, administered dose in accordance with the SmPC/USPI.

The expected number of patients to be randomized in the study is around 90. The patients are randomized in a 2:1 (vaccine treatment arm [i]:control treatment arm [ii]) ratio.

Patients randomized to treatment arm (i) are scheduled for 12 study visits and patients randomized to treatment arm (ii) are scheduled for 10 study visits during a study period of 78 weeks, see list below and Figure 1. The following vists apply for patients participating in the trial

- Screening Visit (Screening)
- Vaccination 1 Visit (Vacc1), applicable for patients randomized to treatment arm (i)
- Vaccination 2 Visit (Vacc2), applicable for patients randomized to treatment arm (i)
- Nephrectomy Visit (Nephrectomy)
- Sunitinib Start Visit (Sun-Start), five (5) to eight (8) weeks after Nephrectomy
- Sunitinib Follow-up Visits (SFU[6W] and SFU[12W]), every 6 weeks for 12 weeks or until locally CT-verified PD whichever occurs first
- Sunitinib Follow-up Visits (SFU[24W], SFU[36W], SFU[48W], and SFU[60W]), every 12 weeks until End-of study or until locally CT-verified PD whichever occurs first
- End-of-Study Visit (End-of-Study)

The above described visits are applicable to all randomized subjects after and including protocol version 4.0. Subjects entering the trial corresponding to protocol versions prior to this, were included following a visit pattern that was different for high and intermediate risk patients. Following this design intermediate risk subjects would only start sunitinib treatment after confirmed PD.

At the two (2) Vaccination Visits, the patients are be administered Intuvax (10 x106 DCs) intratumorally in the viable part of their primary tumor. Vaccine from the same batch (i.e. the same donor) is be used at both occasions. The patient stay at the clinic at least four (4) hours after vaccination. Nephrectomy is done at least 3 days after the second vaccination and maximum 63 days after Screening. Sunitinib treatment is initiated five (5) to eight (8) weeks after nephrectomy, administered dose is in accordance with the SmPC/USPI.

All patients areencouraged to contact the clinic in between study visits if they experience adverse events (AEs) or have any concerns. If follow-up of any symptoms is needed between the planned visits, the patient are scheduled for a visit as soon as possible and applicable assessments are performed.

A diagram of the study design is provided in Figure 1, and a flow chart what all assessments to be conducted per visit are provided in Tables 1 and 2.

Post-study survival data (either patient alive or date of death) will be collected.

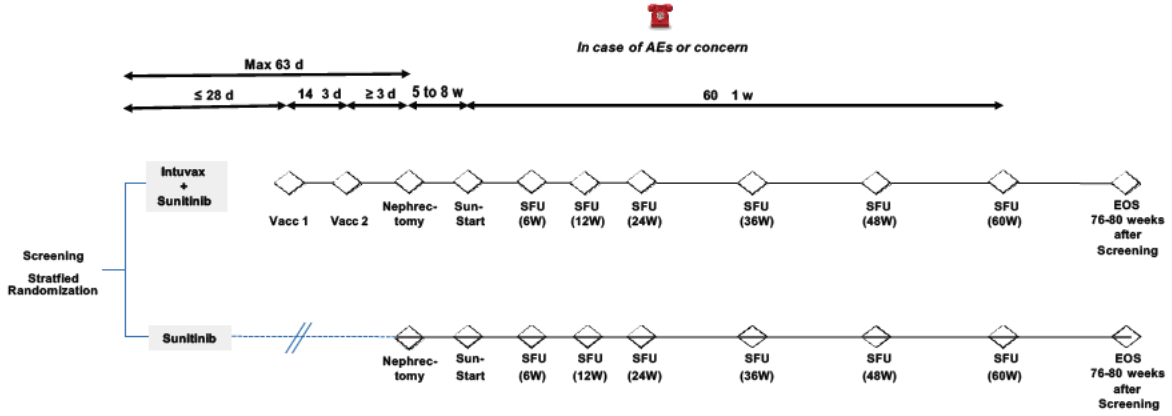

Figure 1 Overall Study Design

Table 1 Study Flow Chart

Visit	**Screening** **Day 1**	**Vacc1** *Intuvax + sunitinib*[c] **Day 2-28** *sunitinib only:* **N/A**	**Vacc2** *Intuvax + sunitinib*[c] **Day 16-42** *sunitinib only:* **N/A**	**Nephrectomy** *Intuvax + sunitinib*[c] **Day 19-63** *sunitinib only:* **Day 63 at the latest**	**Sun-Start** **5 to 8 weeks after Nephr.**[j]	**SFU[6W]** **6w ±7d after Sun-Start** **SFU[12W]** **12w ±7d after Sun-Start** **SFU[24W]** **24w ±7d after Sun-Start** **SFU[36W]** **36w ±7d after Sun-Start** **SFU[48W]** **48w ±7d after Sun-Start** **SFU[60W]**[o] **60w ±7d after Sun-Start**	**End-of-Study** **78w ±2w after Screening**	**Extra visit** **When needed**
Informed consent	X	X[s]						
Demography	X							
Med ca and Surg ca H story	X							
CT/MRI scan[l]	X[m]				X[t]	X[t]	X[t]	
Pr or and/or Concom tant Med cat on	X	X	X	X[a]	X	X	X	X
Phys ca Exam nat on	X	X	X		X	X	X	X
V ta S gns[b]	X	X[c]	X[c]		X	X	X	X
ECG	X							
Hemato ogy and C n. Chem.	X	X[d]	X[d]	X[a d]	X[u]	X	X	X
GFR based on Creat, G uc, TSH, and Thyrox ne (free T4)	X				X	X	X	X[n]
PT-INR	X	X[d]	X[d]	X[a d]				
APTT	X	X[d]	X[d]	X[a d]				
Pregnancy	X[e]	X[e]	X[e]					
Ur na yses	X	X[d]	X[d]	X[a]	X[u]	X	X	X
HIV/HBV/HCV and HLA	X							

Cont. **Table 2 Study Flow Chart**

Visit	**Screening** **Day 1**	**Vacc1** *Intuvax + sunitinib*[b] **Day 2-28** *sunitinib only:* **N/A**	**Vacc2** *Intuvax + sunitinib*[b] **Day 16-42** *sunitinib only:* **N/A**	**Nephrectomy** *Intuvax + sunitinib*[b] **Day 19-63** *sunitinib only:* **Day 63 at the latest**	**Sun-Start** **5 to 8 weeks after Nephr.**[j]	**SFU[6W]** **6w ±7d after Sun-Start** **SFU[12W]** **12w ±7d after Sun-Start** **SFU[24W]** **24w ±7d after Sun-Start**	**SFU[36W]** **36w ±7d after Sun-Start** **SFU[48W]** **48w ±7d after Sun-Start** **SFU[60W]**[o] **60w ±7d after Sun-Start**	**End-of-Study** **78w ±2w after Screening**	**Extra visit** **When needed**
Auto- and A o mmun zat on		X			X				
ECOG performance	X	X[d]	X[d]		X	X		X	X
Karnofsky performance	X								
[redacted]	X			X[a]	X	X		X	
Inc us on/Exc us on cr ter a	X[g]								
Random zat on	X[g]								
Conf rmatory d agnost c b opsy	X[p]								
Nephrectomy				X					
B ops es (tumor x2, adjacent norma t ssue)				X					
Adm n strat on of Intuvax[q]		X[c]	X[c]						
Sun t n b d spense & return[h]					X[i]	X		X[i]	
AEs	X	X[c]	X[c]	X	X	X		X[k]	X
D agnos s Conf rmat on[r]				X					

a Assessment to be comp eted before nephrectomy and may be done the day before nephrectomy for og st ca reasons
Loca y ana yzed Creat n ne for pat ents nc uded n the study before 28 August 2017 (f performed as part of c n ca rout ne) to be recorded n eCRF

b He ght on y at Screen ng. We ght at a v s ts except for Vacc1 and Vacc2 V s ts.

c See spec f c f ow chart, *Table* , for deta ed nstruct ons on pre- and post-vacc nat on assessments.

d Phys ca exam nat on, ECOG performance, and samp es for safety ab and ur na yses may be taken the day before vacc nat on for og st ca reasons
Loca y ana yzed resu ts for Hb, WBC, p ate ets, PT-INR, and APTT need to be ava ab e before vacc nat on

Loca y ana yzed resu ts for Hb, WBC, and c n ca chem stry m ght need to be ava ab e pr or to nephrectomy

Ana ys s of coagu at on status at Nephrectomy s not necessary prov ded the pat ent s not on ant coagu ant treatment. For pat ents on ant coagu ants oca samp ng pract ce app es.

e Pregnancy test n b ood at Screen ng, and n e ther b ood or ur ne at Vacc1 and Vacc2 V s ts. The pregnancy test resu t s needed pr or to each vacc nat on.

f Samp es for auto- and a o mmun zat on ana yses w be co ected pr or to vacc nat on at Vacc1 V s t. Samp ng at Sun-Start V s t on y app cab e for pat ents random zed to Intuvax.

g To be done when the resu ts from a assessments made are ava ab e. Te ephone contact w th pat ent to nform about treatment and t m ng of next study v s t.

h The prescr bed dose to be n accordance w th the SmPC/USPI nc ud ng any dose adjustments.

Return of sun t n b not app cab e at Sun-Start V s t and D str but on not app cab e at End-of-Study V s t. Standard of Care app es after End-of-Study.

j Start of sun t n b adm n strat on w be dependent on wound hea ng. The t me w ndow for n t at on s f ve (5) to e ght (8) weeks after Nephrectomy.

k Post-study co ect on of surv va data.

If CT cannot be used for some reason, MRI s acceptab e. The same moda ty has to be used at a v s ts.

m CT scan to be done w th n 3 weeks before Screen ng un ess a CT scan has been done n c n ca rout ne w th n 6 weeks before Screen ng. Bra n mag ng (preferab y by contrast-enhanced) MRI or CT to be done w th n 3 weeks before Screen ng V s t un ess a CT scan has been performed n c n ca rout ne w th n 6 weeks pr or to Screen ng V s t

n To be done f Extra V s t s schedu ed after Sun-Start V s t

o If SFU[60W] s schedu ed ≥76 weeks s nce Screen ng th s v s t shou d be cons dered the End-of-Study V s t

p Conf rmatory d agnost c b opsy n accordance w th oca rout nes pr or to Vacc1 V s t, f requ red by oca regu at ons and aws

q Abso ute fast ng for four (4) h pr or to Intuvax adm n strat on app es

r Rout ne h sto ogy/Pr mary d agnos s s assessed oca y

s Extra consent for vacc nat on for pat ents random zed to the vacc ne arm, to be taken after random zat on f requ red by oca regu at ons

t The CT scan does not have to be done the very same day as the correspond ng study v s t. However, each CT scan has to be done w th n the spec f ed t me w ndow for the correspond ng v s t

u The aboratory safety b ood and ur ne assessments do not have to be done the very same day as the study v s t. However, t has to be done w th n 3 days pr or to the v s t.

Table 2 Assessments in Connection with Vaccination

Assessment	Pre-vacc nat on	Vacc nat on	Post-vacc nat on					
	> 2 h	0 h	15 m n (±5 min)	30 m n (±10 min)	60 m n (±10 min)	2 h (±10 min)	3 h (±10 min)	4 h (±20 min)
Intuvax nject on		X						
BP	X		X	X	X	X	X	X
HR	X		X	X	X	X	X	X
Body temperature	X			X	X	X	X	X
AEs	X		X	X	X	X	X	X

4.2 Determination of Sample Size

This is a proof of concept study and the number of patients chosen is based on practical considerations and not on a formal statistical power calculation. With around 90 patients randomized 2:1 to vaccination and control, it is expected that 18-month survival rate for high- and intermediate-risk mRCC patients overall can be adequately estimated for exploratory purposes but not to confirm the findings as statistical significant.

5 DATA SETS TO BE ANALYSED

The following analysis sets will be used for the statistical analysis and presentation of data:

- **The safety set**: All randomized patients with at least one safety assessment at Screening.
- **The full analysis set (FAS)**: All randomized patients being evaluable for any efficacy endpoint
- **The per protocol set (PPS)**: All patients randomized to Intuvax who had both doses of Intuvax administered or patient randomized to sunitinib alone, both having the nephrectomy and who continued the trial without any major protocol violations that could interfere with the objectives of this study. The criteria for PPS, regarding which protocol deviations that warrant exclusions will be determined by the following criteria.
    - Violations to inclusion, exclusion and withdrawal criteria
    - Deviations relating to primary and secondary objectives/endpoints
    - Study medication (Intuvax or Sunitinib): That was not stored and/or prepared and/or administered as defined in the protocol
    - Administration of prohibited concomitant medication
    - Availability of required data

The exact criteria that warrant exclusion from PPS will be documented in relation to review of the reported PDs. The patients excluded with reference to the PD leading to exclusion will be listed and signed off in in the *Pre-Analysis Review Form* before DBL.

The FAS is considered as the primary analysis population, and will be used for all primary and secondary efficacy analyses. The primary efficacy analysis will be repeated using the PPS. Any significant discrepancy between the results from the FAS and the PPS will be analysed and discussed.

Secondary efficacy endpoints defined as to be analyzed after start of sunitinib will be based on the subset of subjects in FAS having at least one dose of sunitinib (or as described for PFS, when subjects were included according protocol versions prior to version 4.0).

Baseline and safety will be presented using the safety set.

6 STATISTICAL AND ANALYTICAL PLANS

The planned tables and listings are presented in APPENDIX 1

6.1 Changes in the Planned Analyses

- An additional subgroup is added, see section 6.7.
- The objective and the endpoint related to evaluation of relative number of tumor infiltrating CD8+ T-cells in the resected primary tumor compared to number of infiltrating CD8+ T-cells in available diagnostic pre-biopsy (sample from either primary tumor or metastasis acceptable) will not be done. This is due to no diagnostic pre-biopsies have been available for analyses.
- Survival endpoints (primary and secondary) in this trial will be analysed using log-rank tests according to protocol, however in addtion exploratory corresponding cox regressions will be applied in order to be able to estimate treatment group hazards ratios with corresponding 95% Cis, if possible. Overall analyses will include adjustment for stratification, and the results will be repeated separately by strata.
- [redacted]

6.2 Blind Review

This is an open label trial, therefore any review of ongoing data that is conducted is not blind. In addition to the review of data conducted by the clinical data manager (CDM), as based on pre-defined edit checks, validation checks and manual reviews as described in the DVP, data will be reviewed ongoing during statistical programming by the statistician and statistical programmer. Findings of potential inconsistencies and/or errors in data will be reported to data management for further queries and corrections.

Any changes in the planned analysis decided in connection to the review, will be included in the final version of the SAP. Minor clarifications and/or definitions after the SAP has been finalized may be included in the *Pre-Analysis Review Form,* which will be signed before data base lock (DBL).

Classification of subjects in study populations, as defined in section 5, will be determined and documented in the *Pre-Analysis Review Form*, which will be finalized before DBL.

6.3 Hypotheses and Statistical Methods

6.3.1 Definitions

Baseline	The date of randomization is defined as baseline for OS and 18-month survival rate.

The centrally assessed CT performed at the Sunitinib Start Visit is defined as CT baseline for evaluation of PFS, response rate and TTP after start of sunitinib in intermediate- and high-risk patients

The Screening Visit is defined as baseline for all other assessments than those listed above.

6.3.2 Summary Statistics

In general, data will be summarized by means of summary statistics. Continuous data will be presented with the number of observations, mean value, standard deviation, minimum, Q1, median, Q3 and maximum value. Categorical data will be presented as counts and percentages. All efficacy related variables will be summarized for the FAS population and all safety related data will be summarized for the safety population.

For any assessments being evaluated by visit, an LOCF (Last observation carry forward) approach will be applied, where the last available information will be combined, independently of what the last recorded visit is.

All descriptive statistics will be presented by stratum of high- and intermediate risk patients and pooled together and by treatment group.

6.3.3 Patient Data Listings

Data collected in the CRF will generally be listed in Appendix 16.2 (see section 0). CRF check questions [e.g. Lab samples taken (Yes/No)] and reminders will not always be listed.

Listings will be sorted by treatment group, study centre and patient number, or by patient number and treatment group.

In CRF modules where a date is recorded, the date and the relative day may be included in the corresponding listing. In modules where both a start date and stop date are recorded, the duration may be included in the listing.

6.3.4 Demographic and Other Baseline Characteristics

Patient disposition and discontinuation, Demographics (Age, Sex and Race) and other baseline characteristics (Weight and Height) and Medical History (mRCC): Duration of mRCC, Primary Tumor Stage, mRCC Symptoms and Severity Grade, Karnofsky Performance Status and other Medical history will be presented using summary statistics by treatment group and by intermediate/high risk stratum. The patient disposition and discontinuation will be based on all screened patients, while the other will be summarised for the Safety population.

6.3.5 Primary Efficacy analysis

This is a descriptive proof of concept study and the sample size is not determined based on a statistical power calculation. Even though the trial is descriptive, some exploratory statistical testing will be conducted for primary endpoint, as described below.

Overall Survival

The primary endpoint is median OS, where OS is defined as the time from randomization to the time of death from any cause.

Median OS after randomization in high-risk and intermediate-risk mRCC patients will be calculated and compared overall and by subgroup based on FAS in the following way:

After the last patient has completed the trial, a collection of survival status, for patients still alive when exiting the study will be conducted by [redacted] Drug Safety. Additional collections will be conducted up to 5 years after collection of the last patient's 18 months survival data. For patients who die before end of trial, or patients with a known date of death during the additional collection, the survival time will be calculated as the difference in date of death and randomization date plus 1 day. Patients still alive at last contact, either during the trial or at the additional collection, will be censored at last date patient is known alive. Patients that are lost to follow-up during trial, or alive at end of trial where no follow-up information is available will be censored at last date patient is known alive.

Survival functions will be displayed graphically using Kaplan-Meier plots, and life table statistics will be produced including summaries of number of events and censored observations. Estimates of 25%, 50% (median) and 75% percentiles of time of survival with corresponding 95% confidence intervals will be calculated. Addtionally, analyses where the survival functions will be compared between Intuvax+sunitinib, vs. sunitinib alone will be conducted using a stratified log-rank test, controlling for strata (high/intermediate-risk patients).

The analyses will be done overall, and separately for high/intermediate risk group of patients.

In addition, the primary efficacy endpoint will be evaluated using the PPS.

The analyses will be conducted using Proc Lifetest, SAS®.

18-month survival rate

18-month survival rate is defined as the proportion of patients alive 18 months after randomization, or probability of surviving beond 18 months after randomization.

The 18-month survival rates will be obtained using the same analyses as applied for OS, described above, where the fixed time point estimate, 18-months survival, will be estimated using the kaplan meier estimates as obtained above. The Timelist option in Proc Lifetest will be applied to get the estimated proportions at 18 months. Treatment groups will be compared using a z-test based on the proportions, where the Greenwood formula will be used for caculation of related standard errors. The analysis will be done overall, and separately for high/intermediate risk group of patients. Results will be presented including the estimated proportions with corresponding 95% CIs and the p-value for treatment difference. As the log-rank test for comparison between treatment groups is assessed on the full survival functions, as applied above, while the 18 months survival only utilize a subset of the compete survival data, the results from the treatment comparison based on the latter should be considered with caution.

The endpoint will be evaluated for FAS as the main analysis, although will also be repeated for the PPS population.

6.3.6 Secondary Efficacy Analyses

PFS from start of sunitinib according to RECIST 1.1

PFS from start of sunitinib treatment will be derived as date whichever occurred first of any cause of death or date for first tumor progression (which is date for centrally assessed CT performed, according to RECIST 1.1) minus date for start of sunitinib treatment plus 1 day.

For the analysis of PFS only deaths occuring before end-of-trial will be accounted for in the analysis.

Analysis of PFS will be evaluated the following way:

Survival functions will be displayed graphically using Kaplan-Meier plots, and life table statistics will be produced including summaries of number of events and censored observations. Estimates of cumulative 25%, 50% (median) and 75% percentiles of survival with corresponding 95% confidence intervals will be calculated.

Comparison between Intuvax+sunitinib, vs. sunitinib alone will be done using a stratified log-rank test (controlling for strata intermediate/high risk), separte analyses will also be done by strata.

With protocol versions before version 4.0, intermediate risk patients did not have to initiate treatment with sunitinib at a fixed time point according to the visit schedule. Consequently some patients were never started on sunitinib, and in some cases sunitinib treatment was initiated at a later time point. The sunitinib start date constitutes the baseline time point for PFS according to protocol version 4.0 and after. In the analyses, patients who either had a delay or never started sunitnib will be included under the assumption that sunitinib treatment would have been initiated according to the final design, the date of the visit following the nephrectomy visit will be used as baseline.

Another issue that will be considered in the analysis is that some patients may have been discontinued based on general clinical disease progression as evaluated by investigator from symptoms/signs of disease, rather than based on a PD according to RECIST 1.1. For the analysis such cases will be handled strictly based on the RECIST 1.1 evaluation, thus if a patient is withdrawn without a CT confirmed PD the subject will be censored at last CT

Analyses will be based on FAS and repeated for separately by strata..

<u>Proportion of Objective Response Rate (ORR) and Disease Control Rate (DCR) from start of sunitinib</u>

Proportion of ORR from start of sunitinib treatment will be derived as the proportion of patients with the individual's best overall response scored as "CR" or "PR" (using RECIST 1.1) across all time points from first visit six (6) weeks after sunitib treatment, to end-of-study visit. Similarly, DCR will be derived as proportion of patients with best overall response scored as "CR", "PR" or "SD".

ORR and DCR will be summarised and comparision of treatment groups will be made using the Cochran Mantel-Haenzel test, adjusting for strata.

Duration of response will be derived only for patients meeting the ORR definition CR or PR, at least once, as the date of the first occurrence of PD or death minus the date at which the CR or PR was first observed, plus 1 day. Patients without an occurrence of a PD or death after CR of PR will contribute with the time up till last last tumor assessment. Data will be summarised descriptively.

Duration of clinical benefit will be derived only for patients meeting the DCR definition CR, PR or SD at least once, as the date of the first occurrence of PD or death minus the date at which the CR, PR or SD was first observed, plus 1 day. Patients without an occurrence of a PD or death after CR, PR or SD will contribute with the time up till last last tumor assessment. Data will be summarised descriptively.

The duration of stable disease is calculated for only those patients who exhibited a best response of stable disease response and will be calculated as the date for the first SD

response to the date of the first observed progression of disease or death before end of trial, if the death was due to disease progression (whichever comes first) plus 1 day. Data willl be summarised descriptively.

Response rate from Sunitinib Start Visit

Evaluation of response rate, based on CT and according to the RECIST 1.1 guideline, from Sunitinib Start Visit will be based on the subpopulation from FAS who have been exposed to at least one dose of sunitinib. Number of patients with CR, PR, PD, and SD after start of sunitinib will be summarized using the underlying ordinal scale.

Waterfall charts will be used to display the percent change in target lesion tumour dimension vs best overall response and Two types of Swimmer plots will be created, one with bars showing time from randomization and one from sunitinib start. In these events for progressive diseace, end of trial and vital status will be indicated.

Response rate from Screening to Post-Nephrectomy

The evaluation of RECIST response rate between Screening and Post-Nephrectomy assessment will be summarised in the same way as described for response rate after Sunitinib Start Visit.

Time to tumor progression (TTP)

TTP from start of Sunitinib treatment will be derived as date for tumor progression, or clinical disease progression (other than RECIST 1.1) if occuring before tumor progression, minus date for start of sunitinib treatment plus 1 in the same way as done for PFS but excluding any deaths, if death before tumor or disease progression the subject will be censored at time of last CT during the trial. This variable will be analysed using the same method as for the evaluation of PFS.

Infiltrating CD8+ T-cells

The individual evaluation of intratumoral infiltration of CD8+ T-cells will be conducted as described in the protocol, where each patient will have the number of CD8+ T-cells/mm2 counted from 3 areas in two separate biopsies by [redacted]. Each patients median of the 6 individual counts will be calculated. The patient median number of CD8+ T-cells willl be summarised by treatment group, strata and overall using descriptive statistics for continous data as described in Section 12.1.4.

At the GLP compliant laboratory [redacted] a validated automated quantification of intratumoral CD8+ T cells, using whole slide scanning instruments, will be performed. The tumoral area will be delineated by a trained operator and the surface of CD8+ labeling percentage will be assessed in the delineated areas. Each patients mean percentage from the two (2) primary tumor biopsies will used for statistical evaluations. Patient's mean percentage will be evaluated for the treatment arms per stratum and in total using summary statistics, as described for continuous data in Section 6.3.2.

Relative number of tumor infiltrating CD8+ T-cells in the resected primary tumor compared to number of infiltrating CD8+ T-cells in available diagnostic pre-biopsy (sample from either primary tumor or metastasis), not be be evaluated as described in the protocol due to missing pre-biopsy samples.

As the technology used by [redacted] eliminates much more the subjective measurement of CD8+ infiltration and has been technically validated, the [redacted] approach is widely regarded as the more accepted one in contrast to the the [redacted] approach. Additionally, issues in the quality of the execution had been identified in the beginning of the

trial. Therefore, primarily the data generated by [redacted] will be used and not the [redacted] ones.

Furthermore, an exploratory evaluation of the impact of level of tumor infiltrating CD8+ T-cells (as analysed by [redacted]) on primary endpoint and PFS will be conducted. This will be done, if possible, by including the calculated CD8+ infiltration as a covariate in a cox regression, in addition to included factors for treatment group, strata and a treatment by strata interaction term. If the model can be fitted, then the influence of CD8+ on the outcome will be evaluated. In addition CD8+ infiltration will be summarised in relation to best overall response, ORR and DCR according to RECIST 1.1 during the trial. Similar exploratory analyses will be done by including a baseline factor for TNM staging in the model.

6.3.7 [redacted]

[redacted]

[redacted]

Evaluation of auto- and allo-immunization parameters

Auto- and alloimmunization parameters will be assessed prior to vaccination at Vacc1 Visit and at Sun-Start Visit for patients randomized to Intuvax.

Autoimmunization parameters, anti-nuclear antibodies (IF-ANA), anti-mitochondrial and anti-liver-kidney icrosomal antigens will be assessed as “Negative” or “Positive” and additional assessment of “Weak” or “Strong” will be done for positive results on Homogenous, Speckled, Nucleolar, and Centromere patterns.

Alloimmunization at the humoral level by screening of alloantibodies against HLA-A, B, C (HLA class I) and HLADR, DQ, DP (HLA class II) antigens will be assessed as “Present” or “Not Present”.

The results of auto- and allo-immunization parameters will be tabulated using general summary statistics for categorical data. In addition shift tables will be presented to summarise the changes from the assessment prior to vaccination 1, to the Sun-start visit.

TTF defined as progressing during or after treatment with Intuvax+sunitinib or sunitinib followed by the start of subsequent second line systemic therapy

TTF is defined as progressing during or after treatment with Sunitinib or Intuvax + Sunitinib followed by the start of subsequent second line systemic therapy including immune checkpoint inhibition or tyrosine kinase inhibition, and will be derived as the date of screening until start date of second line treatment following progression. Similar censoring rules as applied for PFS will be used. Patients with PD without any second line treatment will be censored at withdrawal. Similar survival statistics as applied for analysis of PFS will be conducted.

Association between Sunitinib dose density and primary and secondary endpoints

Exploratory analyses will be conducted where the influence of individual Sunitinib dose density on the outcome of primary and secondary endpoints will be evaluated. This will be done by applying a cox regression overall, including treatment group, strata and average dose density during the time leading up to either event or censoring. Initially a treatment group by dose density interaction will be included, if the interaction term is not significant the interaction will be dropped from the model.

Sunitinib dose density will be derived as the total recorded dose during the time leading to event or censoring divided by the corresponding time period.

These analyses will be conducted for evaluation of primary endpoint and PFS and in addition summary statistics for dose density will be provided split by treatment group and best response rate, ORR and DCR.

6.3.8 Exposure to Treatment

All details collected in relation to the Intuvax vaccination will be listed and tabulated. Nephrectomy data will be listed. Exposure data for sunitinib use will be listed by treatment group and by high/intermediate risk stratum. Duration of sunitinib treatment will be summarised by treatment group and strata. Patient sunitinib compliance will be evaluated summarising the number of dispensed tablets minus the number of returned and lost tablets.

6.3.9 Concomitant Medications

All concomitant medications/therapies will be summarised as number of patients being treated with each type of medication/therapy classified according to ATC level 3 group text and World Health Organization (WHO) Drug Dictionary preferred name.

Prior medication/therapy is defined as medication/therapy administered prior to Screening Visit. All medication/therapy administered after Screening Visit are considered concomitant medication/therapy. Prior medication/therapy will be indicated as past or ongoing at Screening.

In summary tables, each patient is only counted once for each drug, on a preferred name level and will be classified according to the first start date of the medication. If there is an occurrence of the same preferred name before and after screening, the medication is only counted as started before screening. For total within each group text, a patient can be counted both before and after screening if one medication is present at screening, and another medication with another preferred name starts after baseline.

6.3.10 Adverse Events

Analyses of AEs will be based on the Safety set. AEs will be coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 17.1.

All AEs will be listed by treatment group, with patient number in addition to type of event (verbatim term, system organ class and preferred term), start and stop day relative to first dose of treatment, seriousness, intensity, action taken, relationship to study drug and outcome of AE. Treatment-emergent status will be flagged in the listing. In addition, corresponding listings of screening AEs, serious AEs (SAEs), AEs leading to discontinuation of study medication, AEs leading to death will be produced.

The total number of AEs will be summarized including the number of patients with at least one AE, the total number of AEs, the number of unique AEs, by seriousness, intensity, action taken, relationship to study drug and by treatment group and in total. The number of AEs per severity (CTCAE) and relation to trial drug will also be included and summarized per treatment group and in total. SAEs will also be summarized separately in a similar manner.

The number of patients and the number of AEs will be tabulated by MedDRA system organ class (SOC) and preferred term in descending order of overall frequency.

AEs occurring during the 4 hours following the Intuvax vaccination will in addition be summarized separately.

Summary statistics of AE will be done by treatment group.

Pre treatment events occurring between first assessment at Screening and first Intuvax dose (for vaccinated patients) and between first assessment at Screening and Nephrectomy (for unvaccinated patients) will be summarized separately.

6.3.11 Other Safety Assessments

Vital Signs

For vital signs parameters (systolic and diastolic blood pressure, supine heart rate and temperature) summary statistics will be produced for observed values by visit. In addition, the difference from baseline to each visit at which they were assessed will be derived and presented.

Vital signs assessed at time points post vaccination will be summarised separately.

Clinical Laboratory Measurements

The laboratory categories are Hematology, Clinical Chemistry, Coagulation, Urine analysis and Pregnancy analysis.

For all laboratory parameters, summary statistics will be produced for observed values by visit. In addition, the difference from baseline to each visit at which they were assessed will be derived and presented. The number of abnormal (low and high) and clinically significant observations will be tabulated for each treatment group by visit. Abnormal values will be flagged in listings.

Shift tables that show the number of patients who changed from low, normal or high at baseline to low, normal or high at each post-baseline time of assessment will be presented.

Physical Examination

Physical examination results will be tabulated including number of subjects with normal, abnormal not clinically significant or clinically significant abnormalities by visit. Corresponding shift tables for changes from baseline will be presented, and all the results will be listed.

6.4 Level of Significance, Multiple Comparisons and Multiplicity

The sample size in this trial is not based on a formal power calculation. Any inferential statistical methods applied in this trial will be regarded as exploratory, therefore no adjustments will be applied to adjust for multiple testing.

6.5 Adjustment for Covariates

Parametric analyses based on statistical models will not be conducted. For primary endpoint a stratified Log-rank test will be done including adjustment for high/intermediat risk strata.

6.6 Handling of Dropouts and Missing Data

Primary and secondary efficacy endpoint

The primary and secondary efficacy endpoint analysis will be conducted on available data (observed cases). Missing data due to loss of follow-up and rules for censoring will be done as described in each corresponding section.

Handling of incomplete dates

Incomplete (partial or missing) dates will be presented in data listings as provided on the eCRF. However, for use in calculations (e.g. to calculate the duration of an AE or medication use) dates will be estimated as follows.

For partial start-dates

- If the year is unknown, then the date will not be imputed and will be assigned a missing value
- If the month is unknown, then:
  - If the year matches the year of the first dose date, then impute the month and day of the first dose date
  - Otherwise, assign 'January'
- If the day is unknown, then:
  - If the month and year match the month and year of the first dose date, then impute the day of the first dose date.
  - Otherwise, assign 'January'.

For partial end-dates,

- If the year is unknown, then the date will not be imputed and will be assigned a missing value.
- If the month is unknown, then assign 'December'.
- If the day is unknown, then assign the last day of the month

If the above rules for end-dates result in a date after the patient was ended the study, then the end date will be replaced with the patient's date of completion/withdrawal. Furthermore, should the above rules not result in the most conservative date (as described below), then the imputed value may be replaced by a date that will lead to a more conservative analysis.

After implementing the rules above, to determine whether AEs with incomplete start or stop dates are pre-treatment or treatment-emergent the following strategy will be used:

- If the start date and stop date are both missing, the most conservative approach is taken and the AE is considered to be treatment-emergent
- If the start date is missing but the stop date is not missing and is on or after the day of first study drug administration but before or on the Week 12 visit date then the most conservative approach is taken and the AE is considered to be treatment-emergent;
- If the start date is missing but the stop date is not missing and is before the day of first study drug administration then the AE is considered to be pre-treatment.

If the date of first and/or last dose of study drug administration is missing then duration of exposure will be set to missing.

Handling of unscheduled visits

Descriptive summaries and by-visit analyses will be presented according to the planned (scheduled) visits, unless otherwise specified.

For patients withdrawing early, where discontinuation data is collected on the end-of-trial visit, the data will be reallocated to the visit nearest to withdrawal, if applicable.

Any data collected on unscheduled visits, will be reallocated to the visit nearest in time to the planned visits where the corresponding information is not already available. This will be done by allocating the unscheduled data within the visit windows by corresponding visit as listed below.

Vacc1	from screening to 28 days
Vacc2	+/- 3 days
Nephrectomy Visit:	At least 3 days after Vacc2 Visit and within 63 days from Screening Visit for patients randomized to Intuvax followed by sunitinib. Within 63 days from Screening Visit for patients randomized to sunitinib only.
Sun-Start Visit:	Five (5) to eight (8) weeks after Nephrectomy Visit
SFU[6W]:	6 weeks (±7 days) after Sun-Start Visit
SFU[12W]:	12 weeks (±7 days) after Sun-Start Visit
SFU[24W]:	24 weeks (±7 days) after Sun-Start Visit
SFU[36W]:	36 weeks (±7 days) after Sun-Start Visit
SFU[48W]:	48 weeks (±7 days) after Sun-Start Visit
SFU[60W]:	60 weeks (±7 days) after Sun-Start Visit
End of Study Visit:	78 ±2 weeks after Screening

6.7 Multicentre Studies

Due to the limited number of patients included in this trial, site level summary statistics will not be produced. A summary of number of patients per country will be generated, and only if relevant additional descriptive statistics for primary and secondary endpoints by country may be produced if any treatment by country effects are suspected.

6.8 Examination of Subgroups

In general be subgroup evaluations will performed in this study based on the stratification levels, high and intermediate risk patients. Statistical analyses will be performed on the primary endpoint of OS and proportion of 18-months survival and for the secondary endpoint of PFS. Analysis will be done for the FAS population.

Also, analysis of subgroup of patients from the site in Gothenburg that performes embolisation the day before operation will be evaluated descriptively for all biopsy data and for corresponding patient characteristics and demographic characteristics.

A summary overview of all Adverse Events, and summary of number of patients by AE intensity and relationship with treatment will be produced split by ilixadencel batch subgroup (INT and CCK).

6.9 Interim Analysis

An interim analysis is not planned for in this study.

6.10 Data Monitoring

Not applicable.

7 REFERENCES

1. Heng DYC, Xie W, Regan MM, Warren MA, Golshayan AR, Sahi C et al. Prognostic factors for overall survival in patients with metastatic renal cell carcinoma treated with vascular endothelial growth factor–targeted agents: Results from a large, multicenter study. J Clin Oncol. 2009; 27(34):5794-99

2. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982; 5(6):649-55

3. Marcello Pagano, Kimberlee Gauvreau. Principles of Biostatistics, 2nd edition, 2000.

4. EORTC QLQ-C30 Scoring Manual, ISBN 2-9300 64-22-6, Third edition, 2001

8 APPENDIX 1

Data from patients screened but not included in the study will not be presented in any listings or tables.

8.1 Tables to be Produced for the Clinical Study Report (Section 14 according to ICH E3)

(Table numbers refer to section numbers in ICH E3)

14.1 DEMOGRAPHIC DATA

(Baseline presentations will be based on the safety set overall and split by stratum if not otherwise stated below)

14.1.1 Patient Disposition in Analysis Sets and Reason for Exclusions (All included patients)
14.1.2 Patient Discontinuation (All included patients)
14.1.3 Number of Patients by Visit (Safety Set)
14.1.4 Demographics: Age, Sex and Race (Safety Set)
14.1.5 Number of Patients by Country (Safety Set)
14.1.6 Other Baseline Characteristics: Weight, Height (Safety Set)
14.1.7 Karnofsky Performance Status (Safety Set)
14.1.8 Medical History (mRCC): Duration of mRCC, TNM Stage, mRCC Symptoms and Severity Grade (Safety Set)
14.1.9 Medical and Surgical History (Excluding mRCC) (Safety Set)

14.2 EFFICACY DATA

(Efficacy presentations will be split by stratum, all presentation will be based on FAS if not otherwise stated below)

Tables

14.2.1 Life table statistics of OS by treatment group (FAS, PPS and Subgroups)
14.2.2 Quartile Estimates (Median) and Confidence Intervals for OS (FAS, PPS and Subgroups)
14.2.3 Log rank test compare survival functions for treatments groups OS (FAS, PPS and Subgroups)
14.2.4 The estimates of the second primary endpoint of the proportion of 18-months survival and corresponding z-test test. (FAS, PPS and Subgroup)

14.2.7 Life table statistics of PFS from start of Sunitinib by treatment group

14.2.8 Quartile Estimates (Median) and Confidence Intervals for PFS from start of Sunitinib (FAS and Subgroup)

14.2.9 Log-Rank test compare survival functions for treatment groups PFS from start of Sunitinib (FAS and Subgroup)

14.2.13 Summary of RECIST 1.1, Number of patients with CR, PR, PD, SD, and "Not Evaluable" by visit from Screening to Sunitinib Start Visit (FAS and Subgroup)

14.2.14 Summary of RECIST 1.1, Number of patients with CR, PR, PD, SD, and "Not Evaluable" by visit after Sunitinib Start Visit (FAS and Subgroup)

14.2.15 Summary of ORR and DCR from start of Sunitinib (FAS and Subgroup)

14.2.16 Cochran Mante -Haenze test for ORR and DCR (FAS and Subgroup)

14.2.17 Summary of duration of response, and duration of clinical benefit (FAS and Subgroup)

14.2.18 Summary of duration of stable disease (FAS and Subgroup)

14.2.19 Life table statistics of TTP from start of Sunitinib by treatment group (FAS and Subgroup)

14.2.20 Quartile Estimates (Median) and Confidence Intervals for TTP from start of Sunitinib (FAS and Subgroups)

14.2.21 Log-Rank test compare survival functions for treatment groups TTP from start of Sunitinib (FAS and Subgroups)

14.2.22 Summary of tumor infiltrating CD8+ T-cells and relative number of tumor infiltrating CD8+ T-cells, [redacted] and [redacted] (FAS and Subgroups)

14.2.23 Summary of ECOG performance by visit (FAS and Subgroups)

14.2.24 [redacted]

14.2.25 Summary of immunohistology parameters (CD8+ T-cells) in a biopsy from adjacent normal kidney tissue collected approximately 2 cm from the tumor margin and in a metastasis biopsy where applicable, [redacted] and [redacted] (FAS and Subgroups)

14.2.26 Summary of degree of MHC mismatch (HLA-A, HLA-B, and HLA-DRB1) between Intuvax (donor) and the patient (receiver) and intratumoral infiltration of CD8+ T-cells, [redacted] and [redacted] (FAS and Subgroups)

14.2.27 Summary table for auto- and allo-immunization parameters. (FAS and Subgroups)

14.2.28 Shift tables for auto- and allo-immunization parameters from prior to vaccination 1 to Sun-Start visit (FAS and Subgroups)

14.2.29 Life table statistics of TTF from Screening by treatment group (FAS and Subgroups)

14.2.30 Quartile Estimates (Median) and Confidence Intervals for TTF from Screening (FAS and Subgroups)

14.2.31 Log-Rank test compare survival functions for treatment groups TTF Screening (FAS and Subgroups)

14.2.32 Summary of CD8+tumor infiltration (FAS) by best overall response, ORR and DCR according to RECIST 1.1 during the trial (FAS and Subgroups)

14.2.33 [redacted]

14.2.34 [redacted]

14.2.35 [redacted]

14.2.36 [redacted]

14.2.37 Summary of Sunitinib dose density (FAS) by ORR, DCR and best overall response according to RECIST 1.1 during the trial (FAS and Subgroups)

14.2.38 [redacted]
14.2.39

Figures

14.2.35 Kaplan-Meier plots OS survival functions by treatment group (FAS, PPS, Subgroups)
14.2.36 Kaplan-Meier plots PFS survival functions by treatment group (FAS, PPS, Subgroups)
14.2.37 Kaplan-Meier plots TTP survival functions by treatment group (FAS, Subgroups)
14.2.38 Kaplan-Meier plots TTF survival functions by treatment group (FAS, Subgroups)
14.2.39 Waterfall charts over the response distribution (FAS and Subgroups)
14.2.40 Swimmer plots time from screening (FAS and Subgroups)
14.2.41 Swimmer plots time from randomization (FAS and Subgroups)
14.2.42 Plot over mismatch patient/donor and CD8+ T-cells (as analysed by [redacted]) and corresponding Spearman correlation (FAS and Subgroups)
14.2.43 Plot over mismatch patient/donor and CD8+ T-cells (as analysed by [redacted]) and corresponding Spearman correlation (FAS and Subgroups)

14.3 SAFETY DATA
(Safety presentations will be based on the safety set unless otherwise stated below)

14.3.1 Displays of Adverse Events

14.3.1.1 Summary of Adverse Events
14.3.1.2 Summary of Adverse Events by ilixadencel batch subgroup
14.3.1.3 Adverse Events by System Organ Class and Preferred term
14.3.1.4 Adverse Events: Number of Patients by Intensity and Relationship by Treatment

14.3.1.5 Adverse Events: Number of Patients by Intensity and Relationship by Treatment by ilixadencel batch subgroup
14.3.1.6 Serious Adverse Events by System Organ Class and Preferred term
14.3.1.7 Related Adverse Events by System Organ Class and Preferred term
14.3.1.8 Adverse Events by CTCAE grade and System Organ C ass and Preferred term
14.3.1.9 Adverse Events occurring 4 hours following the Intuvax vaccination
14.3.1.10 Adverse Events occurring between first assessment at Screening and first Intuvax dose
14.3.1.11 Adverse Events occurring between first assessment at Screening and Nephrectomy
14.2.1.12 Related Serious Adverse Events by System Organ Class and Preferred term

14.3.2 Listings of Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

14.3.2.1 Listings of Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

14.3.4 Abnormal Laboratory Value Listings

14.3.4.1 Abnormal Laboratory Value Listing
14.3.4.2 Other Relevant Laboratory Analyses

14.3.4.3 Summary Statistics by Visit/Timepoint with Difference from Baseline (including the number of abnormal (low and high) and clinically significant observations)

14.3.4.4 Shift Tables

14.3.5 Extent of Exposure

14.3.5.1 Exposure vaccination

14.3.5.2 Exposure sunitinib and sunitinib dose density

14.3.6 Vital Signs

14.3.6.1 Summary Statistics with Difference from Baseline for Vital Signs (Systolic Blood Pressure, Diastolic Blood Pressure, Heart Rate and weight)

14.3.6.2 Vital signs post vaccination

14.3.7 Physical Examination

14.3.7.1 Summary of Physical Examination

14.3.7.2 Shift Tables for Physical Examination

14.3.8 ECG

14.3.8.1 Summary of ECG

14.3.9 Concomitant Medication and Therapy

14.3.8.2 Summary of Concomitant Medication

14.3.8.3 Summary of Sunitinib doses

8.2 Listings of Individual Patient Data and Other Information to be Produced for the Clinical Study Report (Sections 16.1 and 16.2 in ICH E3)

(Listing numbers refer to the relevant appendix number in ICH E3. CRF check questions/reminders will not be listed.)

16.1.7 Randomization Scheme
16.2.1.1 Discontinued Patients, Reason for Discontinuation
16.2.1.2 Visit Dates and Other Important Dates
16.2.1.3 Study Termination
16.2.3.1 Patients Excluded from the Efficacy Analysis (Evaluability, Reason for Evaluability Classification)
16.2.3.2 Treatment Allocation and Evaluability for All Patients
16.2.4.1 Demographic Data
16.2.4.2 Medical History
16.2.4.3 Inclusion Criteria Not Met and Exclusion Criteria Met
16.2.4.4 Existing Symptoms
16.2.4.5 CT/ MRI-scan
16.2.4.6 HLA tissue-typing
16.2.4.7 Karnofsky
16.2.4.8 Heng / Randomization
16.2.4.9 General information
16.2.5.1 Compliance and/or Drug Concentration Data vaccine
16.2.5.2 Compliance and/or Drug Concentration Data sunitinib
16.2.6.1 RECIST 1.1 evaluation
16.2.6.2 Efficacy parameters (ORR, OS, PFS, TTP, TTF)
16.2.6.3 [redacted]
16.2.6.4 ECOG
16.2.7.1 Adverse Event Listings by Treatment, Patient, Relative Day or Week. (Since demographic data and IMP are listed in separate listings, this listing will only contain information on adverse events, for space reasons.)
16.2.7.3 Adverse Event Listings by System Organ Class, Preferred Term, Treatment and Patient
16.2.7.4 Pre-treatment Adverse Event Listings by System Organ Class, Preferred Term, Treatment and Patient
16.2.8.1 Listing of Individual Laboratory Measurements by Patient
16.2.8.2 Listing of Relevant Comments Regarding Laboratory Values
16.2.8.3 Serology
16.2.8.4 Pregnancy
16.2.9.1 Vital Signs
16.2.9.1 Physical Examination
16.2.10.1 ECG
16.2.11.1 Concomitant Medications and Therapy
16.2.12.1 Alloimmunization
16.2.13.1 Surgery-Nephrectomy
16.2.14.1 Immunohistology