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EVALUATION OF TOFACITINIB IN EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS: A PHASE I/II TWO-CENTER SAFETY AND TOLERABILITY STUDY

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Evaluation of Tofacitinib in Early Diffuse Cutaneous Systemic Sclerosis: A Phase I/II Two-Center Safety and Tolerability Study
Final Statistical Analysis Plan

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Contents

1. Endpoints and Other Outcomes

This section describes the primary and secondary efficacy outcomes, as well as safety and other outcomes.

1.1. Primary Endpoint

Objective: To demonstrate acceptable safety and tolerability of tofacitinib in early dcSSc.

The primary endpoint is the proportion of participants who experience Grade 3 or higher (more severe) adverse events that occur at or before Week 24 (double-blind phase).

1.1.1. Primary Analysis of the Primary Endpoint.

The proportion of subjects in the safety population (see Section 2.1) with at least one Grade 3 or higher adverse event that begins at or before Week 24, the double-blind phase of the trial, will be calculated and compared for each of the study treatment arms.

1.1.2. Secondary Analysis of the Primary Endpoint.

To assess the robustness of the results for the primary analysis, an analysis of the total number of Grade 3 (severe) or higher adverse events that begin at or before Week 24 will also be compared for each of the study treatment arms.

1.2. Secondary Endpoints

1.2.1. Secondary Endpoint. Analyses of the Primary Endpoint Over Time.

The analyses of the primary endpoint described in sections 1.1.1 and 1.1.2 will be repeated at Weeks 12 to assess the time course of the safety profile as defined by the occurrence of Grade 3 or higher adverse events.

1.2.2. Secondary Endpoint. Analyses of the Adverse Events at the Grade 2 Threshold.

The analyses described in sections 1.1.1, 1.1.2 and 1.2.1 will be repeated for adverse events beginning at or before the time point of interest that are assessed as at least Grade 2 (moderate) severity.

1.2.3. Secondary Endpoint. % of Subjects with Adverse Events of Special Interest (AESI).

The proportion of subjects in the safety population experiencing an AESI will be compared between the two study treatment arms. Comparisons will be made for at least one AESI of any type, as well as for each of the events that are considered to be of special interest individually. Separate analyses will be performed for AESIs that occur at or before Weeks 12 and 24. AESIs are defined to be any one of herpes zoster, malignancy, serious infection, lymphocytes <500cells mm^3, ANC <500cells mm^3, AST > 3xULN, ALT > 3xULN, Hy's Law criteria met, Hemoglobin drop > 2mg/dL, increase in HDL/LDL ratio > 50%, or an increase in serum creatinine > 50%.

1.2.4. Secondary Endpoint. Change from Baseline in the Modified Rodnan Skin Score (mRSS).

Change from baseline in the mRSS total score will be compared between the two treatment arms to assess skin thickness relative to the initiation of study treatment at the various time points. The analysis will be performed separately at Weeks 12 and 24 on subjects in the modified intent-to-treat (mITT) population (see section 2.1).

1.2.5. Secondary Endpoint. Provisional American College of Rheumatology Combined Response Index in Systemic Sclerosis

CRISS will be compared between the two treatment arms separately at Weeks 12 and 24 on subjects in the modified intent-to-treat (mITT) population (see section 2.1).

1.2.6. Secondary Endpoint. % of Responders as Defined by the mRSS.

Subjects in the mITT population will be assessed for reaching clinical thresholds of decreased skin thickness over time as defined by a percentage reduction in the mRSS from baseline. Time points assessed will be Weeks 12 and 24, and analyzed separately. Within each of these time points, separate analyses will be performed for decreases (responder definition) of at least 20, 40, and 60% relative to the baseline mRSS total score.

1.2.7. Secondary Endpoint. Change from Baseline in the mRSS sub-scores.

Change from baseline in the mRSS representative score and maximum score will be compared between the two study treatment arms for the mITT population of subjects at Weeks 12 and 24 separately.

1.2.8. Secondary Endpoint. Change from Baseline in Physician Global Health Assessment.

Change from baseline in the physician's global health assessment will be compared between the two study treatment arms for the mITT population of subjects at Weeks 12 and 24 separately, to determine overall progression of disease severity as determined by the subject's physician.

1.2.9. Secondary Endpoint. Change from Baseline in Patient Global Health Assessment.

Change from baseline in the patient's global health assessment will be compared between the two study treatment arms for the mITT population of subjects at Weeks 12 and 24 separately, to determine overall progression of disease severity as determined by the subject.

1.2.10. Secondary Endpoint. Change from Baseline in Health Related Quality of Life (HRQoL) using the Patient-Reported Outcomes Measurement Information System (PROMIS-29).

Change from baseline in the HRQoL total score will be compared between the two study treatment arms for the mITT population of subjects at Weeks 12 and 24 separately to determine perceived overall changes in quality of life since the initiation of study treatment as determined by the subject.

1.2.11. Secondary Endpoint. Change from Baseline in the Scleroderma Health Assessment Questionnaire-Disability Index (SHAQ-DI).

Change from baseline in the SHAQ-DI total score will be compared between the two study treatment arms for the mITT population of subjects at Weeks 12 and 24 separately to determine perceived overall changes in the subject's functional ability since the initiation of study treatment as determined by the subject.

1.2.12. Secondary Endpoint. Change from Baseline in the UCLA SCTC Gastrointestinal Symptoms Total Score (GIT).

Change from baseline in the UCLA SCTC GIT will be compared between the two study treatment arms for the mITT population of subjects at Weeks 12 and 24 separately to determine changes in the subject's gastrointestinal symptoms since the initiation of study treatment.

1.2.13. Secondary Endpoint. Change from Baseline in the PRO for Scleroderma-related Skin Symptoms (PRO-SRSS) Total Score.

Change from baseline in the PRO-SRSS will be compared between the two study treatment arms for the mITT population of subjects at Weeks 12 and 24 separately to determine changes in the subject's overall skin symptoms since the initiation of study treatment.

1.2.14. Secondary Endpoint. Change from Screening in Pulmonary Function Tests (PFT).
Change from screening PFTs will be compared between the two study treatment arms for the mITT population of subjects at Weeks 12 and 24 separately for each of percent predicted FVC, FEV and DLCO.

1.2.15. Secondary Endpoint. Change from Screening to Week 24 in Left Ventricular Ejection Fraction (Maximum of Range).
Change from screening ejection fraction will be compared between the two study treatment arms for the mITT population of subjects at Week 24.

1.2.16. Secondary Endpoint. Change from Screening to Week 24 in Tricuspid Regurgitation Jet.
Change from screening tricuspid regurgitation jet will be compared between the two study treatment arms for the mITT population of subjects at Week 24.

1.3. Exploratory Endpoints
Analyses of each of the secondary endpoints will be provided at weeks 36 and 48, provided the item was collected.

1.4. Additional Measures
Additionally, the following measures will be provided descriptively (no inferential analyses) by study treatment arm for the safety population:

- Clinical laboratory values over time.
- Vital signs over time.
- Physical examination findings.
- Concomitant medication.

2. Analysis Strategy

No formal interim analyses of the primary endpoint were conducted, therefore the nominal α level to be used at the final analysis is 0.10 for the primary endpoint. All other secondary outcomes will also be tested at the 10% level, with no adjustment for multiplicity. Given the limited statistical power for a study consisting of 15 subjects, models will not include covariates.

2.1. Study Populations

Two study populations will be defined for these analyses:

- ***Modified Intent to Treat (mITT):*** The mITT analysis set consists of all subjects randomized, receiving at least one dose of treatment, and having at least one post-baseline efficacy assessment for the given parameter. No imputation techniques will be utilized for missing observations.
- ***Safety:*** The safety population consists of all subjects who were randomized and received at least one dose of the study drug.

2.2. Analyses of Primary Endpoint

The primary analysis is a comparison of the percentage of subjects with Grade 3 adverse events that begin within the first 24 Weeks following initiation of study treatment between tofacitinib and placebo. The analysis will be performed on the safety population. The test will be performed using Fisher's Exact Test, given that the largest possible number of patients affected are 10 and 5, respectively, for tofacitinib and placebo. The number and percentage of patients with at least one Grade 3 adverse event will be provided along with Clopper Pearson Exact confidence intervals for proportions at the 90% threshold.

2.2.1. Primary Analysis of the Primary Endpoint.

Proportion of patients with at least one Grade 3 adverse event within the first 24 Weeks

Analysis Set	Safety Population
Methods	Fisher's Exact Test Clopper Pearson Exact Confidence Intervals
Results	• Number and percentage of subjects with at least one Grade 3 adverse event in the first 24 weeks • 90% confidence interval for proportions • P-value from Fisher's Exact Test

2.2.2. Secondary Analysis of the Primary Endpoint.

A sensitivity analysis will be performed to assess how the total number of Grade 3 or higher adverse events, rather than just the proportion of patients experiencing the events, affect the conclusions of the analysis of the primary endpoint. The analysis will employ Poisson Regression methodology, offset for time in the study (the lesser of 24 weeks, or withdrawal from the trial).

Analysis Set	Safety Population
Methods	Poisson Regression offset for time in the study (the lesser of 24 weeks or withdrawal from the trial)
Dependent Variable	Number of grade 3 or higher adverse events experienced within the first 24 weeks on a per patient basis.
Covariate	Treatment
Results	• Total number of Grade 3 adverse event in the first 24 weeks • Relative risk of tofacitinib to placebo. • 90% confidence interval for relative risk • P-value for treatment effect

2.3. Analyses of Secondary Endpoints

2.3.1. Analyses of the primary endpoint over time.

The secondary analyses is a comparison of the percentage of subjects with Grade 3 adverse events that begin within the first 12, 36, and 48 Weeks, respectively, following initiation of study treatment between tofacitinib and placebo. Each of the time points is a standalone analysis, utilizing the methodology described for the primary analysis of the primary endpoint in section 2.2.1

Analysis Set	Safety Population
Time Points	2.3.1a: Week 12, 2.3.1b: Week 36, 2.3.1c: Week 46
Methods	Fisher's Exact Test Clopper Pearson Exact Confidence Intervals

Results	• Number and percentage of subjects with at least one Grade 3 adverse event up to and including the time point of interest • 90% confidence interval for proportions • P-value from Fisher's Exact Test

2.3.2. Secondary analyses of the primary endpoint over time.

Secondary analyses will be performed over time (Weeks 12, 36 and 48) using the same methodology described in section 2.2.2 to explore treatment differences in the total number of Grade 3 or higher adverse events over time. The offset for time in study will be the lesser of the withdrawal date from the trial or the time point of interest.

Analysis Set	Safety Population
Methods	Poisson Regression offset for time in the study (the lesser of the time point of interest or withdrawal from the trial)
Time Points	2.3.2a: Week 12, 2.3.2b: Week 36, 2.3.2c: Week 46
Dependent Variable	Number of grade 3 or higher adverse events experienced within the time point of interest on a per patient basis.
Covariate	Treatment
Results	• Total number of Grade 3 adverse event within the time point of interest. • Relative risk of tofacitinib to placebo. • 90% confidence interval for relative risk • P-value for treatment effect

2.3.3. Secondary analyses for proportion of subjects.

The proportion of subjects in the specified populations above will be compared between the two study treatment arms at the specified time points utilizing Fisher's Exact Test and Clopper Pearson confidence intervals to describe treatment differences.

Analysis Set	See Above
Time Points	See Above

Parameters	• Adverse events of special interest • mRSS responders
Methods	Fisher's Exact Test Clopper Pearson Exact Confidence Intervals
Results	• Number and percentage of subjects with at the parameter of interest. • 90% confidence interval for proportions • P-value from Fisher's Exact Test

2.3.4. Secondary analyses for continuous endpoints.

Continuous parameters will be analyzed utilizing a two-sample t-test to explore treatment differences at the time points described above. There will be no further adjustments. Descriptive statistics (e.g. mean, standard deviation, median, min, and max) will be provided by treatment to further describe the distributions. If there are specific concerns about outliers, suggesting a skewed distribution, a Wilcoxon Rank Sum test will be additionally provided as a sensitivity analysis.

Analysis Set	See Above
Time Points	See Above
Parameters	• Change from baseline in mRSS total score. • CRISS scores at Weeks 12 and 24. • Change from baseline in physician's global health assessment. • Change from Baseline in Patient Global Health Assessment. • Change from Baseline in Health Related Quality of Life (HRQoL). • Change from Baseline in the Scleroderma Health Assessment Questionnaire-Disability Index (SHAQ-DI). • Change from Baseline in the UCLA SCTC Gastrointestinal Symptoms Total Score (GIT). • Change from Baseline in the PRO for Scleroderma-related Skin Symptoms (PRO-SRSS) Total Score. • Change from Screening in Pulmonary Function Tests (PFT) – FVC, FEV and DLCO. • Secondary Endpoint. Change from Screening to Week 24 in Left Ventricular Ejection Fraction (Maximum of Range).

	• Change from screening ejection fraction will be compared between the two study treatment arms for the mITT population of subjects at Week 24. • Secondary Endpoint. Change from Screening to Week 24 in Tricuspid Regurgitation Jet. • Change from screening tricuspid regurgitation jet will be compared between the two study treatment arms for the mITT population of subjects at Week 24. •
Methods	Two sample t-test
Results	• Mean • Standard deviation • Median • Min, Max • P-value from t-test

2.4. Analyses of Exploratory Endpoints

Each of the items above will be analyzed for weeks 36 and 48 using the methodology described for the given time, provided the item was collected at these time points.

3. Table, Listing and Figure Shells

Note: Weeks 36 and 48 are exploratory, and will be provided in separate, supplemental tables following the reporting of primary and secondary endpoints.

3.1.1. Subject Characteristics and Study Conduct

Table 1: TOFA Subject Disposition. All Subjects

Status	Tofacitinib N (%)	Placebo N (%)
ITT Population [1]		
Safety Population [2]		
Open Label Population [3]		
Completed Study Treatment		
Discontinued Study Early		
Reason for Discontinuation		
Subject was determined to be ineligible		
Subject withdrew consent		
Investigator withdrew subject		
Study terminated by Sponsor		
Death		
Lost to follow-up		
Other		
Permanently Discontinued Study Treatment		
Reason for Discontinuation of Study Treatment		
Adverse Event		

Note: Percentages are based on the number of subjects in the Safety Population.
[1] The ITT population includes all patients randomized to TOFA.
[2] The Safety Population includes all randomized subjects who received at least one dose of study medication.
[3] The Open Label Population includes all patients in the Safety Population that have completed 24 weeks (168 Days) of Double-Blind study treatment and not withdrawn from the study.
Data cutoff date: DDMMYY

Listing 1: TOFA Early Termination. ITT Subjects.

Subject ID	Treatment	Reason for Discontinuation	Time on Treatment (Days)	Time in Study (Days)

Conditional Note: No patients have discontinued as of the data cutoff date.

Data cutoff date: DDMMYY

Table 2: TOFA Demographic Characteristics. ITT Population

Variable Statistic or Category	Tofacitinib N=10	Placebo N=5
Age (Years)		
N		
Mean		
SD		

Variable Statistic or Category	Tofacitinib N=10	Placebo N=5
Median		
Min, Max		
Age, n (%)		
18 to 35 years		
>35 to 55 years		
>55 to 70 years		
Gender, n (%)		
Male		
Female		
Of Childbearing Age		
Not of Childbearing Age		
Hysterectomy		
Tubal Ligation		
Post Menopausal		
Other Reason		
Ethnicity, n (%)		
Hispanic or Latino		
Not Hispanic or Latino		
Race, n (%) [1]		
American Indian or Alaska Native		
Asian		

Variable Statistic or Category	Tofacitinib N=10	Placebo N=5
Black or African-American		
Native Hawaiian or Other Pacific Islander		
White		
Not Reported		
Smoking History, n (%) [1]		
Never		
Past History		
Current Smoker		
No Response		

Note: Percentages are 100*n/N
[1] Subjects reporting more than one race are counted in each of the race categories reported.
Data cutoff date: DDMMYY

Table 3: TOFA Baseline Characteristics. ITT Population

Variable Statistic or Category	Tofacitinib N = 10	Placebo N = 5
mRss at Baseline		
N		

Variable Statistic or Category	Tofacitinib N = 10	Placebo N = 5
Mean		
SD		
Median		
Min, Max		
Disease Duration Since 1st Non-Raynaud's Sign or Symptom (Years)		
N		
Mean		
SD		
Median		
Min, Max		
Disease Duration Since Raynaud's Phenomenon (Years)		
N		
Mean		
SD		
Median		
Min, Max		
Interstitial lung disease on HRCT of chest, N (%)		
FVC% - at Screening		
N		
Mean		

Variable Statistic or Category	Tofacitinib N = 10	Placebo N = 5
SD		
Median		
Min, Max		
DLCO% - at Screening		
N		
Mean		
SD		
Median		
Min, Max		
HAQ-DI [theoretical range, 0-3]		
N		
Mean		
SD		
Median		
Min, Max		
SHAQ: Pain From Illness in Past Week (theoretical range, 0-150)		
N		
Mean		
SD		
Median		

Variable Statistic or Category	Tofacitinib N = 10	Placebo N = 5
Min, Max		
SHAQ: Intestinal Problems Interfere with Daily Activities in Past Week [theoretical range, 0-150]		
N		
Mean		
SD		
Median		
Min, Max		
SHAQ: Breathing Problems Interfere with Daily Activities in Past Week [theoretical range, 0-150]		
N		
Mean		
SD		
Median		
Min, Max		
SHAQ: Raynaud's Interfere with Daily Activities in Past Week [theoretical range, 0-150]		
N		
Mean		
SD		
Median		

Variable Statistic or Category	Tofacitinib N = 10	Placebo N = 5
Min, Max		
SHAQ: Finger Ulcers Interfere with Daily Activities in Past Week [theoretical range, 0-150]		
N		
Mean		
SD		
Median		
Min, Max		
Hemoglobin (g/dL) – at Screening		
N		
Mean		
SD		
Median		
Min, Max		
WBC (K/uL) – at screening		
N		
Mean		
SD		
Median		
Min, Max		
Large Joint Contracture N (%)		

Variable Statistic or Category	Tofacitinib N = 10	Placebo N = 5
Small Joint Contracture N (%)		
Tendon Friction Rub (Range 0 to 12) **		
# (%) with 0 positive results		
# (%) with 1 positive result		
# (%) with 2 positive results		
# (%) with ANY positive results		

Data cutoff date: DDMMYY

** Areas of examination include right and left shoulder, elbow, wrist, MCP, knee, and ankle.

Table 4: TOFA Baseline ECHO. ITT Population

Variable Statistic or Category	Tofacitinib N=10	Placebo N=5
Left Ejection Fraction (Maximum of Range)		
N		
Mean		
SD		
Median		

Variable Statistic or Category	Tofacitinib N=10	Placebo N=5
Min, Max		
EV Enlargement: N (%)		
Right Ventricular Diameter For Patients with Enlargement (mm)		
N		
Mean		
SD		
Median		
Min, Max		
RVSP: N (%)		
RVSP Value (mmHg)		
N		
Mean		
SD		
Median		
Min, Max		
Pericardial Effusion Moderate to Large: N (%)		

Data cutoff date: DDMMYY

Table 5: TOFA Study Drug Compliance. ITT Population

Variable Statistic or Category	Tofacitinib N=10	Placebo N=5
Study Drug Exposure (Days)		
N		
Mean		
SD		
Median		
Min, Max		
Study Drug Compliance % (Actual Tablets Used/Expected Tablets Used)		
N		
Mean		
SD		
Median		
Min, Max		
Study Drug Compliance % Thresholds for Dosed Subjects		
Number of Subjects Dosed		
< 75%		
75-85%		
85-95%		
95-99%		

Variable Statistic or Category	Tofacitinib N=10	Placebo N=5
100%		
101-105%		
At least 95% Compliant		

Data cutoff date: DDMMYY

Table 6: TOFA Summary of Immunosuppressive Therapy. Safety Population

Variable	Tofacitinib N=10	Placebo N=5
# of Subjects		
# of Subjects with Immunosuppressive Therapy		
% of Subjects with Immunosuppressive Therapy		

Data cutoff date: DDMMYY

Listing 2: Immunosuppressive Therapy. Safety Population

Treatment	Subject ID	Medication	Start Date	Stop Date	Medication Ongoing

Data cutoff date: DDMMYY

Table 7: TOFA Concomitant Medication Usage. Safety Population [1]

Concomitant Medication	Tofacitinib N=10 n(%)	Placebo N=5 n(%)
Abreva		
Acyclovir		
Adderall XR		
Aleve		
Amlodipine(Norvasc)		
Asprin		
Atorvastatin(Lipitor)		
Augmentin		
Bydureon		
Calcium with Vitamin D		
Carafate		
Celebrex		
Ciprofloxacin(Cipro)		
Clindamycin(Cleocin)		
Clonazepam(Klonopin)		
CoQ10		
Collagenase		
Compezine		
Cymbalta		

Concomitant Medication	Tofacitinib N=10 n(%)	Placebo N=5 n(%)
Diazepam(Valium)		
Diltiazem		
Duloxetine(Cymbalta)		
Esomeprazole magnesium(Nexium)		
Ferrous Sulfate		
Flexeril		
Flonase		
Folic Acid		
Furosemide(Lasix)		
Gabapentin		
Glucophage(Metformin)		
Glucosamine Chondroitin		
Hydrocodone-Acetamenophen		
Ibuprofen (Advil/Motrin)		
Iloprost infusions		
Iron		
Ketorolac tromethamine (Toradol)		
Levemir		
Levothyroxine		

Concomitant Medication	Tofacitinib N=10 n(%)	Placebo N=5 n(%)
Lexapro		
Lisinopril(zestril)		
Lopressor		
Loratidine/pseuoephedrine		
Lyrica		
Medical Marijuana		
Methotrexate		
Miralax		
Multi-vitamin		
Mycophenolate-Mofetil		
Neomycin/polyminyx		
Neurontin(Gabapentin)		
Nexium		
Niacin		
Nifedipine(Procardia)		
Normal Saline IV fluids		
Omeprazole(Prilosec)		
Prednisone		
Prevident		
Probiotic		
Ranitidine(Zantac)		

Concomitant Medication	Tofacitinib N=10 n(%)	Placebo N=5 n(%)
Riociguat		
Sennosides		
Sildenafil		
Tessalon Perles		
Tesslon Pearls		
Tramadol(Ultram)		
Valacyclovir		
Viagra		
Vicodin		
Vitamin C		
Vitamin D3		
Vitamin D3 with Calcium		
Voltaren		
Xifaxin		
Zestoretic 20/12.5		
Zithromax Z-Pak		
alendronate		
amlodipine/olmesartin		
etonogestral Implant		
levothyroxine		
nitrofurantoin		

Concomitant Medication	Tofacitinib N=10 n(%)	Placebo N=5 n(%)
protonix		
riociguat		
trilipix		
zyrtec		

[1] The safety population includes all patients randomized to TOFA who received at least one dose of study medication.
Data cutoff date: DDMMYY

3.1.2. Safety Analyses

Table 8: TOFA Summary of SAEs by System Organ Class Regardless of Relatedness to Intervention. Safety Population

Variable	Tofacitinib N=10	Placebo N=5
# of SAEs		
# of Subjects with SAEs		
# of Subjects		
SAEs per Subject		
% of Subjects with SAEs		

Data cutoff date: DDMMYY

Table 9: TOFA Proportion of Subjects with SAEs by Severity Grade. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Total Events		
Total Subjects With At Least One Event		
Grade 1		
Grade 2		
Grade 3		
Grade 4		
Grade 5		
Grades 3-5		

[1] Percentages are 100*n/N.
The severity grade shown is the greatest grade reported per event for a particular Subject (Grade1 < Grade 2 < Grade 3 < Grade 4 < Grade 5).
Data cutoff date: DDMMYY

Listing 3: TOFA Listing of SAEs. Safety Population.

Treatment	Subject ID	SAE#	New SAE since (*Date of last report*)	SAE Brief Description (Verbatim Term)	Treatment Emergent?	SAE Start Date	SAE Stop Date	Days from Start of Study Medication	Severity Grade	Relationship to Study Treatment	Outcome	Study Drug Action Taken	Study Drug Stop Date	Study Drug Start Date	Treatment Required

There were no SAEs reported as of the data cutoff date.

Treatment emergent adverse events are AEs that are began after the first dose of study medication.

Note: Double-Blind Treatment is expected to last 24 Weeks (168 Days). Those SAEs that started >= Day 169 are assumed to have occurred during the Open Label phase.

Data cutoff date: DDMMYY

Listing 4: TOFA Listing of Deaths. Safety Population

Treatment	Subject ID	SAE#	New SAE since Aug 4, 2017	SAE Primary Category	SAE Description (Verbatim Term)	Treatment Emergent?	SAE Start Date	SAE Stop Date	Days from Start of Study Medication	Severity Grade	Relationship to Study Treatment	Outcome	Study Drug Action Taken	Treatment Required

Conditional Note: There were no deaths reported as of the data cutoff date.

Treatment emergent adverse events are AEs that began after the first dose of study medication.

Data cutoff date: DDMMYY

Table 10: TOFA Proportion of Subjects with Adverse Events by Primary Category. Safety Population.

Preferred Term	Tofacitinib n (%) [1]	Placebo n (%) [1]
# of Safety Patients		
# of AEs		
# of Subjects with AEs		
% of Subjects with AEs		
Primary Category		
General Disorders		
Flu-Like Symptoms		
Common Cold		
Weight Gain		
Weight Loss		
Cardiac Disorders		
Tachycardia		
Renal and Urinary Disorders		
Chronic Kidney Disease		
Non-Obstructive Renal Calculi		
Gastrointestinal Disorders		
GERD		
Increased GERD		
Infections and Infestations		
Ulcer Infection		

Preferred Term	Tofacitinib n (%) [1]	Placebo n (%) [1]
Urinary Tract Infection		
Upper Respiratory Infection		
Otitis Externa		
Investigations		
Hyperkalemia		
Hypercholesterolemia		
Skin and subcutaneous Disorders		
Pruritus (Itching)		
Digital Ulcer Finger		
Nervous System Disorders		
Headache		
Migraine		
Bell's Palsy		
Musculoskeletal and Connective Tissue Disorders		
Joint Pain		
Knee Pain		
Back Pain		
Right Trochanteric Bursitis		
Bilateral Wrist Synovitis		
Respiratory, thoracic and mediastinal disorders		
Maxillary Sinus Inflammation		
Sinus Congestion		
Dyspnea or Exertion		

Preferred Term	Tofacitinib n (%) [1]	Placebo n (%) [1]
Vascular Disorders		
Hypertension		
Hypertensive Urgency		

[1] Percentages are 100*n/N.
Data cutoff date: DDMMYY

Table 11: TOFA Proportion of Subjects with Adverse Events by Severity. Safety Population.

Preferred Term	Tofacitinib n (%) [1]	Placebo n (%) [1]
# of Safety Patients		
# of AEs		
# of Subjects with AEs		
% of Subjects with AEs		
Severity Grade		
No Adverse Events		
Mild		
Moderate		

[1] Percentages are 100*n/N.
The severity shown is the greatest reported per event for a particular Subject (Mild < Moderate < Severe).

Data cutoff date: DDMMYY

Listing 5: TOFA Listing of Treatment Emergent Adverse Events. Safety Population.

Treatment	Subject ID	New AE Since March 5, 2018	CTCAE Classificaiton	AE Primary Category	AE Start Date	AE End Date	Days from Start of Study Medication	Severity	Relationship to Study Treatment	Outcome	Expected / Unexpected	Study Drug Action Taken	SAE?	Worsening of SSC?

Treatment	Subject ID	New AE Since March 5, 2018	CTCAE Classificaiton	AE Primary Category	AE Start Date	AE End Date	Days from Start of Study Medication	Severity	Relationship to Study Treatment	Outcome	Expected / Unexpected	Study Drug Action Taken	SAE?	Worsening of SSC?

Data cutoff date:DDMMYY

Note: Double-Blind Treatment is expected to last 24 Weeks (168 Days). Those AEs that started >= Day 169 are assumed to have occurred during the Open Label phase.

Table 12: Adverse Events of Special Interest. Safety Population.

Preferred Term Category	Tofacitinib N=10 n (%) [1]	Placebo N=5 n(%) [1]
Total Events		
Total Subjects With At Least One Event		
Herpes Zoster		
Malignancies		
Serious Infections		
Lab Value Abnormalities		
Lymphocytes <500cells mm3		
ANC <500cells mm3		
AST/ALT > 3xULN		
Hy's Law Criteria Met		
Hb drop >2gm/dL		
Increase in HDL/LDL > 50%		
Increase in Serum Creatinine > 50%		

[1] Percentages are 100*n/N.
Data cutoff date: DDMMYY

The following set of Figures will be of this format:

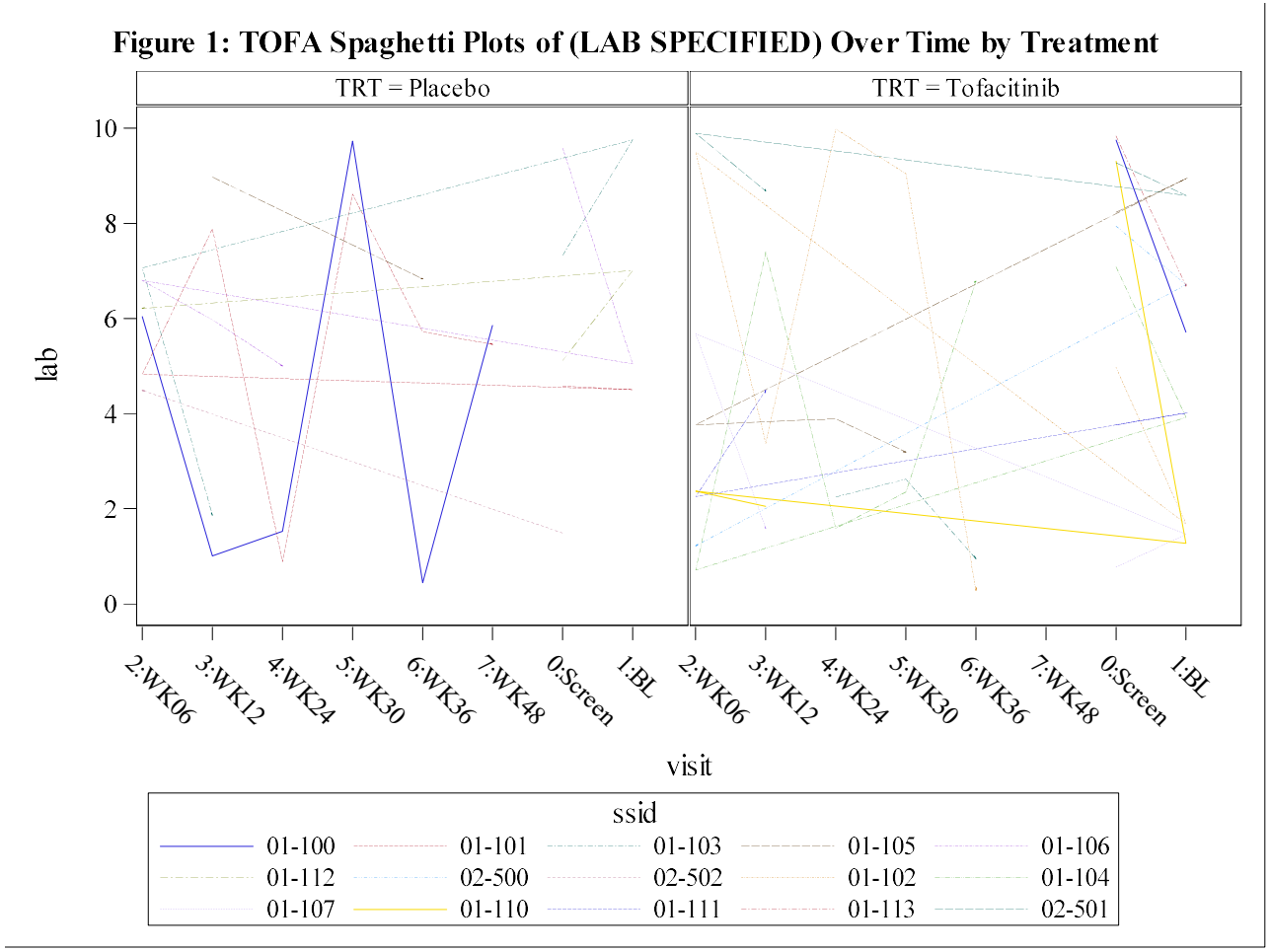

Figure 1: TOFA Spaghetti Plots of Hemoglobin Over Time by Treatment
Figure 2: TOFA Spaghetti Plots of WBC Over Time by Treatment

Figure 3: TOFA Spaghetti Plots of Creatinine Over Time by Treatment
Figure 4: TOFA Spaghetti Plots of Lymphoctyes %Over Time by Treatment
Figure 5: TOFA Spaghetti Plots of Neutrophil % Over Time by Treatment
Figure 6: TOFA Spaghetti Plots of ALT Over Time by Treatment
Figure 7: TOFA Spaghetti Plots of AST Over Time by Treatment
Figure 8: TOFA Spaghetti Plots of Total Cholesterol Over Time by Treatment
Figure 9: TOFA Spaghetti Plots of Triglycerides Over Time by Treatment
Figure 10: TOFA Spaghetti Plots of LDL Over Time by Treatment
Figure 11: TOFA Spaghetti Plots of HDL Over Time by Treatment

Table 13: TOFA Proportion of Subjects with Grade 3 (Severe) or Higher SAEs Within the First 24 Weeks. Primary Outcome. Safety Population.

Adverse Events	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Subjects With At Least One Grade 3 or Higher Event		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Poisson Regression, offset for time in study (lesser of 36 weeks or end of study).
Data cutoff date: DDMMYY

Table 14: TOFA Number of Grade 3 (Severe) or Higher SAEs Within the First 24 Weeks. Secondary Outcome. Safety Population.

Adverse Events	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Total Number of Grade 3 or Higher SAEs		
Relative Risk [2]		
90% Confidence Interval [2]		
p-value [2]		

[1] Percentages are 100*n/N.
[2] Poisson Regression, offset for time in study (lesser of 24 weeks or end of study).
Data cutoff date: 31OCT18

Table 15: TOFA Proportion of Subjects with Grade 3 (Severe) or Higher SAEs Within the First 12 Weeks. Secondary Outcome. Safety Population.

Adverse Events	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Subjects With At Least One Grade 3 or Higher Event		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.

[2] Clopper Pearson Exact confidence intervals for proportions with at least a Grade 3 SAE.
[3] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 16: TOFA Number of Grade 3 (Severe) or Higher SAEs Within the First 12 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Total Number of Grade 3 or Higher SAEs		
Relative Risk [2]		
90% Confidence Interval [2]		
p-value [2]		

[1] Percentages are 100*n/N.
[2] Poisson Regression, offset for time in study (lesser of 12 weeks or end of study).
Data cutoff date: DDMMYY

Table 17: TOFA Proportion of Subjects with Grade 3 (Severe) or Higher SAEs Within the First 36 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Subjects With At Least One Grade 3 or Higher Event		

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Clopper Pearson Exact confidence intervals for proportions with at least a Grade 3 SAE.
[3] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 18: TOFA Number of Grade 3 (Severe) or Higher SAEs Within the First 36 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Total Number of Grade 3 or Higher SAEs		
Relative Risk [2]		
90% Confidence Interval [2]		
p-value [2]		

[1] Percentages are 100*n/N.
[2] Poisson Regression, offset for time in study (lesser of 36 weeks or end of study).
Data cutoff date: DDMMYY

Table 19: TOFA Proportion of Subjects with Grade 3 (Severe) or Higher SAEs Within the First 48 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Subjects With At Least One Grade 3 or Higher Event		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Clopper Pearson Exact confidence intervals for proportions with at least a Grade 3 SAE.
[3] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 20: TOFA Number of Grade 3 (Severe) or Higher SAEs Within the First 48 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Total Number of Grade 3 or Higher SAEs		
Relative Risk [2]		
90% Confidence Interval [2]		
p-value [2]		

[1] Percentages are 100*n/N.
[2] Poisson Regression, offset for time in study (lesser of 48 weeks or end of study).
Data cutoff date: DDMMYY

Table 21: TOFA Proportion of Subjects with Grade 2 (Moderate) or Higher SAEs Within the First 12 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Subjects With At Least One Grade 2 or Higher Event		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Clopper Pearson Exact confidence intervals for proportions with at least a Grade 2 SAE.
[3] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 22: TOFA Number of Grade2 (Moderate) or Higher SAEs Within the First 12 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Total Number of Grade 2 or Higher SAEs		
Relative Risk [2]		

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
90% Confidence Interval [2]		
p-value [2]		

[1] Percentages are 100*n/N.
[2] Poisson Regression, offset for time in study (lesser of 12 weeks or end of study).
Data cutoff date: DDMMYY

Table 23: TOFA Proportion of Subjects with Grade 2 (Moderate) or Higher SAEs Within the First 24 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Subjects With At Least One Grade 2 or Higher Event		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Clopper Pearson Exact confidence intervals for proportions with at least a Grade 2 SAE.
[3] Fisher's Exact Test
Data cutoff date: DDMMYY'

Table 24: TOFA Number of Grade 2 (Moderate) or Higher SAEs Within the First 24Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Total Number of Grade 2 or Higher SAEs		
Relative Risk [2]		
90% Confidence Interval [2]		
p-value [2]		

[1] Percentages are 100*n/N.
[2] Poisson Regression, offset for time in study (lesser of 24 weeks or end of study).
Data cutoff date: DDMMYY

Table 25: TOFA Proportion of Subjects with Grade 2 (Moderate) or Higher SAEs Within the First 36 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Subjects With At Least One Grade 2 or Higher Event		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Clopper Pearson Exact confidence intervals for proportions with at least a Grade 2 SAE.
[3] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 26: TOFA Number of Grade 2 (Moderate) or Higher SAEs Within the First 36 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Total Number of Grade 2 or Higher SAEs		
Relative Risk [2]		
90% Confidence Interval [2]		
p-value [2]		

[1] Percentages are 100*n/N.
[2] Poisson Regression, offset for time in study (lesser of 36 weeks or end of study).
Data cutoff date: DDMMYY

Table 27: TOFA Proportion of Subjects with Grade 2 (Moderate) or Higher SAEs Within the First 48 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Subjects With At Least One Grade 2 or Higher Event		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Clopper Pearson Exact confidence intervals for proportions with at least a Grade 2 SAE.
[3] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 28: TOFA Number of Grade 2 (Moderate) or Higher SAEs Within the First 48 Weeks. Secondary Outcome. Safety Population.

System Organ Class Preferred Term	Tofacitinib N=10 n (%) [1]	Placebo N=5 n (%) [1]
Total Number of Grade 2 or Higher SAEs		
Relative Risk [2]		
90% Confidence Interval [2]		
p-value [2]		

[1] Percentages are 100*n/N.
[2] Poisson Regression, offset for time in study (lesser of 48 weeks or end of study).
Data cutoff date: DDMMYY

Table 29: TOFA Proportion of Subjects with Adverse Events of Special Interest Within the First 12 Weeks. Secondary Outcome. Safety Population.

Preferred Term Category	Tofacitinib N=10 n (%) [1]	Placebo N=5 n(%) [1]
Total Subjects With At Least One Event		
90% Confidence Interval [2]		

Preferred Term Category	Tofacitinib N=10 n (%) [1]	Placebo N=5 n(%) [1]
p-value [3]		
Herpes Zoster		
90% Confidence Interval [2]		
p-value [3]		
Malignancies		
90% Confidence Interval [2]		
p-value [3]		
Serious Infections		
90% Confidence Interval [2]		
p-value [3]		
Lab Value Abnormalities		
Lymphocytes <500cells mm3		
90% Confidence Interval [2]		
p-value [3]		
ANC <500cells mm3		
90% Confidence Interval [2]		
p-value [3]		
AST/ALT > 3xULN		
90% Confidence Interval [2]		
p-value [3]		

Preferred Term Category	Tofacitinib N=10 n (%) [1]	Placebo N=5 n(%) [1]
Hy's Law Criteria Met		
90% Confidence Interval [2]		
p-value [3]		
Hb drop >2gm/dL		
90% Confidence Interval [2]		
p-value [3]		
Increase in HDL/LDL > 50%		
90% Confidence Interval [2]		
p-value [3]		
Increase in Serum Creatinine > 50%		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Clopper Pearson Exact confidence intervals for proportions with at least of the given AE(s).
[3] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 30: TOFA Proportion of Subjects with Adverse Events of Special Interest Within the First 24 Weeks. Secondary Outcome. Safety Population.

Preferred Term Category	Tofacitinib N=10 n (%) [1]	Placebo N=5 n(%) [1]
Total Subjects With At Least One Event		
90% Confidence Interval [2]		
p-value [3]		
Herpes Zoster		
90% Confidence Interval [2]		
p-value [3]		
Malignancies		
90% Confidence Interval [2]		
p-value [3]		
Serious Infections		
90% Confidence Interval [2]		
p-value [3]		
Lab Value Abnormalities		
Lymphocytes <500cells mm3		
90% Confidence Interval [2]		
p-value [3]		
ANC <500cells mm3		
90% Confidence Interval [2]		

Preferred Term Category	Tofacitinib N=10 n (%) [1]	Placebo N=5 n(%) [1]
p-value [3]		
AST/ALT > 3xULN		
90% Confidence Interval [2]		
p-value [3]		
Hy's Law Criteria Met		
90% Confidence Interval [2]		
p-value [3]		
Hb drop >2gm/dL		
90% Confidence Interval [2]		
p-value [3]		
Increase in HDL/LDL > 50%		
90% Confidence Interval [2]		
p-value [3]		
Increase in Serum Creatinine > 50%		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Clopper Pearson Exact confidence intervals for proportions with at least of the given AE(s).
[3] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 31: TOFA Proportion of Subjects with Adverse Events of Special Interest Within the First 36 Weeks. Secondary Outcome. Safety Population.

Preferred Term Category	Tofacitinib N=10 n (%) [1]	Placebo N=5 n(%) [1]
Total Subjects With At Least One Event		
90% Confidence Interval [2]		
p-value [3]		
Herpes Zoster		
90% Confidence Interval [2]		
p-value [3]		
Malignancies		
90% Confidence Interval [2]		
p-value [3]		
Serious Infections		
90% Confidence Interval [2]		
p-value [3]		
Lab Value Abnormalities		
Lymphocytes <500cells mm3		
90% Confidence Interval [2]		
p-value [3]		
ANC <500cells mm3		
90% Confidence Interval [2]		

Preferred Term Category	Tofacitinib N=10 n (%) [1]	Placebo N=5 n(%) [1]
p-value [3]		
AST/ALT > 3xULN		
90% Confidence Interval [2]		
p-value [3]		
Hy's Law Criteria Met		
90% Confidence Interval [2]		
p-value [3]		
Hb drop >2gm/dL		
90% Confidence Interval [2]		
p-value [3]		
Increase in HDL/LDL > 50%		
90% Confidence Interval [2]		
p-value [3]		
Increase in Serum Creatinine > 50%		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Clopper Pearson Exact confidence intervals for proportions with at least of the given AE(s).
[3] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 32: TOFA Proportion of Subjects with Adverse Events of Special Interest Within the First 48 Weeks. Secondary Outcome. Safety Population.

Preferred Term Category	Tofacitinib N=10 n (%) [1]	Placebo N=5 n(%) [1]
Total Subjects With At Least One Event		
90% Confidence Interval [2]		
p-value [3]		
Herpes Zoster		
90% Confidence Interval [2]		
p-value [3]		
Malignancies		
90% Confidence Interval [2]		
p-value [3]		
Serious Infections		
90% Confidence Interval [2]		
p-value [3]		
Lab Value Abnormalities		
Lymphocytes <500cells mm3		
90% Confidence Interval [2]		
p-value [3]		
ANC <500cells mm3		
90% Confidence Interval [2]		

Preferred Term Category	Tofacitinib N=10 n (%) [1]	Placebo N=5 n(%) [1]
p-value [3]		
AST/ALT > 3xULN		
90% Confidence Interval [2]		
p-value [3]		
Hy's Law Criteria Met		
90% Confidence Interval [2]		
p-value [3]		
Hb drop >2gm/dL		
90% Confidence Interval [2]		
p-value [3]		
Increase in HDL/LDL > 50%		
90% Confidence Interval [2]		
p-value [3]		
Increase in Serum Creatinine > 50%		
90% Confidence Interval [2]		
p-value [3]		

[1] Percentages are 100*n/N.
[2] Clopper Pearson Exact confidence intervals for proportions with at least of the given AE(s).
[3] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 33: TOFA Labs Over Time. Safety Population
[1]

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
Hemoglobin	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Hematocrit	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Platelets	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
RBC	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
WBC	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Neutrophils	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Lymphocytes	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Monocytes	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Eosinophils	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Basophils	Screening	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Sodium	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Chloride	Screening	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Potassium	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
AST	Screening	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
ALT	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
Glucose	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Calcium	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
Creatinine	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
eGFR	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
Total Bilirubin	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
BUN	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
Total Protein	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Albumin	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Alkaline Phosphatase	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
ESR	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
CRP	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Total Cholesterol	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
HDL	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
LDL	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
Triglycerides	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		

[1] The safety population includes all patients randomized to TOFA who received at least one dose of study medication.
Note: Lipid panel only done at Screening and Weeks 6, 30, and 36.
Data cutoff date: DDMMYY

Table 34: TOFA Vital Signs Over Time. Safety Population [1]

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
Temperature(C)	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Respiratory Rate	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Systolic Blood Pressure	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Diastolic Blood Pressure	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Pulse	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Height(cm)	Screening	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
Weight(kg)	Screening	N		
		Mean(SD)		
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
BMI	Screening	N		
		Mean(SD)		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
	Baseline	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 6	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 30	N		
		Mean(SD)		
		Median		

Lab	Time	Status	Tofacitinib N=10	Placebo N=5
		Min, Max		
	Week 36	N		
		Mean(SD)		
		Median		
		Min, Max		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		

[1] The safety population includes all patients randomized to TOFA who received at least one dose of study medication.
Data cutoff date: DDMMYY

Table 35: TOFA Physical Examination Findings. Safety Population [1]

Body System	Time	Tofacitinib N (%)	Placebo N (%)
Head Eyes Ears Nose and Throat	Screening		
	Week 6		
	Week 12		
	Week 24		
Respiratory	Screening		
	Week 6		
	Week 12		
Cardiovascular	Screening		
	Week 12		
	Week 24		
	Week 30		
Abdomen	Screening		
	Week 6		
	Week 24		
Musculoskeletal	Screening		
	Week 6		
	Week 12		

Body System	Time	Tofacitinib N (%)	Placebo N (%)
	Week 24		
	Week 30		
Dermatological	Screening		
	Week 6		
	Week 12		
	Week 24		
	Week 30		
	Week 36		
	Week 48		

Note: Percentages are based on the number of subjects with abnormal findings in the Safety Population.
[1] The Safety Population includes all randomized subjects who received at least one dose of study medication.
Data cutoff date: DDMMYY

3.1.3. Efficacy Analyses

Table 36: TOFA Change From Baseline in mRSS Total Score. ITT Population

Status	Tofacitinib N=10	Placebo N= 5
Week 12		
N		

Status	Tofacitinib N=10	Placebo N= 5
Mean(SD)		
Median		
Min, Max		
p-value [2]		
Week 24		
N		
Mean(SD)		
Median		
Min, Max		
p-value [2]		
Week 36		
N		
Mean(SD)		
Median		
Min, Max		
p-value [2]		
Week 48		
N		
Mean(SD)		
Median		
Min, Max		

Status	Tofacitinib N=10	Placebo N= 5
p-value [2]		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests

Data cutoff date: DDMMYY

Table 37: TOFA Responder Status Relative to Baseline in mRSS Total Score. ITT Population [1]

Status	Tofacitinib N=10 n(%)	Placebo N= 5 n(%)	p-value [2]
Week 12			
At least 20% Reduction			
At least 40% Reduction			
At least 60% Reduction			
Week 24			
At least 20% Reduction			
At least 40% Reduction			
At least 60% Reduction			

[1] The ITT population includes all patients randomized to TOFA.
[2] Fisher's Exact Test
Data cutoff date: DDMMYY

Table 38: TOFA Change From Baseline in mRSS Scores. ITT Population [1]

Variable [2]	Tofacitinib N=10	Placebo N=5
Week 12		
Total Score		
N		
Mean(SD)		
Median		
Min, Max		
p-value [2]		
Representative Score		
N		
Mean(SD)		
Median		
Min, Max		
p-value [2]		
Maximum Score		
N		
Mean(SD)		
Median		
Min, Max		
p-value		

Variable [2]	Tofacitinib N=10	Placebo N=5
Week 24		
Total Score		
N		
Mean(SD)		
Median		
Min, Max		
p-value		
Representative Score		
N		
Mean(SD)		
Median		
Min, Max		
p-value		
Maximum Score		
N		
Mean(SD)		
Median		
Min, Max		
p-value		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests
Data cutoff date: DDMMYY

Table 39: TOFA Change From Baseline in Physician Global Health Assessment. ITT Population [1]

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
Week 12	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 24	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 36	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 48	N		

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
	Mean(SD)		
	Median		
	Min, Max		
	p-value		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests
Data cutoff date: DDMMYY

Table 40: TOFA Change From Baseline in Patient Global Health Assessment. ITT Population [1]

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
Week 12	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 24	N		
	Mean(SD)		
	Median		
	Min, Max		

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
	p-value		
Week 36	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 48	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests
Data cutoff date: DDMMYY

Table 41: TOFA Change From Baseline in Health-Related Quality of Life (HRQOL) using PROMIS-29. ITT Population [1]

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
Week 12	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 24	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 36	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 48	N		
	Mean(SD)		
	Median		
	Min, Max		

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
	p-value		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests
Data cutoff date: DDMMYY

Table 42: TOFA Change From Baseline in Scleroderma Health assessment Questionnaire-Disability Index (SHAQ-DI). ITT Population [1]

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
Week 12	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 24	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 36	N		

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 48	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests
Data cutoff date: DDMMYY

Table 43: TOFA Change From Baseline in UCLA SCTC Gastrointestinal Symptoms Total Score. ITT Population [1]

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
Week 12	N		
	Mean(SD)		
	Median		

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
	Min, Max		
	p-value		
Week 24	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 36	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 48	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests
Data cutoff date: DDMMYY

Table 44: TOFA Change From Baseline in Scleroderma-Related Skin Symptoms Assessed by PRO-SRSS. ITT Population [1]

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
Week 12	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 24	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 36	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value		
Week 48	N		
	Mean(SD)		
	Median		
	Min, Max		

Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
	p-value		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests
Data cutoff date: DDMMYY

Table 45: TOFA Change From Screening in PFTs.
ITT Population [1]

PFT	Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
% Predicted FVC	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
		p-value		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
		p-value		
	Week 48	N		

PFT	Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
		Mean(SD)		
		Median		
		Min, Max		
		p-value		
% Predicted FEV	Week 12	N		
		Mean(SD)		
		Median		
		Min, Max		
		p-value		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
		p-value		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
		p-value		
% Predicted DLCO	Week 12	N		
		Mean(SD)		

PFT	Time	Statistic [2]	Tofacitinib N=10	Placebo N=5
		Median		
		Min, Max		
		p-value		
	Week 24	N		
		Mean(SD)		
		Median		
		Min, Max		
		p-value		
	Week 48	N		
		Mean(SD)		
		Median		
		Min, Max		
		p-value		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests
Data cutoff date: DDMMYY

Table 46: TOFA Change From Screening to Week 24 in Left Ejection Fraction (Maximum of Range). ITT Population [1]

Time	Statistic	Tofacitinib N=10	Placebo N=5
Week 24	N		
	Mean(SD)		
	Median		
	Min, Max		
	p-value [2]		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests
Data cutoff date: DDMMYY

Table 47: TOFA Change From Screening to Week 24 in Tricuspid Regurgitation Jet. ITT Population [1]

Time	Statistic	Tofacitinib N=10	Placebo N=5
Week 24	N		
	Mean(SD)		
	Median		
	Min, Max		

Time	Statistic	Tofacitinib N=10	Placebo N=5
	p-value [2]		

[1] The ITT population includes all patients randomized to TOFA.
[2] Two-sample t-tests
Data cutoff date: DDMMYY