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Sponsor: Sanofi	**Study Identifiers:** NCT02321709, 2014-001690-13, U1111-1154-6184
Drug substance(s): SAR113244	**Study code:** TDR11407

Title of the study: A randomized, double-blind, placebo-controlled study of safety, tolerability and pharmacokinetics of repeated ascending subcutaneous doses of SAR113244 and pharmacodynamics of single dose of SAR113244 in male and female lupus patients (TDR11407)

Study center(s): 1 center in Germany

Study period:

Date first patient enrolled: 21/Nov/2014

Date last patient completed: 31/Mar/2016

Phase of development: 1

Objectives:

The primary objective was to assess the tolerability and safety of SAR113244 in male and female lupus patients after once every 4 weeks (Q4W) repeated ascending subcutaneous (SC) doses of SAR113244.

The secondary objectives were to assess in male and female lupus patients:

- The pharmacokinetics (PK) of SAR113244.
- The pharmacodynamics (PD) of SAR113244 for the following parameters:
  - Disease-related parameters: Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic lupus erythematosus disease activity index (SELENA-SLEDAI) score, British Isles Lupus Assessment Group (BILAG; if applicable), systemic lupus erythematosus (SLE) Responder Index and BILAG-based Combined Lupus Assessment values (if applicable); anti-double stranded (ds) DNA antibody levels and plasma complement levels (C3, C4), blood sedimentation (SED) rate and C-reactive protein (CRP),
  - Human CXC chemokine receptor 5 (CXCR5) receptor binding on peripheral B and T cells,
  - Serum and urine CXC chemokine ligand 13 protein (CXCL13) levels,

Peripheral blood B (including plasmablasts and double-negative memory B cells) and T cell subsets.

Methodology: Double-blind, placebo-controlled study consisting of repeated ascending doses of SAR113244 in male and female lupus patients.

Number of patients:

Planned: Up to 40

Randomized: 21 (optional 800 mg dose not administered)

Treated: 21

Evaluated:

Safety: 21

Pharmacokinetics: 15

Pharmacodynamics: 21

Diagnosis and criteria for inclusion:

Male and female lupus patients aged 18 to 75 years, inclusive, who fulfilled American College of Rheumatology or Systemic Lupus International Collaborating Clinics classification criteria for SLE for at least 6 months, with mild-to-moderate active lupus defined as SELENA-SLEDAI score in the range of 2 to 9, inclusive

Study treatments

Investigational medicinal product: SAR113244

Formulation: Vials for injection containing 1.5 mL SAR113244 (at a concentration of 100 mg/mL)

Route of administration: SC

Dose regimen: Two administrations of low dose or high dose Q4W

Investigational medicinal product: Placebo

Formulation: Vials for injection containing 0.9% isotonic saline

Route(s) of administration: SC

Dose regimen: Single doses administered identically to SAR113244

Duration of treatment: Two administrations

Duration of observation: Up to 20 weeks, including screening (within 4 weeks), observation phase from the first dose to the last assessment (112 days) including 2 treatment days within 4 weeks, and an end-of-study (EOS) visit (Day 113).

There was also a poststudy observation on Day 226 for anti-drug antibodies (ADA) assessment for those patients who were positive for ADA at the EOS visit.

Criteria for evaluation:

Safety: Patients were monitored for safety via adverse events (AEs) spontaneously reported by the patients or observed by the Investigator, standard clinical laboratory evaluations (biochemistry, hematology, urinalysis, and serology), serum immunoglobulins, peripheral blood B and T cells, immunogenicity, vital signs (heart rate, systolic and diastolic blood pressure), oral body temperature, standard 12-lead electrocardiograms (ECGs), ECG morphology, physical examination, body weight, and injection site reactions.

Pharmacokinetics: The following PK parameters were calculated for SAR113244 plasma concentrations using noncompartmental methods: maximum plasma concentration observed (C_{max}), first time to reach C_{max} (t_{max}), area under the plasma concentration versus time curve calculated using the trapezoidal method during a dosage interval (AUC_{0-4w}), terminal half-life associated with the terminal slope ($t_{1/2z}$), apparent total body clearance of a drug at steady state from the plasma (CL_{ss}/F), and apparent volume of distribution at the steady state after repeated dose (V_{ss}/F).

Pharmacodynamics: Disease-related biomarkers (anti-dsDNA antibodies, antinuclear antibody [ANA] levels, plasma complement levels, blood SED rate and CRP, anti-Smith, anti-Ro, anti-La, and anti-cardiolipin); disease activity and quality of life scales (SELENA-SLEDAI, BILAG, Physical Global Assessment [PGA], Lupus-Quality of Life [QoL], and Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue), CXCR5 receptor occupancy (RO) on B cells, CXCR5 expression on peripheral B- and T-cells, serum and urine CXCL13 levels, and peripheral blood B and T cell subsets.

Pharmacokinetic sampling times and bioanalytical methods:

Blood samples for the determination of SAR113244 concentrations in plasma were collected at the following times: Day 1 (prior the first dose), Day 2 (24 hours), Day 8 (168 hours), Day 15 (336 hours), Day 29 (prior the second dose, ie 672 hours), Day 30 (696 hours), Day 36 (840 hours), Day 43 (1008 hours), Day 57 (1344 hours), Day 71 (1680 hours), Day 85 (2016 hours) and Day 113 (EOS, 2688 hours).

SAR113244 concentrations were determined in plasma using a validated enzyme-linked immunosorbent assay (ELISA) method with a lower limit of quantification (LLOQ) of 0.04 µg/mL.

In addition, blood samples for immunogenicity assessment were collected at the following times: Day 1 (prior to the first dose), Day 15 (high dose treatment only), Day 29 (prior to the second dose), Day 43 (high dose treatment only), Day 57, Day 85, and Day 113 (EOS). For patients testing positive for ADA on Day 113 (EOS), a last sample was collected on Day 226. The ADA assay was performed using a validated ELISA method.

Pharmacodynamic sampling times and bioanalytical methods:

Samples for the determination of CXCR5 RO on peripheral B cells, and samples for determination of serum and urine CXCL13 were collected at the following times: Days 1 (predose), 8, 15, 29 (predose), 36, 43, 57, 85, and 113.

CXCR5 on the cell surface of B-lymphocytes bound with drug was assessed in whole blood samples using a validated assay and was established on the basis of the CellQuant Calibrator (BioCytex).

CXCL13 was quantified in serum using a validated ELISA method, and in urine using an exploratory ELISA method.

Statistical methods:

Safety: The safety evaluation was based upon the review of the individual values (clinically significant abnormalities) and descriptive statistics (summary tables, graphics). All the safety analyses were performed on the safety population.

For AEs, frequencies of treatment-emergent adverse events (TEAEs) and adverse events of special interest (AESIs) classified by Medical Dictionary for Regulatory Activities (version 18.1) system-organ class and preferred term were tabulated by treatment group.

Counts of patients with potentially clinically significant abnormalities (PCSAs, version 24 May 2014) in clinical laboratory, ECG and vital sign evaluations were summarized by treatment group for each parameter.

Descriptive statistics were provided by treatment group for laboratory data, ECG, vital signs, serum immunoglobulins, and total peripheral blood B and T cells. For local tolerability data, descriptive statistics of the individual erythema and edema peak diameter classification, as well as maximum pain intensity and other skin reactions were provided by treatment group.

For ADA data, the number and percent of patients with pre-existing ADA at baseline was summarized by treatment group; the counts and percent of each ADA status (negative, positive, and inconclusive) and substatuses for positive patients (ie, treatment-boosted ADA patients and treatment-induced ADA patients subdivided in ADA persistent and transient patients) during the study were described by treatment group. Other endpoints (peak titer, time to onset and ADA duration) for treatment-induced ADA patients were also derived and tabulated by treatment group.

Pharmacokinetics: PK parameters of SAR113244 were summarized by descriptive statistics for each treatment. Dose accumulation was assessed using a linear fixed effects model for C_{max} and $AUC_{0\text{-}4w}$. Dose effect was assessed using a linear fixed effects model on log-transformed $t_{1/2z}$. Dose proportionality for C_{max} and $AUC_{0\text{-}4w}$ was assessed using pairwise comparisons for each parameter that was log-transformed. Within-patient and total standard deviations for $\log(C_{max})$ and $\log(AUC_{0\text{-}4w})$ were estimated by equating observed and expected mean squares within the following linear mixed effects model framework.

Pharmacodynamics: Each PD variable was summarized by descriptive statistics by scheduled time for each treatment group, on raw data and change from baseline. Time profile plots of mean (± SEM) raw data, absolute and/or percent change from baseline (depending on the parameters) were also produced by treatment group for selected parameters.

Summary :

Population characteristics:

Of the 21 lupus patients randomized and treated in the study, 19 completed the study treatment period. A total of 16 patients received SAR113244 and 5 patients received placebo. One patient receiving low dose Q4W and 1 patient receiving high dose Q4W withdrew their consent and discontinued from the study early.

At baseline, 1/5 (20.0%) patients receiving placebo was <45 years of age compared to 7/10 (70.0%) patients receiving high dose Q4W. Three of 6 patients (50.0%) receiving low dose Q4W were <45 years of age.

The majority of patients (19/21) were female. All patients receiving SAR113244 were female, 3/5 (60.0%) patients receiving placebo were female and 2/5 (40.0%) were male. The majority of patients (20/21) were Caucasian/White and 1/21 patient receiving high dose Q4W was Asian/Oriental.

Overall, mean disease duration was approximately 10 years. All patients tested positive for ANA at screening and all patients apart from 1 (in the placebo treatment group) tested positive for ANA at baseline. The ADA titers ranged from 0 to 200 IU/mL at screening and from 14 to 500 IU/mL at baseline. All patients had negative QuantiFERON TB Gold Test results at screening.

Overall total SELENA-SLEDAI scores ranged from 2 to 8 at screening and from 4 to 10 at baseline. Overall PGA of disease activity ranged from 9 to 52 mm on Day 1. A total of 12/21 (57.1%) patients were receiving ongoing treatment with prednisolone (total dose ranging from 2.5 to 15 mg) at screening.

Safety results:

The most frequently reported TEAEs (reported in >2 patients) were nasopharyngitis and headache, reported in all treatment groups, and injection site erythema, reported only in patients receiving SAR113244. Postural dizziness, procedural dizziness, and nausea were each reported in 2 patients, and all other TEAEs were single occurrences. There did not appear to be any dose related trends in the type or incidence of AEs reported.

Injection site reactions such as erythema (in 5 patients) and itch (in 1 patient) were reported among the16 patients receiving SAR113244, with no dose relationship. All events of injection site erythema were of mild intensity.

The TEAEs of injection site erythema in Patient Nos. 276001003 and 276001011 in the low dose treatment group, and Patient No. 276001041 in the high dose treatment group each lasted for over 24 hours and were, therefore, reported as AESIs.

One serious adverse event (SAE) occurred during the study; Patient No. 276001048 in the placebo treatment group experienced postmenopausal hemorrhage. This SAE was considered moderate in intensity and not related to the investigational medicinal product (IMP). Study treatment was not changed as a result of this SAE.

There were a few PCSAs for laboratory assessments and vital signs both in patients treated with SAR113244 and the placebo group, with no dose- or treatment-related trends. Few PCSAs for heart rate and QTcF were reported only in patients receiving SAR113244. No QTcF values >480 ms or QTcF increase from baseline >30 ms were reported in any patient.

SAR113244 had no relevant effect on the level of peripheral blood total B and T cells, or immunoglobulins IgA, IgD, IgE, IgG, or IgM.

Pharmacokinetic and ADA results:

SAR113244 plasma concentrations were below the LLOQ in all predose samples on Day 1, for each dose level.

SAR113244 PK parameters after the first and the second dose are summarized in the 2 tables below

SAR113244 plasma PK parameters after the 1st dose of SAR113244

Mean ± SD (Geometric Mean) [CV%]	Plasma SAR113244	
	Low dose	High dose
N	6	9
C_{max}	9.37 ± 3.06	21.3 ± 7.28
(µg/mL)	(9.02) [32.7]	(20.1) [34.1]
t_{max} [a]	168.90	167.95
(h)	(167.85 - 337.53)	(24.00 - 168.95)
AUC_{0-4W}	4410 ± 1560	9040 ± 3300
(µg.h/mL)	(4220) [35.3]	(8470) [36.5]

a Median (Min - Max)
Profile of Subject 276001019 was excluded
Source = PKS Study : TDR11407; Scenario: P-X-A-EV-OD, Version 11
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SAR113244 plasma PK parameters after the 2nd dose of SAR113244		
Mean ± SD (Geometric Mean) [CV%]	**Plasma SAR113244**	
	Low dose Q4W	**High dose Q4W**
N	5	9
C_{max}	15.3 ± 4.09	28.6 ± 11.5
(µg/mL)	(14.9) [26.7]	(26.4) [40.2]
t_{max} [a]	168.38	168.00
(h)	(168.00 - 169.75)	(24.00 - 169.92)
AUC_{0-4W}	6800 ± 2480	13500 ± 5930
(µg.h/mL)	(6520) [36.4]	(12300) [43.9]
$t_{1/2z}$	167 ± 62.2	286 ± 133
(h)	(159) [37.2]	(256) [46.5]
CL_{ss}/F	0.0396 ± 0.00992	0.0450 ± 0.0219
(L/h)	(0.0383) [25.0]	(0.0407) [48.7]
V_{ss}/F	17.9 ± 5.90	24.2 ± 12.2
(L)	(17.3) [32.9]	(22.2) [50.3]

[a] Median (Min - Max)
Source = PKS Study : TDR11407; Scenario: P-X-B-EV-OD, Version 6
Date/Time = 9/13/2016 3:53:43 PM

For both doses, median t_{max} was observed 7 days after the first dose and after the second dose.

As described in the table below, over the range low dose to high dose, for a 2.0-fold increase in dose, mean SAR113244 C_{max} and AUC_{0-4W} increased by 2.23- and 2.01-fold, respectively after a first dose, and by 1.77 and 1.88-fold, respectively after a second dose. Exposure increased with no major deviation from dose proportionality.

Day	Parameter	Dose ratio	Estimate	90% CI
Day 1	C_{max} (ug/mL)	(Ratio low dose / high dose) = 2	2.23	(1.61 to 3.08)
	AUC_{0-4w} (ug.h/mL)	(Ratio low dose / high dose) = 2	2.01	(1.42 to 2.82)
Day 29	C_{max} (ug/mL)	(Ratio low dose / high dose) = 2	1.77	(1.20 to 2.59)
	AUC_{0-4w} (ug.h/mL)	(Ratio low dose / high dose) = 2	1.88	(1.24 to 2.87)

PGM=PRODOPS/SAR113244/TDR11407/CSR/REPORT/PGM/pk_tdr11407.sas.sas OUT=REPORT/OUTPUT/pk_dp_k_t_2_i.rtf (19SEP2016 - 10:41)

After the administration of 2 doses of SAR113244 within 4 weeks, accumulation ratios pooled over low dose and high dose were of 1.47 for C_{max} and of 1.50 for AUC_{0-4W}, as described in the table below.

Parameter	Comparison	Estimate	90% CI
Rac (C_{max})	SAR113244 low dose Q4W	1.64	(1.38 to 1.94)
	SAR113244 high dose Q4W	1.31	(1.16 to 1.49)
	Pooled SAR113244 doses	1.47	(1.32 to 1.63)
Rac (AUC_{0-4w})	SAR113244 low dose Q4W	1.55	(1.34 to 1.78)
	SAR113244 high dose Q4W	1.45	(1.31 to 1.61)
	Pooled SAR113244 doses	1.50	(1.37 to 1.64)

PGM=PRODOPS/SAR113244/TDR11407/CSR/REPORT/PGM/pk_tdr11407.sas.sas OUT=REPORT/OUTPUT/pk_ac_k_t_2_i.rtf (19SEP2016 - 10:38)

No dose effect on $t_{1/2z}$ was observed. When pooled over the low dose to high dose range, the estimate of $t_{1/2z}$ geometric mean was of 202 hours, ie, 8.4 days.

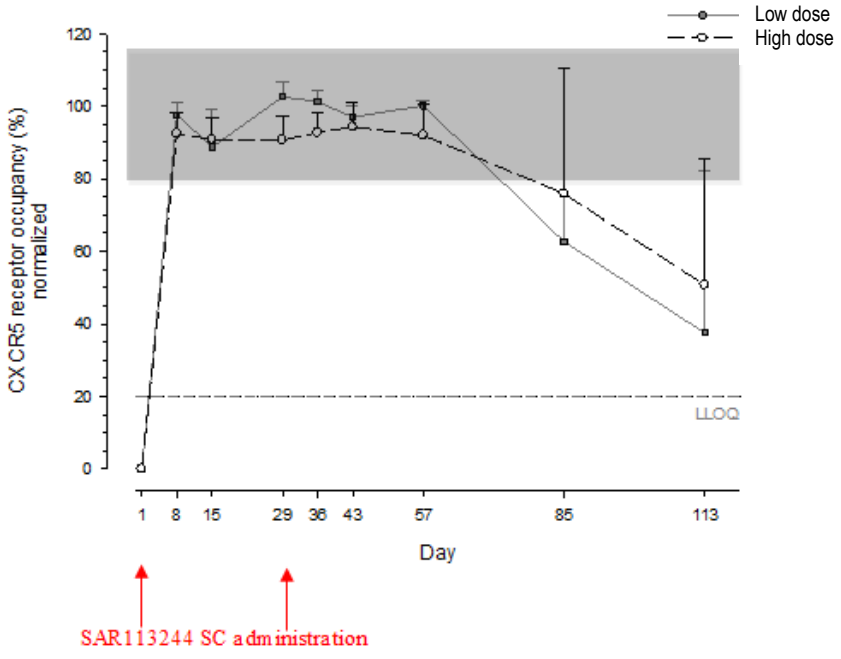
Total variability for SAR113244 C_{max} and AUC_{0-4W} was moderate with respectively 36.6% and 39.5%. Within-subject variability for C_{max} and AUC_{0-4W} was low with respectively 15.0% and 12.5%.

Anti-drug antibodies were not detected in any patients receiving placebo or in any patients prior to the administration of SAR113244. The incidence of treatment-induced ADA in patients receiving low dose Q4W SAR113244 and patients receiving high dose Q4W SAR113244 was 66.7% (4/6) and 20.0% (2/10), respectively. Overall, treatment-induced ADA were detected in 37.5% patients treated with SAR113244.

Pharmacodynamic results:

CXCR5 occupancy

Mean normalized SAR113244 occupancy to CXCR5 on B lymphocytes versus time following a 1st dose and a 2nd dose of Low dose and High dose SAR113244.



Grey zone: saturation is considered to be reached (threshold of RO%>80% based on assay method precision, approximately 20%).

Saturation of CXCR5 by SAR113244 occurred by 7 days after the first dose for all patients at low dose and high dose. The duration of saturation relative to the second dose was 42 days as median value at low dose, and appeared to increase to 56 days as median value at high dose. For both dose groups, normalized RO% had decreased out of the saturation zone by Day 113 in 10/12 patients (in some patients to <LLOQ), although normalized RO% >80% was still observed for 2 patients on Day 113 (1 patient each in the low dose and high dose SAR113244 groups).

Disease-related markers

There did not appear to be any treatment- or dose-related trends in mean percent change from baseline in the anti-dsDNA antibody values from baseline to each of the scheduled visits.

In the placebo treatment group, 4/5 (80%) patients tested positive for ANA on Day 1 (2/5 with a titer of 1:640, 1/5 with a titer of 1:160, and 1/5 with a titer of 1:320), and 5/5 (100%) patients tested positive for ANA on Day 113 (1/5 with a titer of 1:40, 1/5 with a titer of 1:160, 1/5 with a titer of 1:320, 1/5 with a titer of 1:640, and 1/5 with a titer of 1:2560). All patients in the low dose and high dose SAR113244 treatment groups with analyzable samples tested positive for ANA on both Day 1 and Day 113. In the low dose SAR113244 treatment group, at Day 1, 3/6 patients had a titer of 1:80 and 3/6 patients had a titer of 1:160. At Day 113, 1 patient's sample was missing, 1/5 patients had a titer of 1:40, 1/5 patients had a titer of 1:80, 1/5 patients had a titer of 1:160, and 2/5 patients had a titer of 1:320. In the high dose SAR113244 treatment group, at Day 1, 2/10 patients had a titer of 1:40, 1/10 patients had a titer of 1:80, 4/10 patients had a titer of 1:160, 2/10 patients had a titer of 1:320, and 1/10 patients had a titer of 1:640. At Day 113, 1/10 patients had a titer of 1:40, 5/10 patients had a titer of 1:160, 2/10 patients had a titer of 1:320, 1/10 patients had a titer of 1:640, and 1/10 patients had a titer of 1:2560.

There did not appear to be any treatment- or dose-related trends in mean percent change from baseline in plasma complement levels C3 or C4 from baseline to each of the scheduled visits.

There did not appear to be any treatment- or dose-related trends in mean percent change from baseline in blood SED rate or CRP from baseline to each of the scheduled visits.

All patients with analyzable samples in the placebo treatment group and the high dose SAR113244 treatment group tested negative for the anti-Smith antibody on Day 1 and Day 113. Four of 5 (80.0%) patients in the low dose SAR113244 treatment group tested negative for the anti-Smith antibody on Day 1 and all patients in the low dose SAR113244 treatment group with analyzable samples tested negative for the anti-Smith antibody on Day 113. On Days 1 and 113, 3/5 (60.0%) patients and 2/4 (50.0%) patients, respectively, in the placebo treatment group tested negative for the anti-Ro/SS-A antibody. On Days 1 and 113, 4/5 (80.0%) patients in the low dose SAR113244 treatment group tested negative for the anti-Ro/SS-A antibody. On Days 1 and 113, 7/8 (87.5%) patients and 8/10 (80.0%) patients, respectively, in the high dose SAR113244 treatment group tested negative for the anti-Ro/SS-A antibody.

On Days 1 and 113, 4/5 (80.0%) patients and 3/4 (75%) patients, respectively, in the placebo treatment group tested negative for the anti-La/SS-B antibody. All patients with analyzable samples in the low dose SAR113244 treatment group tested negative for the anti-La/SS-B antibody on both Day 1 and Day 113. On Days 1 and 113, 7/8 (87.5%) patients and 9/10 (90.0%) patients, respectively, in the high dose SAR113244 treatment group tested negative for the anti-La/SS-B antibody.

All patients with analyzable samples in the placebo and low dose SAR113244 treatment groups tested negative for anti-cardiolipin antibody (IgG) on Days 1 and 113. On Day 1, 8/9 (88.9%) patients in the high dose SAR113244 treatment group tested negative for the anti-cardiolipin antibody (IgG) and 1/9 (11.1%) patient tested positive. On Day 113, 9/10 (90.0%) patients in the high dose SAR113244 treatment group tested negative for the anti-cardiolipin antibody (IgG), and 1/10 (10.0%) patient tested positive.

All patients with analyzable samples across treatment groups tested negative for the anti-cardiolipin antibody (IgM) on Day 1 and Day 113.

Disease activity and quality of life scales

Mean total SELENA-SLEDAI scores were similar across treatment groups throughout the study, and ranged from 0 to 10. Mean changes from baseline in total score were all <1.3 throughout the study for all treatment groups. BILAG scores at baseline compared to Day 113 were similar. SAR113244 did not appear to have any effect on BILAG scores.

Mean PGA scores were similar across treatment groups from baseline to Day 113. In the high dose SAR113244 treatment group, mean change from baseline in PGA score at Day 113 was an increase of 8.8 in the high dose SAR113244 treatment group compared to a decrease of 5.6 and 0.5 in the placebo and low dose SAR113244 treatment groups, respectively.

Lupus-QoL scores at baseline compared to Day 113 were similar. SAR113244 did not appear to have any effect on Lupus-QoL scores. FACIT-Fatigue scores at baseline compared to Day 113 were similar. SAR113244 did not appear to have any effect on FACIT-Fatigue scores.

Serum CXCL13 levels

No treatment- or dose-related trends were apparent in the CXCL13 concentration data from the time of baseline to Day 113.

Peripheral blood B and T cell subsets

Following dosing with SAR113244 and placebo, several B cell subsets were examined by flow cytometry. Frequencies were determined out of the lymphocytes expressing CD20. For naïve B cells, (CD19+CD27-IgD+), the mean percentage ranged from approximately 59.8% to 64.7% across all postbaseline time points (baseline ranged from 62.0% to 64.5%). For pre-switch memory B cells (CD19+CD27+IgD+), the mean percentage ranged from approximately 6.0% to 8.1% (baseline ranged from 6.5% to 7.9%). For post-switch memory B cells (CD19+CD27+IgD-), the mean percentage ranged from approximately 19.8% to 23.3% (baseline ranged from 19.8% to 21.5%). For double-negative memory B cells (CD19+CD27-IgD-), the mean percentage ranged from approximately 7.4% to 10.6% (baseline ranged from 8.7% to 9.2%).

The baseline percentage of cells expressing CXCR5 for each subset is as follows: naïve B cells 98.4% to 99.2%; pre-switch memory B cells 98.1% to 99.1%; post-switch memory B cells 94.1% to 94.2%; and double-negative memory B cells 63.5% to 79.2%.

Following dosing with SAR113244 on Day 1, a decrease in CXCR5 receptors by SAR113244 was observed at Day 8 (first visit postdose) in the high dose SAR113244 treatment group and at Day 15 (first visit postdose) in the low dose SAR113244 treatment group. Maximal occupancy appeared to continue to Day 85 (last available time point) in the high dose SAR113244 treatment group and Day 43 in the low dose SAR113244 treatment group; by Day 85, RO appeared to be returning to baseline levels.

Following dosing with low dose Q4W SAR113244 on Day 1, of the lymphocytes expressing CD19, the frequency of CD19+CD20+ cells appeared to decrease until Day 15 (baseline: 94.6%, Day 15: 81.0%) and then steadily increase from Day 15 to Day 85 (Day 29: 84.3%, Day 43: 86.7%) returning to levels similar to those observed at baseline (Day 85: 92.0%). The frequency of CD19+CD20-CD27++ cells (antibody-secreting cells), following dosing with low dose Q4W SAR113244 on Day 1, appeared to increase transiently in some patients, returning by Day 85 to levels similar to those observed at baseline. These B cell subsets did not appear to be consistently affected by SAR113244 in the high dose SAR113244 treatment group.

The frequencies of total T cells and T cell subsets were determined.

Following dosing with SAR113244 and placebo, several T cell subsets were examined by flow cytometry. Frequencies were determined out of the lymphocytes expressing CD3. For helper T cells (CD4+), the mean percentage ranged from approximately 51.4% to 70.5% across all postbaseline time points (baseline ranged from 53.6% to 69.5%). For cytotoxic T cells (CD8+), the mean percentage ranged from approximately 21.0% to 38.8% across all postbaseline time points (baseline ranged from 22.1% to 38.9%).

For naïve T cells (CD45RA+CCR7+), of the CD4+ cells, the mean percentage ranged from approximately 41.9% to 50.5% across all postbaseline time points (baseline ranged from 44.8% to 49.0%); of the CD8+ cells, the mean percentage ranged from approximately 38.8% to 53.3% across all postbaseline time points (baseline ranged from 45.8% to 52.4%).

For central memory T cells (CD45RA-CCR7+), of the CD4+ cells, the mean percentage ranged from approximately 25.0% to 30.0% across all postbaseline time points (baseline ranged from 24.9% to 28.1%); of the CD8+ cells, the mean percentage ranged from approximately 3.3% to 8.5% across all postbaseline time points (baseline ranged from 3.6% to 9.0%).

For effector memory T cells (CD45RA-CCR7-), of the CD4+ cells, the mean percentage ranged from approximately 19.9% to 26.6% across all postbaseline time points (baseline ranged from 21.4% to 26.9%), of the CD8+ cells, the mean percentage ranged from approximately 18.2% to 35.2% across all postbaseline time points (baseline ranged from 16.1% to 28.7%).

The mean percentage of CD4+ cells that expressed CXCR5+ at baseline ranged from approximately 8.7% to 17.2%.

Issue date: 23-Mar-2021