STATISTICAL ANALYSIS PLAN

Protocol N° BPS0115 / OP099516.DOM – Part A

Version 1.0 - Date: April 05, 2019

An Ascending Dose Tolerability Study and Pharmacokinetic Assessment in Healthy Male and Female Volunteers after Single & Multiple Oral Administration of DF2755A

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DOCUMENTATION HISTORY

Version	Effective date	Reason for change
Draft 1.1	February 6, 2018	Document creation by Eurofins Optimed
Draft 1.2	May 30, 2018	Integration of Pharmacokineticc analysis by PhinC development
Draft 2	October 24, 2018	Document sent to sponsor for reading
Draft 3	April 04, 2019	Integration of sponsor comments
Version 1.0	April 05, 2019	Final version

LIST OF ABBREVIATIONS

General terms

a.m.	Ante meridian
EOS	End Of Study Visit
ICH	International Conference on Harmonization
IMP	Investigational Medicinal Product
MAD	Multiple administration dose
MedDRA	Medical Dictionary for Regulatory Activities
NTEAE	Non-Treatment Emergent Adverse Event
SAD	Single administration dose

Safety & medical

AE	Adverse Event
BP	Blood pressure
bpm	beats per minute
BW	Body Weight
ECG	Electrocardiogram
HR	Heart Rate
IV	Intravenous
SAE	Serious Adverse Event
SBP	Systolic Blood Pressure
TEAE	Treatment Emergent Adverse Event

Biologics

ALT	Alanine Leucine Transferase
AST	Alanine serine transferase
CHC	Chronic viral hepatitis C
CPK	Creatine phosphokinase
GGT	Gamma Glutamy1 Transferase
HBs	Hepatitis B surface antigen
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus
HIV1	Human Immunodeficiency Virus type 1
HIV2	Human Immunodeficiency Virus type 2
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
PNM	Polimorphonuclear leukocytes
ROS	Reactive Oxygen Spieces
WBC	White Blood Cells

Bioanalysis

ALQ	Above limit of quantification
LOQ	Limit of quantification
ULOQ	Upper limit of quantification

Pharmacokinetics

$\mathbf{A_{e,ur}}$	Amount excreted in urine
$\mathbf{A_{e,f}}$	Amount excreted in feces

AUC	Area under the plasma concentration-time curve
AUC_{0-t}	Area under the plasma concentration-time curve from time zero to the final time point
$AUC_{0-\infty}$	Area under the plasma concentration-time curve from time zero to infinity
AUC_{0-24}	Area under the plasma concentration-time curve from time zero to 24 hours post-dosing
CL/F	Apparent clearance
CL_R	Renal clearance
C_{max}	Maximum plasma concentration
$f_{e,ur}$	Percentage of the dose excreted in the urine
$f_{e,f}$	Percentage of the dose excreted in the feces
PK	Pharmacokinetic(s)
$t_{1/2}$	Terminal half-life
t_{last}	Time of last measurable concentration
t_{max}	Time of maximum plasma concentration
Vz/F	Apparent volume of distribution
λ_z	Terminal phase rate constant

Statistics

CI	Confidence Interval
GM	Geometric mean
Min	Minimum
Max	Maximum
N	Number
PDS	Pharmacodynamic set
PKS	Pharmacokinetic set
RS	Randomized set
SD	Standard Deviation
SEM	Standard Error of the Mean
SS	Safety set

1 INTRODUCTION

In accordance with the main characteristics of the protocol, the Statistical Analysis Plan (SAP) details that the scheduled analyses are to be performed in order to evaluate the tolerability and safety of ascending single and repeated doses of DF2755A in healthy adult male and female volunteers.

Study design

The study is a phase I, single center, double-blind, placebo controlled, randomized, ascending single and repeated doses study in healthy male and female volunteers.
The design consists of a double blind comparison of the test compound versus placebo in which the dose is increased in successive treatment periods.
The Multiple Ascending Dose (MAD) will be initiated only after the authorization, from ANSM of a substantial amendment that will be presented in order to notify the results of Single Ascending Dose (SAD) part of the study. Besides in order to decide to move forward from SAD to MAD, the pharmacokinetic data for all doses administered during SAD will be evaluated (i.e. plasma: quantitative determination of DF2755A bound and unbound; qualitative and preliminary quantitative determination of known metabolites; urine and faeces: qualitative and quantitative determination of parent compound and qualitative and preliminary quantitative investigation of known metabolites).
Dose will be escalated in order to achieve enough safety information on an interval of doses possibly encompassing both the effective dose and the maximum tolerated dose (defined as the highest dose devoid of any clinical signs/symptoms).

Part A: Single doses of 50 mg oad, 150 mg oad, 450 mg oad or 700 mg oad of DF2755A are planned to be tested in healthy male and female volunteers.

Objectives of the study

Primary objectives

- To evaluate the tolerability and safety of ascending single and repeated doses of DF2755A in healthy adult male and female volunteers.

Secondary objectives

- To determine the pharmacokinetics parameters of DF2755A.
- To establish a dose concentration-response relationship over a wide range of doses in order to select a narrower range of dose and dosing regimen to be subsequently studied in patients after single and multiple administration.
- To evaluate the effect of ascending single and repeated doses on the pharmacodynamics parameters.
- To compare metabolites pathway in Human with the one observed in animals.

Criteria for evaluation

Primary evaluation criteria:
AE, vital signs, 12-lead ECG, physical examination, laboratory exams.

Secondary evaluation criteria:

Pharmacokinetics: measurement of pharmacokinetics parameters: C_{max}, t_{max}, λ_z, $t_{1/2}$, AUC_{0-t}, $AUC_{0-\infty}$, V_z/F, CL/F, $A_{e,ur}$, $A_{e,f}$, $f_{e,f}$, $f_{e,ur}$, CL_R, parent:metabolite(s) ratio.

Pharmacodynamics: measurement of leukocyte markers: CD11b, CD18 and reactive oxygen species (ROS).

Study schedule

Table 1: STUDY FLOW CHART – PART A: from cohort 1 to cohort 4

Visit/Period	Screening	Inclusion	Treatment period			End of study visit
Day	D-21 to D-2	D-1	D1	D2	D3	D4
Informed consent	X					
Inclusion/Exclusion criteria[1]	X	X				
Previous Medical / Surgical History	X					
Prior/concomitant medications	X	X	X	X	X	X
Physical/Medical examinations	X	X				X
Body weight, height	X	X				X
Haematology	X	X		X		X
Hemostasis	X	X		X		X
Biochemistry	X	X		X		X
Urinalysis	X	X		X		X
Serology	X					
Urine test for drug abuse	X	X				
Alcohol breath test	X	X				
Admission		X				
Discharge						X
Randomization			X			
Study Drug / Placebo Administration[2]			X			
Vital signs : Blood pressure / Heart rate / Oral body temperature	X	X	X	X		X
12-lead ECG recording[3]	X	X	X	X	X	X
Blood sample for Pharmacokinetics			X	X	X	X
Blood sample for Pharmacodynamic[5]			X	X	X[6]	X[6]
Urine collection		X	X	X	X	X
Faeces collection		X	X	X	X	X
AE collection[4]	⟷					

[1]Confirmation of the Inclusion/exclusion criteria prior to randomization number assignment;
[2]Dose: Cohort 1, 2; 3 & 4; Single dose in the morning; All subjects will be in fasting conditions from the evening before (at least 10 h, overnight);
[3]Safety ECG;
[4]All AEs will be reported
[5] Starting only from the second ascending dose;
[6] T48h or T72h: time will be determined after results of the first dose administered.
When ECG, vital signs and PK are required at the same time, this specific order will be followed: vital signs first, then ECG and blood sample for PK at the end.

Table 2: DETAILED FLOW CHART – PART A

Visit/Period	Inclusion	Treatment period																				
Day	D-1	D1														D2			D3		D4	
Theoretical time (h)		Pre dose	T0	T0,5	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	T12	T16	T24	T36	T40	T48	T60	T72	
Inclusion/Exclusion criteria	X																						
Prior/concomitant medications																							
Physical/Medical examinations	X																					X	
Body weight; height	X																					X	
Haematology	X																X					X	
Hemostasis	X																X					X	
Biochemistry	X																X					X	
Urinalysis	X																X					X	
Urine test for drug abuse	X																						
Alcohol breath test	X																						
Admission	X																						
Discharge																						X	
Randomization			X																				
Study Drug Administration			X																				
Blood pressure / Heart rate / Oral Body Temperature	X	X			X		X		X			X			X		X					X	
12-lead ECG recording	X	X			X	X	X	X		X		X			X		X			X		X	
Blood sample for Pharmacokinetics		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Blood sample for Pharmacodynamics		X	Cmax then Cmax +3h												X		X			X[1]		X[1]	
Urine collection	X		X								X					X		X			X		
Faeces collection	X		X							X								X			X		
AE collection																							

[1] T48h or T72h: time will be determined after results of the first dose administered

2 DEFINITION OF POPULATIONS AND STUDY TREATMENTS

2.1 Randomization

The randomization list was prepared to permit that one of the two first subjects treated per each cohort, received a placebo.
The treatments were allocated at D1 for both parts.

2.2 Justification for number of subjects

No formal sample size calculation was made. The subjects treated with test product and the subjects treated with placebo are considered sufficient to detect drug effects and determine pharmacokinetic parameters before escalating to the next dose level.

SAD cohorts: Thirty -two (**32)** healthy volunteers (HV) + 4 reserve subjects (total 36) will be enrolled to have 4 groups. Three groups of eight (8) male subjects and one group of 4 M +4 F.

MAD cohorts: MAD cohorts: Thirty -six (36) healthy volunteers (HV) + 4 reserve subjects (total 40) will be enrolled to have 3 groups. Two groups of twelve (12) male subjects and group of 6M+6 F.

2.3 Screening, inclusion and randomization numbers

The screening number was S and 3 digits, for example: S003. It was a chronological number. The screening number was used throughout the screening period, until subjects are randomized.

The inclusion number was composed of 7 digits, 3 for the number of centre (001) and 4 for the inclusion number: from 1001 to 1032 for part A. It will be a chronological number.

The randomization number was the same as the inclusion number and the treatment number.

2.4 Analysis populations

The Randomized set (RS) will be defined as all randomized subjects.

The Safety set (SS) will be defined as all included subjects having taken at least one dose of study drug.

The pharmacokinetic set (PKS) will be defined as all the included subjects who have taken at least one dose of study drug without major protocol deviations affecting pharmacokinetics and with available data.

The pharmacodynamic set (PDS) will be defined as all the included subjects who have taken at least one dose of study drug without major protocol deviations affecting pharmacodynamics and with available data.

2.5 Study treatment

Name of the compound:	DF2755A
Pharmaceutical form:	Capsules of 50 mg, and 200 mg
Dose per administration:	Part A: 50 mg oad, 150 mg oad, 450 mg oad or 700 mg oad
Timing for administration:	Part A: Single oral dose administration on D1 according to the randomization. The administration will take place at around 8:00 a.m with 200 ml of tap water, in sitting position, in fasting conditions.

Name of the compound:	Placebo
Pharmaceutical form:	Matching capsule
Dose per administration:	NA
Timing for administration:	Part A: Single oral dose administration on D1 according to the randomization. The administration will take place at around 8:00 a.m with 200 ml of tap water, in sitting position, in fasting conditions.

3 STATISTICAL ELEMENTS

The statistical analysis performed by EUROFINS OPTIMED pertains to description at baseline, conduct of the study and safety analysis with statistical software SAS (version 9.4).

The pharmacokinetic statistical analysis will be performed by PhinC Development.

The Correlation analysis between pharmacokinetic and pharmacodynamic parameters will be performed by EUROFINS OPTIMED.

Interim analysis: For each part of the study, an interim PK analysis on DF2577Y (the acid form of DF2755A) and its metabolites (if any) will be performed after completion of each dose level. This analysis will be done on anonymized data provided by the bioanalytical center to prevent any violation of the double blind condition of the study.

Final PK analysis will be performed using final validated bioanalytical data and actual PK blood sampling times.

For safety parameters (laboratory safety parameters, vital signs, ECG), in case of repeat assessments, the last assessment prior to the administration of the study treatment and the first assessment after the administration will be used for descriptive statistics. All assessments, including the repeat assessment will be included in the data listings and will be flagged accordingly.

3.1 Statistical methods

The methodology presented in this statistical analysis plan takes into account methods planned in the protocol.

3.2 Descriptive statistics

At least the following descriptive statistics will be reported:

- *Continuous variables*: Number of observations (N), mean, standard deviation (SD), standard error of the mean (SEM) minimum (Min), median and maximum (Max).
- *Categorical variables*: Frequency (n) and percentage (%).

3.3 Statistical tests

Safety analysis

The safety analysis will be descriptive.

Pharmacokinetic analysis

In the first time, pharmacokinetic analysis will be performed for the single ascending dose part (part A).

- Descriptive statistics for drug concentrations:

  For descriptive statistics, individual bound and unbound plasma concentrations of DF 2577Y and its related metabolites will be presented by dose level and nominal time points, when applicable.

  Descriptive statistics for the plasma concentrations will be presented as number of available data (N), mean, standard deviation (SD) and will be calculated if at least 2/3 of the plasma values per time-point are above LOQ. For descriptive statistics calculations, concentrations below LOQ will be set to zero (0) if they are reported before the first quantifiable sample or considered as missing data if they are reported after the first quantifiable data.

  Individual measured plasma concentration *vs.* actual time curve will be produced in graphic for each compound (parent and metabolites), for each subject, for each dose level on both linear/linear and log/linear scales where applicable. Similarly, mean plasma concentration *vs.* time curves will also be produced for each dose level.

- Derivation of PK parameters and descriptive statistics for PK parameters:

  For the calculation of the PK parameters from plasma concentrations of DF2755Y and its metabolites (if any) using NCA approach the following rules will be applied:

  - All the plasma concentrations validated by the bioanalytical laboratory and provided to the pharmacokineticist will be used for the PK analysis.
  - The actual blood sampling time points related to the preceding administration will be used.
  - At time points in the lag-time between time zero and the first concentration equal or above the limit of quantification (LOQ), concentrations below LOQ will be set to zero (0). Concentrations below LOQ between 2 concentrations equal or above LOQ will be considered as missing data. Trailing concentrations below LOQ will not be used in calculations.
  - For plasma concentration above the upper limit of quantification (ULOQ) and reported as above the limit of quantification (ALQ) in the final plasma concentration tables, ALQ will be replaced by the first measurement for the PK analysis.
  - Not reported concentration (NR) will be excluded from the PK analysis.
  - Pre-dose concentration is less than or equal to 5% of C_{max} value in a PK profile, the subject's data can be included in all PK measurements and calculations without any adjustments. If the pre-dose value is greater than 5% of C_{max}, the subject will be dropped from all statistical evaluations (applicable only at the predose on day 1).

  The urinary PK parameters will be calculated from the urine concentrations, the volume of urine collected in each collection interval sample and the start and stop time of each interval.

  The fecal PK parameters will be calculated from the fecal concentrations, the weight of feces collected in each collection interval sample and the start and stop time of each interval.

  The following PK parameters of DF 2577Y bound and unbound (or related metabolites) will be derived from for each subject:

- **C_{max}** The observed maximum plasma concentration of DF 2577Y (or metabolites) measured in a subject after dosing identified by inspection of the plasma drug concentration *versus* (*vs.*) time data.
- **t_{max}** The time at which C_{max} was apparent, identified by inspection of the plasma drug concentration *vs.* time data.
- **λ_z** The terminal plasma elimination rate-constant will be estimated from log-linear regression analysis of the terminal phase of the plasma concentration *vs.* time profile. For the slope of the terminal elimination phase to be accepted as reliable, the following criteria will be imposed:
  - a coefficient $r^2 \geq 0.90$,
  - a minimum of 3 data points, including the last measured data point and excluding C_{max}, are available for the regression.

  If these 2 criteria could not be met, the slope of the terminal elimination phase will be considered as not calculable and all the parameters derived from this value ($AUC_{0-\infty}$, $t_{1/2}$, …) will be reported as not calculable (NC).
- **$t_{1/2}$** will be calculated according to the following equation: $t_{1/2} = \ln(2)/ \lambda_z$.
- **AUC_{0-24}** The area under the concentration *vs.* time curve from time zero (pre-dose) to 24 h post-dose will be calculated using a linear trapezoidal method.
- **AUC_{0-t}** The area under the concentration *vs.* time curve from time zero (pre-dose) to the time of last quantifiable concentration will be calculated using a linear trapezoidal method.
- **$AUC_{0-\infty}$** The area under the serum drug concentration *vs.* time curve from time zero to infinity: [$AUC_{0-\infty} = AUC_{0-t} + (C_t/\lambda_z)$, where C_t = the observed concentration of drug for the last sample on the PK profile in which drug was detected, and λ_z as defined above. The percentage of extrapolation of $AUC_{0-\infty}$ should normally not exceed 20% to consider the value as reliable.
- **fu** Fraction of unbound in plasma defined as the ration of the unbound concentration over the total concentration
- **CL/F** The apparent oral clearance will be estimated, for the parent drug only, using the formula:

  $$CL/F = Dose / AUC_{0-\infty}$$
- **Vz/F** The apparent volume of distribution will be calculated for the parent drug only, based on the terminal elimination phase, as follows

  $$Vd/F = CL/F / \lambda_z$$
- Parent to metabolite ratios will be calculated for C_{max} and $AUC_{0-\infty}$ as the ratio of the metabolite (C_{max} or $AUC_{0-\infty}$) over the parent drug (C_{max} or $AUC_{0-\infty}$).
- **$A_{e,ur(t1-t2)}$** Amount of DF 2577Y (or metabolites) excreted in urine over a fraction of time t1 to time t2 from :

  Ae = DF 2577Y (or metabolites) concentration × Urinary volume of the fraction
- **$A_{e,ur(0-72)}$** the cumulative amount excreted in urine from 0 to 72 h as the sum of all the amount excreted over each period of time
- **$f_{e,ur\ (t1-t2)}$** Percentage of the dose excreted in the urine for DF2577Y only, between time t1 and time t2 as ($A_{e,ur(t1-t2)}$/dose)x100
- **$f_{e,ur\ (0-72)}$** Total percentage of the dose excreted in the urine for DF 2577Y only, between 0 and 72 h as ($A_{e,ur(0-72)}$/dose)x100
- **CL_R** Renal clearance determined as the ratio Ae_{0-72}/AUC_{0-72} with t = 24 h post-dose and t_{last}
- **$A_{e,f(t1-t2)}$** Amount of DF 2577Y (or metabolites) excreted in feces over a fraction of time t1 to time t2 from :

Ae = DF 2577Y (or metabolites) concentration × feces weight

- **$A_{e,f(0-72)}$** the cumulative amount excreted in feces from 0 to 72 h as the sum of all the amount excreted over each period of time
- **$f_{e,f\ (t1-t2)}$** Percentage of the dose excreted in the feces for DF 2577Y only, between time t1 and time t2 as ($A_{e,f(t1-t2)}$/dose)x100
- **$f_{e,f\ (0-72)}$** Total percentage of the dose excreted in the feces for DF 2577Y only, between 0 and 72 h as ($A_{e,f(0-72)}$/dose)x100

Individual derived PK parameters will be presented by dose level for each compound (parent and/or metabolites). Descriptive statistics of the PK parameters will be presented as N, mean, SD, standard error (SE), coefficient of variation (CV%), median, minimum (Min), maximum (Max) values, and geometric mean (GM).

Derivation of PK parameters will be carried out using WinNonlin® Professional software (Version Phoenix 6.4 – Pharsight Corporation – Moutain View, California – USA) using the methodology described above.

- Dose proportionality assessment:
  For DF 2577Y bound and unbound and related metabolites, the hypothesis that C_{max}, $AUC_{0-\infty}$ are dose proportional will be formally tested using a power model approach. AUC and C_{max} values, for all dose levels, will be analyzed for dose proportionality using analysis of variance techniques.
  Data will be fitted to the following model:

$$\log(\text{AUC or } C_{max}) = \mu + [\beta \times \log(\text{Dose})]$$

  This is usually referred to as a power model because after exponentiation:

$$AUC_{0-\infty} \text{ or } C_{max} = \alpha \times \text{Dose}^{\beta}$$

  Prior to the analysis, the assumption of a linear relationship between the log $AUC_{0-\infty}$ (C_{max}) and log-dose will be tested using analysis of variance by partitioning the sums of squares for treatments into those for linearity and departures from linearity. If the departures from linearity are significant then the hypothesis of dose proportionality is rejected and the power model analysis will not be performed.
  In case, $AUC_{0-\infty}$ could not be considered as reliable in a majority of subjects (e.g. too large percentage of extrapolation, poor quality of ke determination), dose proportionality assessment will be performed on AUC_{0-t} values.
  The estimate obtained for β is a measure of dose proportionality. The estimate of β together with its 90% confidence interval (CI) (β_l, β_u) will be presented to quantify the degree of non-proportionality.
  The dose proportionality will be confirmed if the 90% CI of β (β_l, β_u) is contained completely within the following critical region:

$$[\Theta_L ; \Theta_H] = \left[1 + \frac{\log(0.8)}{\log(r)} ; 1 + \frac{\log(1.25)}{\log(r)}\right]$$

  where r, defined as the dose ratio, is equal to h/l, h being the highest dose and l the lowest dose.
  Assessment of the dose proportionality will be performed on the complete dose range. In case of departures from linearity or of negative conclusion of dose proportionality on the complete dose, further investigation using the same methodology might be done on a restrained dose range.
  For each day of PK assessment, the individual AUC and C_{max} values will be presented graphically by dose level. The mean AUC and C_{max} values along with the SD will also be displayed graphically by dose level.
  The statistical package SAS® v.9.4 will be used to perform all statistical analyses.

4 STATISTICAL ANALYSES

4.1 Sample size of analysed sets

The objective of analysis presented below is to describe analysis populations.

Criteria	Number of subjects in the Randomized Set (RS) Number of subjects in the Safety Set (SS) Reasons of exclusion from SS Number of subjects in the pharmacokinetic set (PKS) Reasons of exclusion from the PKS Number of subjects in the pharmacodynamics set (PDS) Reasons of exclusion from PDS
Statistical method	Descriptive statistics by dose group and overall.
Title of table	Sample size of analysed sets by dose group and overall.

4.2 Demographic characteristics

The objective of analysis presented below is to describe the demographic and baseline characteristics.

Demography

Criteria	Age (years) Gender (Male/Female) If Female, is she infertile or in post-menopause for at least 2 years? (yes/no) Weight (kg) Height (cm) BMI (kg/m²)
Populations	RS and PKS/PDS/SS Sets (in case different from the RS).
Statistical method	Descriptive statistics.
Title of table	Demographic characteristics by dose group and overall.

Medical and surgical history

Criteria	System Organ Class (SOC), MedDRA dictionary Preferred Term (PT), MedDRA dictionary
Information	All history events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) dictionary.
Populations	RS.
Statistical method	Descriptive statistics as subject count by SOC and PT. Listing of medical history events by dose group and subject.
Title of table	Number and percentage of medical and surgical history events by SOC and PT by dose group and overall. Listing of medical and surgical history by dose group and

	subject.

Previous medications

Criteria	ATC term, Who Drug dictionary preferred name term, Who Drug dictionary
Populations	RS.
Statistical method	Descriptive statistics. A listing will be performed by subject.
Title of table	Number and percentage of previous medications by ATC term and preferred name term by dose group and overall. Listing of previous medications by dose group and subject.

Physical examination at screening and D-1

Criteria	For each examination: assessment (normal/abnormal) and clinically significant (yes/no) At screening Skin and mucous Ear/nose/throat Pulmonary Cardiac Gastro-intestinal Neurological At D-1 Overall examination
Information	Result and clinically significant will be summarised in one 3-class criterion (normal/abnormal NCS/abnormal CS).
Populations	RS.
Statistical method	Descriptive statistics. If relevant, listing of abnormal findings by subject.
Title of table	Physical examination at screening and D-1 by dose group and overall. If relevant, Listing of abnormal findings by dose group and subject.

Urine drug screen

Criteria	Results (negative/positive/not done)
information	Urine drug screen criteria are assessed at screening and at D-1. Results concern: Cannabinoids, amphetamines, cocaine, benzodiazepines, opiates and cotinine.
Populations	RS.
Statistical method	Descriptive statistics.
Title of table	Urine drug screen at screening and at D-1 by dose group and overall.

Alcohol breath test

Criterion	Result (negative/positive)
Information	Alcohol breath test performed at screening and at D-1.
Populations	RS.
Statistical method	Descriptive statistics.
Title of table	Alcohol breath test at screening and at D-1 by dose group and overall.

Serology

Criteria	HIV1 and 2 antibodies (negative/positive/not done) HCV antibodies (negative/positive/not done) HBs antigen (negative/positive/not done)
Information	Serology criteria are assessed at screening.
Populations	RS.
Statistical method	Descriptive statistics.
Title of table	Serology at screening by dose group and overall.

4.3 Pharmacokinetics and pharmacodynamics analyses

Criteria	Cmax (ng/mL); tmax (h); λZ; t1/2(h):; AUC0-24 (h×ng/mL); AUC0-t (h×ng/mL); AUC0-∞ (h×ng/mL); fu VZ/F (DF2577Y only); CL/F (DF2577Y only); $A_{e,ur}$; $f_{e,ur}$ $A_{e,f}$; $f_{e,f}$ CLR; Parent:metabolite(s) ratio for Cmax and AUCs.
Information	Interim analyses will be performed after completion of each dose level, using anonymized data provided by the bioanalytical center Final PK analysis will be performed using validated bioanalytical data and actual PK blood sampling times of the part A of the study
Population	PKS
Statistical method	Descriptive statistics of concentrations and PK parameters Dose proportionality analysis using power model (section 3.3)
Title of tables	List of concentrations Descriptive statistics of concentrations List of PK parameters Descriptive statistics of PK parameters

Pharmacodynamic analysis: correlation between Cmax and pharmacodynamics criteria

Criteria	Pharmacokinetic criterion DF2577Y Cmax (ng/mL) Pharmacodynamic criteria Leukocyte markers: CD11b, CD18
Information	DF2577Y concentration assessed at D1 (pre-dose, T30min, T1h, T2h, T3h, T4h, T5h, T6h, T7h, T8h, T9h, T10h, T11, T12h, T16h), D2 (T24h, T36h, T40h), D3 (T48h, T60h) and D4 (T72h). Leukocytes markers not assessed for first cohort. Leukocytes markers assessed at D1 (Tcmax, Tcmax+3h, T12h), D2 (T24h), D3 (T48h) or D4 (T72h) (time determined after the results of the first dose administered).
Population	PKS
Statistical method	Time matched: D1 (Tcmax, Tcmax+3h, T12h), D2 (T24h), D3 (T48h) or D4 (T72h). The relationship between values of pharmacodynamic parameters time matched with DF2577Y (bound and unbound) plasma concentrations will be first evaluated by visual inspection of graphs relating pharmacodynamic parameters with DF2577Y (bound and unbound) plasma concentrations. In case of reliable relationships, basic models, such as Emax model, will be first developed. Then, the selected models will be optimized by testing covariate such as BMI, age, etc. Further model development might be done depending on the results of each modelling.
Title of tables	Cmax concentration *vs* CD11b for each time matched. Cmax concentration *vs* CD18 for each time matched.

4.4 Safety: Adverse events

The objective of analysis presented below is to evaluate the safety of study drugs through adverse events reported during the study.

Criteria	AE number Description SOC term MedDRA) PT term MedDRA) Start date and time Time since last study drug administration End date and time AE Duration Severity (mild/moderate/severe) Serious (yes/no) Expected (yes/no) Congenital anomaly or birth defect (yes/no) Significant disability (yes/no) Death (yes/no) Life threatening (yes/no) Other medically important event (yes/no) Hospitalization (yes/no) and if yes, date of hospitalization Relationship to study treatment (none / unlikely /possible / probable / highly probable / not assessable) Outcome (recovered-resolved / recovering-resolving / recovered-resolved with sequelae / not recovered-not resolved / fatal /unknown) Action taken with study product (dose increased / dose not changed / dose reduced / dose interrupted / drug withdrawn / not applicable / unknown) Other actions (yes/no) and if yes specify Concomitant medication recorded (yes/no)
Information	AEs will be coded according to the Medical Dictionary for Regulatory Activity (MedDRA). They will be classified into pre-defined standard categories according to chronological criteria: - Treatment emergent AEs (TEAE): AEs that occurs for the first time or if present before worsened during an exposure to drug(s). - Non-treatment emergent AEs (NTEAE): AEs that occurs before the study drug administration. An AE occurring during the run-out will be related to the last day of treatment administration received. AEs will be individually listed per dose group, subject number, presenting: assigned dose group, verbatim, Primary System Organ Class (SOC), Lowest Level Term (LLT), Preferred Term (PT), emergence (yes or no) date and time of onset, date and time of last study drug administration before AE, duration, time from onset since last study drug administration, intensity and seriousness, relationship to

	study drug, the required action taken and outcome. The non-treatment emergent AEs will be summarised by SOC and PT for the safety set. The treatment emergent AEs will be summarised by SOC, PT and dose group for the safety set. It will consist in the evaluation of the number of AEs and the number of subjects reporting these AEs.
Population	SS.
Statistical method	For each part: The TEAEs will be summarized by dose group and overall. The analysis will include the evaluation of the number of adverse events, the number of subjects reporting these adverse events and the % of subjects within the dose group. In case of few adverse events (≤ 5), only a listing will be prepared by dose group and subject. TEAEs will be individually listed per dose group, subject, emergence, day, SOC, LLT, PT, date and time of onset and offset, time since last product administration, duration, intensity and seriousness, relationship to study product, action taken and outcome. NTEAEs will be summarised by dose group and subject. Serious adverse events (SAEs) will be summarised by dose group and subject.
Title of tables	For each part: Treatment emergent AEs - SS - By dose group. Listing of treatment emergent AEs - SS - By dose group, subject, SOC, LLT and PT. NTAEs - By dose group. Listing of NTAEs by dose group, subject, SOC, LLT and PT. - SS. SAEs - By dose group. Listing of SAEs by dose group, subject, SOC, LLT and PT - SS.

4.5 Safety: Laboratory criteria

The objective of analysis presented below is to evaluate the safety laboratory variables.

Biochemistry, hematology and hemostasis criteria

Criteria	Biochemistry Creatinine (µmol/L) Glucose (mmol/L) Total protein (g/L) Urea (mmol/L) Albumin (g/L) Globulin (albumin/globulin ratio) Total cholesterol (mmol/L) Triglycerides (mmol/L) Sodium (mmol/L) Potassium (mmol/L) Chloride (mmol/L) Calcium (mmol/L) Uric acid (IU/L) AST (IU/L) ALT (IU/L) GGT (IU/L) Alkaline phosphatase (IU/L) CPK (IU/L) Total bilirubin (µmol/L) Conjugated bilirubin (µmol/L) LDH (IUl/L) LDL (mmol/L) HDL (mmol/L) Phosphore (mmol/L) Hematology Hemoglobin (g/L) Hematocrit (no unit) Red blood cells (Tera/L) White blood cells (Giga/L) Neutrophils (Giga/L) Eosinophils (Giga/L) Basophils (Giga/L) Lymphocytes (Giga/L) Monocytes (Giga/L) Platelets (Giga/L) Reticulocytes (Giga/L) MCV (fL) MCH (fmol) MCHC (mmol/L) Hemostasis aPTT subject (s) aPTT ratio Prothrombin time (s) Prothrombin level

Information	Part A: criteria assessed at screening, D-1, D2 and at end of study visit (D4.). Part A, baseline: last assessed value at D-1. Emergent value is defined as any normal value at pre-dose assessment (baseline value) according to laboratory range becoming abnormal at post-dose assessment or lower (upper) abnormal baseline value becoming upper (lower) abnormal at post-dose assessment. Laboratory ranges are reported in database.
Population	SS.
Statistical method	<u>For each criterion</u> Values, position according to laboratory range and clinical assessment will be described at screening, baseline, each scheduled assessment during treatment phase and at end of study visit overall. Change between the values from baseline to each scheduled assessment during treatment phase and end of study visit will be described by dose group and overall. Listing of emergent values according to laboratory range from Baseline to each scheduled assessment during treatment phase and end of study visit by dose group and subject.
Title of tables	<u>For each criterion</u> Name of criterion (unit): Values, position according to laboratory range and clinical assessment at screening, baseline, during treatment phase and at end of study visit. Change between the values from baseline to during treatment phase and to end of study visit. Listing of emergent values from baseline to during treatment phase and to end of study visit by dose group and subject.

Urinalysis and microscopic criteria

Criteria	Urine appearance (clear/slightly cloudy/cloudy/opaque) Urine color (pale yellow/dark yellow/brown/red) <u>For each criterion, result and clinical assessment (normal/abnormal NCS/abnormal CS)</u> <u>Urinalysis</u> pH Ketone bodies (negative/positive) Protein (negative/positive) Glucose (negative/positive) Blood (negative/positive) Leucocytes (negative/positive) Nitrite (negative/positive) Urobilinogen bodies (negative/positive) Bilirubin bodies (negative/positive) Nitrite (negative/positive)

	Specific density <u>Microscopic analysis</u> Red blood cells Crystallography Flat cells Round cells Cylinders Mucus Bacteria
Information	Part A: criteria assessed at screening, D-1, D2 and at end of study visit (D4). Part A: baseline: last assessed value at D-1. Emergent value is defined as any normal value at pre-dose assessment (baseline value) according to laboratory range becoming abnormal at post-dose assessment or lower (upper) abnormal baseline value becoming upper (lower) abnormal at post-dose assessment. Laboratory ranges are reported in database.
Population	SS.
Statistical method	pH and specific density: same method as for biology criteria. For each qualitative criterion Result will be described at screening, baseline, each scheduled assessment during treatment phase and at end of study visit. Listing of emergent values from baseline to each scheduled assessment during treatment phase and to end of study visit by dose group and subject. Microscopic criteria Listing of microscopic criteria by subject and visit.
Title of table	pH and specific density: same tables as for biology criteria. For each qualitative criterion: Name of criterion: Result at screening, baseline, during treatment phase and at end of study visit by dose group and overall. Listing of emergent values from baseline to during treatment phase and to end of study visit by dose group and subject. Microscopic criteria Listing of microscopic criteria by dose group, subject and visit.

4.6 Safety: Vital signs

The objective of analysis presented below is to evaluate the safety of study drugs through vital signs criteria.

Blood pressure, heart rate and oral body temperature

Criteria	Supine systolic blood pressure (mmHg) Supine diastolic blood pressure (mmHg) Supine heart rate (bpm) Standing systolic blood pressure (mmHg) Standing diastolic blood pressure (mmHg) Standing heart rate (bpm) Oral temperature (°C) Result (normal/abnormal) Clinically significant (yes/no) Abnormal Finding/Relevant comments Orthostatic hypotension (yes/no)
Information	Criteria assessed at screening, D-1, D1 (pre-dose, T1h, T3h, T5h, T8h, T12h), D2 (T24h) and at end of study visit (D4) Part A:, baseline: last assessed value at D1 pre-dose. Emergent value is defined as any normal value at pre-dose assessment (baseline value) according to normal range becoming abnormal at post-dose assessment or lower (upper) abnormal baseline value becoming upper (lower) abnormal at post-dose assessment. Normal ranges values are reported in appendix. Result and clinically significant will be summarised in one 3-class criterion (normal/abnormal NCS/abnormal CS). Systolic orthostatic hypotension: when (supine-standing) SBP ≥20 mmHg. Diastolic orthostatic hypotension: when (supine-standing) DBP ≥20 mmHg.
Population	SS.
Statistical method	<u>For each criterion</u> Values, position according to normal ranges values will be described at screening, D-1, baseline, each scheduled assessment during treatment phase and at end of study visit overall. Change between the values from baseline to each scheduled assessment during treatment phase and end of study visit will be described by dose group and overall. Listing of emergent values according to normal ranges values from baseline to each scheduled assessment during treatment phase and end of study visit by dose group and subject. Orthostatic hypotension reported will be listed by dose group,

	subject and day(time)-point.
Title of tables	For each criterion Name of criterion (unit): Values, position according to normal ranges values at screening, D-1, baseline, during treatment phase and at end of study visit and change from baseline. Listing of emergent values from baseline to end of study visit by dose group and subject. Vitals: Result and clinical significance at each day(time) point assessment from screening to end of study. Orthostatic hypotension: Listing by dose group, subject and daytime-point.

Weight

Criteria	Weight (kg)
Information	Criteria assessed at D-1 and at end of study visit (D4) Baseline: last assessed value at D-1.
Population	SS
Statistical method	Value at baseline and at end of study visit and change from baseline by dose group and overall.
Title of tables	Weight (kg): Value at baseline and at end of study visit and change from baseline by dose group and overall.

4.7 Safety: Physical examination

The objective of analysis presented below is to evaluate the safety of study drugs through physical examination.

Physical examination

Criteria	Result (normal/abnormal) Clinically significant (yes/no) Abnormal findings
Population	SS.
Information	Physical examination is assessed at end of study visit (D4).
Statistical method	Physical examination: listing of abnormal findings by subject.
Title of table	Physical examination: Listing of abnormal findings at end of study visit – By dose group and subject.

4.8 Safety: ECG

The objective of analysis presented below is to evaluate the safety of study drugs through ECG criteria.

Criterion	Heart rate (bpm) PR (ms) QRS (ms) QT (ms) QTc Fridericia (ms) Result (normal/abnormal) Comment Clinically significant (yes/no)
Information	Part A: criteria assessed at screening, D-1, D1 (pre-dose, T1h, T2h, T3h, T4, T6h, T8h, T12h), D2 (T24h), D3 (T48h) and at end of study visit (D4). Baseline: last assessed value at D1 pre-dose. Emergent value is defined as any normal value at pre-dose assessment (baseline value) according to normal range becoming abnormal at post-dose assessment or lower (upper) abnormal baseline value becoming upper (lower) abnormal at post-dose assessment. Normal ranges values are reported in appendix. Result and clinically significant will be summarised in one 3-class criterion (normal/abnormal NCS/abnormal CS).
Population	SS.
Statistical method	<u>For each criterion</u> Values, position according to normal ranges values will be described at screening, D-1, baseline, each scheduled assessment during treatment phase and at end of study visit overall. Change between the values from baseline to each scheduled assessment during treatment phase and end of study visit will be described by dose group and overall. Listing of emergent values according to normal ranges values from Baseline to each scheduled assessment during treatment phase and end of study visit by dose group and subject.
Title of tables	<u>For each criterion</u> Name of criterion (unit): Values, position according to normal ranges values at screening, D-1, baseline, during treatment phase and at end of study visit and change from baseline. Listing of emergent values from baseline to end of study visit by dose group and subject. ECG: Result and clinical significance at each day(time) point assessment from screening to end of study.

4.9 Conduct of the study

The objective of analysis presented below is to describe the parameters of the conduct of study.

Duration of the study

Criterion	Duration of the study (days)
Definition	End of the study date – screening date + 1
Populations	RS and PKS/PDS/SS Sets (in case different from the RS).
Statistical method	Descriptive statistics - By dose group and overall
Title of table	Duration of the study (days) – By dose group and overall.

Study normally completed

Criteria	Subject successfully completed the study (yes/no) If no: Reason for the withdrawal (lost to follow-up/adverse clinical experience/adverse laboratory experience/deviation from protocol/consent withdrawal/other)
Information	If necessary, reason of withdrawal will be listed by dose group and subject.
Population	RS.
Statistical method	Descriptive statistics by dose group and overall
Title of table	Subject who successfully completed the study – By dose group and overall.

Concomitant medications

Criteria	ATC term, Who Drug dictionary preferred name term, Who Drug dictionary
Population	RS.
Statistical method	The concomitant treatments started after the first treatment administration will be summarized by ATC term and preferred name term and by dose group and overall. The analysis consists in the evaluation of the number of concomitant treatments, in the number of subjects reporting these concomitant treatments and the % of subjects within the dose group. Concomitant treatments started after the first treatment administration will be listed by dose group and subject. If relevant, concomitant treatments started before the first treatment administration will be listed by dose group and subject.
Title of table	Concomitant treatments started after the first treatment administration by ATC term and preferred name term – By dose group and overall. Listing of concomitant treatments started after the first treatment administration by dose group and subject. Listing of concomitant treatments started before the first treatment administration by dose group and subject.

5 INDIVIDUAL DATA

Individual data listings, included unscheduled evaluations, will be presented by dose group, subject, visit and time, if relevant, for following criteria:

- **Discontinued subjects**

Completion/discontinuation date
Status (completed / adverse event / lost to follow-up / withdrawal by subject / physician decision / death / protocol violation / study terminated by sponsor /other) and if other, specify

- **Eligibility of subject**

Are all the inclusion criteria answered Yes (yes/no) and if no: number of criteria and comment
Are all the exclusion criteria answered No (yes/no) and if no: number of criteria and comment
Is the subject eligible to participate in the study? (yes/no)
Date of confirmation of eligibility

- **Visit dates**

Date of visit
Date of randomization

- **Analysed populations**

Subject in Randomized Set (yes/no)
Subject in Safety Set (yes/no)
Subject in Pharmacokinetic Set (yes/no)
Subject in Pharmacodynamic Set (yes/no)

- **Informed consent and demography**

Date of consent
Date of birth
Age (years),
Gender (Male/Female)
If Female, is she infertile or in post-menopause for at least 2 years? (yes/no)
Weight (kg)
Height (cm)
BMI (kg/m²)

- **General medical and surgical history**

Medical/surgical history (yes/no) and if yes:
Start date, nature
MedDRA codes
Ongoing (yes/no)
Start date
End date

- **Previous medication**

Medication number
Medication
Dose
Unit
Route
Indication

Frequency
Start date
End date
ATC term (Who-drug dictionary)
Preferred name term (Who-drug dictionary)

- **Physical examination at screening**

For each examination: assessment (normal/abnormal), clinically significant (yes/no) and abnormal findings
At screening
Skin and mucous
Ear/nose/throat
Pulmonary
Cardiac
Gastro-intestinal
Neurological
At D-1
Overall examination

- **Serology**

Sample number for:
HIV1 and 2 antibodies (negative/positive/not done)
HCV antibody (negative/positive/not done)
HBs antigen (negative/positive/not done)

- **Urine drug screen**

Sample number
Date and time
Result (negative/positive/not done)

- **Alcohol breath test**

Date and time of test
Result (negative/positive/not done)

- **Concomitant medications**

Medication number
Medication
Dose
Unit
Route
Indication
Frequency
Start date
End date
On-going (yes/no)
ATC term (Who-drug dictionary)
Preferred name term (Who-drug dictionary)

- **Study drug administration**

Date and time of drug administration
Administered dose (mg)
Administration performed according to the protocol (yes/no) and if no, comment

- **Pharmacokinetics blood sampling**

Scheduled time
Actual date/time
Sample collected (yes/no)
Before meal (yes/no/unknown)
Fasting state (yes/no/unknown)

- **Pharmacokinetic concentration and criteria**

Sample number
Concentration
Comment (Sample not received/analytical problem (yes/no)
Cmax (ng/mL);
tmax (h);
λZ;
t1/2(h):;
AUC0-24 (h×ng/mL);
AUC0-t (h×ng/mL);
AUC0-∞ (h×ng/mL);
fu
VZ/F (DF2577Y only);
CL/F (DF2577Y only);
$A_{e,ur}$; $f_{e,ur}$
$A_{e,f}$; $f_{e,f}$
CLR;
Parent:metabolite(s) ratio for Cmax and AUCs.

- **Pharmacodynamic blood sampling**

Scheduled time
Actual date/time
Sample collected (yes/no)
Fasting state (yes/no/unknown)

- **Pharmacodynamic criteria**

CXCL1 (Gro alfa)
CXCL2 (Gro beta) (Biorad)
CXCL5 (ENA-78)
CXCL6 (GCP-2)
CXCL8 (IL-8)

- **Urine sample**

Sample collected (yes/no)
Time interval
Start date and time
End date and time
Urine volume collected (mL)
Comment

- **Faeces sample**

Sample collected (yes/no)
Time interval
Start date and time
End date and time
Faeces weight (mg)

Comment

- **Adverse events**

AE number
Description
SOC term MedDRA)
PT term MedDRA)
LLT term MedDRA)
HLT term MedDRA)
HLGT term MedDRA)
Start date and time
Time since last study drug administration
End date and time
AE Duration
Severity (mild/moderate/severe)
Serious (yes/no)
Expected (yes/no)
Congenital anomaly or birth defect (yes/no)
Significant disability (yes/no)
Death (yes/no)
Life threatening (yes/no)
Other medically important event (yes/no)
Hospitalization (yes/no) and if yes, date of hospitalization
Relationship to study treatment (none / unlikely /possible / probable / highly probable / not assessable)
Outcome (recovered-resolved / recovering-resolving / recovered-resolved with sequelae / not recovered-not resolved / fatal /unknown)
Action taken with study product (dose increased / dose not changed / dose reduced / dose interrupted / drug withdrawn / not applicable / unknown)
Other actions (yes/no) and if yes specify
Concomitant medication recorded (yes/no)

- **Biochemistry**

Date and time of assessment
Fasting state (yes/no/unknown)
Value, laboratory range and clinical at each assessment, change and emergent value (yes/no) according to laboratory ranges from baseline for:
Creatinine (µmol/L)
Glucose (mmol/L)
Total protein (g/L)
Urea (mmol/L)
Albumin (g/L)
Globulin (albumin/globulin ratio)
Total cholesterol (mmol/L)
Triglycerides (mmol/L)
Sodium (mmol/L)
Potassium (mmol/L)
Chloride (mmol/L)
Calcium (mmol/L)
Uric acid (IU/L)
AST (IU/L)
ALT (IU/L)
GGT (IU/L)

Alkaline phosphatase (IU/L)
CPK (IU/L)
Total bilirubin (µmol/L)
Conjugated bilirubin (µmol/L)
LDH (IUl/L)
LDL (mmol/L)
HDL (mmol/L)
Phosphore (mmol/L)
Comments

- **Hematology**

Date and time of assessment
Value, laboratory range and clinical at each assessment, change and emergent value (yes/no) according to laboratory ranges from baseline for:
Hemoglobin (g/L)
Hematocrit (no unit)
Red blood cells (Tera/L)
White blood cells (Giga/L)
Neutrophils (Giga/L)
Eosinophils (Giga/L)
Basophils (Giga/L)
Lymphocytes (Giga/L)
Monocytes (Giga/L)
Platelets (Giga/L)
Reticulocytes (Giga/L)
MCV (fL)
MCH (fmol)
MCHC (mmol/L)
Comments

- **Hemostasis**

aPTT subject (s)
aPTT ratio
Prothrombin time (s)
Prothrombin level
Comments

- **Urinalysis**

Date and time of assessment
Urine appearance (clear/slightly cloudy/cloudy/opaque)
Urine color (pale yellow/dark yellow/brown/red)
Result, laboratory range (if relevant) and clinical at each assessment and emergent value (yes/no) according to laboratory ranges from baseline (or baseline values for qualitative criteria) for:
<u>Urinalysis</u>
pH
Ketone bodies (negative/positive)
Protein (negative/positive)
Glucose (negative/positive)
Blood (negative/positive)
Leucocytes (negative/positive)
Nitrite (negative/positive)
Urobilinogen bodies (negative/positive)

Bilirubin bodies (negative/positive)
Nitrite (negative/positive)
Specific density

Microscopic analysis
Red blood cells
Crystallography
Flat cells
Round cells
Cylinders
Mucus
Bacteria

- **Vitals**

Scheduled time
Position (supine/standing)
Actual time position
Actual time measurement
Supine systolic blood pressure value (mmHg)
Supine diastolic blood pressure value (mmHg)
Supine heart rate value (bpm)
Oral temperature (°C)
Weight (kg)
Result (normal/abnormal)
Clinically significant (yes/no)
Comment

- **Physical examination at end of study visit**

Results (normal/abnormal) and if relevant
Clinically significant (yes/no)
Abnormal physical finding

- **ECG**

Scheduled time
Time performed
Heart rate (bpm)
PR (ms)
QRS (ms)
QT (ms)
QTc Fridericia (ms)
Result (normal/abnormal)
Clinically significant (yes/no)
Comment

- **Duration of study**

Duration of study (days)

- **Study restrictions**

Did the subject respect the study restrictions throughout the course of the study? (yes/no) and if no, specify

- **Study comments**

Comments

6 APPENDIX: Normal ranges for clinical criteria

	Criterion	Unit	Normal ranges
Vital signs	Oral body temperature	°C	[36.3 – 37.5[
	Supine SBP	mmHg	[90 – 140] for ≤ 45 years [90 – 150] for > 45 years
	Supine DBP	mmHg	[50 – 90]
	Supine HR	bpm	[40 – 100]
Electrocardiogram	PR	ms	[120 – 210[
	QRS	ms	[0 – 120[
	QTc Fridericia	ms	[0 – 430] for male and [0 – 450] for female

16.1.10 Documentation of inter-laboratory standardisation methods and quality assurance procedures

Vérifié le : 3.1.19 CF 04.01.19 FVL

LABORATORY NORMAL RANGES

STUDY OP099516.DOM/BPS0115

HAEMATOLOGY	UNIT	VALUES MAN	VALUES WOMAN
Red blood cells	T/L	4,44 – 5,61	3,92 – 5,08
Haemoglobin	g/L	135 – 169	119 – 146
Haematocrit	%	40,0 – 49,4	36,6 – 44,0
MCV	fl	81,8 – 95,5	82,9 – 98,0
MCH	pg	27,0 – 32,3	27,0 – 32,3
MCHC	g/dL	32,4 – 35,0	31,8 – 34.7
White blood cells	G/L	3,91 – 10,90	4,49 – 12,68
Neutrophils	G/L	1,80 – 6,98	2,10 – 8,89
Eosinophils	G/L	0,03 – 0,59	0,01 – 0,40
Basophils	G/L	0,01 – 0,07	0,01 – 0,07
Lymphocytes	G/L	1,26 – 3,35	1,26 – 3,35
Monocytes	G/L	0,29 – 0,95	0,25 – 0,84
Platelets	G/L	166 – 308	173 - 390

HAEMOSTASIS	UNIT	VALUES MAN /WOMAN
Prothrombin level	%	> 75
Prothrombin Time (STA – NeoPTimal®)	s	12,0 – 16,3
APTT	s	Lot Reactif dependant
APTT reference	s	Lot Reactif dependant
APTT ratio		(0,80 – 1,20)

BLOOD BIOCHEMISTRY	UNIT	VALUES MAN	VALUES WOMAN
Glucose	mmol/L	4,11 – 5,89	4,11 – 5,89
Creatinine	µmol/L	59 – 104	45 – 84
Urea	mmol/L	1,60 – 7,50	1,60 – 7,30
SGOT/ASAT	U/L	< 35	< 31
SGPT/ALAT	U/L	< 42	< 31
GGT	U/L	8 – 61	5 – 36
Alkalin phosphatase	U/L	40 – 129	35 – 104
Lacto - dehydrogenase	U/L	135 – 225	135 – 214
CPK	U/L	< 170	< 145
Total Bilirubin	µmol/L	< 19	< 19
Conjugated Bilirubin	µmol/L	< 5	< 5
Acide urique	µmol/L	202 – 416	143 – 339
Cholesterol	mmol/L	3,87 – 5,18	3,87 – 5,18
Triglycerides	mmol/L	< 1,70	< 1,70
HDL Cholesterol	mmol/L	> 1,00	> 1,00
LDL Cholesterol (dosed)	mmol/L	< 4,10	< 4,10
Sodium	mmol/L	136 – 145	136 – 145
Potassium	mmol/L	3,9 – 5,1	3,9 – 5,1
Chlore	mmol/L	98 – 106	98 – 106
Calcium	mmol/L	2,15 – 2,50	2,15 – 2,50
Phosphorus 18 - 19 years > 19 years	mmol/L	0,96 – 1,66 0,86 – 1,44	0,96 – 1,53 0,86 – 1,44
Total protein	g/L	66 – 87	66 – 87
Albumin	g/L	35 – 52	35 – 52
Globulines	g/L	21,2 – 34,9	21,2 – 34,9
Albumin/globulin ratio		1,20 – 1,80	1,20 – 1,80

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GROUPE Oriade noviale

Vérifié le : 3.01.19
04.01.19 FK

SEROLOGY	RESULT
P24 antigen & HIV ½ antibodies	Negative
HCV antibodies detection	Negative
HBs antigen detection	Negative

POSITIVE URINARY SCREENING	UNITS	VALUES MAN/WOMAN
Glucose	mmol/L	< 1,10
Protein	g/L	< 0,12
Creatinin	mmol/L	Man: 3,54 – 24,60 Woman: 2,55 – 20,00
Red Blood Cell count	/mL	< 10 000
White Blood Cell count	/mL	< 10 000
Crystals		Few Negative Many phosphates ammoniaco – magnesiens Many phosphates Rare Many urates Few oxalate calcium
Epithelial cells		Negative/Positive
Epithelium renal cells		Negative/Positive
Cylinders		Negative/Positive
Mucous		Negative/Positive
Bacteria		Negative/Positive

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Oriade noviale GROUPE

Vérifié le : 03 DEC 18
dr 26/03/18 FK

LABORATORY NORMAL RANGES

STUDY OP099516.DOM/BPS0115

HAEMATOLOGY	UNIT	VALUES MAN	VALUES WOMAN
Red blood cells	T/L	4,44 – 5,61	3,92 – 5,08
Haemoglobin	g/L	135 – 169	119 – 146
Haematocrit	%	40,0 – 49,4	36,6 – 44,0
MCV	fl	81,8 – 95,5	82,9 – 98,0
MCH	pg	27,0 – 32,3	27,0 – 32,3
MCHC	g/dL	32,4 – 35,0	31,8 – 34.7
White blood cells	G/L	3,91 – 10,90	4,49 – 12,68
Neutrophils	G/L	1,80 – 6,98	2,10 – 8,89
Eosinophils	G/L	0,03 – 0,59	0,01 – 0,40
Basophils	G/L	0,01 – 0,07	0,01 – 0,07
Lymphocytes	G/L	1,26 – 3,35	1,26 – 3,35
Monocytes	G/L	0,29 – 0,95	0,25 – 0,84
Platelets	G/L	166 – 308	173 - 390

HAEMOSTASIS	UNIT	VALUES MAN /WOMAN
Prothrombin level	%	> 75
Prothrombin Time	s	9,9 – 13,8
APTT	s	Lot Reactif dependant
APTT reference	s	Lot Reactif dependant
APTT ratio		(0,80 – 1,20)

BLOOD BIOCHEMISTRY	UNIT	VALUES MAN	VALUES WOMAN
Glucose	mmol/L	4,11 – 5,89	4,11 – 5,89
Creatinine	µmol/L	59 – 104	45 – 84
Urea	mmol/L	1,60 – 7,50	1,60 – 7,30
SGOT/ASAT	U/L	< 35	< 31
SGPT/ALAT	U/L	< 42	< 31
GGT	U/L	8 – 61	5 – 36
Alkalin phosphatase	U/L	40 – 129	35 – 104
Lacto - dehydrogenase	U/L	135 – 225	135 – 214
CPK	U/L	< 170	< 145
Total Bilirubin	µmol/L	< 19	< 19
Conjugated Bilirubin	µmol/L	< 5	< 5
Acide urique	µmol/L	202 – 416	143 – 339
Cholesterol	mmol/L	3,87 – 5,18	3,87 – 5,18
Triglycerides	mmol/L	< 1,70	< 1,70
HDL Cholesterol	mmol/L	> 1,00	> 1,00
LDL Cholesterol (dosed)	mmol/L	< 4,10	< 4,10
Sodium	mmol/L	136 – 145	136 – 145
Potassium	mmol/L	3,9 – 5,1	3,9 – 5,1
Chlore	mmol/L	98 – 106	98 – 106
Calcium	mmol/L	2,15 – 2,50	2,15 – 2,50
Phosphorus 18 - 19 years > 19 years	mmol/L	0,96 – 1,66 0,86 – 1,44	0,96 – 1,53 0,86 – 1,44
Total protein	g/L	66 – 87	66 – 87
Albumin	g/L	35 – 52	35 – 52
Globulines	g/L	21,2 – 34,9	21,2 – 34,9
Albumin/globulin ratio		1,20 – 1,80	1,20 – 1,80

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SEROLOGY	RESULT
P24 antigen & HIV ½ antibodies	Negative
HCV antibodies detection	Negative
HBs antigen detection	Negative

POSITIVE URINARY SCREENING	UNITS	VALUES MAN/WOMAN
Glucose	mmol/L	< 1,10
Protein	g/L	< 0,12
Creatinin	mmol/L	Man: 3,54 – 24,60 Woman: 2,55 – 20,00
Red Blood Cell count	/mL	< 10 000
White Blood Cell count	/mL	< 10 000
Crystals		Few Negative Many phosphates ammoniaco – magnesiens Many phosphates Rare Many urates Few oxalate calcium
Epithelial cells		Negative/Positive
Epithelium renal cells		Negative/Positive
Cylinders		Negative/Positive
Mucous		Negative/Positive
Bacteria		Negative/Positive

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16.1.11 Publications based on the study

Not applicable.

16.1.12 Important publications referenced in the report

Not applicable.