Suprasorb® C

Post-Market Clinical-Follow-Up Study of Suprasorb® C collagen wound dressing

STATISTICAL ANALYSIS PLAN

Version 2.0 – 10/12/2020

Written by RCTs

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1. STATISTICAL ANALYSIS PLAN - APPROVAL FORM

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2. VERSION HISTORY

Version	Date	Author	Comment / changes
0.1	22/05/2019	RCTs	Initial draft version (based on protocol version 4.0 dated 18OCT2018 and CRF version 6.0 dated 13DEC2018 and Local Care CRF version 5.0 dated 17OCT2017 and planimetry forms dated 09FEB2018 and 06APR2018)
0.2	13/06/2019	RCTS	Integration of Sponsor's comments
1.0	14/06/2019	RCTS	First approved and signed version
1.1	13/08/2020	RCTs	Update of the primary endpoint analysis
2.0	10/12/2020	RCTs	Second approved and signed version

3. ABBREVIATIONS

Abbreviation	Description
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
CI	Confidence Interval
CRF	Case Report Form
PMCF	Post Market Clinical Follow up
TS	Treated Set
MedDRA	Medical Dictionary for Regulatory Activities
OQOL	Overall Quality of Life
PPS	Per Protocol Set
PT	Preferred term
Q1	First quartile
Q3	Third quartile
QOL	Quality of Life
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
WHAT	Wound Healing Analysing Tool
WHO-DD	World Health Organization Drug Dictionary

4. PROTOCOL

This Statistical Analysis Plan is based on the Suprasorb® C Protocol version 4.0 dated 18OCT2018.

The overall study design, plan description, study objectives, inclusion and exclusion criteria and sample size calculation are presented in the protocol.

5. ANALYSIS SETS AND SUBGROUPS

5.1. Analysis sets

The analysis sets are defined below.

- **Treated Set (TS):** all patients treated initially at least once with Suprasorb® C,
- **Per Protocol Set (PPS):** all patients treated with Suprasorb® C according to the protocol, meaning with no major protocol deviation.

Note: at the time of writing, the following patients have been identified as having a major protocol deviation: (cf. final data review minutes for further details).

Centre	Patient	Major Protocol Deviation
24	01	Age inclusion criteria not met
39	01	Age inclusion criteria not met
40	01	Age inclusion criteria not met
45	01	Age inclusion criteria not met; Target ulcer diameter inclusion criteria not met
61	01	Target ulcer diameter inclusion criteria not met
67	01	Target ulcer diameter inclusion criteria not met
68	01	Target ulcer diameter inclusion criteria not met
69	01	Target ulcer diameter inclusion criteria not met

5.2. Analysis subgroups

No subgroup is defined.

6. ENDPOINTS

6.1. Primary endpoint

As stated in the protocol section 9:

Progression of healing after application of Suprasorb® C collagen wound dressing is used as parameter for evaluation of performance. The progression towards healing will be measured by reduction of wound area and formation of granulation tissue. A progression of healing, i.e. success of treatment, strongly points toward the absence of adverse events in the healing period. Progression of healing will be assessed in 8 weeks after start of treatment with Suprasorb® C. Success of treatment is defined as a wound area reduction of at least 15 %, or as a shift from the healing phase to the granulation phase in more than 50% of the wound area.

The primary endpoint is therefore a combined endpoint. The primary endpoint and its components will be computed as follows.

Progression of healing at week 8 (=primary endpoint):

The primary endpoint will be computed as follows:

- Success:
  - if relative change in wound area from baseline to W8 ≤ -15%
  - and/or
  - if relative change in granulation from baseline to W8 > 50%
- Failure:
  - if relative change in wound area from baseline to W8 > -15%
  - and
  - if relative change in granulation from baseline to W8 ≤ 50%.

Note: in other cases, the primary endpoint will be considered as missing (i.e. not computable).

Relative change in wound area from baseline to W8 (%):

The following algorithm will be used:

- Relative change in wound area from baseline to W8 (%) = 100 x (Area W8-W0) / W0.

Note:

After receipt of the photos, the analysis tool “WHAT” will not be able to perform an objective measure of the size of the wound. So, to evaluate the parameter “reduction of wound area”, the wound healing will be determined with the planimetry measures.

Missing planimetry wound area will be replaced using wound area as measured by an independent expert using photos. At the time of writing, 3 patients have a missing planimetry graph at D0: patients 21-01, 24-01 and 47-01. Missing wound area at D0 of patients 21-01 and 24-01 will be replaced by 63.7 cm^2 and 13.8 cm^2, respectively. No photos were available for patient 47-01.

Follow-up patients with missing area at W8 and for whom variable “Healing of the wound” is Yes at W4, W8 or Early discontinuation visit will be replaced by 0 cm^2. No patient in the current database has “Healing of the wound” ticked Yes at visit i followed by “Healing of the wound” ticked No at a subsequent visit i+1 or i+2.

Relative change in wound area from baseline to W8 ≤ -15% (yes/no):

This endpoint will be derived as follows:

- Yes, if relative change in wound area from baseline to W8 ≤ -15%.
- No, if relative change in wound area from baseline to W8 > -15%.

Shift from the healing phase to the granulation phase:

The parameter "shift of phase" will be analysed by Lohmann & Rauscher. However, to compute the combined primary endpoint, the following endpoints will be computed:

- Relative change in granulation from baseline to W8 (%) = 100 x (granulation at W8-W0) / W0.

This endpoint will be derived as follows:

- Yes, if relative change from baseline in granulation to W8 > 50%.
- No, if relative change from baseline in granulation to W8 ≤ 50%.

Note:

Granulation (%) of the wound area has been measured by an independent expert using photos. Granulation data of each patient at each visit will be sent by Lohmann & Rauscher to RCTs. RCTs will import the granulation data into the SAS database. Please refer to the Data Transfer Specifications for further details.

6.2. Secondary endpoints

Secondary endpoints are:

- Duration of Suprasorb® C use (days): date of last removal of Suprasorb® C[1] – date of inclusion +1

[1] Date of last removal of Suprasorb® C =

- Date of last removal of Suprasorb® C at D28 assessment if 'Healing of the wound' ticked "Yes" at assessment at D28
- **Or** Date of last removal of Suprasorb® C at D56 assessment if 'Healing of the wound' ticked "Yes" at assessment at D56
- **Or** the most recent date among: Date of assessment at D56 (i.e. date of last assessment) and **Date of study withdrawal before D56***

*** Some patients have both a date of study withdrawal and a date of assessment at D56**

If date of last removal of Suprasorb® C is filled at D28 and D56, the most recent date will be used.

All secondary endpoints relative to safety, adverse events or side effects are described in section 6.3. Safety endpoints

6.3. Safety endpoints

6.3.1. Adverse events

Adverse events will be coded using the MedDRA dictionary (version 21.1).

Safety will be evaluated by the frequency and nature (SOC/PT) of adverse events (AEs) (non serious and serious) and serious adverse events (SAEs):

- All adverse events (AE)

- Serious adverse events (SAE)
- AE by severity (mild/moderate/severe)
- AE with certain, probable or possible causal relationship with Suprasorb® C
- AE with certain, probable or possible relationship with the study procedure

AEs will be reviewed during data review meeting to decide whether they correspond to known risk and side effects (i.e wound infection, allergic disorders, pain and maceration).

A description of the following endpoints will be presented:

- At least one AE – *derived variable*
- At least one SAE – *derived variable*
- Time to onset (days) – *derived variable*
- Outcome (resolved / ongoing)
  - If resolved, duration (days) – *derived variable*
- Severity (mild / moderate / severe)
- Causal relationship to Suprasorb® C (Certain / Probable / Possible / Improbable / Excluded)
- Related to Suprasorb® C (Yes / No) – *derived variable*
  - Yes if Certain or Probable or Possible or Improbable
- Causal relationship to study procedure (Certain / Probable / Possible / Improbable / Excluded)
- Related to study procedure (Yes / No) – *derived variable*
  - Yes if Certain or Probable or Possible or Improbable

Individual listing of AEs and SAEs will be provided.

6.4. Other endpoints and variables

6.4.1. Demographic data and other baseline characteristics

The following standard characteristics (gender, age, etc.) will be used as recorded in the CRF:

- Demographic data
  - Sex (Male/Female)
  - Age (years)
  - Weight (kg)
  - Height (cm)
  - BMI (kg/m^2) – *derived variable*
    - $BMI=Weight/Height^2$
  - BMI will be classified as follows – *derived variable*
    - <18.5 = underweight
    - [18.5-24.9] = Healthy weight
    - [25-29.9] = Overweight
    - >30 = Obesity

- Characteristics of target ulcer at baseline (i.e. inclusion visit)

The following characteristics will be used as recorded in the CRF:

- Appearance of wound.

- Length × width (cm^2) (categorical variable)
- Exudation of wound (None / Mild / Moderate / Severe)
- Color segmentation (%)
  - Closed wound;
  - Pink ± red;
  - Only red;
  - ± yellow/white;
  - ± black
- Perilesional skin (Normal or Erythematous, Oedematous, Macerated, Eczema, Other)
  - In addition, a concatenation of all possible abnormal perilesional skin will be derived.

- Planimetric assessment of wound
  - Performed (Yes/No)
  - Largest diameter of wound (cm)
- Depth of the wound (cm)
- Pictures of wound
  - Pictures of wound after cleansing with saline solution (Yes/No)
  - If no, the main reason.
- Indication of use of Suprasorb® C (venous ulcer / mixed ulcer)

- Removal of primary wound dressing on D0:

The following characteristics will be used as recorded in the CRF:

- Presence of the wound dressing at inclusion (Yes/No)
- Bleeding of the wound when the dressing was removed (Yes/No)
- If yes, the bleeding was (mild, moderate, severe, very severe)

- Local treatment of target ulcer on D0:
  - Local treatment provided
    - Wound cleansing with saline solution (Yes/No)
    - Debridment of the wound (Yes/No)
    - Removal of fibrin/slough (Yes/No)
    - Local or oral analgesia provided prior to treating the wound (Yes/No)
  - Placement of Suprasorb® C
    - Number of dressings applied (One/Two/Three)
      - Numerical variable – *derived variable*
    - Was the dressing cut to size before application? (Yes/No)
    - Was the dressing moistened before application? (Yes/No)
    - Ease of application (Very easy/Easy/Difficult/Very difficult)
    - Conformability to wound (Very good/Good/Poor/Very Poor)
    - If any boxes of 3 or 4 are ticked, specify the reason
    - Did the dressing overlap the perilesional skin? (Yes/No)
    - Material used for the secondary dressing (Compresses/Gauze, Absorbent dressing pad, Superabsorber, Gel, Other material, Foam, Fixation, Hydrocolloid, Film)
      - If other, specify
    - Was the compression applied? (Yes/No)

    - If yes, specify the tradename

- Quality of life
    - Pain Score (1 to 10) + numerical – *derived variable*
    - Mobility (1 to 10) + numerical – *derived variable*
    - Social life (1 to 10) + numerical – *derived variable*
    - Psychic aspect (1 to 10) + numerical – *derived variable*

- Overall quality of life
    - How is your quality of life? (1 to 10) – categorical and numerical variables
    - How satisfied are you with your overall quality of life? (1 to 10) – categorical and numerical variables

- Planimetry
    - Wound perimeter (cm): mean of 1st data entry and 2nd data entry (*derived variable*)
    - Wound surface area (cm²): mean of 1st data entry and 2nd data entry (*derived variable*)

6.4.2. Other endpoints

6.4.2.1.Assessment since the last visit (day 28 and day 56)

- Healing of the wound
    - Healing of the wound (Yes/No)
        - if yes, time from inclusion to healing (days): Date of healing* – Date of inclusion + 1

* : date of healing=minimum date between date of healing at D28 , premature withdrawal if the wound has healed and date of healing at D56.

6.4.2.2.Characteristics of target ulcer at each visit (day 28 and day 56)

The following characteristics will be used as recorded in the CRF.

- Appearance of the wound
    - Length × width (cm²) – categorical variable
    - Exudation of wound
    - Color segmentation (%)
    - Perilesional skin (Normal, Erythematous, Oedematous, Macerated, Eczema, Other)
- Planimetric assessment of wound
    - Planimetric assessment performed? (Yes/No)
    - If no, specify the main reason
    - If yes:
        - Wound perimeter (cm): mean of 1st data entry and 2nd data entry (*derived variable*)
        - Change from baseline in wound perimeter (cm): Wound perimeter at D28/D56 – Wound perimeter at baseline (*derived variable*)
        - Wound surface area (cm²): mean of 1st data entry and 2nd data entry (*derived variable*)
        - Change from baseline in wound surface area (cm²): Wound surface area at D28/D56 – Wound surface area at baseline (*derived variable*)
- Depth of the wound (cm)

- Change from baseline in depth of wound (*derived variable*)

- Picture of wound
  - Two pictures of wound after cleansing with saline solution (Yes/No).
  - If no, specify the main reason

6.4.2.3.Removal of Suprasorb® C (day 28 and day 56)

The following characteristics will be used as recorded in the CRF.

- Rests of Suprasorb® C to the wound surrounding skin? (Yes/No)
- Removal of Suprasorb® C from the wound edges possible? (Yes/No)
- Removal of Suprasorb® C residues from the wound possible? (Yes/No)

6.4.2.4.Local treatment of target ulcer (day 28 and day 56)

The following characteristics will be used as recorded in the CRF.

- Local treatment provided
  - Was the wound cleaned with saline solution? (Yes/No)
  - Was the wound debrided? (Yes/No)
  - Was fibrin/slough removed? (Yes/No)
  - Was local or oral analgesia provided prior to treating the wound? (Yes/No)
- Placement of Suprasorb® C
  - Suprasorb® C applied on D28/D56? (Yes/No)
    - If no, specify the main reason
    - If yes,
      - How many dressings were applied (One/Two/Three) + numerical – *derived variable*
      - Was the dressing cut to size before application? (Yes/No)
      - Was the dressing moistened before application? (Yes/No)
      - Ease of application (Very easy/Easy/Difficult/Very difficult)
      - Conformability to wound (Very good/Good/Poor/Very Poor)
        - If any boxes of 3 or 4 are ticked, specify the reason
      - Did the dressing overlap the perilesional skin? (Yes/No)
      - Material used for the secondary dressing (Compresses/Gauze, Absorbent dressing pad, Superabsorber, Gel, Other material, Foam, Fixation, Hydrocolloid, Film)
        - If other, specify
      - Was the compression applied? (Yes/No)
      - If yes, specify the tradename

6.4.2.5.Overall assessment of efficacy of study dressing

The following characteristics will be used as recorded in the CRF.

- Efficacy (Very good/ Good/ Moderate/ Poor/ Very poor)
- Tolerance with regard to perilesional skin (Very good/ Good/ Moderate/ Poor/ Very poor)
- Stagnating wound showed healing tendency (Very good/ Good/ Moderate/ Poor/ Very poor)
- Conformability of dressing to the wound (Very good/ Good/ Moderate/ Poor/ Very poor)
- Patient comfort (Very good/ Good/ Moderate/ Poor/ Very poor)
- Acceptability by patient (Very good/ Good/ Moderate/ Poor/ Very poor)

In addition, the following variables will be computed:

- Changes from D28 to D56 (stagnation/deterioration/improvement) – derived variables

6.4.2.6.Quality of life

- Pain Score (1 to 10) + numerical – *derived variable*
- Mobility (1 to 10) + numerical – *derived variable*
- Social life (1 to 10) + numerical – *derived variable*
- Psychic aspect (1 to 10) + numerical – *derived variable*

For each of the previous score, change from baseline at day 28 and day 56 will be computed as follows (QOL day 28 – QOL baseline, QOL day 56 – QOL baseline).

6.4.2.7.Overall quality of life

- How is your quality of life (1 to 10) – categorical and numerical variables
- How satisfied are you with your overall quality of life (1 to 10) – categorical and numerical variables

Change from baseline at day 28 and day 56 will be computed as follows (OQOL day 28 – OQOL baseline, OQOL day 56 – OQOL baseline).

6.4.3. Nurse diary

Local treatment data at each day will be analysed as recorded in the Study nurse diary.

- Treatment planned (yes/no)
- Complete re-epithelialization of the wound (yes/no)
- Appearance of the secondary dressing BEFORE the dressing removal
  - Normal
  - Saturated
  - Bloody
  - Leakage of exudate
- Appearance of wound
  - Maceration
  - Exudation
  - Foul-smelling odor
  - Irritation/deterioration of PPL
- Local treatment
  - Cleansing of wound
  - Care of PPL
- Application of dressing
  - Moistening of dressing before application
  - Difficulty in applying
  - Problem with conformability
  - Number of dressings used
- Secondary dressing
  - Compresses / gauze
  - Foam
  - Absorbing dressing pad
  - Fixation
  - Superabsorber

- Hydrocolloid
- Gel
- Film
- Other
- Application of venous compression

- Comments

6.4.4. Medical history

Medical history data will be used as recorded in the eCRF.

In addition, the following variable will be computed:

- At least one medical history.

6.4.5. Prior and concomitant therapies

The prior and concomitant therapies will be coded with WHO-DD version SEP 2013 C Version.

The following prior/concomitant treatments will be analysed:

- All prior treatments and care recorded in the CRF ("Prior treatment and care (excluding wound dressings)" form at inclusion).
- Concomitant treatments and care recorded in the CRF. Concomitant therapies are recorded in the "Main on-going general treatment (oral and/or systemic)" form at inclusion and "change in main treatment (oral/systemic)" form at each follow-up visit.

7. DATA ANALYSIS CONSIDERATIONS

7.1. Statistical software

The statistical analysis will be performed using SAS® software v9.4.

7.2. Type I error, handling of multiplicity issues and alpha adjustment procedures

The type I error rate is set to to $\alpha = 0.05$ (two-sided).

However, no formal comparison (i.e. implying a statistical test) is planned.

No multiplicity issue is foreseen; consequently, no procedure for alpha adjustment are planned.

7.3. Site effect and pooling of sites

No site effect will be included into the model, as the site size is expected to be small.

7.4. Descriptive analyses of quantitative and qualitative variables

Quantitative variables will be described by: N (number of patients with non-missing data), mean, standard deviation (SD), minimum, maximum, median, first quartile (Q1) and third quartile (Q3). 95% CIs (binomial) for the means will be presented if they are relevant to the analysis.

Categorical variables will be described by frequency and percentage (over non-missing data) of patients in each category with the 95% CIs. Percentages will be expressed with one decimal place.

7.5. Definition of baseline, time-windows and analysis periods

Baseline:

Baseline is defined as data recorded at the inclusion visit.

Analysis periods: not applicable.

Time-windows: not applicable.

7.6. Handling of missing data and outliers

No missing data will be imputed. AEs with missing relationship, missing seriousness, and/or missing severity will be considered as related to study drug, serious, and severe for the analysis, respectively.

8. PLANNED STATISTICAL ANALYSES

All analyses will be performed on the TS and the PPS.

8.1. Disposition of patients

The following will be provided:

- Number of included patients
- Number of treated patients (i.e. TS)
- Among treated patients, number and percentage of patients who withdraw from the study at Day 56, number and percentage of patients who withdraw from the study before Day 56 and reasons for withdrawal

In addition, the following data will be provided:

- Date of first patient in (i.e. first visit performed)
- Date of last patient out (i.e. last visit performed)

Study duration (days) = date of last patient last visit - date of first patient first visit
The template in section 11.4 will be used.

8.2. Protocol deviations

Protocol deviations will be reviewed during the final data review meeting (prior to database lock). The scientific committee will adjudicate them, i.e. decide which deviations are major and should lead to exclusion from the PP set. Decisions from the scientific committee will be documented in the data review minutes.

The following potential major protocol deviations will be reviewed (but not limited to):

- Inclusion criteria not met and/or exclusion criteria met
- Attestation from investigator not available
- Date of inclusion anterior to date of attestation
- Patients who stop Suprasorb® C for reason other than healing of wound
- Withdrawal from the study for reason other than healing of wound
- Missing duration of treatment exposure
- Missing pictures of wound (i.e. “Two pictures of wound after cleansing with saline solution” not ticked “Yes” (i.e. ticked “No” or missing) at Day 28 or Day 56 if the wound is not healed yet.
- Any intermediate therapy (e.g. using different wound dressing) within the treatment period of Suprasorb® C prior to the beginning of granulation
- Missing healing date.

Patients with at least one major protocol deviation will be excluded from the Per Protocol Set.

8.3. Analysis sets

Frequency and percentage of patients included in each analysis set defined in Section 5.1 will be provided.

8.4. Demographic data and baseline characteristics, including medical history and therapies

8.4.1. Demographic data and baseline characteristics

Descriptive analyses will be provided on the TS population using templates available in section 11.1 and 11.2.

8.4.2. Medical history

Descriptive analyses will be provided on the TS population using the template available in section 11.2.

8.4.3. Prior/concomitant treatments

Descriptive analyses of prior treatments and care (excluding wound dressings) will be provided on the TS population using the template available in section 11.2.

Concomitant therapies will be analyzed by WHO-DD preferred name and ATC3 at each visit and overall. The ATC3 will be sorted alphabetically, and WHO-DD preferred names will be sorted by descending frequency (within ATC3, on « total » column) using the template in section 11.3. Treatments recorded in the CRF at D26 and D56 with "Treatment was" variable ticked "stopped" will not be presented in this analysis. Those treatments will only be listed.

8.5. Analysis of the primary endpoint

Reduction of wound area:

A descriptive analysis will be provided overall, on the Treated Set using the template provided in section 11.1.

8.6. Analysis of the secondary endpoints

Frequency and severity of adverse events as well as incidence and side effects in the group of allergic disorders, pain and maceration:

An analysis of AEs will be provided overall, on the TS using the template provided in section 11.5.

All AEs and known risks and side effects will be analyzed as number of events and number and percentage of patients who experienced at least one event.

Known risk and side effects:

AEs related to the known risks and side effects described in section 6.3.1 will be described using the template provided in **Erreur ! Source du renvoi introuvable.**

Duration of Suprasorb® C use for wound treatment:

A descriptive analysis will be provided overall, on the Treated Set using the template provided in section 11.1.

A descriptive analysis of the endpoints defined in section 6.3.12 will be provided overall, on the TS using the template provided in section 11.1 and 11.2.

Individual data listings will be provided on the TS.

8.7. Safety analysis

All safety analyses will be performed on the Treated Set.

8.7.1. Adverse events

Overall summary table:

For all AE categories defined in Section 6.3.1, the number of patients who experienced at least one AE of the corresponding category will be provided overall, on the TS, using the template provided in section 11.5.

All AEs will be listed.

All SAEs will be listed.

Analysis by SOC and PTs:

For all AE categories defined in Section 6.3.1, a descriptive analysis by SOC and PT will be provided on the TS, overall. Tables will summarize the total number of events and the number and percentage of patients experiencing the event. The SOC will be sorted alphabetically, and PT will be sorted by descending frequency (within SOC, on « total » column) according to the MedDRA classification (System Organ Class and Preferred Term).

The template provided in section 11.6 will be used.

8.8. Other endpoints

All the following endpoints will be provided on the Treated Set.

8.8.1. Assessment since the last visit

A descriptive analysis will be provided at day 28 and day 56 using the template provided in in section 11.1 and 11.2.

8.8.2. Characteristics of target ulcer

A descriptive analysis will be provided at day 28 and day 56 using the template provided in section 11.1 and 11.2.

8.8.3. Removal of primary Suprasorb® C

A descriptive analysis will be provided at day 28 and day 56 using the template provided in section 11.1 and 11.2.

8.8.4. Local treatment of target ulcer

A descriptive analysis will be provided at day 28 and day 56 using the template provided in section 11.1 and 11.2.
Listing will be provided for text free variables.

8.8.5. Overall assessment of efficacy of study dressing

A descriptive analysis will be provided at day 28 and day 56 using the template provided in section 11.1 and 11.2.

8.8.6. Quality of life

A descriptive analysis will be provided at day 28 and day 56 using the template provided in section 11.1 and 11.2

8.8.7. Overall quality of life at each visit

A descriptive analysis will be provided at day 28 and day 56 using the template provided in section 11.1 and 11.2.

8.8.8. Nurse diary

A descriptive analysis will be provided using the template provided in section 11.2.
Listing will be provided for text free variables

9. CHANGES IN THE STATISTICAL METHODS FROM THOSE STATED IN THE PROTOCOL

This SAP is based on protocol version 4.0, CRF version 6.0, Nurse diary version 5.0 and planimetry forms dated 09FEB2018 and 06APR2018.

The intention to treat set was renamed as the Treated Set to be more coherent with the definition, stated in the protocol.

10. QUALITY CONTROL

A self-validation will be performed by the statistician in charge of the analysis as follows: each derived variable will be validated exhaustively (i.e. on all patients) whenever possible. Exhaustive controls can be performed using either contingency tables (i.e. displaying all qualitative variables and minimum/maximum values of quantitative variables involved in the derivation rules) or individual data listings that are considered as not too large (i.e. no more than 50 rows). An exhaustive control is considered possible when the corresponding output contains up to 50 rows. For validation outputs considered as too large (i.e. more than 50 rows), the validation can be performed on a minimum of 10% patients randomly drawn. If the validation output is still too large (i.e. more than 50 rows), the validation will be performed on a subset of 50 rows (minimum).

Validation outputs will be reviewed by a third party (i.e. head of biostatistics or another statistician).

11. TEMPLATES

The following templates will be used.

11.1. Table template for numerical data

	Total **N=XXX**
Label of variable (unit)	
Non-missing	XXX
Mean (sd)	XXX(XXX)
Median	XXX
Q1;Q3	XXX; XXX
Min;max	XXX; XXX
Missing	XXX
Etc…	

11.2. Table template for categorical data

	Total **N=XXX**
Label of variable	
Modality 1 [n (%)]	XXX (XXX.X)
Modality 2 [n (%)]	XXX (XXX.X)
Missing [n (%)]	
Non-missing [n (%)]	
Etc.	

11.3. Table template for treatment data

	Total N=XXX		
ATC3/ Pharmaceutical substance(s)	**Nb TRT**	**Nb pat**	**% pat**
Any treatments	XX	XX	XX.X
ATC3 A	XX	XX	XX.X
Pharmaceutical substance 1	XX	XX	XX.X
Pharmaceutical substance 2	XX	XX	XX.X
ATC3 B	XX	XX	XX.X
Pharmaceutical substance 1	XX	XX	XX.X
Etc.	XX	XX	XX.X

11.4. Table template for the disposition of patients

	Total N=XXX
Included [n]	XXX
Treated [n]	XXX
Study withdrawal at Day 56 [n (%)]	XXX (XX.X)
Study withdrawal before Day 56 [n (%)]	XXX (XX.X)
Reason(s) for withdrawal [n]	XXX
	XXX
	XXX

11.5. Table template for the overall summary of AEs

	Total N=XXX
All adverse events (AE)	xxx (xx%)
Serious adverse event (SAE)	xxx (xx%)
Related AE with the study drug according to the investigator	xxx (xx%)
Related AE with the study procedure according to the investigator	xxx (xx%)
AE leading to discontinuation of the study drug	xxx (xx%)
Mild severity AE	xxx (xx%)
Moderate severity AE	xxx (xx%)
Severe severity AE	xxx (xx%)

11.6. Table template SOC and PT analysis

	Total N=XXX		
System Organ Class/ Preferred Term	**Nb AE**	**Nb pat**	**% pat**
Any adverse events	XX	XX	XX.X
SOC A	XX	XX	XX.X
PT 1	XX	XX	XX.X
PT 2	XX	XX	XX.X
SOC B	XX	XX	XX.X
PT 1	XX	XX	XX.X
Etc.	XX	XX	XX.X

SuprasorbC - Statistical Analysis Plan - v2.0 10122020

Final Audit Report 2020-12-10

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