STATISTICAL ANALYSIS PLAN

DRUG:	SGX945 (Dusquetide)
STUDY NUMBER(S):	DUS-AUBD-01
PROTOCOL(S) TITLE:	Pilot Study of SGX945 (Dusquetide) in the Treatment of Aphthous Ulcers in Behçet's Disease
IND NUMBER:	[redacted]
SPONSOR:	Soligenix, Inc.
VERSION NUMBER:	1.0
VERSION DATE:	September 5, 2024

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STATISTICAL ANALYSIS PLAN APPROVAL FORM

Protocol Title: Pilot Study of SGX945 (Dusquetide) in the Treatment of Aphthous Ulcers in Behçet's Disease

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This Statistical Analysis Plan (SAP) was subject to critical review and has been approved by the appropriate protocol review committee of the sponsor. The information contained in this SAP is consistent with the protocol requirements and intent.

Name and Title	Approval	Signature	Date
Author: [redacted]	☒ Yes ☐ No (select one)	[redacted]	
Medical Affairs: [redacted]	☒ Yes ☐ No (select one)	[redacted]	
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Quality Assurance: [redacted]	☒ Yes ☐ No (select one)	[redacted]	
Other: [redacted]	☒ Yes ☐ No (select one)	[redacted]	

1 INTRODUCTION

This statistical analysis plan (SAP) provides a more technical and detailed elaboration of the statistical analyses of efficacy and safety as outlined and/or specified in the DUS-AUBD-01 study protocol. Because this is an exploratory, proof of concept study, the clinical study report may contain additional analyses not included in this plan that will be considered hypothesis generating. Similarly, specifications of tables, figures, and data listings are contained in a separate document although additional items may be included in the clinical study report.

1.1 Dusquetide

Dusquetide is a five amino-acid peptide that binds to the intracellular p62 protein (Yu 2009, Zhang 2022) resulting in modulation of the innate immune response to both infection and tissue damage by reducing induction of inflammation and increasing macrophage activation/recruitment, resulting in increased bacterial clearance and tissue healing (Scott 2007, Kudrimoti 2016, North 2016). Preclinical studies with dusquetide revealed a significant reduction in both duration and peak intensity of oral mucositis (OM, mouth aphthous ulcers) in a fractionated radiation-induced hamster model (Kudrimoti 2016). Efficacy was dose responsive and effective at 25 mg/kg (allometric equivalent for humans 1 to 2 mg/kg) dosed every third day during fractionated radiation therapy. The small peptide molecule is rapidly metabolized by peptidases and administered by slow intravenous (IV) infusion over 4 minutes.

Dusquetide has been studied in a large Phase 1 trial where it was found to be well tolerated at doses up to the maximum administered of 8.0 mg/kg with a circulating half-life of minutes. In vitro testing of blood samples from the normal volunteers confirmed the modulation of the cytokine profiles following stimulation of the samples with lipopolysaccharide (LPS) that lasted for 48 hours following administration at which time no dusquetide was present.

In a double-blind, placebo-controlled Phase 2 trial of 111 patients with head and neck cancer (HNC) undergoing chemoradiation therapy (CRT), patients receiving 1.5 mg/kg of dusquetide had a decrease in their mean duration of severe oral mucositis (SOM) by 50% (from 18 to 9 days), a 39% reduction in the mean area-under-the-curve (AUC) of their WHO-grade-time calculation, and a 7% reduction in the incidence of SOM. Dusquetide appeared to have the highest effectiveness in subpopulations expected to have the longest duration of SOM. In the subpopulation of patients receiving the most aggressive cisplatin therapy who received 1.5 mg/kg of the drug, there was a 67% decrease in the median duration of SOM (from 30 to 10 days), a 51% reduction in the median AUC WHO grade-time calculation, and an 18% relative reduction in incidence of SOM compared to placebo.

In a double-blind, placebo-controlled, international Phase 3 trial of 266 patients receiving CRT for the treatment of HNC, dusquetide increased the number of patients without SOM from 30% in the placebo group to 41% and decreased the median time with SOM from 20 days in the placebo group to 12.5 days in the dusquetide group. The increase in variability noted across the treatment groups compared to the Phase 2 trial resulted in these differences failing to reach statistical significance.

1.2 Behçet's Disease (BD)

BD is an uncommon, chronic multisystem, variable vessel vasculitis characterized by oral ulcers, genital ulcers, uveitis, skin lesions, neurologic involvement, and gastrointestinal involvement (Yazici 2018, Hatemi 2020, Hatemi 2021). There is substantial geographic and ethnic variability of the disease with higher incidence of disease in the Middle East and Eastern Asia and low incidence in the US (Hammam 2021). The onset of disease is usually in the third decade of life (Bozkurt 2023). The most common symptoms of the disease include recurrent oral ulcers in ~95% of patients, genital aphthous ulcers in 80%, vascular involvement in 15 to 50%, ocular involvement in 40 to 50%, and neurologic involvement in <5% (Leccese 2021). The disease course involves spontaneous remission and exacerbation and is thought to share both autoimmune and autoinflammatory disease features (Le Joncour 2023).

BD has been increasingly associated with genetic abnormalities causing or concurrent with innate immune amplification (Shimizu 2023). Skin histopathology indicates neutrophilic dermatitis or panniculitis while pathergy tests in BD patients result in persistent lymphocyte and monocyte infiltrations compared to healthy individuals (Shimizu 2023). In both oral and genital lesions, lymphocyte infiltration is frequently observed in the lamina propia. In addition to neutrophil infiltration, macrophages have also been shown to have altered response profiles in response to BD sera, suggesting a prevalence of M1 type macrophages in BD patients (Shimizu 2023). Similarly, impairment of M2 mediated anti-inflammatory function has been proposed as an underlying etiology of BD (Hirahara 2022). IL-1β, IL-6 and TNFα are all known to be elevated in serum from patients with BD (Li 2023, Shimizu 2023).

2 STUDY METHODS

This is an open-label trial enrolling patients with BD and a history of oral and/or genital ulcers with at least two active oral ulcers and/or one active genital ulcer and with well documented details of prior treatments and responses to that treatment. Patients will receive dusquetide (1.5 mg/kg based on the patient's Baseline body weight) administered every 3 days (-1/+2) as a 4-minute infusion.

Patients will be treated for a total of 4 weeks (8 treatments), with weekly follow-up visits for an additional 4 weeks. At Baseline and at each visit, the number of genital ulcers, the

number of oral ulcers, the pain due to oral ulcers, the pain due to genital ulcers, and vital signs will be recorded. Female patients reporting symptoms will undergo a pelvic exam at the Baseline visit in order to note any genital ulcers that may be present internally. The pelvic exam will be repeated at Week 4 Treatment 2 and the Week 8 follow-up visit if the patient states that they have vaginal ulcers. At each infusion visit, vital signs will be collected once prior to the infusion, as well as four times post-infusion (every 5 minutes for 20 minutes). The degree of oral and genital ulcer scarring and quality of life and disease severity assessments (Leeds Behçet's Disease Quality of Life Assessment [BD-QoL], Behçet's Disease Current Activity Form [BDCAF], Behçet's Syndrome Activity Score [BSAS], peripheral joint count and evaluation for tenderness and swelling, and both Physician and Patient global assessment [PGA and PtGA] of skin lesions) will additionally be assessed at Baseline, at the last treatment visit (Week 4 Treatment 2) and at the last follow-up visit (Week 8). Physical examinations and safety labs (hematology and chemistry) will be analyzed at Baseline, at the last treatment visit (Week 4 Treatment 2) and at the last follow-up visit (Week 8). The Behçet's Disease History Patient Questionnaire (BDHPQ) will be assessed at the Baseline Visit and at the last treatment visit (Week 4 Treatment 2). AEs will be recorded throughout the study.

3 DATA SOURCE

Data will be entered into a paper CRF and monitored by personnel from Soligenix's designee, Mene Health Group, against the medical record/source documents. Data will be entered into Excel files and analyzed in both Excel (Office 2019 or later) and Prism (version 10.0 or higher).

4 ANALYSIS OBJECTIVES

This is an open label, pilot, proof-of-concept trial. Data generated will be compared to prior, published data of apremilast versus placebo in a similar population from the same site (Hatemi 2019). Historical safety and efficacy comparisons will be made with both the placebo and apremilast treatment groups from published data as well as a comparison of patient outcomes compared to their own historical medical history of flares.

5 PATIENT POPULATIONS AND SUBGROUPS

This is a single group trial and analyses will include all patients who have been enrolled and receive at least one dose of dusquetide. The entry criteria are as follows.

Inclusion Criteria:

In order to be enrolled into the trial, subjects must meet ***all*** of the criteria below:

1. ≥18 years of age.

2. Patients must have a clinical diagnosis of BD meeting the International Study Group criteria.

3. Patients must have at least two oral ulcers and/or one genital ulcer on the day of randomization.

4. Patients willing to follow the clinical protocol and voluntarily give their written informed consent.

5. Female patients not pregnant or nursing and willing to undergo a pregnancy test prior to treatment initiation and at the end of the treatment period.

Exclusion Criteria:

In order to be enrolled into the trial, subjects cannot have any of the following criteria:

1. Pregnancy or mothers who are breast-feeding.

2. All women of childbearing potential (WOCBP) and males with female partners who are WOCBP NOT WILLING to agree to the use of effective contraception during the trial.

3. Evidence of significant renal, hepatic, hematologic or immunologic disease.

4. Subject has any condition that, in the judgment of the PI, is likely to interfere with participation in the study.

5. Use of any investigational medication within 4 weeks prior to enrollment or 5 pharmacokinetic/pharmacodynamic half-lives (whichever is longer).

6. Having received concomitant immune modulating therapy (except colchicine) within:

    a. Ten days prior to enrollment for azathioprine and mycophenolate mofetil

    b. Four weeks (28 days) prior to enrollment for cyclosporine, methotrexate, cyclophosphamide, thalidomide and dapsone

    c. Oral and topical corticosteroids must have been tapered as appropriate and discontinued 3 days prior to day of enrollment

    d. At least 5 terminal half-lives for all biologics including, but not limited to, those listed below; within:

        i. Four weeks prior to enrollment for etanercept

ii. Eight weeks prior to enrollment for infliximab

iii. Ten weeks prior to enrollment for adalimumab, golimumab, certolizumab, abatacept, and tocilizumab

iv. Six months prior to enrollment for secukinumab

7. Having received oral or parenteral corticosteroids within 6 weeks (42 days) prior to enrollment.

8. Having received apremilast (Otezla®) within 4 weeks prior to enrollment.

9. Presence of non-BD related genital ulcers, including both infectious and non-infectious etiologies.

10. Active organ involvement requiring immunosuppressive treatment.

6 ENDPOINTS AND COVARIATES

This is a pilot study to determine the efficacy and safety of SGX945 (dusquetide) in BD patients with oral and/or genital ulcers. Efficacy statistics will be performed comparing the results to the apremilast study (Hatemi 2019) results (both the placebo and apremilast treatment groups) but, because of the small sample size of the trial, the results are not expected to meet the threshold for statistical significance. Similarly, the outcomes for the individual patient will be compared to their personal history of previous flares. This subjective data will be presented as "Worse", "Same", "Better".

All reported data will be presented as tables, figures, and patient listings.

6.1 Baseline Characteristics

The demographic and Baseline characteristics of the dusquetide study will be presented and the reported data from the apremilast study included in the tables for reference.

6.2 Efficacy Endpoints

Endpoints for this proof-of-concept, open-label study will include:

- Proportion of patients with complete resolution of oral ulcers
    - Dichotomous variable
    - Yes/No at 4 weeks

  - Comparisons to the apremilast study results (using the 6-week values since this is the earliest result published although the number of successes is expected to be higher in the apremilast than the 4-week dusquetide value) analyzed using a chi-squared test unless the expected value in any one of the 2×2 table is less than 5 in which case an exact Fisher's p-value will be calculated

- Proportion of patients with complete resolution of genital ulcers
  - Dichotomous variable
  - Yes/No at 4 weeks
  - Given that the apremilast study only reported the 12-week resolution of genital ulcer data, no formal statistical tests will be done
- AUC of the number of oral ulcers over time throughout the 4-week treatment window
  - Continuous variable
  - A linear trapezoid method will be used to calculate the AUC for each reported timepoint and the AUC will be the sum of the AUCs in each time period through 4 weeks
  - Comparison made to apremilast study drug and placebo rates estimated from the Figure 2 graph through 4 weeks using a student's t-test
  - Comparison made to apremilast study drug and placebo rates versus the dusquetide rate using the Kaplan-Meier method and the curves compared using a log-ranked test
- AUC of the number of genital ulcers over time throughout the 4-week treatment window
  - Continuous variable
  - A linear trapezoid method will be used to calculate the AUC for each reported timepoint and the AUC will be the sum of the AUCs in each time period through 4 weeks
  - No comparison to the apremilast study is possible since this data was not presented
- Number of oral ulcers over time throughout the 4-week treatment window

- Continuous variable
- Presented as the mean, standard deviation, median, range and 95% confidence intervals

- Number of genital ulcers over time throughout the 4-week treatment window
  - Continuous variable
  - Presented as the mean, standard deviation, median, range and 95% confidence intervals

- Time to complete resolution
  - Genital ulcers (if present)
  - Oral ulcers (if present)
  - Any ulcers
  - All
    - Continuous variable
    - Presented as table of all patients with number of ulcers (categorized by type: oral/genital/all) and visit through 4 weeks
    - No comparison to the apremilast study since apremilast data reported either at 12 weeks (oral or genital) or not reported (any ulcer)

- Time to recurrence or new occurrence of genital ulcers
  - Continuous variable
  - Presented as the mean, standard deviation, median, range and 95% confidence intervals
  - No comparison to the apremilast study is possible since only treatment phase data was presented

- Time to recurrence or new occurrence of oral ulcers
  - Continuous variable

- Presented as the mean, standard deviation, median, range and 95% confidence intervals
- No comparison to the apremilast study is possible since only treatment phase data was presented

- Change from Baseline score of pain due to genital ulcers
  - Continuous variable
  - Presented as the mean, standard deviation, median, range and 95% confidence intervals
  - No comparison to the apremilast study is possible since only 12 week data was presented
- Change from Baseline score of pain due to oral ulcers
  - Continuous variable
  - Presented as the mean, standard deviation, median, range and 95% confidence intervals
  - Given that the apremilast study results only reported the 12-week oral ulcer pain data, no formal statistical tests will be done
- Change from Baseline score in the BD-QoL
  - Continuous variable
  - Presented as the mean, standard deviation, median, range and 95% confidence intervals
  - Given that the apremilast study results only reported the 12-week BD-QoL data, no formal statistical tests will be done
- Change from Baseline score in the BDCAF
  - Continuous variable
  - Presented as the mean, standard deviation, median, range and 95% confidence intervals

- Given that the apremilast study results only reported the 12-week BDCAF data, no formal statistical tests will be done

- Change from Baseline score in the BSAS
  - Continuous variable
  - Presented as the mean, standard deviation, median, range and 95% confidence intervals
  - No comparison to the apremilast study is possible since this data was not presented

- Change from Baseline score in number of peripheral joints with arthralgia, severity of pain
  - Continuous variable (counts)
  - Presented as the mean, standard deviation, median, range and 95% confidence intervals
  - No comparison to the apremilast study is possible since this data was not presented

- Change from Baseline score in number of peripheral joints with arthritis, severity of swelling, and severity of tenderness
  - Continuous variable (counts)
  - Presented as the mean, standard deviation, median, range and 95% confidence intervals
  - No comparison to the apremilast study is possible since this data was not presented

- Change from Baseline score in the PGA and PtGA of skin lesions
  - Continuous variable
  - Presented as the mean, standard deviation, median, range and 95% confidence intervals
  - No comparison to the apremilast study is possible since this data was not presented

- Number of ulcers with a clinical diagnosis of infection
    - Continuous variable (counts)
    - Presented as the mean, standard deviation, median, range and 95% confidence intervals
    - No comparison to the apremilast study is possible since this data was not presented
- Presence and severity of any scarring within 4 weeks post-treatment
    - Continuous variable
    - Presented as the mean, standard deviation, median, range and 95% confidence intervals
    - No comparison to the apremilast study is possible since this data was not presented

Data will be compared to historical outcomes for each patient with respect to resolution of genital and oral ulcers (descriptive analysis) and historical resolution rates for both genital and oral ulcers over time in the literature.

6.3 Safety Endpoints

6.3.1 Treatment Emergent Adverse Events (TEAEs)

A summary overview of TEAEs will be presented in each of the following categories by the number and percentage of patients experiencing at least one of the described TEAE as shown in Table 1.

Table 1: Summary of TEAEs

Measurement	Patients with at Least 1 Reported TEAE SGX945 N = 25
Any TEAE	
Moderate or Severe TEAE	
Severe TEAE	
Moderate or Severe "Administration related TEAE" [a]	

Severe "Administration related TEAE" [a]
TEAE "Related" to Study Drug
TEAE "Possibly Related" to Study Drug
TEAE "Possibly Related" or "Related" to Study Drug
TEAE leading to patient withdrawal
Serious Adverse Event (SAE)

[a] Administration related TEAE includes all AEs categorized as "General disorders and administration-site conditions" that include "Administration or infusion related" in the Preferred Term description

A listing of each System Organ Class (SOC) and Preferred Term (PT) reported TEAE by treatment group with all reported PTs presented for each SOC listed. TEAEs by severity and relatedness will be presented in which each PT reported for a given SOC will be listed. Where a given patient has more than one event for a given PT/SOC, it will only be counted once and assigned the maximum severity or relatedness reported if there are different judgements among the reports of the same event in that patient.

6.3.2 Safety Laboratory Results

For all laboratory data, if the reported value of a clinical laboratory parameter cannot be used in a statistical summary table due to, for example, that a character string is reported for a parameter of the numerical type, then a coded value needs to be appropriately determined and used in the statistical analyses as shown in Table 2. However, the actual values as reported in the database will be presented in data listings.

Table 2: Example for Coding of Special Character Values for Clinical Laboratory Parameters

Lab Test	Possible Lab Results (in SI unit)	Coded Value for Analysis
Chemistry: ALT	<5	5
Chemistry: AST	<5	5
Chemistry: Bilirubin, Total	<2	2

Categorization of laboratory results into low/normal/high group will be done using the single local laboratory's lower and upper limits of normal value.

6.3.3 Vital Signs

Vital signs data and change from Baseline will be summarized using descriptive statistics. Criteria for clinically significant values have been defined as shown in Table 3. Shift in number of patients with clinically significant values at Baseline will be displayed.

Table 3: Vital Signs Clinically Significant Value

Vital Sign Variable	Absolute Value
Systolic Blood Pressure	≥180 mmHg and increase of ≥20 mmHg from Baseline ≤90 mmHg and decrease of ≥20 mmHg from Baseline
Diastolic Blood Pressure	≥105 mmHg and increase of ≥15 mmHg from Baseline ≤50 mmHg and decrease of ≥15 mmHg from Baseline
Pulse	≥120 bpm and increase of ≥15 bpm from Baseline ≤50 bpm and decrease of ≥15 bpm from Baseline

Listings of all vital sign values will note values that are identified as abnormal and the PIs as to whether these are clinically significant.

6.3.4 Physical Examinations

Reported findings from the general physical examination will by listed by patient.

7 HANDLING OF MISSING VALUES AND OTHER DATA CONVENTIONS

7.1 Missing Efficacy Data

Any efficacy data point missing will be considered censored for that timepoint in summary analyses. No imputed values will be used. All reported data points will be included in the patient listings.

7.2 Missing Safety Data

Any safety data point missing will be considered censored for that timepoint in summary analyses. No imputed values will be used. All reported data points will be included in the patient listings.

For TEAEs missing the judgement of relatedness will be considered to be "Related". For TEAEs missing the judgement of severity will be considered to be "Severe". For TEAEs missing an end date will be considered to be "Ongoing".

7.3 Missing Date Data

7.3.1 General Missing Date Information

For events occurring within the study period, missing dates for any activity required during that visit will have the visit date imputed.

7.3.2 Missing Dosing Date Information

If the date of dosing of the study medication is missing, it will be assigned the associated visit date. If the date of the imputed stop date is before the start date (imputed or non-imputed start date), then the imputed stop date will be equal to the start date.

7.3.2.1 Missing day and month

If the year of the incomplete stop date is the same as the year of the last dose date of study medication, then the day and month of the last dose date will be assigned to the missing fields.

If the year of the incomplete stop date is prior to the year of the last dose date of study medication, then December 31 will be assigned to the missing fields.

If the year of the incomplete stop date is after the year of the last dose date of study medication, then January 1 will be assigned to the missing fields.

7.3.2.2 Missing month only

Treat day as missing and replace both month and day according to the above procedure.

7.3.2.3 Missing day only

If the month and year of the incomplete stop date are the same as the month and year of the last dose date of study medication, then the day of the last dose date will be assigned to the missing day.

If either the year is before the year of the last dose date of study medication or if both years are the same but the month is before the month of the last dose date of study medication, then the last day of the month will be assigned to the missing day.

If either the year is after the year of the last dose date of study medication or if both years are the same but the month is after the month of the last dose date of study medication, then the first day of the month will be assigned to the missing day.

8 PROCEDURES TO REDUCE BIAS

This is an open-label trial with all patients receiving dusquetide.

9 STATISTICAL PROCEDURES

9.1 Methodology and Conventions

All efficacy endpoints will be analyzed using all the patients enrolled and having received at least one dose of study drug. Baseline information and efficacy assessments will be listed for all patients for all available time points. As a single site study, local lab results will be utilized for all evaluations. All data collected will be included in data listings.

9.2 Additional Data Handling Rules and Presentation Specifications

The following general guidelines will apply to all statistical analyses and data presentations:

- All patient data, will be summarized and presented
- Baseline is defined as the last available value obtained prior to the first administration of study drug.
- By default, US conventional units will be used for laboratory value presentations. A set of lab summary tables in International Standard Units (SIU) will also be provided based on tables, listings and figures (TLF) index.
- Age is calculated as of date that the informed consent form was signed.
    - age = floor((date of Informed Consent – birth date+1)/365.25)
- Duration of treatment or days in treatment is calculated as: last dose date – first dose administration date + 1
- Study day of assessment is calculated as: assessment date – first dose administration date + 1 for assessments occurring on or after first dose administration date. Study day of assessment is calculated as: assessment date – first dose administration date for assessments occurring prior to first dose administration date.
- Body weight, height and temperatures will be converted using the following formula:
    - kg = pounds/2.2

- cm = 2.54 × inches

- All percentages will be rounded to one decimal place and lined up by the decimal place. The percentage will be suppressed when the count is zero. Percentages of 100% will have the decimal place suppressed and will be presented as 100%.

- For continuous variables that are recorded as "< X" or "> X", the value of "X" will be used in the calculation of summary statistics. The original values will be used for the listings.

- Decimal points will be presented as follows:

  - Number of patients (N) and the numbers of patients with characteristic of interest (n) will be presented without a decimal point.

  - Minimum and maximum in same precision (number of places after the decimal point) as in the database.

  - Mean and median in one more places after the decimal point than minimum and maximum.

  - Standard deviation (SD) in one more decimal than mean and median.

9.3 Analyses

Continuous variables presentations will include the statistics as shown in Table 3.

Table 4: Summary Statistics of Continuous Variables

Statistic	Software	Function
Mean	Excel	= AVERAGE(*array*)
Standard Deviation	Excel	= STDEV.P(*array*)
Median	Excel	= MEDIAN(*array*)
Minimum of range	Excel	= MIN(*array*)
Maximum of range	Excel	= MAX(*array*)
Minimum of CI range	Excel	= MEAN(*array*)-CONFIDENCE.T(0.05, STDEV.P(*array*), size)
Maximum of CI range	Excel	= MEAN(*array*)+CONFIDENCE.T(0.05, STDEV.P(*array*), *size*)
Group comparisons	Excel	= TTEST(*array1,array2*, 2, 2)
Graphs	GraphPad Prism	

CI= 95% confidence interval

Categorical data presentations will include the statistics as shown in Table 4.

Table 5: Summary Statistics of Categorical Variables

Statistic	Software	Function
N	From database	
n	From database	
Percent	Excel	= n ÷ N
Group comparisons with all cells with expected value >5	Excel	= CHISQ.TEST(*array of actual values, calculated array of the ratio of the product of row totals and column totals to the grand total*, 2, 2)
Group comparisons with all cells with expected value ≤5	GraphPad Prism	Fisher's exact test using contingency format
Kaplan-Meier curves	GraphPad Prism	Survival format used with start and last dates columns used for each patient. Log-Rank test p-value reported

n = number of patients in category
N = total number of patients in group

10 INTERIM ANALYSIS

No Interim Analysis will be conducted.

11 SENSITIVITY ANALYSES

Given the limited sample size, no sensitivity analyses are planned although results for subgroups defined by sex (male/female), age (< median, ≥ median), and ulcer type (oral, genital, and oral/genital) will be presented.

12 ADJUSTMENTS OF MULTIPLICITY, CONFOUNDERS, AND HETEROGENEITY

Given the limited sample size and single-arm design, no formal statistical adjustments are planned.

13 SAMPLE SIZE CALCULATION

No formal sample size calculation was conducted to determine the number of patients to be entered into this exploratory, open-label, pilot study.

14 LISTING OF TABLES, FIGURES, AND LISTINGS

This information is provided in a separate document, "Tables, Figures, and Listings".

15 COMPUTER SOFTWARE

Data will be entered into Microsoft Excel (version 2019 Microsoft Office Professional Plus or higher) and the analyses listed in Section 9 will be performed using the built-in function, as indicated. All graphs, Fisher's exact p-values calculations, and Kapan-Meier time to event analyses will be performed using GraphPad Prism (version 10.0 or higher).

16 PROCEDURES OF MAINTAINING PATIENT CONFIDENTIALITY

All data shared with Soligenix and included in the database will be identified only by the subject number without names or initials included. The degree of anonymity of data will be included in the Informed Consent Form signed by the patients.

17 REFERENCES

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