Official Title: A Multicenter, Open-label, Study of StrataGraft Skin Tissue in Adult Subjects with Deep Partial-thickness Thermal Burns

NCT Number: NCT04123548

Document Date: SAP (Version 1): 11 March 2022

STATISTICAL ANALYSIS PLAN

Protocol Number: MNK01053115

A Multicenter, Open-label, Study of StrataGraft® Skin Tissue in Adult Subjects with Deep Partial-thickness Thermal Burns

Product: StrataGraft®

Regulatory Agency Identification Number (IND): 010,113

Original Protocol (V1) Date: 26 August 2019
Amendment 1 (V2) Date: 02 October 2020
Study Phase: 3b

Original SAP Date: 11 May 2020
SAP V1 Date: 25 February 2022

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Statistical Analysis Plan Approval

Title:	A Multicenter, Open-label, Study of StrataGraft Skin Tissue in Adult Subjects with Deep Partial-thickness Thermal Burns
Protocol Number:	MNK01053115
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ABBREVIATIONS

Abbreviation	Term
AE	Adverse event
autograft	Transplant of skin tissue from 1 location to another on same person
CI	Confidence Interval
CSR	Clinical Study Report
DPT	Deep partial-thickness (has intact dermal elements)
eCRF	Electronic case report form
FDA	Food and Drug Administration
HCRU	Health care resource utilization
ICH	International Council for Harmonisation
MedDRA	Medical Dictionary for Regulatory Activities
OR	Operating Room
POSAS	Patient and observer scar assessment scale
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SG	StrataGraft
SoC	Standard of Care
TBSA	Total body surface area
TEAE	Treatment-emergent adverse event
xenograft	The transplant of an organ, tissue, or cells to an individual of another species.

1 INTRODUCTION

This Statistical Analysis Plan (SAP) describes the planned analysis for Mallinckrodt Pharmaceuticals protocol MNK01053115 (A Multicenter, Open-label, Study of StrataGraft Skin Tissue in Adult Subjects with Deep Partial-thickness (DPT) Thermal Burns; the StrataCAT Study). This phase 3b study is being completed to assess safety, clinical outcomes, and healthcare resource utilization (HCRU) for a single application of StrataGraft in the post excision treatment of thermally induced DPT burn that contain intact dermal elements in an adult patient population.

The following documents were reviewed in preparation of this SAP:

- Protocol MNK01053115, issued on 26 August 2019. [Amendment 1, V2, 02 October 2020]
- Case report form (CRF), issued on 20 August 2021
- ICH (E9) Guidance on Statistical Principles for Clinical Trials.

The purpose of the SAP is to ensure the credibility of the study results by pre-specifying the statistical approaches for the study analysis prior to database lock. The analyses outlined in this SAP supports the completion of the Clinical Study Report (CSR) and may be included in regulatory submissions and/or future manuscripts. Unplanned, exploratory analyses performed to support the clinical development program may not necessarily be identified in the SAP and will be identified in the CSR.

2 PROTOCOL SUMMARY

2.1 Study Design

This is a prospective, open-label, single-arm study assessing the safety and clinical outcomes of StrataGraft in the treatment of DPT thermal burn injuries with intact dermal elements. Study enrollment will be approximately 100 subjects but will continue until StrataGraft becomes commercially available or until the Sponsor decides to close the study. Enrollment will include subjects with a minimum of 3% and up to 50% TBSA of partial +/- full thickness thermal burn. Treatment will include a single application of up to 1:1 meshed StrataGraft on prepared DPT wound(s) totaling no more than approximately 2000 square centimeters in area (no more than 3 study treatment thermal burn areas and no more than 20 StrataGraft constructs applied per subject). The wound bed must be clean, excised and have bleeding controlled prior to StrataGraft application. The constructs may be anchored with tissue adhesive, staples, or sutures, and then covered with a nonadherent, nonocclusive contact layer and additional secondary dressings per institutional standard of care (dressings should not contain silver). Safety assessments will include monitoring of treatment emergent adverse events (TEAEs), serious adverse events (SAEs), wound infections, and clinically significant changes in vital signs, laboratory test results, and

immunological changes. Wound assessments will include measurements for average depth, length, and width for calculations of area and percent epithelialization. Wound assessments will be facilitated by photographs taken by the subject and/or taken by the clinical study site staff at study visits throughout the study. Scar evaluation will be conducted using the Patient and Observer Scar Assessment Scale (POSAS). Additionally, HCRU data will be collected. All eligible subjects were provided the opportunity to consent to be part of a contact database and follow-up registry; subjects will have the choice to decline with no impact to their participation in the StrataCAT study. In addition, a subset of 10 subjects (sourced from across all the sites) with closed wounds will be separately consented to have a punch biopsy (measuring 3 mm) taken from the center of the healed burn wound, and another punch biopsy measuring 3 mm taken from non-burned healthy skin. A histological evaluation of both samples will be done to analyze and contrast the skin architecture in the healed burn wound with healthy skin. The biopsy will happen at the Week 12, regardless of when wound closure occurs.

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Table 1: Schedule of Assessments

Procedure	Screening +/-14 days	Day 1 Baseline	Week 1[a] ± 2 days	Week 2[a] ± 2 days	Week 4[a] ± 3 days	Week 8[b] ± 3 days	Week 12[b] ± 7 days	Week 24[b] ± 7 days	Visit for Confirmation of Healing[c]
Informed consent for study treatment	√								
Consent for direct contact by Sponsor and safety registry post study [d]		√	—	—	—√—	—	—	—	—√
Medical history, physical examination, and height and weight	√								
Pregnancy test	√								-
Vital signs	√	√	√	√	√	√	√	√	√
Infection assessment	√	√	√	√	√	√	√	√	√
Concomitant medications/procedures	√	√	√	√	√	√	√	√	√
Prescription drugs given at discharge from the hospital for wound-related events including pain control, itch, psychotropics, and antibiotics		√	√	√	√	√	√	√	√
Safety laboratory tests[e]		√[f]					√		
Archival plasma and leukocyte collection		√							

Procedure	Screening +/-14 days	Day 1 Baseline	Week 1[a] ± 2 days	Week 2[a] ± 2 days	Week 4[a] ± 3 days	Week 8[b] ± 3 days	Week 12[b] ± 7 days	Week 24[b] ± 7 days	Visit for Confirmation of Healing[c]
Blood collection for PRA testing (HLA I and II)		√			√		√		
StrataGraft application		√							
AE[g] /SAE /TEAE assessment	√	√	√	√	√	√	√	√	√
Photograph of treatment sites[h]	√	√	√	√	√	√	√	√	√
Assessment of wound closure/continued closure			√	√	√	√	√	√	√
Skin quality outcome of treatment sites							√	√	
HCRU Assessments	√	√	√	√	√	√	√	√	√
Biopsies[i]							√		

[a] In public state of emergency situations, the Weeks 1 and 2 visit windows can be expanded to include ± 5 days.

[a] In public state of emergency situations, the Week 4 visit window can be expanded to include ± 12 days.

[b] In public state of emergency situations, the Weeks 8, 12, and 24 visit windows can be expanded to include ± 14 days.

[c] This visit may be scheduled at any time during the study to occur at least 2 weeks after initial observation of complete wound closure.

[d] Consent for post study registry can be obtained at any study visit beginning at Screening (together with the consent for the study treatment), during the study treatment, or at the final study visit.

[e] Any testing abstracted from the medical record from the time of admission throughout the study treatment period.

[f] May be performed within 48 hours of surgery.

[g] AEs will be assessed on an ongoing basis; AEs (serious and non-serious) occurring from time of signing informed consent until completion of the Final Visit and follow-up until resolution of any ongoing TEAE at the time of study treatment completion or subject withdrawal.

[h] A weekly photo taken by subject (or designate) of the treatment site(s) for the first 12 weeks and then every other week to Week 24. Photos submitted during a week when there's no in-person visit would serve as an allowable proxy for observing wound characteristics. If a subject's wound is noted to be closed for the first time via a submitted photo that should prompt a confirmation of wound healing visit 2 weeks later.

[i] Biopsies of a closed wound and of the normal skin will be taken from a subgroup of 10 subjects.

2.2 Study Objectives and Endpoints

2.2.1 Primary Objective

The primary objective of this study is to assess the safety of a single application of StrataGraft in the treatment of adults with thermally induced DPT burns that contain intact dermal elements.

2.2.2 Other Objectives

Demonstrate the clinical outcomes of a single application of StrataGraft in the post excision treatment of thermally induced DPT burns that contain intact dermal elements.

2.2.3 Exploratory Objective

Assess for healthcare resource utilization (HCRU) throughout the study period.

2.2.4 Modification from the Statistical Section of the Final Protocol

No major modification from the latest protocol is made.

2.3 Sample Size Considerations

No sample size determination was made for this study, as this is a single treatment group, non-randomized study designed to accumulate supplemental safety and outcome data for the use of StrataGraft for the treatment of DPT wounds with intact dermal elements. This study will enroll approximately 100 subjects from up to 18 clinical study centers that previously participated in the phase 3 STRATA2016 study.

2.4 Randomization and Blinding

This study is designed as an open-label, single arm study. No randomization will be conducted, and no blinding is required for the study.

2.5 Interim Analysis (IA)

No statistical interim analyses for efficacy are planned for this study.

3 STATISTICAL METHODS AND CONVENTIONS

3.1 General Conventions

- Unless otherwise noted, the number of subjects (N), mean, standard deviation, median, minimum, and maximum will be presented for continuous variables and frequency and percentage of subjects in each category will be presented for discrete variables.
- Unless otherwise noted, confidence intervals (CIs) will be 2-sided 95% CIs.
- Listings will be sorted by subject identification, and date of the procedure or event.
- Statistical analyses will be done using Statistical Analysis Software (SAS®) version 9.4 or higher.
- The Kaplan-Meier estimate will be computed to determine the median time to first confirmed complete wound closure without autograft placement (date of closure is the date of the first observation of complete epithelialization without use of an autograft and confirmed with a second observation of complete closure at least 2 weeks after the first.). The 95% CI will be constructed with a generalized Brookmeyer and Crowley method.
- The Proportion and 95% CI of subjects will be calculated using the normal approximation to the binomial distribution.
- Listing will be provided for all related summary tables.

3.1.1 Handling of Missing Data

No imputation for missing values will be conducted. All observed values (i.e., excluding missing values for visit) will be used for the analyses.

3.1.2 Date/Time Derived Variable Conventions

Study Day 1 (application of StrataGraft) will be considered as baseline for the endpoint calculation. If the value is not available at Study Day1, the last available observed value prior to application of StrataGraft will be used.

3.2 Analysis Populations

All safety and efficacy analyses will be based on the mITT population.

3.2.1 Modified Intention to Treat Population

The modified intention-to-treat (mITT) population will include all subjects who enrolled and received StrataGraft.

3.2.2 Major/Minor Protocol deviation

Protocol deviation (i.e., Major, Minor) will be determined before data base lock by sponsor clinical team. The major and minor protocol deviations will be listed.

3.3 Demographics and Baseline Characteristics

Demographic characteristics, including age, age category (<65, ≥65 year), sex, race, ethnicity, weight, height, BMI, baseline condition based on the Baux score and its category (<50, ≥50), Modified Baux score and its category (<90, ≥90), and overall TBSA burned and its category (<median, ≥median) will be summarized by all subjects on mITT population and completers which is defined as subjects complete study.

The Modified Baux score is calculated as:

Modified Baux score = age + TBSA burned + [17 x (inhalation Injury, 1 = yes, 0 = no)], where TBSA burned includes only 2nd and 3rd degree burns.

The Baux score is calculated as:

Baux score = age + TBSA burned, where TBSA burned includes only 2nd and 3rd degree burns.

The following parameters will also be summarized:

- Time of first assessment at any medical center to StrataGraft treatment, and its category (≤7, >7 days)
- Time of first assessment at any medical center to assessment at this medical center (days)
- Time of burn injury date to application of StrataGraft date
- Time of burned injury date to application of StrataGraft date (≤7, >7 days)
- Mean total StrataGraft (SG) treatment site area and its category (≤500 cm^2, >500 cm^2, & ≤1000 cm^2, >1000 cm^2) by subject, respectively
    - SG treatment site A area and its category (≤500 cm^2, >500 cm^2)
    - SG treatment site B area and its category (≤500 cm^2, >500 cm^2)
    - SG treatment site C area and its category (≤500 cm^2, >500 cm^2)

  - StrataGraft Treatment by location (Anterior trunk, Anterior Upper Extremity (upper arm + forearm), Anterior Lower Leg, Anterior Thigh, Posterior Trunk, Posterior Upper Extremity (upper arm + forearm), Posterior Lower Leg, Posterior Thigh)

- Mean total StrataGraft (SG) treatment site area and its category (≤500 cm^2, >500 cm^2, & ≤1000 cm^2, >1000 cm^2) by treatment site regardless of their label A, B or C
- Other burn area not treated with StrataGraft (%TBSA)
- Donor site area (cm^2)

3.4 Medical History and Physical Examination

Medical history terms will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 23.0. The frequency and percentage of subjects with medical history within each system organ class will be summarized.

The limited Physical Examination will be conducted at Screening to include evaluation of lungs, heart, abdomen, and extremities. The findings (normal, abnormal, abnormal clinical significance) of the physical examination will be recorded on the eCRF and summarized.

The acute burn history, which the subject has any relevant history associated with the subject's acute burn event, will be tabulated by body system.

3.5 Concomitant Medications

Medications will be coded using the WHODRUG dictionary (Global B3 September 2020) by using Anatomical-Therapeutic-Chemical (ATC) classification and preferred term name. ATC category (i.e., ATC 4) and Preferred term will be summarized by location (SG treatment sites, non-SG burn area, donor site, other site) and all subjects.

3.6 Concomitant Procedures

Concomitant procedure (including transfusions, use of xenograft or allogenic products, negative pressure wound therapy, etc.) will be summarized with the records throughout the duration of the study. The total number of concomitant procedure and number of subjects who had at least one concomitant procedure will be summarized by SG treatment site, non-SG burn area, not applicable and all subjects.

3.7 Treatment and Exposure

The number of subjects with 1, 2, and 3 burn sites, and numbers of StrataGraft constructs applied (per site and total per subject) will be summarized.

The observation duration from Day 1 (application of StrataGraft) to end of study will be summarized.

3.8 Efficacy and Safety Analysis

There is no hypothesis testing for the study. All analyses are descriptive.

3.8.1 Primary Endpoint Analysis

The primary endpoint of this study is:

- **Count and percentage of subjects with TEAEs.**

  The TEAE is defined as those adverse events with onset date and time after the first placement of study product or those events in which the onset date and time are before the first placement of study product but worsened after the first placement of study product. To be conservative, in the case of a missing start date for an AE, the AE will be considered a TEAE. All the subjects with TEAEs will be summarized with frequency and percent in mITT population.

  More analyses will be performed as described in section 3.9.1.

  The subgroup analyses of TEAE will be performed as described in section 3.8.3.

3.8.2 Other Endpoint Analyses

The other endpoints of this study are:

- **Proportion of subjects with confirmed complete wound closure of all treatment sites without autograft (i.e., complete re-epithelialization without drainage and subsequently verified with confirmation assessment) on or before Week 12, supported by photodocumentation.**

  Complete wound closure is defined as 100% skin re-epithelialization in absence of drainage and without autograft placement. Successful wound closure in this study requires that complete wound closure on or before Week 12 is achieved without autograft placement and is confirmed at least 14 days following the initial observation of complete closure.

The investigator will evaluate the confirmation of complete wound closure either by direct clinician observation or by subject-provided photodocumentation.

The proportion of subject with all confirmed complete treatment site closure(s) including two-sided 95% confidence intervals based on the normal approximation to the binomial will be calculated and presented.

- **Proportion of subjects with confirmed complete wound closure of all treatment sites without autograft (verified with confirmation assessment) at each visit, supported by photodocumentation.**

  The planned visits are Week 1, Week 2, Week 4, Week 8, Week 12, and Week 24. However, the subjects may show up at any visit, and number and percentage will be summarized. For each visit, the denominator of the proportion of subjects is based on the total number of subjects who provided data for the visit.

- **Proportion of subjects maintaining durable wound closure by Week 24.**

  Durable wound closure by Week 24 is achieved when a subject with confirmed wound closure is observed as remaining closed at least 90 days after complete wound closure through Week 24. Two summaries will be performed: 1. Denominator is mITT population 2. The denominator will be based on subjects with confirmed wound closure of all treatment sites without autograft by Week 12. The number, percentage and two-sided 95% confidence intervals based on the normal approximation to the binomial will be calculated and presented.

- **Proportion of treatment sites with confirmed complete wound closure without autograft (i.e., complete re-epithelialization without drainage and subsequently verified with confirmation assessment) on or before Week 12 and supported by photodocumentation.**

  The treatment sites will be analyzed regardless of subject. Treatment site with confirmed wound closure requires treatment site complete closure on or before Week 12 is achieved without autograft placement and is confirmed at least 14 days following the initial observation of complete closure.

  The investigator will evaluate the confirmation of complete treatment site closure either by direct clinician observation or by subject-provided photodocumentation.

The proportion of confirmed complete treatment site closure including two-sided 95% confidence intervals based on the normal approximation to the binomial will be calculated and presented.

- **Proportion of treatment sites maintaining durable wound closure by Week 24.**

  The treatment sites will be analyzed regardless of subject.

  Durable wound closure by Week 24 is achieved when a confirmed wound is observed as remaining closed at least 90 days after a confirmed complete wound closure through Week 24. Two summaries will be performed: 1. Denominator is all treatment sites 2. The denominator will be based on a confirmed treatment site wound closure by Week 12. The number, percentage and two-sided 95% confidence intervals based on the normal approximation to the binomial will be calculated and presented.

- **Time to first confirmed complete wound closure of all treatment sites in a subject without autograft (verified with confirmation assessment at least 14 days later).**

  The event for Kaplan-Meier method will be the first occurrence of all confirmed complete wound closure without autograft in a subject (first observation of complete closure verified with a second observation of complete closure at least 14 days later). The time to first confirmed wound closure will be analyzed by the Kaplan-Meier estimation method. The period for this analysis is calculated as (the date of having the first confirmed event – the date of Day 1 + 1). Subjects not having any confirmed complete closure event during the study will have their time censored at the last available date in the study. Kaplan-Meier estimates by StrataGraft treatment area with confirmed wound closure will be presented for the following categories: ≤ 500 cm^2, > 500 cm^2.

  The Kaplan-Meier estimate will be computed to determine the median time to confirmed complete wound closure without autograft placement.

  In addition, the event for Kaplan-Meier method will be the first occurrence of complete wound closure without grafting (which includes autograft, allograft, xenograft and other skin substitute) will also be generated.

- **Skin quality and cosmesis of treated sites assessed by POSAS scores**

  The scar evaluation will use the POSAS total scores at Week 12 and Week 24. The POSAS (The Patient and Observer Scar Assessment Scale) scales are evaluated separately by clinician (observer) and subject (patient), resulting in two total scores.

  Total POSAS Score of each treatment site is the sum of the scores for vascularization, pigmentation, thickness, relief, pliability and surface area scored for that treatment site, and each item is scored numerically on a ten-step scale.

  Each of the individual POSAS items and the total POSAS score, represented as the mean score across all items and supported by photo-documentation, will be summarized by treatment site and overall mean score of all of the treatment sites of the subject, by clinician and subject, and for both Week 12 and Week 24.

  POSAS will be summarized by clinical visit in person and remotely, respectively.

- **Number of subjects with wound-infection related events.**

  Local wound infection will be determined by the clinical investigator and may include confirmatory microbiological assessment. Similarly, systemic infection will be determined by the clinical investigator and may include documentation of such signs as positive blood and/or wound cultures, fever (defined as >38.5°C) and/or elevated white blood cell count.

  Study treatment sites will be examined by the investigator for signs and symptoms of infection at every study visit. Cultures of the treatment sites may be obtained for microbiological evaluation at the discretion of the clinical investigator or per institutional SoC at any time during treatment. The clinical investigator will evaluate the wound culture results for clinical significance.

  The wound-infection related events will be summarized by visit and SG treatment site by subject.

To evaluate the effects of initial re-grafting on SG treatment sites, initial complete wound closure with or without confirmation is not required. Grafting includes allograft, xenograft and other skin substitute, and autografting, which is separately calculated. The following endpoints evaluating the combination of initial complete wound closure, confirmation of complete closure, and grafting/autografting will be summarized by SG treatment site and overall (across all treatment sites per subject):

- Summary of subjects with re-grafting on StrataGraft treatment sites

- Proportion and 95% confidence intervals of subjects who achieved initial wound closure on or before Week 12
- Proportion of subjects who achieved initial wound closure for at least one wound site without grafting on or before Week 12
- Proportion of subjects who achieved initial wound closure for at least one wound site without autograft on or before Week 12
- Proportion of subjects who achieved initial wound closure at each visit up to Week 12
- Proportion of subjects who achieved initial wound closure without grafting at each visit up to Week 12
- Proportion of subjects who achieved initial wound closure without autograft at each visit up to Week 12
- Proportion of subjects who achieved initial wound closure with grafting at each visit up to Week 12
- Proportion of subjects who achieved initial wound closure with autograft at each visit up to Week 12
- Proportion of subjects who achieved ≥95% wound closure without autograft at each visit up to Week 12
- Proportion of treatment sites ≥ 95% wound closure without autograft at each visit up to Week 12
- Proportion and 95% confidence intervals of subjects who achieved confirmed wound closure on or before Week 12
- Proportion of subjects who achieved initial confirmed wound closure at each visit up to Week 12
- Proportion of subjects who achieved initial confirmed wound closure without grafting at each visit up to Week 12
- Proportion of subjects who achieved initial confirmed wound closure without autograft at each visit up to Week 12
- Proportion of subjects who achieved initial confirmed wound closure with grafting at each visit up to Week 12
- Proportion of subjects who achieved initial confirmed wound closure with autograft at each visit up to Week 12

- Proportion of subjects with confirmed wound closure without grafting at each visit
- Proportion of subjects with confirmed wound closure without autograft at each visit

3.8.3 Subgroup Analyses

The Proportion of subjects with confirmed complete wound closure without grafting on or before Week 12 and TEAE endpoints will be summarized by the following demographic and baseline characteristics:

- Race (white, non-white)
- Ethnicity (Hispanic, non-Hispanic)
- Age (<65, ≥ 65)
- Sex (Male, Female)
- StrataGraft treatment area (≤ 500 cm^2, > 500 cm^2)
- StrataGraft treatment area (≤ 1000 cm^2, > 1000 cm^2)
- Overall TBSA of wound burden defined as burns plus donor site area (< Median, ≥ Median)
- Burn location (Anterior trunk, Anterior Upper Extremity (includes forearm + upper arm), Anterior Lower Leg, Anterior Thigh, Posterior Trunk, Posterior Upper Extremity (includes forearm + upper arm), Posterior Lower Leg, Posterior Thigh)

To further evaluate the burn location effect, Percent of Re-epithelialization without Grafting at each Visit, Proportion of subjects maintaining durable wound closure and POSAS by clinical visit in person by burn location will be summarized.

3.8.4 Exploratory Analyses

Results from all Health Care Resource Utilization (HCRU) parameters as exploratory efficacy endpoints will be summarized with descriptive statistics. The exploratory endpoints are as following:

- Location of care for StrataGraft application (e.g. inpatient hospital, outpatient/ambulatory hospital, clinic, etc.)
- Treatments used for all other burn areas following excision and %TBSA treated with each (other than StrataGraft treatment sites)

- Number of Operation Room (OR) procedures required for burn treatment: excisions, application of StrataGraft and all other grafting procedures, including autografts allografts, and xenografts
- Duration of OR procedure
- Length of hospital stay
- Prescription drugs given at discharge from the hospital for wound-related events including pain control, itch, psychotropics, and antibiotics
- Re-admission within 30 days after discharge
- Whether a re-admission is planned
- Length of hospital stay of re-admission

3.8.5 Multiplicity

Adjustment for multiplicity does not apply to analysis of the endpoints for this study.

3.9 Safety

3.9.1 Adverse Events

All adverse events (AEs) will be assessed and recorded before or after the first placement of study product. Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 23.0. Adverse event information includes system organ class, preferred term, severity, and seriousness, and the investigator's assessment of the relationship of the adverse event to the placement of study product.

The TEAE definition is described in section 3.8.1 .

The number of TEAE as well as the number and percentage of subjects who experienced at least one TEAE will be summarized for each system organ class and each preferred term. TEAE will also be summarized by maximum severity and by strongest relationship to SG treatment site for each system organ class and each preferred term.

The sites will be presented as SG treatment sites (A, B, C), pooled SG treatment sites, Non-SG Burn area, donor sites, and other. The pooled SG treatment site is counted if the event occurs for at least one of the treatment sites.

The following TEAEs will be summarized by frequency and percentage of subjects:

- All TEAEs by sites and overall
- TEAEs by maximum severity, site and overall

- TEAEs by relationship, site and overall
- TEAEs at SG treatment sites by relationship
- TEAEs at SG treatment sites by relationship and maximum severity
- TEAEs leading to withdrawal by sites and overall
- TEAEs leading to withdrawal at SG treatment site by relationship
- TEAEs of wound-infection by sites and overall
- Serious Treatment Emergent adverse events (TEAEs) by sites and overall
- Serious TEAEs at SG treatment sites by relationship

3.9.2 Laboratory Assessments

Hematology and biochemistry will be collected at baseline (Day 1 or possibly within 48 hours of surgery) and Week 12. Summaries of baseline assessment and change from baseline for laboratory assessments will be summarized by number of subjects, mean, standard deviation, median, minimum and maximum.

Hematology and biochemistry laboratory results will be classified as status of 'Low', 'Normal' and 'High' as defined by central lab', and in some cases, by the sites' laboratory normal range. Shift tables summarizing status of changes from baseline at Week 12 according to baseline status will be provided for subjects with both baseline and Week 12 results.

Hematology and biochemistry parameters will be categorized as normal, non-clinical significance and clinical significance at Baseline and Week 12 by the clinician according to the institutional SoC in the evaluation of study subjects. Shift tables of change from baseline to Week 12 will be created for laboratory results using clinically significant categories.

3.9.3 Vital Signs

Patients vital sign data was collected at each visit and visit for confirmation of healing. The average values and change from baseline in vital signs of body temperature, systolic blood pressure (SBP), diastolic blood pressure (DBP), HR, and respiratory rate, will be summarized for each visit.

3.9.4 Assessment of Tissue Architecture

A subset of 10 subjects (sourced from across all the sites) with closed wounds (from subjects who have achieved wound closure, across all the sites) will be separately consented to have a punch biopsy (measuring 3 mm) taken from the center of the healed burn wound, and another punch biopsy measuring 3 mm taken from non-burned healthy skin. A histological evaluation of both samples will be done to analyze and contrast the skin architecture in the healed burn wound with healthy skin. The biopsy will happen at the study visit Week 12, regardless of when wound closure occurs. The histological evaluation results will be summarized by healed burn wound and non-burned healthy skin.

3.9.5 Immunology Assessments

Immunological evaluations will include Panel Reactive Antibodies (PRA) with HLA class I and II screening and testing for allelic reactivity at Day 1, Week 4 and Week 12. The number (%) of subjects that are HLA Class I and II positive will be provided for each visit.

4 AMENDMENTS TO THE SAP

This is the SAP based on the protocol amendment 1 (v2) on 02 October,2020.

5 PROGRAMMING SPECIFICATIONS AND CONSIDERATIONS

The corresponding programming specifications for variables for this SAP will be provided in a separate document.

6 TABLE, LISTING, AND FIGURE (TLF) SHELLS

The corresponding Table, Listing and Figure shells for this SAP will be provided in a separate document.

7 APPENDIX

No Appendix is included.

8 REFERENCES

No reference is included.