A Single-Arm, Open-Label Study of Bimekizumab in Pyoderma Gangrenosum: Biweekly Dosing Through Week 16, Then Every 4 Weeks to Week 24

NCT Number: to be assigned

Document Date: 8/10/2026

A single-arm open-label study assessing efficacy of bimekizumab in adult participants with pyoderma gangrenosum over 24 weeks (BEAT-PG)

Protocol Version Number:	**1**
Protocol Version Date:	**July 2026**
Investigational Product:	Bimekizumab
IND/IDE Status:	IND Exempt-178503
Principal Investigator	Alex G Ortega Loayza, M.D., MCR (PI) Department of Dermatology Oregon Health & Science University, Center for Health and Healing 3303 S Bond Ave, CH16D Portland, OR 97239 Phone: 503-494-3376 Fax: 503-346-8105 Email: ortegalo@ohsu.edu
Sponsor:	Oregon Health & Science University
Funding Source:	Union Chimique Belge (UCB)
Trial Configuration	Single-arm, open-label, interventional

CLINICAL PROTOCOL SYNOPSIS

Title	A Single-Arm, Open-Label Study of Bimekizumab in Pyoderma Gangrenosum: Biweekly Dosing Through Week 16, Then Every 4 Weeks to Week 24
Principal Investigator	Alex G Ortega Loayza, M.D.
Objectives	To determine whether bimekizumab provides clinical improvement for participants with PG who are candidates for systemic therapy.
Trial Configuration	Single-arm, open-label, proof-of-concept, interventional
Setting	The trial will recruit 15 adults with PG (defined by the investigator and a second reviewer on the basis of results from clinical, histological and laboratory assessments) through dermatologist offices, recruitment letters, and advertisement. Study visits will occur at Screening, **weeks 0 (baseline), 2, 4, 6, 8,10, 12, 14, 16, 20, and 24.** Study visits at weeks **0, 2, 4, 6, 8, 10, 12, 14, 16, 24, and 36 will be required in-person**; the remaining visits at **week 20, and 28** can be in-person or performed via institutionally approved secure videoconferencing software.
Sample Size Estimate	A sample size of 15 accounting for 10% drop out achieves 80% power to detect a difference in the proportion of patients with complete re-epithelialization, defined as 100% re-epithelialization without any drainage, of the target ulcer at week 24 (P1 – P0) of 0.41 using a two-sided z-test of one proportion with a target significance level of 0.05. These results assume that the population proportion under the null hypothesis (P0) is 0.50.
Number of Participants	15
Eligibility Criteria	**Inclusion criteria** **Age** 1. At least 18 years of age (or the legal age of consent in the jurisdiction in which the study is taking place) **Type of participant and Disease characteristic** 2. Have a diagnosis of at least one PG ulcer defined by the investigator on the basis of results from clinical and/or histological and/or laboratory assessments: Classic PG defined as deep ulceration with undermining violaceous borders and PARACELSUS score >10. If multiple ulcers are present, the largest ulcer (defined by greatest surface area) will be designated the target ulcer and followed throughout the study. 3. Subject has a minimum of 1 evaluable ulcer ($4cm^2$ – $225cm^2$) at screening. 4. Be a candidate for systemic therapy. **Concomitant medications, treatments, and procedures**

	5. Undergoing at least once a week wound care at home or at a wound care facility. 6. Participants must be on a stable dose of prednisone of 20 mg/day for at least two weeks prior to first drug administration (baseline) and must follow the baseline Prednisone tapering algorithm. 7. Subjects on existing immunosuppression and systemic therapies for managing underlying comorbidities associated with PG but are not intended to treat PG specifically will be included in trial and allowed to continue these medications while on trial. The comorbidity must be on a stable clinical course and clinical treatment must be stable for at least 1 month prior to screening. Dosage of medication used to treat underlying comorbidities will be documented at each visit. Please refer to exclusion criteria 2-4 for prohibited medications and washout periods. **Sex and contraceptive/Barrier requirements** 8. Males ages 18 and above must agree to not father a child or donate sperm while on study and for at least 12 weeks following last dose of the study drug. A subject who is a sexually active with a woman of childbearing potential and who has not had a vasectomy must agree to use a reliable form of birth control and confirm that female partner(s) are using birth control, or remain abstinent. 9. Females ages 18 and above must be either of non-childbearing potential or of childbearing potential who test negative for pregnancy at screening, agree to urine pregnancy testing before receiving study intervention administration and agree to use at least two reliable methods of birth control or remain abstinent during the study and for at least 12 weeks following the last dose of bimekizumab Female subjects must agree to not donate eggs while on study or for 12 weeks after the last dose of bimekizumab. **Informed consent** 10. Must sign an informed consent form (ICF) indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study. 11. Be willing and able to adhere to the prohibitions and restrictions specified in this protocol. 12. Be willing to travel to site for all study visits, and willing/able to participate in remote videoconferencing visits with access to a computer with internet and webcam capabilities. 13. Be willing to undergo perilesional and nonlesional skin biopsy at week 0 and week 24 resulting in 4 biopsies during the course of the study. Participants can choose if they are willing to provide 2 additional biopsies (perilesional and nonlesional) at week 16. Refusal to give consent for any of the optional

	research samples does not exclude a participant from participation in the study. **Exclusion criteria** **PG treatment** 1. Any drug treatment specifically for PG including but not limited to biologicals (or biosimilar of), experimental antibodies, small molecules and oral immunosuppressives used within washout periods specified below, prior to first dose of study drug: a. 4 weeks for any therapeutic agent directly targeted to INTERLEUKIN-17 including, but not limited to, secukinumab, brodalumab, ixekizumab b. 8 weeks for infliximab; c. 6 weeks for adalimumab; d. 4 weeks for cyclosporine A, etanercept, inhibitors of the JAK/TYK pathway and PD4 inhibitors; e. 2 weeks for Calcineurin inhibitor topicals (including but not limited to pimecrolimus and tacrolimus) and other advanced topicals (including but not limited to roflumilast and tapinarof). If not specified specifically, a time of 4 weeks or 5 half-lives of the drug (whichever is longer) prior to first drug administration. 2. Intralesional corticosteroids within 4 weeks of screening. 3. Individuals with active clinically infected ulcers. Individuals will be eligible for enrollment following completed treatment and resolution of infection. Antibiotics for wound superinfection are allowed. **Non-PG treatment** 4. Immunomodulating medications for managing underlying comorbidities associated with PG, but not PG itself (e.g., for rheumatoid arthritis), are allowed as combination therapy except for Methotrexate (MTX) and Leflunomide which are allowed individually but not in combination. **Coexisting Medical Conditions or Past History:** 5. Individuals will be screened for IBD using a calprotectin test at screening. Individuals with inflammatory bowel disease (IBD) will be excluded from study. 6. Concurrent skin disease that is deemed to interfere with assessment of ulcer. 7. Have signs or symptoms suggestive of possible lymphoproliferative disease, including lymphadenopathy or splenomegaly or a history of lymphoproliferative disease within 5 years before screening; or currently has a known malignancy or has a history of malignancy within 5 years before screening, with the exception of a nonmelanoma skin cancer that has been adequately treated with no evidence of recurrence for at least 3 months before the first study drug administration or cervical carcinoma in situ that has been treated with no

	evidence of recurrence for at least 3 months before the first study drug administration. 8. Recent (within past 6 months) cerebrovascular accident, myocardial infarction, coronary stenting. Uncontrolled hypertension – confirmed systolic blood pressure >160 mmHg or diastolic blood pressure >100 mm Hg. 9. Clinically significant (per investigator's judgement) drug or alcohol abuse within the last 6 months preceding the Baseline Visit. 10. Has not fully recovered from major surgery (e.g., requiring general anesthesia and hospitalization) within 8 weeks before screening, or has such surgery planned during the time the participant is expected to participate in the study (40 weeks) which in the opinion of the investigator would pose an unacceptable risk to the subject. 11. Presence of significant uncontrolled respiratory, hepatic, renal, endocrine, hematologic, neurologic, or neuropsychiatric disorders, or abnormal laboratory screening values that, in the opinion of the investigator, pose an unacceptable risk to the subject if participating in the study or of interfering with the interpretation of the data. 12. Participants with pyoderma gangrenosum with comorbid necrotizing ulcer features or disease will be excluded from study. 13. Have clinical laboratory test results at screening that are outside the normal reference range of the population and are considered clinically significant, or have any of the following specific abnormalities: a. Neutrophil count <1500 cells/μL b. Lymphocyte count <500 cells/μL c. Platelet count <100,000 cells/μL d. AST or ALT or alkaline phosphatase > 2 times the upper limit of normal e. Hemoglobin <10 g/dL f. Serum creatinine ≥1.5 mg/dL (SI: ≤137 μmol/L) g. White blood cells <3500 cells/ μL 14. Participant has known allergies, hypersensitivity, or intolerance to bimekizumab or its excipients (refer to Investigator's brochure) 15. Individuals who are pregnant, lactating or breastfeeding. **Infections or Predisposition to Infection:** 16. History of chronic or recurrent infections, or active, untreated, acute infection, or immunocompromised to an extent that participation in the study would pose an unacceptable risk to the subject based on the investigator's clinical assessment. 17. Clinically serious infection or received intravenous antibiotics for an infection, within 8 weeks before first dose. 18. Have signs or symptoms suggestive of active TB upon medical history and/or physical examination. a. Have had recent close contact with a person with active TB for which a physician specializing in TB has not ruled out latent TB or has not received appropriate

	treatment before the first study drug administration. b. Have a positive QuantiFERON®-TB Gold test result within 2 months before the first administration of study drug in which active TB has not been ruled out and for which appropriate treatment for latent TB has not been initiated before the first administration of study dug. i. An exception is made for participants who are currently receiving treatment or will initiate treatment for latent TB prior to first administration of study intervention. For participants with a history of treated latent TB there must be documentation of appropriate treatment prior to the first administration of study intervention. It is the responsibility of the investigator to verify the adequacy of previous TB treatment and provide appropriate documentation. IGRA testing is not required at screening for participants with a history of treated latent TB or ongoing treatment for latent TB. 19. Positive for human immunodeficiency virus (HIV), active hepatitis B virus, or hepatitis C virus. A positive Hepatitis B surface antibody test with a corresponding negative hepatitis B surface antigen test indicates immunity to the disease and will not be exclusionary. 20. Symptomatic herpes zoster infection within 12 weeks of screening or recurrent or disseminated (even a single episode) herpes zoster. 21. Symptomatic herpes simplex or disseminated (even a single episode) herpes simplex at the Week 0 (baseline) visit. 22. History of disseminated opportunistic infections (e.g., listeriosis and histoplasmosis). 23. Have received a live vaccine within 12 weeks prior to baseline or intend to have a live vaccine during the course of the study or 4 weeks after last study drug administration or 12 weeks after last study drug administration for Bacillus Calmette-Guérin (BCG) vaccine. **Other Exclusions:** 24. Has any condition that, in the opinion of the investigator, would make participation not be in the best interest (e.g., compromise the well-being) of the participant or that could prevent, limit, or confound the protocol-specified assessments. 25. Are investigator site personnel directly affiliated with this study and/or their immediate families (spouse, parent, child, or sibling). 26. Are currently enrolled in or discontinued from a clinical trial involving an investigational product or non-approved use of a drug or device within the last 4 weeks or a period of at least 5 half-lives of the last administration of the drug, whichever is longer, or concurrently enrolled in any other type of medical research judged not to be scientifically or medically compatible with this study.

Description of Interventions	Participants with PG will be treated with bimekizumab 320 mg in a pre-filled syringe to be injected subcutaneously at week 0, and every 2 weeks for 16 weeks and then once every 4 weeks for 8 weeks.
Duration of Study	The duration of the study will be 36 weeks.
Outcome Measures	Proportion of participants that achieve a PGA score of ≤ 1 at week-24. This scale has been used in previous trials: 0 = total resolution of target ulcer with no signs of active PG 1= almost completely healed target ulcer with only minimal signs of active PG 2 = evidence of target ulcer healing which involves at least 50% of ulcer/ulcer margin 3 = evidence of target ulcer healing which involves less than 50% of ulcer/margin 4 = no evidence of target healing ulcer Secondary outcomes: 1. To determine whether bimekizumab provides healing (complete re-epithelialization without drainage or dressing requirements) for subjects with PG who are candidates for systemic therapy. 2. To determine the safety of bimekizumab for the treatment of subjects with PG who are candidates for systemic therapy 3. To determine the improvement in quality of life measured by the Skindex Mini, participant global assessment and participant physical function assessment, PHQ-9 and GAD-7. 4. To determine the improvement in pain by NRS scale in the last 7 days and the peak pain by NRS scale in the last 24 hours 5. To determine time to healing 6. To determine time to recurrence 7. Determine differences in pro-inflammatory cytokine and chemokine expression (peripheral blood and lesion) 8. Examine lymphocyte and neutrophil function and migration upon treatment (peripheral blood and lesion) 9. Examine changes to tissue remodeling before, during and after treatment using ultrasound imaging Exploratory outcomes: 10. Evaluation of cytokine gene expression before and after treatment in skin and blood samples 11. Presence and amount of hyperechoic oval structures, hair tracts, and U-shaped vessels found with high frequency ultrasound
Statistical Methods	Primary endpoint analysis: 1. The proportion of participants that achieve a PGA score of ≤ 1 after treatment with bimekizumab at Week 24. The

	proportion will be reported with 95% confidence interval using the Wilson method. Secondary endpoint analysis: 2. The proportion of participants who achieve complete re-epithelialization (healing) of the target ulcer without drainage or dressing requirements. The proportion will be reported with a 95% confidence interval using the Wilson method. 3. The proportion of participants who experience one or more adverse events (AEs) or serious adverse events (SAEs) during the study period. Safety will be summarized descriptively by type, frequency, and severity of AEs. 4. The mean change from baseline in quality of life scores as measured by the Skindex Mini, participant global assessment, physical function assessment, PHQ-9 and GAD-7. Changes will be evaluated using paired t-tests or Wilcoxon signed-rank tests as appropriate. 5. The mean change from baseline in average pain (NRS) over the past 7 days and peak pain in the past 24 hours. Change will be assessed using paired t-tests or Wilcoxon signed-rank tests. 6. The median time to complete re-epithelialization of the target ulcer. Time to healing will be analysed using Kaplan-Meier survival analysis and reported with a 95% confidence interval. 7. The median time to recurrence of PG after initial healing. Time to recurrence will be analysed using Kaplan-Meier survival analysis and reported with a 95% confidence interval. 8. The change in pro-inflammatory cytokine and chemokine expression (in peripheral blood and lesional tissue) from baseline to post-treatment. Differences will be evaluated using paired t-tests or non-parametric alternatives. Multiple comparisons will be adjusted using the Benjamini-Hochberg procedure. 9. The change in lymphocyte and neutrophil function and migration in peripheral blood and lesional tissue after treatment. Outcomes will be analysed using paired t-tests or mixed-effects models, depending on data structure. 10. The change in ultrasound-based measures of tissue remodelling from baseline through treatment and follow-up. Quantitative imaging features will be assessed using repeated measures ANOVA or linear mixed-effects models.

Table of Contents

CLINICAL PROTOCOL SYNOPSIS **4**

ABBREVIATIONS **14**

1. BACKGROUND **16**

1.1. Overview of Pyoderma Gangrenosum (PG) and Bimekizumab 16

1.2. Hypothesis 16

2. OBJECTIVES **16**

2.1. Primary Objective 16

2.2. Secondary Objectives 16

2.3. Exploratory Objectives 17

3. STUDY DESIGN AND ENDPOINTS **17**

3.1. Study Design Overview 17

3.2. Study Endpoints 18

3.2.1 Primary Endpoints *18*

3.2.2. Concept Secondary Endpoints *19*

3.2.3. Exploratory/Mechanistic Endpoints *19*

3.2.4. Intercurrent Events (ICEs) *20*

4. STUDY ENROLLMENT AND WITHDRAWAL **20**

4.1. Inclusion Criteria 20

4.2. Exclusion Criteria 21

PG treatment 21

4.3. Recruitment and Identification of Participants 23

4.4. Vulnerable Populations 23

5. STUDY PROCEDURES, EVALUATIONS, AND SCHEDULE **23**

5.1 Study Visit Procedures 23

5.1.1. Wound Care *23*

5.1.2. Patient Reported Outcomes *24*

5.1.3. Debridement *24*

5.1.4. Photography *24*

5.1.5. Imaging via Ultra High Frequency Ultrasound *25*

5.1.6. Laboratory Testing *25*

5.1.7 Genetic and Genomic Biomarker Testing *25*

5.2. Study visits 26

5.2.1. Screening *26*

5.2.2. Enrollment *26*

5.2.3. Week 0 (baseline) *26*

5.2.4. Week 2 (+/- 5 days) *27*

5.2.5. Week 4 (+/- 5 days) *28*

5.2.6. Week 6 (+/- 5 days) *28*

5.2.7. Week 8 (+/- 5 days) *29*

5.2.8. Week 10 (+/- 5 days) *29*

5.2.9. Week 12 (+/- 5 days) *30*

5.2.10. Week 14 (+/- 5 days) *31*

5.2.11. Week 16 (+/- 5 days) *31*

5.2.12. Week 20 (+/- 5 days) *32*

5.2.13. Week 24 (+/- 5 days) *32*
5.2.14. Week 36 (+/- 5 days) *33*
5.3. DOSE MODIFICATION AND DISCONTINUATION 34
5.3.1. Skin Infection without systemic symptoms *34*
5.3.2. Early Withdrawal *34*
5.3.3. Stopping Rules. Criteria for Subject Discontinuation and Treatment Failure *35*
5.3.4 Suicide Risk Monitoring and Contingency Plan *36*
5.4. TABLE 1: STUDY SCHEDULE OF EVENTS 38

6. INVESTIGATIONAL PRODUCT AND TREATMENT PLAN 39
6.1. INVESTIGATIONAL PRODUCT: BIMEKIZUMAB 39
6.2. DOSING AND ADMINISTRATION 39
6.3. MISSED AND DELAYED DOSES 39
6.4. IMPROPER DOSING 39
6.5. STORAGE 39
6.6. CONCOMITANT MEDICATIONS, TREATMENTS, AND PROCEDURES 40
6.6.1. Concomitant Medication Recording *40*
6.6.2. Prohibited Medications, Treatments, and Procedures *40*
6.6.3. Permitted Medications, Treatments, Rescue Treatments and Procedures *40*

7. STATISTICAL CONSIDERATIONS 41
7.1. SAMPLE SIZE COMPUTATION AND POWER ANALYSIS 41
7.2. STATISTICAL ANALYSIS PLAN 41
7.2.1. Primary Endpoint Analysis: *41*
7.2.3. Exploratory Endpoint Analyses: *42*
7.2.4. Randomization method: *43*
7.2.5. Handling of Missing Data: *43*

8. SAFETY AND ADVERSE EVENT DEFINITIONS AND REPORTING 43
8.1. SPECIFICATION OF SAFETY PARAMETERS 43
8.2. DEFINITIONS 43
8.2.1. Adverse Event (AE) *43*
8.2.2. Serious Adverse Event (SAE) *43*
8.2.3. Unanticipated Problems (UP) *44*
8.3. ADVERSE EVENT ASSESSMENT AND FOLLOW-UP 44
8.4. REPORTING PROCEDURES 45
8.4.1. OHSU IRB Reporting of Unanticipated Problems and Adverse Events *45*
8.4.2. SAE Reporting to the Study Drug Manufacturer *45*
8.5. DATA SAFETY MONITORING PLAN 45
8.6. POTENTIAL RISKS 46
8.6.1 Risk due to study procedures *46*
8.6.2 Risk due to study intervention (bimekizumab) *47*
8.7. PARTICIPANT REMOVAL FROM THE TRIAL DUE TO ADVERSE EVENTS 49

9. DATA HANDLING & MANAGEMENT RESPONSIBILITIES **49**
9.1. PARTICIPANT & DATA CONFIDENTIALITY 49
9.2. DATA COLLECTION & STORAGE: PRIVACY, CONFIDENTIALITY & SECURITY 50
9.2.1. Data Collection *50*
9.2.2. Data Monitoring *50*
9.2.3. Data Confidentiality *50*

9.2.4. Sample Long Term Retention *50*
9.2.5. Data Storage *50*
9.2.6. Data Recording in the Electronic Medical Record (Epic) *51*
9.2.7 Digital Photography *51*
9.2.8. Telemedicine Platform *51*
10. ETHICS/PROTECTION OF PARTICIPANTS 51
10.1. ETHICAL STANDARD 51
10.2. INSTITUTIONAL REVIEW BOARD 52
10.3. INFORMED CONSENT 52
10.4. CONSENT PROCEDURES AND DOCUMENTATION 52
10.5. PROTOCOL REVIEW 52
10.6. CHANGES TO PROTOCOL 52
11. PUBLICATION AND DISSEMINATION POLICY 53
12. REFERENCES 53
12. APPENDIX 54

ABBREVIATIONS

AE	Adverse Event
ANC	Absolute Neutrophil Count
ANOVA	Analysis of Variance
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CD4	T-helper cell
CMP	Comprehensive Metabolic Panel
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
DNA	Deoxyribonucleic acid
DOB	Date of Birth
DSMB	Data Safety Monitoring Board
EDC	Electronic Data Capture
ELISA	Enzyme-Linked Immunosorbent Assay
GAD-7	Generalized Anxiety Disorder Questionnaire-7
GCP	Good Clinical Practice
PGA	Physicians Global Assessment
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IL1	Interleukin 1
IND	Investigational New Drug
INTERLEUKIN-	Interleukin-17
IL23	Interleukin-23
IND	Investigational New Drug
MRN	Medical Record Number
NRS	Numeric Rating Scale
OHRP	Office for Human Research Protections
OHSU	Oregon Health and Science University
PGA	Physician's Global Assessment
PHI	Protected Health Information
PHQ-9	Patient Health Questionnaire-9
PI	Principal Investigator
PPD	Purified Protein Derivative
PRO	Patient Reported Outcome
RNA	Ribonucleic acid
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan

Th1	T Helper 1 cell
Th17	T Helper 17 cell
TBSP	Tablespoons
UP	Unanticipated Problem

1. BACKGROUND

1.1. Overview of Pyoderma Gangrenosum (PG) and Bimekizumab

Pyoderma Gangrenosum (PG) is a painful neutrophilic dermatosis that presents as chronic nonhealing skin ulcers. There are no FDA approved treatments and first-line cyclosporine and corticosteroid therapies show limited efficacy and pose serious long-term side effects1. The overproduction of Interleukin-17 driven by Th1/Th17 dysregulation has been implicated in the pathogenesis of neutrophilic dermatoses such as PG, with INTERLEUKIN-17 induced Matrix Metalloproteinase (MMP) production and neutrophil recruitment hypothesized to play key roles in the self-sustaining inflammatory cycle driving PG ulcerations 2,3 There is mounting evidence supporting INTERLEUKIN-17 as a treatment target for PG with case reports demonstrating the effectiveness of direct and downstream INTERLEUKIN-17 inhibition in PG treatment 4,5. Histological examination has shown overexpression of INTERLEUKIN-17 in patients with PG, further highlighting its role as an important treatment target in PG. INTERLEUKIN-17 6.

INTERLEUKIN-17A and INTERLEUKIN-17F cytokines are expressed as either homodimers or the INTERLEUKIN-17AF heterodimer. These bind INTERLEUKIN-17 RA and INTERLEUKIN-17 RC to form the INTERLEUKIN-17 receptor complex protein to initiate INTERLEUKIN-17 production7 Bimekizumab is a monoclonal body that inhibits binding of INTERLEUKIN-17A, INTERLEUKIN-17F and INTERLEUKIN-17AF the INTERLEUKIN-17 receptor complex, thus inhibiting the release of INTERLEUKIN-17 and downstream inflammatory cytokines such as STAT-3 and NFkB, two transcripts shown to be overexpressed in lesional PG skin8,9.

INTERLEUKIN-17's pivotal role in generating positive feedback loops of inflammation make it an ideal candidate for PG therapy 3. The Food and Drug Administration (FDA), Health Canada and the European Medicines Agency (EMA) currently approve Bimekizumab for treatment of moderate to severe plaque psoriasis in adults. Additional clinical trials to assess its efficacy and safety for Hidradenitis Suppurativa (HS) have shown improved patient outcomes 10,11. It is plausible INTERLEUKIN-17 inhibition will be similarly effective in treating PG, given similarities in the autoimmune dysregulation present in both HS and PG 12,13.

This will be the first clinical trial to test INTERLEUKIN-17 inhibition in the treatment of PG and the first study to correlate outcome measures such as ulcer size with inflammatory markers in skin and blood. Based on the effects of Bimekizumab's dual IL-17A and IL-17F inhibition on downstream inflammatory cytokines overexpressed in PG lesional tissue, Bimekizumab is expected to a safe and effective therapy for PG and lead to improved treatment outcomes for patients.

1.2. Hypothesis

Treatment of participants with PG with bimekizumab once every 2 weeks for 16 weeks, followed by once every 4 weeks for 8 weeks will lead to a Physician's Global Assessment (PGA) score of ≤ 1 at week 24.

2. OBJECTIVES

2.1. Primary Objective

To determine whether bimekizumab provides clinical improvement for participants with PG who are candidates for systemic therapy measured by the proportion of participants what achieve a PGA score of ≤ 1 at week 24.

2.2. Secondary Objectives

1. To determine whether bimekizumab provides healing (complete re-epithelialization without drainage or dressing requirements) for subjects with PG who are candidates for systemic therapy.

2. To determine the safety of bimekizumab for the treatment of subjects with PG who are candidates for systemic therapy
3. To determine the improvement in quality of life measured by the Skindex Mini, participant global assessment,participant physical function assessment, PHQ-9 and GAD-7
4. To determine the improvement in pain by NRS scale in the last 7 days and the peak pain by NRS scale in the last 24 hours
5. To determine time to healing
6. To determine time to recurrence
7. Determine differences in pro-inflammatory cytokine and chemokine expression (peripheral blood and lesion)
8. Examine lymphocyte and neutrophil function and migration upon treatment (peripheral blood and lesion)
9. Examine changes to tissue remodeling before, during and after treatment using ultrasound imaging

2.3. Exploratory Objectives

1. Evaluation of cytokine gene expression before and after treatment in skin and blood samples
2. Presence and amount of hyperechoic oval structures, hair tracts, and U-shaped vessels found with high frequency ultrasound

3. STUDY DESIGN AND ENDPOINTS

3.1. Study Design Overview

This will be a single-arm, open-label, interventional, collaborative study of 15 participants with PG treated with bimekizumab 320mg subcutaneous injections every 2 weeks for 16 weeks, followed by every 4 weeks until week 24. Clinical improvement will be assessed by PGA at Week 24 after completion of study treatment. A recurrence follow-up visit will be performed at Week 28 to assess sustained remission, patient reported outcomes and adverse events. A safety follow-up visit will be performed at Week 36 to assess patient reported outcomes, sustained remission, and adverse events.

Blood tests will be performed for screening and safety at Screening, Week 0, Week 12, Week 24, and week 36. Blood samples for cytokine expression analysis will be obtained in tandem with each blood test: before the first dose (Week 0), Week 12, and Week 24. Biopsies for cytokine expression analysis will be obtained before the first dose (Week 0) and at Week 24. Wound drainage fluid (if ulcer is not closed) for further analysis will be collected for all participants at Week 0, Week 6, Week 12, Week 16, and Week 24. Ultrasound imaging will be conducted with imaging at Week 0, Week 6, Week 12, Week 16, and Week 24.

We hope that by coupling the use of bimekizumab and ultrasound, we will be able to find novel connections between ulcer structures and healing timelines.

To investigate the healing process, we plan to use ultrasound as an objective tool for evaluating progress. Some characteristics have been described in literature in pyoderma gangrenosum, such as hyperechoic oval structures, hair tracts, and U-shaped vessels.[1] Additional ultrasound characteristics that will be evaluated and recorded at each time point include echogenicity (hyperechoic, hypoechoic, mixed echogenicity) and vascularity (hyperemic/increased vascularity, moderate, decreased vascularity) both within the wound bed and in surrounding wound borders. Measurements of wound thickness, extent of undermining, fistulous tracts, and hypoechoic subepidermal low echogenic band (SLEB) thickness, if present, will be recorded using machine calipers. Remodeling of the deep dermis and subcutaneous cellular tissue will be analyzed for progression.

While some of these ultrasound characteristics have been utilized in small populations for inflammatory conditions and wound healing, to our knowledge there has not been a standardized protocol for ultrasound use in wounds or specific findings characteristic of wound inflammatory and

non-inflammatory stages. Our aim is to identify patterns noted in wounds and correlate with clinical and histological healing.

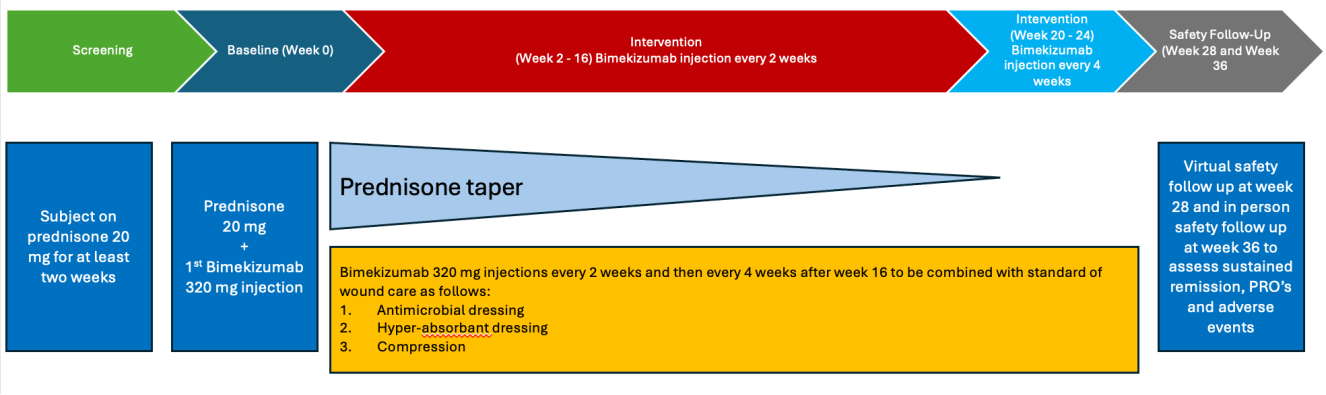
All wounds will be imaged using high-frequency ultrasound at each time point. The operator of the ultrasound equipment will have sufficient training to collect several imaging clips of ulcers for review and analysis. The transducer will be placed perpendicular to the wound surface with light pressure and a coupling agent for optimal sound transmission. The focal zone will be optimized to the central portion of the lesion. Multiple three-second video clips will be obtained to include the entirety of the wound and all borders. The most representative images of each wound will be selected for analysis, which will include wound depth, SLEB, fistulous tracts, and undermining measurements, and descriptions of vascular features, echogenic texture, hyperechoic oval structures, hair tracts, and u-shaped vessels.

Participants will be required to complete a series of questionnaires, detailed in the appendix, at the start of each in person visit.

Microbiological tissue and wound cultures will be also obtained at the first visit and throughout the study as necessary.

Each participant will undergo a standardized wound care regimen during the trial to include: an antimicrobial dressing, a hyper absorbent dressing and compression. All PG involving the lower extremities will require compression to be decided by investigator. Participants with allergies to any dressing listed will utilize a similar, non-allergenic product at the discretion of the investigator. All participants will undergo at least 1 dressing change weekly. Adherence to this wound care regimen will be recorded in the EDC along with the number of weekly dressing changes for each patient. Sharp debridement of wounds will be performed at investigator discretion and recorded in the EDC.

Figure 1: Overview of the study design



3.2. Study Endpoints

3.2.1 Primary Endpoints

1. The primary endpoint will assess the proportion of participants that achieve a PGA score of ≤ 1 after treatment with Bimekizumab at week-24. The proportion will be reported with 95% confidence interval using the Wilson method.

   This scale has been used in previous trials:

   0 = total resolution of target ulcer with no signs of active PG

   1= almost completely healed target ulcer with only minimal signs of active PG

   2 = evidence of target ulcer healing which involves at least 50% of ulcer/ulcer margin

   3 = evidence of target ulcer healing which involves less than 50% of ulcer/margin

   4 = no evidence of target healing ulcer

3.2.2. Concept Secondary Endpoints

1. The proportion of participants who achieve healing; defined as the complete re-epithelialization (ulcer size 0) without drainage or dressing requirements of the target ulcer at Week 24 will be assessed with 95% CI using a Wilson method.
2. The proportion of participants that achieve PGA of 0/1 from week 0 to week 24. The proportion will be reported with 95% confidence interval using the Wilson method
3. The proportion of participants that achieve PGA of 0 from week 0 to week 24. The proportion will be reported with 95% confidence interval using the Wilson method
4. The proportion of participants with a decrease in ulcer area size of at least 50% from week 0 to 24. The proportion will be reported with 95% confidence interval using the Wilson method
5. Mean decrease in ulcer area size from week 0 to week 16. The change will be reported with mean and 95% confidence interval.
6. Mean decrease in ulcer area size from week 0 to Week 24. The change will be reported with mean and 95% confidence interval.
7. The proportion of patients with a decrease in ulcer area size of at least 50% from Week 0 to 16. The proportion will be reported with 95% confidence interval using the Wilson method.
8. Mean change in Skindex Mini score from week 0 to week-24 will be reported with two-sided 95% confidence interval. Change in Skindex Mini score will be analyzed using a paired t-test with 0.05 significance level. Generalized estimating equation (GEE)methods will be further used to characterize changes in Skindex Mini score over time.
9. The proportion of participants achieving a minimum of a 2-point decrease in the NRS at week 0 and week 24 The pain NRS is a subject-administered, 11-point horizontal scale anchored at 0 and 10, with 0 representing “no pain” and 10 representing “worst pain imaginable” in the last 7 days. The proportion will be reported with 95% confidence interval using the Wilson method.
10. The proportion of participants achieving an improvement in reported peak pain NRS assessment at week 0 and week 24. The peak pain NRS assessment is a subject-administered, 11-point horizontal scale anchored at 0 and 10, with 0 representing “no pain” and 10 representing “worst pain imaginable” in the last 24 hours. The proportion will be reported with 95% confidence interval using the Wilson method.
11. The mean change in participant physical function from week 0 to week 24. Physical function is a subject-administered 5 category scale that assesses the impact of PG on participant physical function. Change in physical function score will be analyzed using a paired t-test with 0.05 significance level.
12. The mean change in participant global assessment from week 0 to week 24. The participant global assessment is a subject administered 5 category scale that measures participant perspective of the status of their skin disease.
13. The proportion of participants with target ulcer that remains healed by week 48. The proportion will be reported with 95% confidence interval using the Wilson method
14. Time to recurrence defined as the duration of time from documented target lesion healing and further episodes of PG at any site. The Kaplan-Meier survival curve will used to estimate median time to recurrence with two-sided 95% confidence interval.
15. The number of participants experiencing treatment failure. Treatment failure occurs if a patient experiences treatment intolerance or switches to standard of care.

3.2.3. Exploratory/Mechanistic Endpoints

- Normalization and characterization of systemic and cutaneous inflammatory cytokines at Week 24. In order to better understand the inflammatory pathways involved in PG, one skin biopsy from perilesional skin and unaffected skin (nonlesional) respectively will be obtained from participants at Week 0 prior to the first dose of bimekizumab, and again at Week 24. Two biopsies (perilesional and nonlesional) will be collected at Week 0 and Week 24.
- One tube of 10 ml of blood and wound drainage fluid (if ulcer is not closed) will be obtained at Week 0, Week 12, and Week 24. Systemic and cutaneous inflammatory cytokines will be analyzed, and therapeutic response to bimekizumab is expected to correlate with normalization of cytokine levels.

- High frequency ultrasound will be taken at Week 0, Week 12, and Week 24 to evaluate images for presence of hyperechoic oval structures, hair tracts, and U-shaped vessels which may correlate with healing timeline.

3.2.4. Intercurrent Events (ICEs)

Participants who initiate protocol prohibited medication/therapies or discontinue study intervention due to efficacy are considered to be non-responders. Please refer to SAP for ICE definitions.

If a patient experiences a worsening of PG, defined as an increase in any active ulcer surface area by 33% and/or the appearance of 3 or more large ulcers (large ulcer defined as >4cm square surface area), the patient will be discontinued from study and will be considered a treatment failure.

4. STUDY ENROLLMENT AND WITHDRAWAL

4.1. Inclusion Criteria

Age

1. At least 18 years of age (or the legal age of consent in the jurisdiction in which the study is taking place)

Type of participant and Disease characteristic

2. Have a diagnosis of at least one PG ulcer defined by the investigator on the basis of results from clinical, histological and laboratory assessments: Classic PG defined as deep ulceration with undermining violaceous borders and PARACELSUS score >10. If multiple ulcers are present, the largest ulcer (defined by greatest surface area) will be designated the target ulcer and followed throughout the study.
3. Subject has a minimum of 1 evaluable ulcer ($4cm^2$ – $225cm^2$) at screening.
4. Be a candidate for systemic therapy.

Concomitant medications, treatments, and procedures

5. Undergoing at least once a week wound care (as described in 5.1.1) at home or at a wound care facility.
6. Participants must be on a stable dose of prednisone of 20 mg/day for at least two weeks prior to first drug administration (baseline) and must follow the baseline Prednisone tapering algorithm.
7. Participants on existing immunosuppression and systemic therapies for managing underlying comorbidities associated with PG but are not intended to treat PG specifically will be included in trial and allowed to continue these medications while on trial. The comorbidity must be on a stable clinical course and clinical treatment must be stable for at least 1 month prior to screening. Dosage of medication used to treat underlying comorbidities will be documented at each visit.
   Please refer to exclusion criteria 2-4 for prohibited medications and washout periods.

Sex and contraceptive/Barrier requirements:

8. People with testes ages 18 and above must agree to not father a child or donate sperm while on study and for at least 12 weeks following last dose of the study drug. A subject who is a sexually active with a woman of childbearing potential and who has not had a vasectomy must agree to use a reliable form of birth control and confirm that female partner(s) are using birth control, or remain abstinent.
9. People who are able to get pregnant ages 18 and above must be either of non-childbearing potential or of childbearing potential who test negative for pregnancy at screening, agree to blood or urine pregnancy testing before receiving study intervention administration and agree to use at least two reliable methods of birth control or remain abstinent during the study and for at least 12 weeks following the last dose of bimekizumab. Participants must agree to not donate eggs while on study or for 12 weeks after the last dose of bimekizumab.

Informed consent:

10. Must sign an informed consent form (ICF) indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study.
11. Be willing and able to adhere to the prohibitions and restrictions specified in this protocol.
12. Be willing to travel to site for all study visits, and willing/able to participate in remote videoconferencing visits with access to a computer with internet and webcam capabilities.
13. Be willing to undergo perilesional and nonlesional skin biopsy at Week 0 and Week 24 resulting in 2 biopsies during the course of the study. Refusal to give consent for any of the optional research samples does not exclude a participant from participation in the study.

4.2. Exclusion Criteria

PG treatment

1. Any drug treatment specifically for PG including but not limited to biologicals (or biosimilar of), experimental antibodies, small molecules and oral immunosuppressives used within washout periods specified below, prior to first dose of study drug:

a. 4 weeks for any therapeutic agent directly targeted to INTERLEUKIN-17 including, but not limited to, secukinumab, brodalumab, ixekizumab
b. 8 weeks for infliximab;
c. 6 weeks for adalimumab;
d. 4 weeks for cyclosporine A, etanercept, inhibitors of the Janus kinase (JAK) / tyrosine kinase (TYK) pathway and PD4 inhibitors;
e. 2 weeks for Calcineurin inhibitor topicals (including but not limited to pimecrolimus and tacrolimus) and other advanced topicals (including but not limited to roflumilast and tapinarof).
i. If not specified specifically, a time of 4 weeks or 5 half-lives of the drug (whichever is longer) prior to first drug administration.

2. Intralesional corticosteroids within 4 weeks of screening.
3. Individuals with active clinically infected ulcers. Individuals will be eligible for enrollment following completed treatment and resolution of infection. Antibiotics for wound superinfection are allowed.

Non-PG treatment

4. Immunomodulating medications for managing underlying comorbidities associated with PG, but not PG itself (e.g., for rheumatoid arthritis), are allowed as combination therapy except for MTX and Leflunomide which are allowed individually but not in combination.

Coexisting Medical Conditions or Past History:

5. Individuals will be screened for IBD using a calprotectin test at screening. Individuals with inflammatory bowel disease (IBD) will be excluded from study.
6. Concurrent skin disease that is deemed to interfere with assessment of ulcer.
7. Have signs or symptoms suggestive of possible lymphoproliferative disease, including lymphadenopathy or splenomegaly or a history of lymphoproliferative disease within 5 years before screening; or currently has a known malignancy or has a history of malignancy within 5 years before screening, with the exception of a nonmelanoma skin cancer that has been adequately treated with no evidence of recurrence for at least 3 months before the first study drug administration or cervical carcinoma in situ that has been treated with no evidence of recurrence for at least 3 months before the first study drug administration.
8. Recent (within past 6 months) cerebrovascular accident, myocardial infarction, coronary stenting. Uncontrolled hypertension – confirmed systolic blood pressure >160 mmHg or diastolic blood pressure >100 mm Hg.

9. Clinically significant (per investigator's judgement) drug or alcohol abuse within the last 6 months preceding the Baseline Visit.
10. Has not fully recovered from major surgery (e.g., requiring general anesthesia and hospitalization) within 8 weeks before screening, or has such surgery planned during the time the participant is expected to participate in the study (40 weeks) which in the opinion of the investigator would pose an unacceptable risk to the subject.
11. Presence of significant uncontrolled respiratory, hepatic, renal, endocrine, hematologic, neurologic, or neuropsychiatric disorders, or abnormal laboratory screening values that, in the opinion of the investigator, pose an unacceptable risk to the subject if participating in the study or of interfering with the interpretation of the data.
12. Participants with pyoderma gangrenosum with comorbid necrotizing ulcer features or disease will be excluded from study.
13. Have clinical laboratory test results at screening that are outside the normal reference range of the population and are considered clinically significant, or have any of the following specific abnormalities:

1. Neutrophil count <1500 cells/µL
2. Lymphocyte count <500 cells/µL
3. Platelet count <100,000 cells/µL
4. AST or ALT or alkaline phosphatase > 2 times the upper limit of normal
5. Hemoglobin <10 g/dL
6. Serum creatinine ≥1.5 mg/dL (SI: ≤137 µmol/L)
7. White blood cells <3500 cells/ µL

14. Participant has known allergies, hypersensitivity, or intolerance to bimekizumab or its excipients (refer to Investigator's brochure)
15. Individuals who are pregnant, lactating or breastfeeding.

Infections or Predisposition to Infection:

16. History of chronic or recurrent infections, or active, untreated, acute infection, or immunocompromised to an extent that participation in the study would pose an unacceptable risk to the subject based on the investigator's clinical assessment.
17. Clinically serious infection or received intravenous antibiotics for an infection, within 8 weeks before first dose.
18. Have signs or symptoms suggestive of active TB upon medical history and/or physical examination.

Have had recent close contact with a person with active TB for which a physician specializing in TB has not ruled out latent TB or has not received appropriate treatment before the first study drug administration.

Have a positive QuantiFERON®-TB Gold test result within 2 months before the first administration of study drug in which active TB has not been ruled out and for which appropriate treatment for latent TB has not been initiated before the first administration of study dug.

An exception is made for participants who are currently receiving treatment or will initiate treatment for latent TB prior to first administration of study intervention. For participants with a history of treated latent TB there must be documentation of appropriate treatment prior to the first administration of study intervention. It is the responsibility of the investigator to verify the adequacy of previous TB treatment and provide appropriate documentation. Interferon-Gamma Release Assay (IGRA) testing is not required at screening for participants with a history of treated latent TB or ongoing treatment for latent TB.

19. Positive for human immunodeficiency virus (HIV), active hepatitis B virus, or hepatitis C virus. A positive Hepatitis B surface antibody test with a corresponding negative hepatitis B surface antigen test indicates immunity to the disease and will not be exclusionary.
20. Symptomatic herpes zoster infection within 12 weeks of screening or recurrent or disseminated (even a single episode) herpes zoster.

21. Symptomatic herpes simplex or disseminated (even a single episode) herpes simplex at the Week 0 (baseline) visit.
22. History of disseminated opportunistic infections (e.g., listeriosis and histoplasmosis).
23. Have received a live vaccine within 12 weeks prior to baseline or intend to have a live vaccine during the course of the study or 4 weeks after last study drug administration or 12 weeks after last study drug administration for Bacillus Calmette-Guérin (BCG) vaccine.

Other Exclusions:

24. Has any condition that, in the opinion of the investigator, would make participation not be in the best interest (e.g., compromise the well-being) of the participant or that could prevent, limit, or confound the protocol-specified assessments.
25. Are investigator site personnel directly affiliated with this study and/or their immediate families (spouse, parent, child, or sibling).
26. Are currently enrolled in or discontinued from a clinical trial involving an investigational product or non-approved use of a drug or device within the last 4 weeks or a period of at least 5 half-lives of the last administration of the drug, whichever is longer, or concurrently enrolled in any other type of medical research judged not to be scientifically or medically compatible with this study.

4.3. Recruitment and Identification of Participants

The trial will recruit participants with PG, either newly diagnosed or failing other therapies due to side effects or lack of efficacy. A number of recruitment strategies will be utilized for this study proven effective by our group in previous studies.

- Institutional and community dermatology clinics
- Cohort Discovery tool to identify participants with PG via Epic, and a phone call to those participants.
- Publicity on the PG Support Groups Facebook page
- Publicity on PI's Instagram and Facebook accounts
- Publicity through physician and patient advocacy organizations, including an email to members
- Research Match

We have prepared a recruitment script that will be used for any advertising through social media, Research Match, PG support groups, and Mychart. We have prepared flyers detailing the basic outline of the study with contact information for those interested. These will be posted to the PI's professional Facebook and Instagram accounts. Participants may be asked to perform video interviews detailing their experience, and a corresponding media release form will be filled out. These video interviews will be submitted for IRB approval prior to posting on the PI's professional Facebook and Instagram accounts. The study team will also use the physician letter that has been uploaded to reach out to other physicians in hopes of their help referring potentially eligible participants. Additionally, to prescreen these potential eligible participants, the uploaded telephone script will be used. None of these recruitment materials will be used unless approved by the IRB.

4.4. Vulnerable Populations

Children, neonates, people who are pregnant, and people who are incarcerated will not be enrolled in the study.

5. STUDY PROCEDURES, EVALUATIONS, AND SCHEDULE

5.1 Study Visit Procedures

5.1.1. Wound Care

Each participant will undergo a standardized wound care regimen while on trial to include:

1) An antimicrobial dressing

2) A hyper absorbent dressing
3) Compression

Wound care will be provided by study staff at each in-person visit. Participants will receive detailed instructions on wound care to perform at home dressing changes. Study staff will coordinate with participants' home wound care institutions to ensure the regimen is as standardized as possible.

Dressing changes will occur as follows: the dressing will be removed, and the wound will be cleansed with sterile saline. Vaseline will be applied around the wound edge. A new dressing will be re-applied. Any changes or additions to the wound care regimen, including the use of any new topical ointments permitted while on study, will be recorded in REDCap.

All PG involving the lower extremities will require compression dressings to be decided by investigator. Participants with allergies to any dressing listed will utilize a similar, non-allergenic product at the discretion of the investigator. This will be recorded in REDCap. All participants will have at least one dressing change per week. Details of and adherence to this wound care regimen will be recorded in the REDCap along with the number of weekly dressing changes for each patient. Participants with heavy drainage of wounds may utilize an additional abdominal pad and/or gauze wrap. This will be recorded in REDCap.

5.1.2. Patient Reported Outcomes

Participants will complete the Pain Numeric Rating Scale (NRS), Skindex Mini, physical function assessment, wound drainage assessment, and participant global assessment at the start of each study visit prior to any test, procedure or evaluation. All of these instruments have been validated as reliable measures of patient reported outcomes. The proportion of patients achieving a pain reduction related to the target ulcer of at least 2 points compared to baseline or reaching 0 at any time between Week 0 and End of treatment (EOT) will be calculated as a trial endpoint. This minimum of a 2-point reduction in the NRS score has been determined to correspond to "very much" improvement for patients with severe pain in prior studies[15]. The proportion of patients achieving a peak pain assessment reduction related to the target ulcer compared to baseline or reaching 0 at any time between Week 0 and EOT will be calculated as a trial endpoint.

5.1.3. Debridement

The presence of necrotic tissue can interfere with wound healing. Sharp debridement of wounds will be performed at investigator discretion using a sterile curette. The wound will be photographed and measured before and after debridement. The procedure and pre and post debridement measurements will be recorded in the REDCap.

5.1.4. Photography

Photographs of the target ulcer and of all active PG ulcers will be recorded at each in person study visit. Photographs will be taken using a designated digital camera. A black background will be positioned behind the ulcer as best allowed by location on body. The ulcer will be centered in the frame as much is allowed by the anatomical ulcer position. Photos will be taken from between 1-2 feet away from the ulcer. All active PG ulcers will be photographed at each visit.

The maximum longitudinal length will be measured from a position of 12' o clock to 6' o clock as if the wound were a clock face. The maximum perpendicular width of the target ulcer will be measured from 9'o clock to 3'o clock. This will be converted to an approximate area using the formula: length × width × 0.785, which approximates an ellipse.

All additional PG ulcers outside of the target ulcer will be measured and photographed at each in person visit.

5.1.5. Imaging via Ultra High Frequency Ultrasound

High Frequency Ultrasound imaging will be performed on target PG ulcers for each participant, where available, at Week 0, Week 6, Week 12, Week 16, and Week 24. Ultrasound will be performed using designated ultrasound systems.

5.1.6. Laboratory Testing

Laboratory testing will be performed at screening to determine eligibility for study and at Week 0, Week 12, and Week 24. Specific laboratory tests to be performed include: CBC with differential, CD4+ count, Complete Metabolic Panel (CMP) to include: glucose, BUN, creatinine, EGFR CKD-EPI Male and Female, Sodium, Potassium, Chloride, Total CO2, Calcium, Bilirubin, Total protein, Albumin, Alkaline phosphatase, AST, ALT, Anion Gap, BUN/creatinine ratio, globulin level, albumin/globulin ratio, calcium (albumin corrected), anion gap (albumin corrected), Estimated sedimentation rate (ESR), C-reactive protein (CRP), Lipid Panel (non-fasting), hepatitis B core antibody, hepatitis B surface antibody qualitative test, hepatitis B surface antigen, hepatitis C virus with confirmation, HIV antibody/antigen with reflex, hepatitis C virus w/ confirmation, Quantiferon TB test will be performed while on study. The schedule of tests to be drawn at visits is outlined beginning in section 5.2.2 through 5.2.14.

Pregnancy testing will be performed at screening (blood or urine) and before administering drug at every dosing visit (blood or urine) for participants of child-bearing potential.

5.1.7 Genetic and Genomic Biomarker Testing

In addition to the protein biomarker analyses described in Section 3.2.3, this study will collect blood samples for genetic and genomic research to better characterize the molecular basis of PG and its response to bimekizumab.

Genetic/genomic sample collection: at Week 0, Week 12, and Week 24, and additional blood tube will be collected from each participant for DNA and RNA analysis. These samples will be used to:

- Characterize gene expression changes associated with treatment response to bimekizumab
- Evaluate genetic variants that may be associated with PG susceptibility or disease course
- Compare genetic and transcriptomic profiles between participants with differing clinical responses

Genetic testing performed under this section will not be used to determine study eligibility and will not be reported back to participants or their treating providers. Any testing performed under this section will be for Research Use Only.

Whole genome sequencing sample: Of the blood collected for genetic and genomic biomarker testing, the samples may optionally be used for whole genome sequencing to explore genetic difference between individuals with and without PG and between PG and related wound conditions. Declining to provide sample for this optional analysis will not affect the participants ability to take part in any other aspect of the study. And as such results are made available, will not be shared with participants or their providers.

Sample handling and storage: Genetic/genomic samples will be coded with a unique study identifier prior to any analysis or transfer. Only approved study staff will retain the ability to link the code to participant identify. Samples may be sent to non-OHSU laboratory for genetic/genomic analysis and may be retained by the study sponsor (UCB pharmaceutical) for an indefinite period for use in this study, and where permitted under the informed consent, future related research, consistent with Section 9.2.4.

5.2. Study visits

5.2.1. Screening

Participants will read the informed consent form, and all questions about the study will be answered by a study investigator and research staff. If the subject is interested in participating in the study, they will sign the consent form.

The screening window is defined as 8 weeks after signing the informed consent form and the time that the baseline visit (Week 0) must occur. Screening labs may be performed up to 4 weeks prior to the baseline visit (Week 0).

Screening questions will be asked, and eligibility will be determined by qualified research staff. Participants will be asked about vaccine history to ensure that recommended vaccines are up to date, and participants will be reminded that live vaccines (such as the intranasal influenza vaccine or live varicella zoster vaccine (Zostavax) are not permitted during the study (for details refer to exclusion criteria). An investigator will perform an initial assessment to determine the target lesion and the number of lesions. If all other criteria are met, a blood sample will be drawn to screen for HBV, HCV, HIV, and tuberculosis, and to check CBC CMP, ESR and CRP. PPD skin testing may be used if blood testing for tuberculosis is unavailable. If participants have had HBV, HCV, HIV, and tuberculosis testing within 1 months prior to screening, records of these results will be sufficient, and the tests will not be repeated. A blood or urine pregnancy test will be performed for people of childbearing potential at screening and before each drug administration. A bacterial swab to rule out superinfection will be obtained at this visit and all subsequent visits if clinically indicated.

Upon confirmation of normal blood tests as defined in the exclusion criteria, and receipt of the signed consent form, participants will be scheduled for an enrollment and Week 0 (baseline) visit as appropriate for any medication washout period required in the exclusion criteria. If blood tests are abnormal, the subject will be informed and referred to her or his primary care physician for assessment.

For Spanish-speaking participants, the English-written consent form will be verbally translated with the help of a Spanish interpreter. All questions regarding the study will be translated to study staff and answered to patient satisfaction. Participants will then be provided the adapted boilerplate consent, “Consent Form – Short – Spanish,” to sign. A copy of both signed consents will be provided to the patient and uploaded in the patient’s chart.

5.2.2. Enrollment

The inclusion/exclusion criteria will be re-reviewed and participants may proceed with Week 0 (baseline visit) on the same day if they continue to meet criteria.

5.2.3. Week 0 (baseline)

- Study personnel will gather the following information from the participants and record the results in REDCap:
    - Demographics (sex, gender, race, ethnicity)
    - Current medications
    - Drug allergies
    - Use of alcohol, tobacco, and other substances
    - PG medical history
    - General medical history
    - Family medical history
    - Review of Systems
    - Height and weight
    - Blood pressure

    - Pulse
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PHQ-9
    - GAD-7
    - NIMH Suicide Risk Screening Tool
- The subject will be clinically examined by the principal or other qualified investigator who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- A pregnancy test for people of childbearing potential will be performed (blood or urine)
- Each affected body region of the target ulcer will be evaluated by standard of care measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- Ultra-high frequency ultrasound imaging will be performed by the PI or other qualified clinician as outlined in section 5.1.5.
- Participants will undergo a punch biopsy (4-8 mm punch biopsy) from perilesional skin of the target ulcer, performed by one of the investigators. One additional 4-8 mm punch biopsy will be obtained from nonlesional skin as a control. For consistency, skin of any arms will be chosen for biopsy of controls. If arms skin is not available, alternate sites in order of preference will include: leg, chest or back. Location of the biopsy will be carefully documented.
- Blood will be drawn for biomarker gene expression and protein analysis.
- Wound fluid will be collected.
- A bacterial swab to rule out a superinfection will be obtained at this visit and all subsequent visits if clinically indicated. Topical or systemic antibiotics may be used as needed for evidence of superinfection, positive culture results, malodor and/or discolored discharge.
- Blood will be drawn on the date of the visit or before starting the study drug and includes CBC, CMP, ESR, CRP, G-6PD, Lipid panel.
- The first dose of 320 mg bimekizumab will be administered subcutaneously by trained study personnel and participants will receive training on how to self-administer at home (see section 6.2 on dose administration)

5.2.4. Week 2 (+/- 5 days)

- Study personnel will gather the following information from the participants:
    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Weight
    - Blood pressure
    - Pulse
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA
    - PHQ-9
    - GAD-7
    - NIMH Suicide Risk Screening Tool

- The subject will be clinically examined by an investigator (clinician or research nurse) who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- A pregnancy test for people of childbearing potential will be performed (blood or urine).
- Each affected body region of the target ulcer will be evaluated by standard of care, measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- The study drug will be administered by trained study staff or by participants themselves at home. Study staff will monitor and be available during subject's self-administration of study drug.

5.2.5. Week 4 (+/- 5 days)

- Study personnel will gather the following information from the participants:
    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Weight
    - Blood pressure
    - Pulse
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA
    - PHQ-9
    - GAD-7
    - NIMH Suicide Risk Screening Tool
- The subject will be clinically examined by an investigator (clinician or research nurse) who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- A pregnancy test for people of childbearing potential will be performed (blood or urine).
- Each affected body region of the target ulcer will be evaluated by standard of care, measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- The study drug will be administered by trained study staff or by participants themselves at home. Study staff will monitor and be available during subject's self-administration of study drug.

5.2.6. Week 6 (+/- 5 days)

- Study personnel will gather the following information from the participants:
    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Weight
    - Blood pressure
    - Pulse
    - Skindex Mini
    - Physical function assessment

    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA
    - PHQ-9
    - GAD-7
    - NIMH Suicide Risk Screening Tool
- The subject will be clinically examined by an investigator (clinician or research nurse) who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- A pregnancy test for people of childbearing potential will be performed (blood or urine).
- Each affected body region of the target ulcer will be evaluated by standard of care, measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- Ultra-high frequency ultrasound imaging will be performed by the PI or other qualified clinician as outlined in section 5.1.5.
- Wound fluid will be collected
- The study drug will be administered by trained study staff or by participants themselves at home. Study staff will monitor and be available during subject's self-administration of study drug.

5.2.7. Week 8 (+/- 5 days)

- Study personnel will gather the following information from the participants:
    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Weight
    - Blood pressure
    - Pulse
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA
- The subject will be clinically examined by an investigator (clinician or research nurse) who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- A pregnancy test for people of childbearing potential will be performed (blood or urine).
- Each affected body region of the target ulcer will be evaluated by standard of care, measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- The study drug will be administered by trained study staff or by participants themselves at home. Study staff will monitor and be available during subject's self-administration of study drug.

5.2.8. Week 10 (+/- 5 days)

- This visit can be conducted virtually via secure video or over the phone
- Study personnel will gather the following information from the participants:

    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA
    - PHQ-9
    - GAD-7
    - NIMH Suicide Risk Screening Tool
- Photographs and measurements will be taken of the target ulcer and all active ulcers and will be sent via MyChart by participant at wound care dressing change or wound care center visit.
- The study drug will be administered by participants themselves at home. Study staff will monitor and be available during subject's self-administration of study drug for counselling/training
    - If participant is unable to self administer drug, a nursing visit will be scheduled with study staff to administer drug.

5.2.9. Week 12 (+/- 5 days)

- Study personnel will gather the following information from the participants:
    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Weight
    - Blood pressure
    - Pulse
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA
- The subject will be clinically examined by an investigator (clinician or research nurse) who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- A pregnancy test for people of childbearing potential will be performed (blood or urine).
- Each affected body region of the target ulcer will be evaluated by standard of care, measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- Ultra-high frequency ultrasound imaging will be performed by the PI or other qualified clinician as outlined in section 5.1.5.
- Participants will undergo a punch biopsy (4-8 mm punch biopsy) from perilesional skin of the target ulcer, performed by one of the investigators. One additional 4-8 mm punch biopsy will be obtained from nonlesional skin as a control. For consistency, skin of any arms will be chosen for biopsy of controls. If arms skin is not available, alternate sites in order of preference will include: leg, chest or back. Location of the biopsy will be carefully documented.
- Blood will be drawn for biomarker gene expression and protein analysis.
- Wound fluid will be collected.

- A bacterial swab to rule out a superinfection will be obtained at this visit and all subsequent visits if clinically indicated. Topical or systemic antibiotics may be used as needed for evidence of superinfection, positive culture results, malodor and/or discolored discharge.
- Blood will be drawn on the date of the visit or before starting the study drug and includes CBC, CMP, ESR, CRP, G-6PD, Lipid panel.
- The study drug will be administered by trained study staff or by participants themselves at home. Study staff will monitor and be available during subject's self-administration of study drug.

5.2.10. Week 14 (+/- 5 days)

- Study personnel will gather the following information from the participants:
    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Weight
    - Blood pressure
    - Pulse
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA
    - PHQ-9
    - GAD-7
    - NIMH Suicide Risk Screening Tool
- The subject will be clinically examined by an investigator (clinician or research nurse) who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- A pregnancy test for people of childbearing potential will be performed (blood or urine).
- Each affected body region of the target ulcer will be evaluated by standard of care, measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- The study drug will be administered by trained study staff or by participants themselves at home. Study staff will monitor and be available during subject's self-administration of study drug.

5.2.11. Week 16 (+/- 5 days)

- Study personnel will gather the following information from the participants:
    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Weight
    - Blood pressure
    - Pulse
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA

- The subject will be clinically examined by an investigator (clinician or research nurse) who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- A pregnancy test for people of childbearing potential will be performed (blood or urine).
- Each affected body region of the target ulcer will be evaluated by standard of care, measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- Ultra-high frequency ultrasound imaging will be performed by the PI or other qualified clinician as outlined in section 5.1.5.
- Wound fluid will be collected
- The study drug will be administered by trained study staff or by participants themselves at home. Study staff will monitor and be available during subject's self-administration of study drug.

5.2.12. Week 20 (+/- 5 days)

- Study personnel will gather the following information from the participants:
    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Weight
    - Blood pressure
    - Pulse
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA
    - PHQ-9
    - GAD-7
    - NIMH Suicide Risk Screening Tool
- The subject will be clinically examined by an investigator (clinician or research nurse) who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- A pregnancy test for people of childbearing potential will be performed (blood or urine).
- Each affected body region of the target ulcer will be evaluated by standard of care, measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- The study drug will be administered by trained study staff or by participants themselves at home. Study staff will monitor and be available during subject's self-administration of study drug.

5.2.13. Week 24 (+/- 5 days)

- Study personnel will gather the following information from the participants:
    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Weight
    - Blood pressure

    - Pulse
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA
    - PHQ-9
    - GAD-7
    - NIMH Suicide Risk Screening Tool
- The subject will be clinically examined by an investigator (clinician or research nurse) who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- A pregnancy test for people of childbearing potential will be performed (blood or urine).
- Each affected body region of the target ulcer will be evaluated by standard of care, measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- Ultra-high frequency ultrasound imaging will be performed by the PI or other qualified clinician as outlined in section 5.1.5.
- Participants will undergo a punch biopsy (4-8 mm punch biopsy) from perilesional skin of the target ulcer, performed by one of the investigators. One additional 4-8 mm punch biopsy will be obtained from nonlesional skin as a control. For consistency, skin of any arms will be chosen for biopsy of controls. If arms skin is not available, alternate sites in order of preference will include: leg, chest or back. Location of the biopsy will be carefully documented.
- Blood will be drawn for biomarker gene expression and protein analysis.
- Wound fluid will be collected.
- A bacterial swab to rule out a superinfection will be obtained at this visit and all subsequent visits if clinically indicated. Topical or systemic antibiotics may be used as needed for evidence of superinfection, positive culture results, malodor and/or discolored discharge.
- Blood will be drawn on the date of the visit or before starting the study drug and includes CBC, CMP, ESR, CRP, G-6PD, Lipid panel.
- The study drug will be administered by trained study staff or by participants themselves at home. Study staff will monitor and be available during subject's self-administration of study drug.

5.2.14. Week 36 (+/- 5 days)

- Study personnel will gather the following information from the participants:
    - Change in medications since the last visit
    - Adverse events
    - Change in personal medical history since the last visit
    - Weight
    - Blood pressure
    - Pulse
    - Skindex Mini
    - Physical function assessment
    - Participant global assessment
    - Wound drainage assessment
    - NRS for skin pain
    - PGA
    - PHQ-9
    - GAD-7
    - NIMH Suicide Risk Screening Tool

- The subject will be clinically examined by an investigator (clinician or research nurse) who will assess the following and record the results in REDCap:
    - Full body skin exam with documentation of target ulcer and measurements, degree of inflammation of target ulcer and PGA
    - Presence of peripheral edema
- Each affected body region of the target ulcer will be evaluated by standard of care, measurements and digital photography to visually record extent of disease.
- Photographs and measurements will be taken of the target ulcer and all active ulcers as outlined in section 5.1.4.
- Blood will be drawn for biomarker gene expression and protein analysis.
- Blood will be drawn on the date of the visit or before starting the study drug and includes CBC, CMP, ESR, CRP, G-6PD, Lipid panel.

5.3. Dose Modification and Discontinuation

5.3.1. Skin Infection without systemic symptoms

The presence of wound infection will be evaluated by the investigator at each study visit. Temperature will be recorded at each visit as part of safety monitoring for potential infection. Should a participant show signs concerning for an infection, a wound culture will be taken and a CBC with differential will be obtained. The participant will not dose with bimekizumab while the CBC with differential and wound culture results are pending. If the wound culture is positive for infection, appropriate therapy will be initiated for the infection. The wound infection treatment regimen will be guided by standard of care practices at the discretion of the investigator, and this will be documented in the REDCap.

The participant will return for an unscheduled clinic visit to assess infection 2 weeks after treatment initiation. If the infection is not resolved, the participant will receive further treatment at the discretion of the site investigator and the participant will be re-assessed for infection at their next scheduled visit. If the investigator determines the infection has cleared, the participant will dose with bimekizumab per protocol. If the infection persists, the participant will skip the scheduled dose planned for that time point and continue treatment for infection. This will be recorded as a protocol deviation.

5.3.2. Early Withdrawal

Participants can withdraw from the study at any time. Reason for withdrawal will be recorded. Participants may also be withdrawn from the study by the local site investigator and in agreement with the study PI for any of the following but not limited to reasons:

1. New or worsening medical conditions (e.g., cancer, renal disease, end-stage cardiopulmonary disease, uncontrolled diabetes, etc.) that may interfere with study procedures or otherwise pose concern for subject health or safety.

2. Have identified (per the clinical judgement of the PI) mental health risks and a score of 15 or higher on the PHQ-9, and an acute or non-acute positive screen on NIMH Suicide Risk Screening Tool during any time throughout the study.

3. The subject becomes pregnant

4. Inability of participants to comply with study procedures

5. Other reasons deemed important to subject safety or data quality raised by the DSMB, IRB, FDA, or any other regulatory body that has the authority to do so.

If the subject wishes to withdraw from the trial before Week 24, they will be asked to attend a final trial (early termination) visit. At this visit, if the subject is willing, the same procedures as for the primary

outcome / Week 24 visit will be carried out. If the subject withdraws after the Week 24 visit, the final Week 36 visit will be carried out early instead.

Study participants who discontinue early from the study who have received at least one dose of study medication will be asked to complete Week 24 procedures AND study staff will follow-up with the participant 12 weeks after their last dose of study medication. If a subject wants to withdraw from the study, the subject will contact the site study staff using the contact information and procedures on the ICF and request withdrawal. If a subject withdraws or is removed from the study for any reason and is unable or unsuitable to continue the study procedures off study medication, the reason and date of discontinuation of the study medication is recorded. At the time of study discontinuation, every effort will be made to schedule the subject for an early termination visit following the procedures for Week 24.

Participants withdrawn due to reportable serious adverse events and participants with serious adverse events thought related to the study that are ongoing at the final study visit are followed until resolved or lost to follow-up after demonstration of due diligence with follow-up efforts, defined as 2 documented attempts to contact patients spaced at least 3 weeks apart.

5.3.3. Stopping Rules. Criteria for Subject Discontinuation and Treatment Failure

- If a patient experiences a worsening of PG, defined as an increase in any active ulcer surface area by 33% and/or the appearance of 3 or more large ulcers (large ulcer defined as >4cm square surface area), the patient will be discontinued from study and will be considered a treatment failure.
- Bimekizumab will be permanently discontinued if any of the following are observed:

    - white blood cell count <1000 cells/µL (1.00×10^3/µL or 1.00 GI/L)
    - ANC <500 cells/µL (0.50×10^3/µL or 0.50 GI/L)
    - lymphocyte count <200 cells/µL (0.20×10^3/µL or 0.20 GI/L)
    - hemoglobin <6.5 g/dL (<65.0 g/L)
    - ALT or AST >8 × ULN
    - ALT or AST >5 × upper limit of normal (ULN) for more than 2 weeks
    - ALT or AST >3 × ULN and TBL >2 × ULN
    - ALT or AST >3 × ULN and symptomatic
    - ALP >3 × ULN
    - ALP >2.5 × ULN and TBL >2 × ULN
    - ALP >2.5 × ULN and symptomatic

In addition, patients will be discontinued from bimekizumab in the following circumstances:

- Malignancy (except for successfully treated basal or squamous cell skin carcinoma)
- Anaphylactic reaction or serious hypersensitivity reaction to bimekizumab,
- Certain prohibited medications are taken per Section 6.4.1 (Prohibited Medications and Procedures)
- Any incidence of myocardial infarction or trans ischemic attack
- Any infection requiring hospitalization

- Pregnancy
- The investigator believes that for safety or tolerability reasons, it is in the best interest of the participant to discontinue study intervention

5.3.4 Suicide Risk Monitoring and Contingency Plan

5.3.4.1 Overview

Suicidal ideation (SI) will be monitored throughout the study using the National Institue of Mental Health (NIMH) Suicide Risk Screening Tool at baseline and each study encounter. If a participant voices suicidal thoughts, intent, or plan at any point, or screens positive using the NIMH tool, the study drug will be discontinued immediately, and the participant will be withdrawn from the study.

5.3.4.2 Definition of a Positive Screen

A participant is considered to have a positive suicide risk screen if any of the following occur:

1. The participant answers "Yes" to any of Questions 1-4 on the NIMH Suicide Risk Screening Tool, or
2. The participant refuses to answer the screening questions.

Question #5 will be used to determine acuity level (acute vs. non-acute).

5.3.4.3 Required Action When a Positive Screen Occurs

In all cases of a positive screen:

- Study drug will be stopped immediately.
- The participant will be withdrawn from the study.
- A safety evaluation will be initiate immediately.
- The participant will not leave the clinic until evaluated or transitioned to a higher level of care.

Acute Positive Screen (Imminent Risk Identified)

1. Keep the participant under continuous supervision. Do not leave the participant alone.
2. Remove any potentially harmful objects from the environment
3. Notify the PI and clinician responsible for participant's care
4. The PI or study clinician will:
    a. Contact the Emergency Department triage or attending physician
    b. Communicate the screening results and clinical concerns
    c. Request urgent psychiatric evaluation
5. Arrange safe transport (clinic staff escort, hospital security transport, or ambulance transport if participant if off-site or medically unstable).
6. Document all findings, actions, and communications in both the research record and medical record

Non-Acute Positive Screen (Potential Risk Identified)

1. Conduct a brief suicide safety assessment to determine next steps.
2. Notify the clinician responsible for participant care

If the participant demonstrates plan and intent but refuses evaluation:

- The PI or clinician may initiate involuntary psychiatric hold per ORS 426.232

If the participant endorses passive ideation only (no plan or intent), the PI or study clinician will:

1. Arrange same-day urgent psychiatry referral.
2. Involve social work for support and care coordination.
3. Develop a safety plan with the participant.

4. Provide crisis resources including 988 Suicide & Crisis Hotline and local 24-hour crisis response resources

All refusals, referrals, and safety planning activities will be documented.

5.4. Table 1: Study Schedule of Events

Week	Screening	WK 0	WK 2	WK 4	WK 6	WK 8	WK 10	WK 12	Wk 14	WK 16	Wk 20	WK 24	WK 28	Wk 36
Informed consent	X													
Demographics		X												
Counseling/training[a]		X					X							
Study drug administration[b]		X	X	X	X	X	X	X	X	X	X	X		
Vital Signs[c]	X	X	X	X	X	X		X	X	X	X	X	X	X
Physical exam	X	X	X	X	X	X		X	X	X	X	X	X	X
Ulcer measurement and photography		X	X	X	X	X		X	X	X	X	X	X	X
Patient Reported Outcomes[d]		X	X	X	X	X	X	X	X	X	X	X	X	X
PGA		X	X	X	X	X	X	X	X	X	X	X	X	X
Blood draw: Lab testing[e]	X	X						X				X		
Blood draw: Cytokines & Genetic/Genomic testing		X						X				X		
High Frequency Ultrasound		X			X			X		X		X		
Wound drainage collection[f]		X			X			X		X		X		
Pregnancy testing[g]		X	X	X	X	X		X	X	X	X	X	X	
Skin biopsy		X										X		
Review Medical History	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Review Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events		X	X	X	X	X	X	X	X	X	X	X	X	X

[a] Participants will be counseled on how to appropriately inject medication by site personnel according to the bimekizumab package insert which will be provided. Participants may either self-administer medication with site personnel present for any support or questions or request site personnel to perform the injection. See section 6.2 for more details.

[b] Bimekizumab pre-filled syringes will be dispensed at 320mg every 2 weeks for the first 16 weeks and then every 4 weeks until week 24. Participants will be provided the package insert for bimekizumab that includes instructions for proper storage and home injection. Participants will be trained during their first visit on proper drug injection.

[c] Vital signs to include blood pressure, weight and temperature

[d] Patient reported outcomes to include Skindex Mini, participant global assessment, physical function assessment, wound drainage scale, NRS, PHQ-9, GAD-7, and NIMH Suicide Risk Screening Tool

[e] Laboratory studies will include: HBV, HCV, HIV, tuberculosis, CBC, CMP, ESR, CRP, lipid panel, pregnancy testing for people who may be able to become pregnant, and markers of disease activity at the screening visit. For all other visits, CBC, CMP, ESR, and CRP will be drawn. Creatinine clearance calculations will be performed when CMP is obtained.

[f] Wound drainage will be collected if wound is draining

[g] Pregnancy testing will be performed at screening (blood or urine) and before study intervention administration at every dosing visit (blood or urine).

6. INVESTIGATIONAL PRODUCT AND TREATMENT PLAN

6.1. Investigational Product: Bimekizumab

Bimekizumab mechanism of action is as a monoclonal IgG1 antibody, a protein designed to attach to interleukin 17A (INTERLEUKIN-17A) and interleukin 17F (INTERLEUKIN-17F), which are messenger proteins in the immune system that increase inflammation. Bimekizumab attaches to INTERLEUKIN-17A and INTERLEUKIN-17F.

6.2. Dosing and Administration

Bimekizumab will be administered at 320 mg by subcutaneous injection at Week 0 by study staff. Participants will be trained in self-administration at Week 0 by study staff according to the instructions on page 10-16 of the Bimekizumab package insert (See appendix 1). These instructions will be provided to each participant. Bimekizumab will be self-administered by participants at a dose of 320 mg by subcutaneous injection every 2 weeks until Week 16 and then every 4 weeks until week 24. Participants who prefer to have the clinic staff administer study drug may request study staff to perform injections during all visit timepoints.

For all scheduled visits that coincide with a Bimekizumab dosing time point outside of Week 0, Bimekizumab self-administration will be monitored on site by study staff. For visits performed via institution approved secure videoconferencing software, a staff member will be available to monitor and support the subject's self-administration. For dose administration that falls outside of a regularly scheduled visit, a staff member will be available for a short videoconference to support the subject self-administration. The lot number and batch number of each pre-filled syringe of Bimekizumab will be recorded in the EDC for accountability purposes.

Used sharps will be disposed of on site during all in-person visits. Should participants choose to complete administration at home, they will be instructed to dispose of sharps in a puncture resistant container and counselled on the importance of not re-using needles. They will be directed to check their local governance guidelines for the proper disposal of sharps.

Participants will return all unused drug to the site for proper disposal following completion of study.

6.3. Missed and Delayed Doses

participants who miss their scheduled Bimekizumab dose will be instructed to complete their missed dose within 7 days of their scheduled timepoint. Participants who do not make up their dose within this 7 day window will be instructed to skip the dose for that time point and this will be marked as a protocol deviation. Participants who miss more than 2 doses will be discontinued from study.

Participants should never receive 2 doses of study drug within a time frame of less than 3 weeks apart. This will be noted as a protocol deviation.

6.4. Improper Dosing

Should a subject administer medication improperly resulting in an underdose, the dose will be marked as an improper dose and a protocol deviation. The subject will be retrained in proper dose administration (see appendix 1).

6.5. Storage

The study drug will be stored in the Research Pharmacy and all applicable Research Pharmacy policies and procedures will be followed.

Since participants may be self-administering study drug at home, they will receive detailed instructions for study drug storage and handling at home.

6.6. Concomitant Medications, Treatments, and Procedures

6.6.1. Concomitant Medication Recording

All concomitant medications taken during the study must be recorded. Participants will be asked about concomitant medications at each study visit.

6.6.2. Prohibited Medications, Treatments, and Procedures

The following therapies will not be permitted for participants enrolled in the trial during the course of the study:

- Treatment with systemic therapy intended to treat PG within the washout period specified in the exclusion criteria. These medications could have a negative safety impact on the participants enrolled and confound the results of the study.
- Live vaccines

Participants will be instructed that these therapies are not permitted.

6.6.3. Permitted Medications, Treatments, Rescue Treatments and Procedures

The following medications will be permitted during the course of the study:

- Topical therapies such as topical antibiotics and wound care dressings as well as oral antibiotics may be used as needed for evidence of superinfection by swap result, positive culture results, malodor and/or discolored discharge.
- Systemic medications intended to treat conditions comorbid with PG will be allowed on study (see inclusion criteria)
- Non-live vaccines (such as the non-live annual influenza vaccine, rabies, or tetanus) except for non-live herpes zoster vaccine (Shingrix) and/or emergency vaccines are allowed
- All participants are required to be on a baseline dose of 20mg of Prednisone two weeks prior to study initiation (Week 0). The baseline prednisone tapering algorithm noted in Table 2 below will be followed while participants are on study.
- Participants will maintain their usual medication regimen for other concomitant diseases throughout the study unless specifically excluded in the protocol. Participants taking concomitant medications should be on a stable dose throughout the study and at least 1 month prior unless changes need to be made for an AE or for appropriate medical management. Additional systemic drugs are to be avoided during the study, unless required to treat an AE. Other medications may be allowed, if approved by the investigator. Any changes in medications should be discussed with the investigator. Participants should be instructed to consult the investigator or other appropriate study personnel at the site before taking any new medications or supplements.

Table 2: Baseline Prednisone tapering algorithm

Time (week)	Prednisone (mg)
0	20
1	15
2	10
3	7.5
4	5
5	2.5
6	0

*Participants must be on stable dose of 20 mg for 2 weeks prior to baseline. Prednisone less than 8 mg is considered a physiological dose.

7. STATISTICAL CONSIDERATIONS

7.1. Sample Size Computation and Power Analysis

Currently 55% of PG patients treated with standard of care experience a PGA score of ≤ 1 by Week 24. We expect that 85% of PG participants treated with Bimekizumab will achieve PGA of 0 or 1 in 24 weeks. 17 patients will be recruited with an accounted drop out rate of 10%. A sample size of 15 is sufficient to provide 80% power to detect a difference of 30% using a one-sided Z-test with a significance level of 0.05. As a major secondary endpoint, we will estimate the proportion of participants with target ulcer that shows complete healing by Week 24. Our projected sample size of 15 will produce a two-sided Wilson exact 95% confidence interval of 0.448-0.870 (width=0.452), assuming the sample proportion is 0.7.

Sample Size	Dropout Rate	Dropout-inflated Enrollment Sample size	Proportion Given H0 P0	Proportion Given H1 P1	Difference P1 -- P0	Target Alpha	Power
9	10%	10	0.50	0.91	0.41	0.05	80%
10	10%	12	0.50	0.92	0.42	0.05	80%
12	10%	14	0.50	0.87	0.37	0.05	80%
14	10%	16	0.50	0.83	0.33	0.05	80%
16	10%	18	0.50	0.80	0.30	0.05	80%
18	10%	20	0.50	0.82	0.32	0.05	80%

7.2. Statistical Analysis Plan

An intent-to-treat analysis set will include those who are enrolled in the trial regardless of the number of treatments received. All primary and secondary analyses will be conducted using the intent-to-treat analysis set, unless otherwise indicated below. A safety analysis set will include those who receive at least one treatment. Toxicity and safety analyses will be conducted using the safety analysis set. A per-protocol analysis set will include those who are compliant with the protocol. As sensitivity analyses, we will analyze the endpoints using the per-protocol analysis set.

7.2.1. Primary Endpoint Analysis:

The proportion of participants with target ulcer that show a PGA score of ≤ 1 from Week 0 to week 24. The proportion will be reported with 95% confidence interval using the Wilson method.

7.2.2. Secondary Endpoint Analyses:

1. The proportion of participants with complete re-epithelialization (ulcer size 0) of the target ulcer at Week 24 will be assessed with 95% Confidence interval using a Wilson method.
2. The proportion of participants with target ulcer that show a PGA 0 from Week 0 to week 24. The proportion will be reported with 95% confidence interval using the Wilson method.

3. The proportion of participants with target ulcer that show a decrease in ulcer area size of at least 50% from Week 0 to Week 24. The proportion will be reported with 95% confidence interval using the Wilson method.
4. The mean decrease of the target ulcer size from Week 0 to Week 24. The change will be reported with mean and 95% confidence interval.
5. The mean decrease in target ulcer size from Week 0 to Week 12. The change will be reported with mean and 95% confidence interval.
6. The proportion of patients with target ulcer that show a decrease in ulcer area size of at least 50% from Week 0 to Week 12. The proportion will be reported with 95% confidence interval using the Wilson method.
7. Mean change in Skindex Mini score from Week 0 to Week-24 will be reported with two-sided 95% confidence interval. Change in Skindex Mini score will be analyzed using a paired t-test with 0.05 significance level. Generalized estimating equation (GEE)methods will be further used to characterize changes in Skindex Mini score over time.
8. The proportion of participants achieving an improvement in reported peak pain NRS assessment at Week 0 and Week 24. The peak pain NRS assessment is a subject-administered, 11-point horizontal scale anchored at 0 and 10, with 0 representing “no pain” and 10 representing “worst pain imaginable” in the last 24 hours.
9. The mean change in participant physical function from Week 0 to Week 32. Physical function is a subject-administered 5 category scale that assesses the impact of PG on participant physical function. Change in physical function score will be analyzed using a paired t-test with 0.05 significance level.
10. The mean change in participant global assessment from Week 0 to Week 24. The participant global assessment is a subject administered 5 category scale that measures participant perspective of the status of their skin disease.
11. The proportion of participants with at least a two-point decrease in pain NRS from Week 0 to Week 32 will be estimated with 95% confidence interval using the Wilson method.
12. The proportion of participants with target ulcer that remains healed by Week 36. The proportion will be reported with 95% confidence interval using the Wilson method.
13. Time to recurrence defined as the duration of time from documented target lesion healing and further episodes of PG at any site. The Kaplan-Meier survival curve will used to estimate median time to recurrence with two-sided 95% confidence interval.
14. The number of treatment failures will be reported using descriptive statistics. Treatment failure occurs if a patient experiences treatment intolerance, switches to standard of care, or experiences unhealed target lesions by Week 24.
15. Mean change in GAD-7 and PHQ-9 score from Week 0 to Week-24 will be reported with two-sided 95% confidence interval. Change in GAD-7 and PHQ-9 scores will be analyzed using a paired t-test with 0.05 significance level. Generalized estimating equation (GEE)methods will be further used to characterize changes in GAD-7 and PHQ-9 scores over time.
16.

7.2.3. Exploratory Endpoint Analyses:

- Treatment response (PGA between 0 and 2 and/or decrease in ulcer area size of at least 50%), will be stratified by over expression of Th17 downstream JAK-STAT cytokines. The epithelial expression of INTERLEUKIN-23 will be assessed qualitatively by a trained dermatopathologist who is blinded to the biopsy collection time (before or after therapy) and the over-expression of INTERLEUKIN-23 in biological samples (skin, blood) will be assessed before and after therapy by ELISA.
- Changes in cutaneous cytokines and chemokines within the tissue biopsy and blood, before and 32 weeks after treatment initiation.
- Presence and amount of hyperechoic oval structures, hair tracts, and U-shaped vessels found with high frequency ultrasound

7.2.4. Randomization method:

- Not applicable

7.2.5. Handling of Missing Data:

- No missing data will be imputed. Whenever possible, all available data will be included in the analysis. A sample size for each analysis will be clearly stated along with the reason for exclusion, if any subject is excluded from the analysis due to missing data.

8. SAFETY AND ADVERSE EVENT DEFINITIONS AND REPORTING

8.1. Specification of Safety Parameters

The PI is responsible for monitoring the safety of participants who have enrolled in the study. Safety assessments will be based on medical review of adverse events and the results of safety evaluations at specified time points as described in Section 5.1 Study Visit Procedures. Any clinically significant adverse events persisting at the end of treatment visit will be followed by the Investigator until resolution/stabilization or death, whichever comes first.

8.2. Definitions

8.2.1. Adverse Event (AE)

An adverse event is defined as any undesirable physical, psychological or behavioral effect experienced by a participant during their participation in an investigational study, in conjunction with the use of the investigational product, whether or not considered intervention-related. In general, this includes signs or symptoms experienced by the participant from the time of signing the informed consent to completion of the study.

AEs may include, but are not limited to:

- Subjective or objective symptoms spontaneously offered by the participant and/or observed by the Investigator or medical staff.
- Clinically significant laboratory abnormalities.
- A significant worsening of the participant's condition from study entry.
- Disease signs and symptoms and/or laboratory abnormalities existing prior to the use of the study treatment that resolve but then recur after treatment.
- Disease signs and symptoms and/or laboratory abnormalities existing prior to the use of the study treatment which increase in frequency, intensity, or a change in quality after treatment.

8.2.2. Serious Adverse Event (SAE)

An AE or suspected adverse reaction is considered "serious" if, in the view of either the Investigator, it results in any of the following outcomes:

- Death,
- A life-threatening adverse event,
- In-patient hospitalization or prolongation of existing hospitalization,
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or
- A congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and/or participant may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include:

- Allergic bronchospasm requiring intensive treatment in an emergency room or at home,
- Blood dyscrasias or convulsions that do not result in in-patient hospitalization, or
- The development of drug dependency or drug abuse.

8.2.3. Unanticipated Problems (UP)

- Modification of inclusion or exclusion criteria to mitigate the newly identified risks
- Implementation of additional safety monitoring procedures
- Suspension of enrollment of new participants or halting of study procedures for enrolled participants
- Modification of informed consent documents to include a description of newly recognized risks
- Provision of additional information about newly recognized risks to previously enrolled participants

The Office for Human Research Protections (OHRP) considers UPs involving risks to participants or others to include, in general, any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than previously known or recognized.

This study will use the OHRP definition of UP.

8.3. Adverse Event Assessment and Follow-Up

The occurrence of an UP, AE or SAE may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by the PI. All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate CRF. Information to be collected includes event description, time of onset, clinician's assessment of severity based on CTCAE v5.0 grade 1-5 (see below for instructions on assessing severity), seriousness, expectedness, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and date of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

At each study visit, the Investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

The Investigator will record all reportable events with start dates occurring any time after informed consent is obtained until the week-36 follow-up study visit. Any SAE that occurs after treatment with

alternative therapy will be reported only if the Investigator or current treating physician has assessed the SAE as related to the study treatment.

Assessment of Severity

The severity of AEs will be assessed using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 Grades 1 through 5. If an event is not classified by CTCAE, the severity of the AE will be graded according to the scale below to estimate the grade of severity. The investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the following categories:

- Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; treatment not indicated.
- Grade 2: Moderate; minimal, local, or noninvasive treatment indicated; limiting age-appropriate activities of daily living.
- Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living.
- Grade 4: Life-threatening consequences; urgent treatment indicated.
- Grade 5: Fatal.

8.4. Reporting Procedures

8.4.1. OHSU IRB Reporting of Unanticipated Problems and Adverse Events

Unanticipated Problems and AEs will be reported to OHSU IRB according to the policies, procedures and guidelines posted on the OHSU IRB web site.

Events that must be reported by the Investigator to the IRB are detailed in the OHSU IRB Investigator Guidance: Prompt Reporting Requirements (HRP-801). At a minimum, events requiring reporting to the IRB include:

- Any new or increased risk related to the research, including AEs or IND safety reports that require a change to the protocol or consent,
- New FDA black box warning,
- Publications identifying new risks,
- Data Safety Monitoring Board/Committee letters recommending changes or discussing new risks
- Unauthorized disclosure of confidential participant information

8.4.2. SAE Reporting to the Study Drug Manufacturer

SAEs will also be reported to Lilly's Global Patient Safety at 1-800-lilly-RX and via fax within 24 hours with a causality assessment.

8.5. Data Safety Monitoring Plan

Subject safety will be monitored in an ongoing way throughout the study. Concomitant medications will be recorded at every study visit. Vital signs including blood pressure, temperature and pulse (measured a minimum of 5 minutes after resting), and weight/BMI will be recorded at every study visit. Laboratory testing will be performed at the screening visit, visit 3 (week-4), and visit 9 (week-24) at a minimum. This will include screening for HIV, HVB, HCV, and tuberculosis as detailed in the exclusion criteria. Baseline, week-4 and week-24 laboratory testing will include complete blood counts with differential, a comprehensive metabolic panel (including GFR and creatinine clearance calculations) , sedimentation rate, c-reactive protein and lipid panel. In the event of abnormal laboratory values, additional and/or repeat laboratory testing may be requested at the discretion of the study investigator to ensure patient safety.

Subjects will be encouraged to report any potential problems at any time to qualified research staff or PI. The occurrence of adverse events will be assessed at each study visit and details including diagnosis, severity, possibility of relationship to the study medication (bimekizumab), and action taken will be recorded on the AE log in REDCap.

Data safety monitoring will involve real-time review of adverse events (AE), dropouts, complaints or breaches of confidentiality. The review of AEs will be performed by the PI (Dr. Ortega) in real time, with review by the sub-investigator (Dr. Greiling) if Dr. Ortega is unavailable.

Data collected during study visits will be entered into the REDCap database by study personnel and study subjects as outlined in the description of visits above. The PI, who has no financial conflict of interest with UCB, will review the data at least monthly.

The study will be monitored for GCP compliance.

8.6. Potential Risks

The risks associated with participation in this study include risks due to study procedures and risks due to study intervention (bimekizumab). The full drug package insert will be available at the visit and can be provided to patient.

8.6.1 Risk due to study procedures

Risks of Blood Draw

Risks of blood draw include discomfort, and a small chance of bleeding, bruising, infection, or fainting.

Risks of biopsy

Risks of biopsy include allergic reaction to the local anesthetic (1 in 10,000 risk), pain, infection, bleeding, and scarring.

Risks of Ultrasound

Ultrasound imaging will be performed on target PG ulcers for each participant, where available, at Week 0, Week 6, Week 12, Week 16 and Week 24. Ultrasound will be performed using designated ultrasound systems. Ultrasound imaging has been used for over 20 years. It is based on non-ionizing radiation, so it does not have the same risks as X-rays or other types of imaging systems that use ionizing radiation. Ultrasound imaging is generally considered safe when used prudently by appropriately trained health care providers. Ultrasound energy does have the potential to produce biological effects on the body. Ultrasound waves can heat the tissues slightly. In some cases, it can also produce small pockets of gas in body fluids or tissues (cavitation). The long-term consequences of these effects are still unknown.

Risk of Injection Site Reaction

Risk of injections include redness, itching, bleeding, bruising, swelling and rash.

Risk of bacterial swabs and wound fluid collection

Risks of bacterial swab collection and wound fluid collection are minimal as they use sterile applicators to the wound surface. Participants may experience brief discomfort, irritation or a very small risk of infection.

Risk of Interviews/Questionnaires

Risks of completing PROs may cause participants to feel upset or uncomfortable. Some questions may be skipped. If answering questions causes distress the study team will aide in accessing counseling support for the participant.

8.6.2 Risk due to study intervention (bimekizumab)

Suicidal Ideation and Behavior

An increased incidence of new onset or worsening suicidal ideation and behavior was observed in subjects treated with BIMZELX. A causal association between treatment with BIMZELX and increased risk of suicidal ideation and behavior has not been definitively established.

Suicidal ideation and behavior were prospectively monitored using the Columbia Suicide Severity Rating Scale (C-SSRS) in clinical trials. The C-SSRS is an interview-based instrument used to monitor for the presence and severity of suicidal ideation (ranging from “none” to “active suicidal ideation with specific plan and intent”) and behaviors (rating the injury and potential lethality of self-injury, if present).

Plaque Psoriasis

During the two 16-week, placebo-controlled periods of Trials Ps-1 and Ps-2, higher rates of suicidal ideation as assessed by C-SSRS were reported in BIMZELX-treated subjects than in subjects receiving placebo. Pooled analysis of C-SSRS data indicated that 12/670 (1.8%) BIMZELX-treated subjects and 1/169 (0.6%) subjects receiving placebo reported passive suicidal ideation with an estimated relative risk of 3.0 (95% confidence interval: 0.39, 22.74). Subjects without a prior history of SI/B treated with BIMZELX also reported a higher rate of new onset suicidal ideation on the C-SSRS than subjects receiving placebo (1.3% vs 0.6%). During the open-label extension trial, one completed suicide was reported in a BIMZELX-treated subject [see Adverse Reactions (6.1)].

Psoriatic Arthritis

Pooled analysis of C-SSRS data from the two 16-week, placebo-controlled periods of Trials PsA-1 and PsA-2 indicated that 2/698 (0.3%) BIMZELX-treated subjects and 3/413 (0.7%) subjects receiving placebo reported passive suicidal ideation with an estimated relative risk of 0.35 (95% confidence interval: 0.05, 2.29) [see Adverse Reactions (6.1)].

Non-Radiographic Axial Spondyloarthritis

Analysis of C-SSRS data from a 16-week, placebo-controlled period of Trial nr-axSpA-1 indicated that no subjects, being treated either with BIMZELX or placebo, reported suicidal ideation [see Adverse Reactions (6.1)].

Ankylosing Spondylitis

Analysis of C-SSRS data from a 16-week, placebo-controlled period of Trial AS-1 indicated that no subjects, being treated either with BIMZELX or placebo, reported suicidal ideation [see Adverse Reactions (6.1)].

Hidradenitis Suppurativa

During the two 16-week, placebo-controlled periods of Trials HS-1 and HS-2, higher rates of suicidal ideation as assessed by C-SSRS were reported in BIMZELX-treated subjects than in subjects receiving placebo. Based on a pooled analysis of the first 16 weeks of the placebo controlled clinical trials, 16/861 subjects in the BIMZELX group (1.9 %) reported suicidal ideation on the C-SSRS compared to 1/146 subjects in the placebo group (0.7%) with an estimated relative risk of 2.70 (95% confidence interval: 0.36, 20.12). Subjects without a prior history of SI/B treated with BIMZELX also reported a higher rate of new-onset suicidal ideation on the C-SSRS than subjects treated with placebo (0.9% vs. 0%). [see Adverse Reactions 6.1]. Consider the potential risks and benefits before prescribing BIMZELX to patients with a history of severe depression or suicidal ideation or behavior. Advise patients, their caregivers, and families to monitor for the emergence or worsening of depression, suicidal ideation, or other mood changes. If such changes occur, instruct patients to promptly seek medical attention or call the National Suicide and Crisis Lifeline at 988 [see Patient Counseling Information (17)]. Refer BIMZELX-treated patients with new or worsening symptoms of depression or suicidal ideation and/or behavior to a mental health professional, as appropriate. Re-evaluate the risks and benefits of continuing treatment with BIMZELX if such events occur.

Infections

BIMZELX may increase the risk of infections, including serious infections. Do not initiate treatment with BIMZELX in patients with any clinically important active infection until the infection resolves or is adequately treated. In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing BIMZELX. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur. If a patient develops such an infection or is not responding to standard therapy, monitor the patient closely and discontinue BIMZELX until the infection resolves.

Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with BIMZELX. Avoid the use of BIMZELX in patients with active TB infection. Initiate treatment of latent TB prior to administering BIMZELX. Consider anti-TB therapy prior to initiation of BIMZELX in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Closely monitor patients treated with BIMZELX for signs and symptoms of active TB during and after treatment.

Liver Biochemical Abnormalities

Treatment with BIMZELX was associated with increased incidence of liver enzyme elevations compared to treatment with placebo in randomized clinical trials. Liver serum transaminase elevations > 3 times the upper limit of normal were reported in subjects treated with BIMZELX [see Adverse Reactions (Package insert section 6.1)]. Elevated liver serum transaminases resolved after discontinuation of BIMZELX. Test liver enzymes, alkaline phosphatase, and bilirubin at baseline, periodically during treatment with BIMZELX and according to routine patient management. If treatment-related increases in liver enzymes occur and drug-induced liver injury is suspected, interrupt BIMZELX until a diagnosis of liver injury is excluded. Permanently discontinue BIMZELX in patients with causally associated combined elevations of transaminases and bilirubin. Patients with acute liver disease or cirrhosis may be at increased risk for severe hepatic injury; avoid use of BIMZELX in these patients.

Inflammatory Bowel Disease

Cases of inflammatory bowel disease (IBD) have been reported in patients treated with INTERLEUKIN-17 inhibitors, including BIMZELX [see Adverse Reactions (6.1)]. Avoid use of BIMZELX in patients with active IBD. During BIMZELX treatment, monitor patients for signs and symptoms of IBD and discontinue treatment if new onset or worsening of signs and symptoms occurs.

Immunizations

Prior to initiating therapy with BIMZELX, complete all age-appropriate vaccinations according to current immunization guidelines. Avoid the use of live vaccines in patients treated with BIMZELX. Limited data are available regarding coadministration of BIMZELX with non-live vaccines [see Clinical Pharmacology (12.2)].

Risks of Prednisone

Prednisone risks are as follows (inserted from the package insert found on “Up to Date”):

- Cardiovascular: Cardiac failure (in susceptible participants), hypertension
- Central nervous system: Emotional lability, headache, increased intracranial pressure (with papilledema), myasthenia, psychiatric disturbance (including euphoria, insomnia, mood swings, personality changes, severe depression), seizure, vertigo
- Dermatologic: Diaphoresis, facial erythema, skin atrophy, urticaria
- Endocrine & metabolic: Cushing’s syndrome, decreased serum potassium, diabetes mellitus, fluid retention, growth suppression (children), hypokalemic alkalosis, hypothyroidism (enhanced), menstrual disease, negative nitrogen balance (due to protein catabolism), sodium retention
- Gastrointestinal: Abdominal distention, carbohydrate intolerance, pancreatitis, peptic ulcer (with possible perforation and hemorrhage), ulcerative esophagitis

- Hematologic & oncologic: Bruise, Kaposi's sarcoma, petechia
- Hepatic: Increased serum alkaline phosphatase, increased serum ALT, increased serum AST
- Hypersensitivity: Anaphylaxis, hypersensitivity reaction
- Infection: Infection
- Neuromuscular & skeletal: Amyotrophy, aseptic necrosis of bones (femoral and humeral heads), osteoporosis, pathological fracture (long bones), rupture of tendon (particularly Achilles tendon), steroid myopathy, vertebral compression fracture
- Ophthalmic: Exophthalmos, glaucoma, increased intraocular pressure, subcapsular posterior cataract
- Miscellaneous: Wound healing impairment
- <1%, postmarketing, and/or case reports: Venous thrombosis (Johannesdottir 2013)
- Risk of Pneumocystis jirovecii pneumonia (PCP or PJP) is elevated in participants taking greater than 20mg of Prednisone in conjunction with immunosuppressive medications such as bimekizumab. Antibiotic Bactrim (trimethoprim/sulfamethoxazole (TMP/SMX)) will be prescribed as a prophylaxis to all participants taking greater than 20mg of Prednisone to counteract this risk. Antibiotic selection for participants with allergies or sensitivities to Bactrim is up to the investigator's discretion.

8.7. Participant Removal from the Trial due to Adverse Events

Any participant who experiences an adverse event may be withdrawn from the trial at the discretion of the Investigator and/or the subject's request.

If a subject suffers any injury and/or damage from this research project through the fault of the Oregon Health & Science University, its officers or employees, they will have the right to bring legal action against the University to recover the damage done subject to the limitation and conditions of the Oregon Tort Claims Act.

9. DATA HANDLING & MANAGEMENT RESPONSIBILITIES

9.1. Participant & Data Confidentiality

The information obtained during the conduct of this clinical study is confidential, and unless otherwise noted, disclosure to third parties is prohibited. Information contained within this study will be maintained in accordance with applicable laws protecting participant privacy, including the provisions of the Health Insurance Portability and Accountability Act (HIPAA).

Participant confidentiality is strictly held in trust by the participating Investigator(s) and study team. This confidentiality is extended to cover testing of biological samples in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence.

Representatives of the IRB or manufacturer supplying study product may inspect all documents and records required to be maintained by the Investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

Upon enrollment, participants will be assigned a code that will be used instead of their name, medical record number or other personally identifying information. Electronic files for data analysis will contain only the participant code. Codes will not contain any part of the 18 HIPAA identifiers (e.g., initials, DOB, MRN). The key associating the codes and the participants' personally identifying information will be restricted to the Investigator and study staff. The key will be kept secure on a restricted OHSU network drive in a limited access folder.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by local IRB and institutional regulations.

9.2. Data Collection & Storage: Privacy, Confidentiality & Security

9.2.1. Data Collection

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site Investigator. The Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. Standard institutional practices will be followed as described in the OHSU's Information Security Directives and Ohio State University's information security directives to maintain the confidentiality and security of data collected in this study. Study staff will be trained regarding these procedures.

The sites will work closely to set up and maintain the study database, create policies and procedures for the study, and monitor data quality and accuracy. Reports from all study sites regarding adverse events (AE), serious adverse events (SAE), unexpected problems (UP), and protocol deviations (PD) will be compiled according to institutional guidelines and recorded in the EDC

Data will be collected for US-based sites (OHSU). This database is not compliant with 21 CFR Part 11 guidelines and is not required to be as no data will be submitted to the FDA for submissions.

9.2.2. Data Monitoring

Data monitoring for accuracy and timely completion of records is the responsibility of the clinical trial staff at the site under the supervision of the site Investigator and will be performed to assess critical study procedures including study data endpoints, subject safety, protocol compliance, and regulatory compliance. The monitoring may include the following: Audit data listings to source documentation, ensure subject eligibility, verify reporting of adverse events, assess compliance with protocol, audit regulatory files, and ensure adequate site personnel training. Drug accountability may be reviewed.

9.2.3. Data Confidentiality

Loss of participant confidentiality is a risk of participation. Efforts will be made to keep study participant identities confidential except as required by law. Participants' samples will be identified by code only. Specifically, each consenting participant will be assigned a unique coded identifier consisting of numbers. This identifier will be associated with the participant throughout the duration of their participation in the trial. The coded identifier will also be used to identify any participant specific samples.

9.2.4. Sample Long Term Retention

Samples collected in this study may be stored for up to 15 years (or according to local regulations) for additional research. Additionally, de-identified blood, biopsy and wound samples will be stored indefinitely for future analysis of gene association associated with PG. Samples will only be used to understand bimekizumab, to understand PG, to understand differential intervention responders, and to develop tests/assays related to bimekizumab and PG. The research may begin at any time during the study or the post-study storage period. The start of the storage period will be the time at which the Clinical Study Report is issued. Stored samples will be coded throughout the sample storage and analysis process and will not be labeled with personal identifiers. Participants may withdraw their consent for their samples to be stored for research.

9.2.5. Data Storage

Basic accrual tracking information (demographic, consent, visit information) will be captured in OHSU's electronic clinical information research system (eCRIS), hosted on OHSU secure servers and managed by OHSU's information technology group at their data center in downtown Portland, Oregon.

Any additional printed documents containing participant identifiers, such as those from the medical record to confirm eligibility or paper consents, will be filed in binders and kept in a locked, secure location.

Study outcome data will be captured in electronic case report forms (eCRFs) using an electronic data capture (EDC) system (on secure servers), which facilitates information being stored in a unified format and location. To further preserve confidentiality, PHI in the EDC system will be limited to birth date and visit dates, city of residence, and email address. The system is password protected and encrypted with role-based security and administered by designated informatics staff. All users of the database are assigned a unique ID, username, and password and must complete training appropriate to their role before they are authorized to enter, access, and store data in the database.

Data from correlative studies will be entered into the EDC system by study personnel at. All other electronic data extracts will be stored only on computers and restricted drives, limited only to study investigators and staff with authorization to access the data.

Individual participant medical information obtained as a result of this study is considered confidential, and disclosure to third parties is prohibited. Research materials obtained specifically for the purposes of this study will include ultrasound images, biopsies and blood draws for mechanistic studies, and blood tests for CBC, CMP, HIV, HBV, HCV, tuberculosis. All samples used for mechanistic testing will be coded and blinded to the investigator. Data regarding medical history and symptom questionnaires will be obtained during the course of this study. Absolute confidentiality will be maintained. Only the principal investigator and study coordinator will have access to identifiable private information to facilitate subject recruitment and subject reimbursement. All data not stored in a secure online database are stored in locked compartments and are not released without the consent of the participants. If data are used in scientific presentations or publications, individuals are never identified. Medical information gathered during the course of the study may be given to the participant's medical team and all appropriate medical personnel responsible for the participant's welfare.

9.2.6. Data Recording in the Electronic Medical Record (Epic)

An Epic research encounter will be created for each in-person visit. A brief S.O.A.P. note that includes study drug administration will be entered into Epic to facilitate communication with the subject's other healthcare providers. Additionally, all serious adverse events will be recorded as a brief note in Epic.

9.2.7 Digital Photography

Photographs of the skin involvement in each subject will be captured as digital files using, digital photography coded with the subject's study number and visit number and kept on institutionally approved secure storage devices. For purposes of publication or education (i.e., viewing by anyone other than study personnel), any identifying features such as the eyes, jewelry, or a tattoo will be digitally blocked out of the photo.

9.2.8. Telemedicine Platform

The study will use a HIPAA-compliant video conferencing platform called WebEx. All protected health information will be stored unless it is deliberately captured and downloaded by one of the participants in the videoconference session. For convenience, we will choose a platform that works natively within a browser with the use of static plugins and that allows participants to access the study "room" via a specific URL without need for preregistration. The platform will use standard audio/video capabilities and will allow access through mobile devices.

10. ETHICS/PROTECTION OF PARTICIPANTS

10.1. Ethical Standard

The Investigator will ensure that this study is conducted in adherence with the protocol and International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP).

10.2. Institutional Review Board

The protocol, informed consent form, recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

10.3. Informed Consent

Written informed consent will be obtained from all participants, or the legally authorized representative of the participant, participating in this trial, as stated in the Informed Consent section of 21 CFR Part 50. If a participant's signature cannot be obtained, the Investigator must ensure that the informed consent is signed by the participant's legally authorized representative. Documentation of the consent process and a copy of the signed consent shall be maintained in the participant's medical record.

10.4. Consent Procedures and Documentation

Informed consent is a process that is initiated prior to the individual's agreement to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of participation will be provided to the participants and their families as appropriate. Consent forms will be IRB-approved and the participant will be asked to read and review the document. The Investigator will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks/benefits of the study, alternatives to participation, and of their rights as research participants.

Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants will have the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. The consent form will be completed using DocuSign software.

The participants may withdraw consent at any time throughout the course of the trial. A copy of the informed consent document will be given to the participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study. Consent and reconsent of Spanish-speaking participants will be obtained through the help of an interpreter.

Participants at OHSU who will be participating in the imaging/ultrasound sub-study will be required to sign a separate imaging informed consent.

10.5. Protocol Review

The protocol and informed consent form for this study must be reviewed and approved in writing by the IRB prior to any participant being consented on this study.

10.6. Changes to Protocol

Any modification of this protocol must be documented in the form of a protocol revision or amendment submitted by the Investigator and approved by the IRB before the revision or amendment may be implemented. The only circumstance in which the amendment may be initiated without regulatory approval is for a change necessary to eliminate an apparent and immediate hazard to the participant. In that event, the Investigator must notify the IRB within 5 business days after the implementation.

11. PUBLICATION AND DISSEMINATION POLICY

The study results will be published in a peer-reviewed journal. Participants will not be identified in any publications.

This protocol will be registered in the ClinicalTrials.gov website. This registration will occur after IRB approval.

12. REFERENCES

1. Ormerod AD, Thomas KS, Craig FE, et al. Comparison of the two most commonly used treatments for pyoderma gangrenosum: results of the STOP GAP randomised controlled trial. *Bmj*. Jun 12 2015;350:h2958. doi:10.1136/bmj.h2958
2. Gaffen SL, Jain R, Garg AV, Cua DJ. The INTERLEUKIN-23-INTERLEUKIN-17 immune axis: from mechanisms to therapeutic testing. *Nat Rev Immunol*. Sep 2014;14(9):585-600. doi:10.1038/nri3707
3. Langrish CL, Chen Y, Blumenschein WM, et al. INTERLEUKIN-23 drives a pathogenic T cell population that induces autoimmune inflammation. *J Exp Med*. Jan 17 2005;201(2):233-40. doi:10.1084/jem.20041257
4. McPhie ML, Kirchhof MG. Pyoderma gangrenosum treated with secukinumab: A case report. *SAGE Open Med Case Rep*. 2020;8:2050313x20940430. doi:10.1177/2050313x20940430
5. Guenova E, Teske A, Fehrenbacher B, et al. Interleukin 23 expression in pyoderma gangrenosum and targeted therapy with ustekinumab. *Arch Dermatol*. Oct 2011;147(10):1203-5. doi:10.1001/archdermatol.2011.168
6. Ortega-Loayza AG, Friedman MA, Reese AM, et al. Molecular and Cellular Characterization of Pyoderma Gangrenosum: Implications for the Use of Gene Expression. *J Invest Dermatol*. Apr 2022;142(4):1217-1220.e14. doi:10.1016/j.jid.2021.08.431
7. Adams R, Maroof A, Baker T, et al. Bimekizumab, a Novel Humanized IgG1 Antibody That Neutralizes Both INTERLEUKIN-17A and INTERLEUKIN-17F. *Front Immunol*. 2020;11:1894. doi:10.3389/fimmu.2020.01894
8. Ortega-Loayza AG, Nugent WH, Lucero OM, Washington SL, Nunley JR, Walsh SW. Dysregulation of inflammatory gene expression in lesional and nonlesional skin of patients with pyoderma gangrenosum. *Br J Dermatol*. Jan 2018;178(1):e35-e36. doi:10.1111/bjd.15837
9. Ji YZ, Liu SR. Koebner phenomenon leading to the formation of new psoriatic lesions: evidences and mechanisms. *Biosci Rep*. Dec 20 2019;39(12)doi:10.1042/bsr20193266
10. Glatt S, Jemec GBE, Forman S, et al. Efficacy and Safety of Bimekizumab in Moderate to Severe Hidradenitis Suppurativa: A Phase 2, Double-blind, Placebo-Controlled Randomized Clinical Trial. *JAMA Dermatol*. 2021;157(11):1279-1288. doi:10.1001/jamadermatol.2021.2905
11. Kimball AB, Jemec GBE, Sayed CJ, et al. Efficacy and safety of bimekizumab in patients with moderate-to-severe hidradenitis suppurativa (BE HEARD I and BE HEARD II): two 48-week, randomised, double-blind, placebo-controlled, multicentre phase 3 trials. *The Lancet*. 2024/05/22/ 2024;doi:https://doi.org/10.1016/S0140-6736(24)00101-6
12. Neutrophil migration in hidradenitis suppurativa. *British Journal of Dermatology*. 2023;188(5):e36-e36. doi:10.1093/bjd/ljad093
13. Garg A, Malviya N, Strunk A, et al. Comorbidity screening in hidradenitis suppurativa: Evidence-based recommendations from the US and Canadian Hidradenitis Suppurativa Foundations. *Journal of the American Academy of Dermatology*. 2022/05/01/ 2022;86(5):1092-1101. doi:https://doi.org/10.1016/j.jaad.2021.01.059

Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues.

Spitzer, R. L., Kroenke, K., Williams, J. B.,

Lowe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. Archives of internal medicine, 166(10), 1092-1097.

12. Appendix

Patient Reported Outcomes

Physician Global Assessment

Total resolution of target ulcer with no signs of active PG	Almost completely healed target ulcer with only minimal signs of active PG	Evidence of target ulcer healing which involves at least 50% of target ulcer/ margin	Evidence of target ulcer healing which involves less than 50% of target ulcer/ margin	No evidence of target ulcer healing
0	1	2	3	4

Skindex Mini

During the past week, how often have you been:	**Never Bothered 0**	**1**	**2**	**3**	**4**	**Always Bothered 5**
1. Bothered by symptoms of your skin problems (eg itching, stinging, burning, hurting or skin irritation)	**0**	**1**	**2**	**3**	**4**	**5**
2. Emotionally bothered by your skin problem (eg, worry, embarrassment, frustration).	**0**	**1**	**2**	**3**	**4**	**5**
3. Bothered by the effects of your skin problem on your ACTIVITIES (eg, going out, accomplishing what you want, work activities, or your relationships with others).	**0**	**1**	**2**	**3**	**5**	**5**

Please check you have answered EVERY question. Thank you.

Participant Global Assessment

From your perspective, how would you describe the status of your skin problem (select one)	Clear	Almost Clear	Mild	Moderate	Severe

	☐	☐	☐	☐	☐

Participant Physical Function Assessment

In the past 7 days, how much difficulty did you have doing your daily physical activities because of your ulcer?	No difficulty at all	A little bit of difficulty	Some difficulty	A lot of difficulty	Can't do because of ulcer
	☐	☐	☐	☐	☐

NRS Pain Assessment: Peak Pain Reported in the last 24 hours

During the past 24 hours, how would you rank your skin pain?	**No pain**										**Worst Pain**
	0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

NRS Pain Assessment: Average pain reported over the last 7 days

During the past 7 days, how would you rank your skin pain?	**No pain**										**Worst Pain**
	0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

Patient Assessment of Wound Drainage over the last 7 days

In the past 7 days, how would you describe the drainage? (select one)	Clear	Almost Clear	Mild	Moderate	Severe
	☐	☐	☐	☐	☐

Patient Health Questionnaire-9 (PHQ-9)

Over the last two weeks, how often have you been bothered by any of the following problems?	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
Little interest or pleasure in doing things	0	1	2	3
Feeling down, depressed, or hopeless	0	1	2	3
Trouble falling or staying asleep, or sleeping too much	0	1	2	3

Feeling tired or having little energy	0	1	2	3
Poor appetite or overeating	0	1	2	3
Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
Moving or speaking so slowly that other people could have noticed? Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

NIMH Suicide Risk Screening Tool

In the past few weeks, have you wished you were dead?	Yes	No
In the past few weeks, have you felt that you or your family would be better off if you were dead?	Yes	No
In the past week, have you been having thoughts about killing yourself?	Yes	No
If yes, how?		
When?		
If answered YES to any of the above, ask the following acuity question:		
Are you having thoughts of killing yourself right now?	Yes	No
If yes, please describe:		

Generalized Anxiety Disorder Questionaire-7 (GAD-7)

Please read each statement and select from “Not at all” to “Nearly every day” to indicate how much the statement applied to you over the past two weeks.

	Not at all	**Several days**	**More than half the days**	**Nealy every day**
Feeling nervous, anxious, or on edge	0	1	2	3

Not being able to stop or control worrying	0	1	2	3
Worrying too much about different things	0	1	2	3
Trouble relaxing	0	1	2	3
Being so restless that it is hard to sit still	0	1	2	3
Becoming easily annoyed or irritable	0	1	2	3
Feeling afraid as if something awful might happen	0	1	2	3