6. Study Population

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, are not permitted.

6.1. Inclusion Criteria

Patients are eligible to be included in the study only if they meet all of the following criteria within the screening period, which is ≤28 days prior to the start of study treatment unless otherwise defined:

Type of Patient and Disease Characteristics

[1] Present with chronic plaque psoriasis based on the investigator-confirmed diagnosis of chronic psoriasis vulgaris for at least 6 months prior to baseline, and meet the following criteria:

A. Plaque psoriasis involving ≥10% body surface area (BSA) and absolute PASI score ≥12 in affected skin at screening (Visit 1) and baseline (Visit 2), and

B. sPGA score of ≥3 at screening (Visit 1) and baseline (Visit 2).

[2] Candidate for systemic therapy and/or phototherapy.

Patient Characteristics

[3a] Male patients:

No male contraception required except in compliance with specific local government study requirement.

[3b] Female patients:

Women not of childbearing potential may participate and include those who are:

A. Infertile due to surgical sterilization (hysterectomy, bilateral oophorectomy, or tubal ligation), congenital anomaly such as mullerian agenesis,

OR

B. Postmenopausal, defined as:

i. A woman at least 50 years of age with an intact uterus, not on hormone therapy, who has had either:

a. Cessation of menses for at least 1 year,

OR

b. At least 6 months of spontaneous amenorrhea with a follicle stimulating hormone >40 mIU/mL,

OR

ii. A woman 55 years or older not on hormone therapy, who has had at least 6 months of spontaneous amenorrhea,

OR

iii. A woman at least 55 years of age with a diagnosis of menopause prior to starting hormone replacement therapy.

Women of childbearing potential:

A. Must test negative for pregnancy prior to initiation of treatment as indicated by a negative serum pregnancy test at the screening visit followed by a negative urine pregnancy test within 24 hours prior to exposure.

B. Must agree to either remain abstinent, if complete abstinence is their preferred and usual lifestyle, or remain in same-sex relationships, if part of their preferred and usual lifestyle, without sexual relationships with males. Periodic abstinence (for example, calendar, ovulation, symptothermal, post-ovulation methods), declaration of abstinence just for the duration of a trial, and withdrawal are not acceptable methods of contraception.

   OR

   Must use 2 effective methods of contraception for the entirety of the study. Abstinence or contraception must continue for 12 weeks following completion of investigational product administration.

   i. Two effective methods of contraception (such as male or female condoms with spermicide, diaphragms with spermicide or cervical sponges) will be used. The patient may choose to use a double-barrier method of contraception. Barrier protection methods without concomitant use of a spermicide are not a reliable or acceptable method. Thus, each barrier method must include use of a spermicide. It should be noted that the use of male and female condoms as a double-barrier method is not considered acceptable due to the high failure rate when these methods are combined.

   ii. Of note, one of the two methods of contraception may be a highly effective (less than 1% failure rate) method of contraception (such as combination oral contraceptives, implanted contraceptives or intrauterine devices).

When local guidelines concerning highly effective or effective methods of birth control differ from the above, the local guidelines must be followed.

[4] Are at least 18 years of age at the time of screening.

[5] Have adequate organ function, including:

A. Hematology:

i. Absolute neutrophil count ≥1.5 x 10^9/L (≥1.5 x 10^3/µL or ≥1.5 GI/L),

ii. Platelet count ≥100 x 10^9/L (≥100 x 10^3/µL or ≥100 GI/L),

iii. Hemoglobin level ≥10.0 g/dL (≥100 g/L),

iv. Lymphocyte count >500 cells/µL (>0.50 x 10^3/µL or >0.50 GI/L),

v. Total white blood cell count ≥3.0 x 10^9/L (≥3.0 x 10^3/µL or ≥3.0 GI/L).

B. Chemistry:

i. Serum creatinine ≤2x the upper limit of normal (ULN),

ii. Alanine aminotransferase (ALT) ≤2x ULN,

iii. Aspartate aminotransferase (AST) levels ≤2x ULN,

iv. Total bilirubin level <1.5x ULN (patients with Gilbert's syndrome must have serum direct bilirubin <1.5 mg/dL or <25.7 µmol/L),

v. Alkaline phosphatase (ALP) <1.5x ULN.

(Note: The tests for AST and ALT may be repeated once within a week if the initial response exceeds this limit, and the repeat value may be accepted if it meets this criterion. Other laboratory tests should not be repeated unless there is a technical error or clinical reasons to believe a result may be erroneous, and requires approval by the Eli Lilly and Company [Lilly]-designated medical monitor.)

[6] Are reliable and willing to make themselves available for the duration of the study and are able and willing to follow study procedures, including use of electronic device for recording of data.

Informed Consent

[7] Have given written informed consent as a legal adult according to local regulations.

6.2. Exclusion Criteria

Patients will be excluded from study enrollment if they meet any of the following criteria at screening, unless otherwise specified:

Medical Conditions

[8] Have an abnormality in the 12-lead electrocardiogram (ECG) that, in the opinion of the investigator, increases the risks associated with participating in the study.

[9] Have an unstable or uncontrolled illness, including but not limited to a cerebro-cardiovascular, respiratory, hepatic, renal, gastrointestinal, endocrine, hematologic, or neurologic disease or abnormal laboratory values at screening, that in the opinion of the investigator, would potentially affect patient safety within the study or of interfering with the interpretation of data.

[10] Presence of significant uncontrolled neuropsychiatric disorder or judged at-risk of suicide in the opinion of the investigator;

OR

marked "yes" to Columbia-Suicidality Severity Rating Scale (C-SSRS) question 4 or 5 on ideation at Visit 1, or prior to dosing at Visit 2;

OR

"yes" to C-SSRS suicide behaviors question 1 month prior to Visit 1, or prior to dosing at Visit 2;

OR

Has a history of suicide attempt within 1 month prior to screening.

[11] Have human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) or test positive human HIV antibodies at screening.

[12] Have hepatitis C or test positive for hepatitis C virus (HCV) at screening, defined as: positive result for hepatitis C antibody and positive confirmatory HCV ribonucleic acid (RNA) test (see Section 9.4.5.5). Patients in sustained virologic response after HCV therapy, and patients who have spontaneously cleared HCV infection (see Section 9.4.5.5), can be included in this study.

[13] Have hepatitis B or test positive for hepatitis B virus (HBV) at screening, defined as:

A. Positive for hepatitis B surface antigen (HBsAg+),

OR

B. Positive for hepatitis B core antibody (HBcAb+) in conjunction with positive confirmatory HBV deoxyribonucleic acid (DNA) test

OR

C. Positive HBV DNA test, regardless of anti-hepatitis B surface antibody (HBsAb) status.

[14] Are women who are breastfeeding or plan to breastfeed during study.

[15] Have donated blood of >500 mL within 14 days prior to baseline.

[16] Have had serious, opportunistic (see Section 9.2.3 and Appendix 4), or chronic/recurring infection within 3 months prior to screening. Examples include, but are not limited to, infections requiring IV antibiotics, hospitalization, or prolonged treatment.

[17] Have received a systemic (including oral) anti-infective agent for an infection within 28 days of baseline (see Section 6.4 for information on rescreening).

[18] Have had, according to the investigator, clinically significant herpes zoster within 3 months of screening.

[19] Have evidence of active or latent tuberculosis (TB) (refer to Section 9.4.5.2 for details on full TB exclusion criteria and Section 6.4 for information on rescreening).

[20] Have received a Bacillus Calmette-Guerin (BCG) vaccination within 12 months or received live vaccine(s) (including attenuated live vaccines) within 12 weeks of baseline or intend to receive either during the study.

[21] Have history of hypersensitivity events to any components of the mirikizumab product formulation.

[22] Have active or history of lymphoma, leukemia, or any malignancy. *Exceptions:* the following conditions are not exclusionary: successfully treated basal cell skin carcinoma, squamous cell skin carcinoma, or cervical carcinoma in situ, with no evidence of recurrence or metastatic disease within the 5 years prior to baseline.

[23] Have any other skin conditions (excluding plaque psoriasis) that would affect interpretation of the results (including, but not limited to, scleroderma, eczema, drug-induced psoriasis, guttate psoriasis, pustular psoriasis, parapsoriasis, or cutaneous manifestations of other autoimmune diseases such as systemic lupus erythematosus).

Prior/Concomitant Therapy

[24] Have received systemic nonbiologic therapy (including, but not limited to, oral psoralen and ultraviolet A [PUVA] light therapy; cyclosporine; corticosteroids; methotrexate; oral retinoids; apremilast; tofacitinib; mycophenolate mofetil; thioguanine; hydroxyurea; sirolimus; tacrolimus; azathioprine; leflunomide; fumaric acid derivatives; or 1,25-dihydroxyvitamin D3 and analogues) or phototherapy (including either oral and topical PUVA light therapy, ultraviolet B, excimer laser, or self-treatment with tanning beds or therapeutic sunbathing) within 28 days prior to baseline.

[25] Have received topical treatment (including, but not limited to, corticosteroids [mild or least potent topical steroids will be permitted for use limited to the face, axilla, or genitalia], crisaborole, anthralin, calcipotriene, topical vitamin D derivatives, retinoids, tazarotene, pimecrolimus, tacrolimus, emollients and other nonprescription topical products containing urea, >3% salicylic acid, alpha- or beta-hydroxyl acids, or medicated shampoos [for example, those that contain >3% salicylic acid, corticosteroids, coal tar, or vitamin D3 analogues]) within 14 days prior to baseline.

[26] Have received anti-TNF targeting biologics within 8 weeks prior to baseline, or anti-IL-17 targeting biologics within 12 weeks prior to baseline.

[27] Have previous exposure to any biologic therapy targeting IL-12/23 (p40 subunit), or IL-23 (p19 subunit), either marketed or investigational.

[28] Are unable or unwilling to avoid excessive sun exposure or use of tanning booths for at least 4 weeks prior to baseline and during the study.

Prior/Concurrent Clinical Trial Experience

[29] Are currently enrolled in any other clinical study involving an investigational product or any other type of medical research judged not to be scientifically or medically compatible with this study.

[30] Have participated, within the last 30 days, in a clinical study involving an investigational product.

If the previous investigational product has a long half-life, 3 months or 5 half-lives (whichever is longer) should have passed prior to screening.

[31] Have previously completed or withdrawn from this study or any other study investigating mirikizumab.

Other Exclusions

[32] Are investigator site personnel directly affiliated with this study and/or their immediate families. Immediate family is defined as a spouse, parent, child, or sibling, whether biological or legally adopted.

[33] Are Lilly employees or employees of third-party organization involved with the study who require exclusion of their employees.

[34] Are unsuitable for inclusion in the study in the opinion of the investigator or Sponsor for any reason that may compromise the patient's safety or confound data interpretation.