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Design of a phase 2a, double-blind, placebo-controlled, global trial of MK-6194, a modified form of IL-2, in participants with non-segmental vitiligo.

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Introduction & Objectives:

Current systemic treatments for vitiligo offer limited efficacy, have potential safety concerns with extended use and can be burdensome or undesirable in application. In vitro and in vivo data suggests regulatory T cells (Tregs) are involved in the pathogenesis of Vitiligo. Treg expansion using low dose IL-2 has shown preliminary evidence of clinical efficacy in a variety of autoimmune diseases. However, its use is limited by a narrow therapeutic window of dose for minimizing activation of the cytotoxic immune cells and frequent injections due to its short half-life.

MK-6194 is a modified form of IL-2 that selectively expands Tregs without significant effects on other immune cell types. MK-6194 administered subcutaneously is generally well tolerated in the completed and ongoing Phase 1 clinical studies at single doses up to 10 mg. In healthy adults, the half-life of MK-6194 is ~20–28 hours after single-dose administration, with dose-related increases in total Tregs.

This study will evaluate the efficacy and safety of MK-6194 at two dose regimens in patients with nonsegmental vitiligo (NCT06113328).

Materials & Methods:

This phase 2a, multicentre, randomized, double-blind, placebo-controlled trial is enrolling adults (aged 18-75 years) with a clinical diagnosis of non-segmental vitiligo of ≥6 months (**Figure 1**). Eligible participants (**Table 1**) will be randomized to receive subcutaneous administration of either placebo or one of the dose regimens of MK-6194 for 24 weeks (double-blind placebo controlled treatment period) and followed-up in a further 24 weeks double-blinded extension. In the double-blinded extension period, participants will continue their original treatment regimen if treated with MK6194 in the double-blind treatment period and participants will be randomized to receive one of the two MK-6194 regimens if previously treated with placebo.

The study will also be stratified by history of previous JAKi use (yes vs no) and stable vs active non-segmental vitiligo at randomization. The primary efficacy endpoint is percent change from baseline in Facial Vitiligo Area Scoring Index (F-VASI) and the primary safety endpoint is number of adverse events (AE) and discontinuation due to AEs at Week 24. Percentage change from baseline in total Vitiligo Area Scoring Index (T-VASI, including the face) will be assessed as a secondary endpoint at Week 24, along with other exploratory endpoints, including patient-reported outcomes, pharmacokinetics and pharmacodynamics.

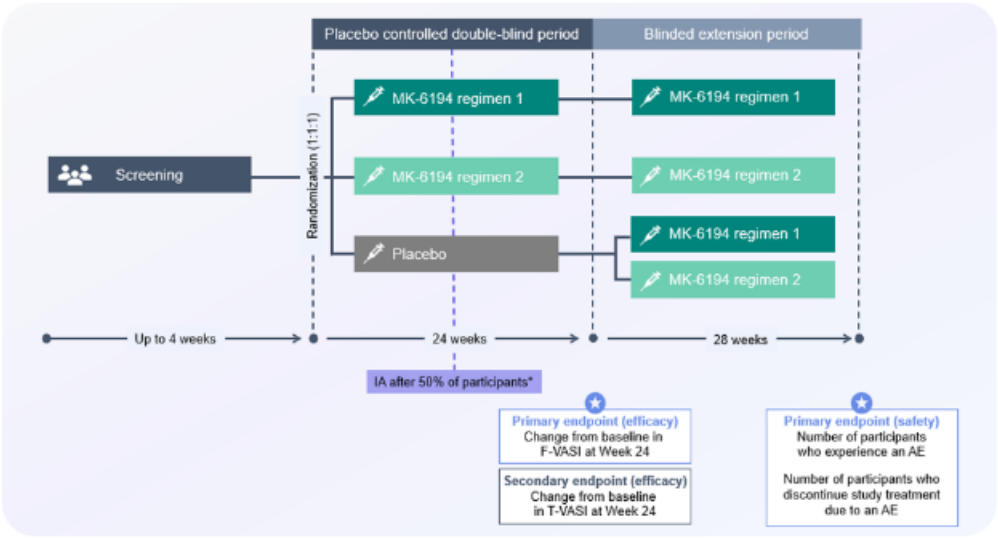
Results:

Approximately 165 participants (55 per treatment group) will be randomized in Europe, USA, Canada and the Asia Pacific region. The study is actively recruiting; no data are yet available.

Conclusion:

This phase 2a trial will outline the efficacy, safety, and tolerability of MK-6194 compared with placebo in patients with non-segmental vitiligo.

Figure 1. Study design and key endpoints



*An interim futility analysis will be performed when the first 50% randomized participants complete the Week 24 evaluation or prematurely discontinue.
AE, adverse event; F-VASI, Facial Vitiligo Area Scoring Index; IA, interim analysis; T-VASI, Total Vitiligo Area Scoring Index (including the face).

Table 1. Inclusion/exclusion criteria

Key inclusion criteria	Key exclusion criteria

• Adults (18–75 years) of any sex/gender
• Clinical diagnosis of non-segmental vitiligo for a duration of ≥6 months*
• At screening and baseline:
  • Depigmentation contributing to F-VASI ≥0.3
  • Depigmented facial BSA ≥0.3%
  • T-VASI ≥4
  • Total body vitiligo area ≥4%†
  • Candidate for systemic therapy based on investigator judgment
	• Segmental vitiligo or ≥50% leukotrichia on face or body
	• History of (or current) inflammatory condition that could interfere with vitiligo evaluation‡
	• Known systemic hypersensitivity to IL-2, or modified IL-2 including MK-6194, or its inactive ingredients
	• Known history of hypereosinophilic syndrome or an eosinophil-related condition§
	• Active clinically significant infection,¶ any infection requiring treatment with IV anti-infectives ≤4 weeks prior to randomization, or oral/intramuscular anti-infectives ≤2 weeks prior to randomization
	• Symptomatic heart failure (NYHA class III or IV) or MI or unstable angina pectoris within 6 months prior to screening
	• Severe chronic pulmonary disease requiring oxygen therapy
	• Has a transplanted organ which requires continued immunosuppression, had major surgery within 3 months prior to screening or has a major surgery planned during the study
	• History of any malignancy, except for successfully treated non-melanoma skin cancer or localized carcinoma *in situ* of the cervix

For full details on the inclusion and exclusion criteria please refer to NCT06113328.

*Vitiligo diagnosis must be made by a trained physician who is a board-certified dermatologist (or local equivalent). Disease duration is defined as the length of time since onset of symptoms; †Excluding hand and foot involvement; ‡In the opinion of the investigator; §For example, eosinophilic pulmonary disease including eosinophilic asthma, eosinophilic esophagitis, eosinophilic nephritis, eosinophilic granulomatosis with polyangiitis; ¶Including COVID-19, HBV, HCV, HIV and TB.

BSA, body surface area; COVID-19, coronavirus disease 19; F-VASI, Facial Vitiligo Area Scoring Index; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IL, interleukin; IV, intravenous; MI, myocardial infarction; NYHA, New York Heart Association; TB, tuberculosis; T-VASI, Total Vitiligo Area Scoring Index (including the face).