IL-6 Inhibition With Vamikibart in Patients With Uveitic Macular Edema: Phase 3 MEERKAT and SANDCAT Trials

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Unmet Need/Purpose

- UME is the most common vision-threatening complication in NIU,[1] affecting ~one-third of patients[2]
- There is a high unmet need in UME for non-steroidal therapies that target specific mediators of the immune response
  - Although NIU may be controlled with systemic immunosuppressive or immunomodulatory agents, UME persists in ~40% of eyes[3,4]
  - Steroids are used to treat UME but have well-recognised side effects
- Currently, there are no approved biological treatments for IVT use in uveitis, including for UME
- Targeting IL-6 is a potential therapeutic strategy for retinal diseases with an inflammatory component, including UME and DME (**Figure 1**)
- Vamikibart (RG6179) is an anti–IL-6 monoclonal antibody that has promising exploratory phase 1 data in UME[5]
- **Here, we report the study design of 2 identical, parallel, ongoing phase 3 trials of IVT vamikibart in UME secondary to NIU**

Abbreviations

AE, adverse event; BCVA, best-corrected visual acuity; CD, cluster of differentiation; CI, co-investigator; CST, central subfield thickness; DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; Fc, fragment crystallisable; IgG2, immunoglobulin G2 isotype; IL-6, interleukin 6; IL-6R, IL-6 receptor; IOP, intraocular pressure; IVT, intravitreal; mAb, monoclonal antibody; NIU, noninfectious uveitis; OCT, optical coherence tomography; PI, principle investigator; PRN, pro re nata (as needed); $t_{1/2}$, half-life; Th17, T helper 17 cell; T_{reg}, regulatory T cell; UME, uveitic macular edema; VEGF, vascular endothelial growth factor.

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Study and Product Disclosures

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The ongoing phase 3 MEERKAT and SANDCAT program is designed to evaluate vamikibart and its potential to address the unmet need for effective non-steroidal IVT treatments in patients with UME

IL-6 Is a Potential Target to Address the Inflammatory Cascade in Retinal Diseases

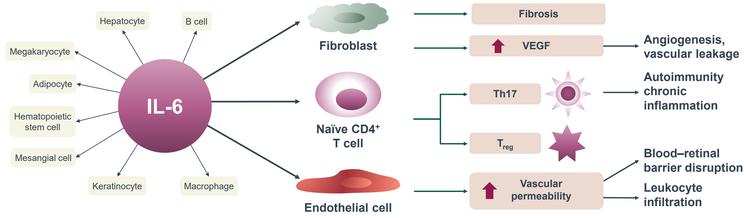
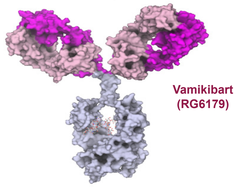


Figure 1. Roles of IL-6[5]

- IL-6 is a pleiotropic, pro-inflammatory cytokine
- Dysregulated IL-6 signaling plays an important role in a variety of retinal diseases and macular edema
- It is produced by multiple cells in response to pathogen- or damage-associated molecular patterns

Vamikibart Is an Anti–IL-6 mAb Engineered for IVT Use



- Specifically engineered for IVT delivery
- Fc region designed for fast systemic clearance and to minimise the potential for systemic AEs
- $t_{1/2}$ after IVT dosing = ~7 days (similar to faricimab)[a]
- Restores blood–retina barrier integrity[b]
- Vamikibart inhibits both cis- and trans–IL-6 signalling

[a] Preliminary data. [b] Preclinical data presented at ARVO 2023.[6]

Preclinical and Clinical Evidence Support Targeting IL-6 in UME Secondary to NIU

High ocular fluid IL-6: Multiple studies demonstrate high IL-6 in NIU[7-9]
High ocular: plasma IL-6 ratio supports local ocular production[10]

Preclinical and clinical evidence for IL-6 inhibition in UME

IVT anti–IL-6 mAb attenuates inflammation in experimental autoimmune uveitis[11]
- Significantly decreased clinical uveitis scores
- Decreased vasculitis on fluorescein angiography
- Reduced retinal/choroidal infiltration and protected retinal anatomy

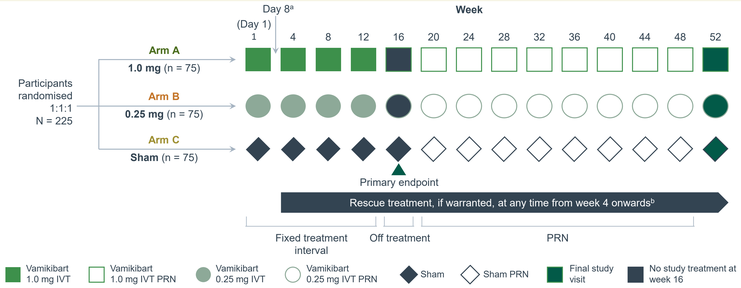
→ Clinical studies with systemic IL-6R inhibition in NIU demonstrated a specific benefit in patients with UME[12]

→ Preliminary results from the phase 1 DOVETAIL trial to assess the safety, tolerability, efficacy and pharmacokinetic/pharmacodynamic profile of vamikibart in patients with UME (n = 37) suggest that[5]:
- 3 IVT injections with vamikibart every 4 weeks (weeks 0, 4 and 8) lead to improvements from baseline in BCVA and CST over 36 weeks
- Vamikibart was well tolerated, with no treatment-related serious AEs, IOP increase or new cataracts

The totality of preclinical and clinical evidence with IL-6 targeting in UME supported progression directly from phase 1 to the phase 3 trial program of IVT vamikibart in UME

MEERKAT/SANDCAT Trials Will Evaluate Efficacy, Safety and Pharmacokinetics/Pharmacodynamics of Vamikibart

MEERKAT (study GR44277, NCT05642312) and SANDCAT (study GR44278, NCT05642325) are 2 identical, global, randomised, double-masked, sham comparator–controlled, phase 3 trials of IVT vamikibart in patients with UME



KEY ELIGIBILITY CRITERIA

UME secondary to NIU
- NIU: active or inactive, acute or chronic, all etiologies and all anatomic types
- UME with CST ≥ 325 µm on macular OCT and BCVA 73–19 letters (ETDRS)
- Age ≥ 18 years old
- Prior local ocular steroids permitted[c]
- Systemic immunosuppression and systemic biologic and topical/oral steroid permitted at baseline and during the study[d]

[a] BCVA and OCT also captured at day 8 safety visit. [b] Predefined rescue criteria permitted rescue treatment from week 4 with standard-of-care therapies.
[c] With washouts or within protocol-defined specifications. [d] If within protocol-defined timelines and permitted doses.

PRIMARY ENDPOINT: Proportion of patients with a ≥ 15-letter BCVA gain from baseline at week 16

Key secondary endpoints

Visual function:
- Proportion of patients with a ≥ 15-letter gain from baseline at week 20 (8 weeks after last study drug dose)
- Change in BCVA score from baseline at week 16

Anatomical:
- Change in CST from baseline at week 16

Other secondary endpoints

Pharmacokinetics/pharmacodynamics: aqueous humour/serum

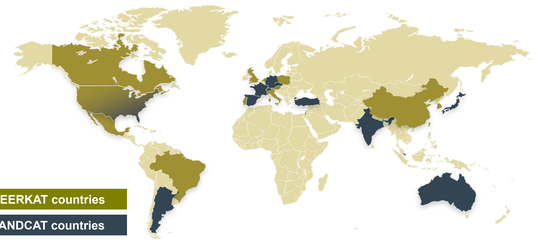
Immunogenicity analyses

Additional functional, anatomical and patient-reported outcomes, including:
- Time to and number of PRN/rescue interventions

Exploratory endpoints: biomarkers

Safety outcomes include the incidence, seriousness and severity of AEs

Study Site Map



The UK is participating in MEERKAT study with 11 study sites:
- Birmingham – Balini Balasubramaniam (PI)
- Bradford – Helen Devonport (PI)
- Brighton – Edward Hughes (PI)
- Bristol – Simon Epps (PI)
- Cardiff – Sanjiv Banerjee (PI)
- Gloucestershire – Quresh Mohamed (PI)
- Liverpool – Nima Ghadiri (PI)
- London (Moorfields Eye Hospital) – Carlos Pavesio (CI), Will Tucker (PI)
- London (Western Eye Hospital) – Rashmi Akshikar (PI)
- Maidstone – Goncalo Almeida (PI)
- Middlesbrough – Ahmed Saad (PI)

Actively enrolling patients

If you have patients who might be interested in taking part in the **MEERKAT** or **SANDCAT** trials, please find more information via the links:

MEERKAT GR44277
clinicaltrials.gov; eucliniclatrials.eu

SANDCAT GR44278
clinicaltrials.gov; eucliniclatrials.eu