SYNOPSIS

<table>
<tr><td>Name of Sponsor/Company:
Akari Therapeutics Plc</td><td rowspan="3">Individual Study Table Referring to Part of the Dossier

Volume:

Page:</td><td rowspan="3">(For National Authority Use only)</td></tr>
<tr><td>Name of Finished Product:
Nomacopan</td></tr>
<tr><td>Name of Active Ingredient:
Nomacopan, rVA576 (also known as coversin, OmCI or rEV576)</td></tr>
<tr><td colspan="3">Title of Study:
TRACKER: Topical rVA576 for treatment of atopic keratoconjunctivitis: a randomised placebo controlled double masked parallel trial.</td></tr>
<tr><td colspan="3">Investigators:
▪ UK – 001 - Dr Sajjad Ahmad
▪ UK – 002 - Dr Kieren Darcy
▪ UK – 003 - Dr Vito Romano
▪ UK – 004 - Professor Fransisco Figueiredo
▪ UK – 005 - Rosalind Stewart
▪ UK – 006 - Dr James Meyerscough
▪ UK – 007 - Dr John Sharp
▪ Spain – ESP001 - Dr Maria Teresa Sainz De La Maza Serra
▪ Spain – ESP002 - Dr Margarita Calonge Cano</td></tr>
<tr><td colspan="3">Study Centres:
▪ 001 - Moorfields Eye Hospital
▪ 002 - Bristol Eye Hospital
▪ 003 - Royal Liverpool University Hospital
▪ 004 - Royal Victoria Infirmary, Newcastle-Upon-Tyne
▪ 005 - St James's University Hospital, Leeds
▪ 006 - University Hospital NHS Foundation Trust
▪ 007 - Addenbrookes Hospital
▪ ESP001 - Hospital Clinic de Barcelona
▪ ESP002 - Instituto Universitario de Oftalmobiología Aplicada</td></tr>
<tr><td colspan="3">Publication (reference):
N/A</td></tr>
<tr><td colspan="2">Studied period:
4th March 2019 (1st patient, 1st dose).
30th April 2020 (last patient, last visit).</td><td>Phase of development:
I/II</td></tr>
<tr><td colspan="3">Objectives:
Primary Objective:
Safety and tolerability of topical rVA576 for AKC, VKC and severe allergic conjunctivitis (SAC or PAC).</td></tr>
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Secondary Objective:

Efficacy of topical rVA576 for the treatment of patients with AKC, VKC, and severe allergic conjunctivitis (SAC or PAC).

Methodology:

Randomised, double masked, placebo controlled parallel group comparison with open label sentinel group.

Part 1: The first 3 patients selected for the study were to be treated with active drug in open-label manner at intervals of one week and had weekly clinic visits until Day 14, after which the visits were every two weeks. When the first 3 patients had completed two weeks of treatment and the safety and tolerability data was to be reviewed by the PI and an independent clinician to ensure safety, the randomisation process began (Part 2). The first 3 Part 1 patients were to continue treatment for a total of eight weeks.

Part 2: Sixteen patients were to be randomised 1:1. between active and placebo, and were to be assessed at bi-weekly intervals until the end of the study by a masked observer.

Number of patients (planned and analysed):

Planned: 3 (Part 1), and 16 (Part 2)
Analysed: 3 (Part 1), and 9 (Part 2)

Diagnosis and main criteria for inclusion:

- Aged 18 and above
- Diagnosis of moderate to severe AKC, VKC, or severe allergic conjunctivitis (seasonal or perennial). Defined as:
  - AKC, VKC - a composite symptom/sign score from one eye of ≥ 18 out of 33
  - Severe allergic conjunctivitis (SAC or PAC) - a composite symptom/sign score from one eye of ≥ 15 out of 27
- Received some topical therapy during the last 3 months without improvement but not currently receiving systemic immunotherapy
- Had at least 7 days without topical ocular corticosteroids prior to entry

Test product, dose and mode of administration:

rVA576 (2.5 mg/mL) eye drops. One drop to each eye every 12 hours.

Duration of treatment:

56 days each for active and placebo dosing plus 7 (±2) days between screening and entry and 28 (±2) days between final trial visit and follow up visit.

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Reference therapy, dose and mode of administration:
Placebo eye drops. One drop to each eye every 12 hours.

Criteria for evaluation:

Primary Endpoint:
Incidence of ocular treatment emergent adverse events during the treatment period (adverse events which occurred during the 56 days following randomisation (Part 2 of the study only).

Secondary Endpoints included:

- Post-instillation comfort, as graded on patient diary cards at Days 1-14, 15-28, 29-42 and 43-56
- Visual acuity by Early Treatment Diabetic Retinopathy Study (ETDRS) charts comparison from Day 1 to Day 56
- Change from Day 1 in composite clinical scores at Day 14, 28, 42 and 56
- Number and percentage of patients with MMP-9 positive levels at Days 1, 28 and 56
- Change from Day 1 in Tear film break up time (TBUT) at Day 14, 28, 42 and 56

Statistical Methods:
The two parts of the study are reported separately. Data from patients included in Part 1 are listed. For patients included in Part 2, ocular adverse events which occurred during the treatment period were considered in the analysis of the primary safety outcome. The difference between the two treatments in the proportion of patients experiencing any ocular treatment-emergent AEs are reported with its associated 95% confidence interval.

Summary - Conclusions
Three patients were enrolled in Part 1 of this study to assess the ability of patients to use the eye dropper and vials correctly, as this was the first study using nomacopan via topical ocular administration. This part of the study was successful and a further nine patients entered Part 2 of the study, three patients treated with nomacopan, and six with placebo.

The patients in Part 2 of the study had a median age of 32.7 years (range 22 - 43), sex ratio of five males to four females, seven patients with atopic or vernal keratoconjunctivitis, and two patients with seasonal or perennial allergic conjunctivitis.

Safety Results
Overall, nomacopan was well tolerated in this study. The primary endpoint was the number of Treatment Emergent Ocular Adverse Events. All three patients in Part 1 of the study (nomacopan) experienced an ocular adverse event compared with two nomacopan patients (66.7%) in Part 2, and three placebo patients (50.0%) in Part 2. There was no difference in the number of treatment emergent ocular adverse events between placebo and nomacopan either in Part 2 of the study, or overall (both Parts 1 and 2).

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As expected in this patient population, the most frequently reported TEAEs were eye disorders. A total of 14 eye disorder events were reported in eight patients overall, with no obvious difference between the treatment groups. Atopic keratoconjunctivitis occurred in two patients (one event in nomacopan Part 1 and two events in one patient in nomacopan Part 2), keratitis occurred in two patients (one in each of nomacopan Part 1 and placebo Part 2), and ocular hyperaemia occurred in two patients (both in nomacopan Part 1). The remaining eye disorders (conjunctival hyperaemia, dry eye, eyelid eczema, eye discharge, eye pruritus, eye swelling and blurred version) all occurred in no more than one patient.

There were no severe TEAEs and no Serious Adverse Events (SAEs) reported.

Efficacy Results

This was a small study with the primary endpoint being safety, and limited efficacy conclusions can be drawn due to the low patient numbers.

The average comfort score classification over time remained consistent throughout the study period with patients registering scores in the comfortable/acceptable or moderately uncomfortable categories in each treatment group. There were no average classification scores in either of the very uncomfortable or severely/unacceptably uncomfortable categories. However, only two patients in the nomacopan group had data to assess comfort score, so meaningful interpretation is difficult.

Similarly, due to the low patient numbers on nomacopan with efficacy data in Part 2, meaningful interpretation of the parameters assessed (ETDRS Visual Acuity, clinical (derived total) score, MMP-9, TBUT, use of rescue medication, and CH50) is difficult.

All of the PK samples analysed were below the assay lower limit of quantification (<1.00 ng/mL), indicating a very low systemic absorption of nomacopan using this route of administration.

Conclusion

Overall, nomacopan was well tolerated in this study, there was no difference between nomacopan and placebo in the number of treatment emergent ocular adverse events, and further studies using nomacopan given by topical ocular administration to similar patient groups are warranted.

The study was terminated early because the onset of the COVID-19 pandemic in 2020 caused all of the participating hospitals to close their ophthalmic outpatients departments for this type of non-urgent investigational study. This meant that the total numbers of participating patients was too low for many meaningful conclusions to be drawn. However, the overall favourability of the safety and comfort results and the lack of measurable systemic absorption means that, when conditions allow, this study or another of similar design will be resumed when, it is hoped, larger numbers will enable more meaningful results to be obtained given that there is still a substantial unmet need for therapeutic agents for this group of ocular diseases.

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Date of the report: 2nd December 2021		