A Trial-based Health Utility Analysis in Patients with Acanthamoeba Keratitis

CO144

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Key messages

- Acanthamoeba keratitis (AK) is one of the most severe causes of microbial keratitis.
- Treatment for AK is an unmet need for which there are no licensed drugs.
- The ODAK (Orphan drug for Acanthamoeba keratitis) trial is a prospective randomized, double-masked, active-controlled, multicenter, phase 3 trial. It is the first pivotal trial and the largest prospective study ever conducted in this disease.
- Secondary outcomes of the trial included best-corrected vision acuity (BCVA), and health-related quality of life (HRQoL) data were measured using EQ-5D-5L.
- In this trial-based analysis we explored the impact of Acanthamoeba infection, and visual acuity on HRQoL.
- Thanks to this analysis we observe that patients cured with good vision have a higher utility score than the poor vision one's.

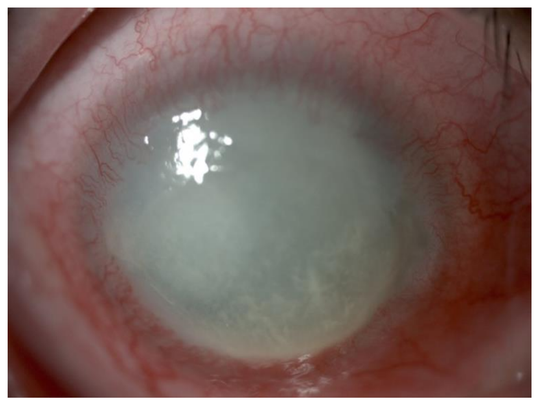

Figure 1. Corneal melting and vascularization in a patient with AK[1]

Background and objective

AK is a rare, but potentially devastating, microbial keratitis caused by *Acanthamoeba* spp, an ubiquitous free-living amoeba. Patients with AK may suffer from pain, which may be disproportionate to clinical findings, and is associated with photophobia, blurred vision, and tearing[2]. The natural history of untreated disease is characterized by poor vision, potential blindness and the need for surgical procedures, such as keratoplasty or enucleation. There are currently no approved medicinal products for treating AK in any country, nor are there any clinical guidelines for the management of the disease[3].

The objective of this analysis was to estimate the health-related quality of life (HRQoL) of patients with AK and to explore the impact of *Acanthamoeba* infection and visual acuity on HRQoL.

Methods

The ODAK (Orphan drug for Acanthamoeba keratitis) Phase 3 trial aimed to evaluate efficacy, safety, and tolerability of 0.8 mg/ml polihexanide (PHMB) plus placebo compared with 0.2 mg/ml PHMB plus 1 mg/ml propamidine for AK treatment (ClinicalTrials.gov NCT03274895)[4]. The main outcome was the cure rate, defined as clinical evidence of *Acanthamoeba* elimination 30 days after discontinuing anti-inflammatory and antiamoebic therapy. Secondary outcomes included the improvement of BCVA and EQ-5D-5L. The BCVA was assessed at baseline and end-of-study and different visual levels were defined (Table 1).

Descriptive analyses were conducted on the full analysis population (n=127). A mixed model for repeated measures (MMRM) was fitted to map the relationship between HRQoL (EQ-5D-5L), and BCVA levels, where good vision is the intercept. In this model, all observations from both arms and all visits were pooled. Utilities were calculated using the Hernandez-Alava mapping.

Table 1. Definition of the BCVA levels

BCVA levels	BCVA	Rationale
Good vision	≥20/40	Based on the required minimum best-corrected visual acuity for the driving license in England and European countries (20/40)[5]
Poor vision	≥20/200 and <20/40	-
Severe vision loss	<20/200	Based on the threshold used by Papa et al.[6] to define severe vision loss and the classification of severity of vision impairment defined by the World Health Organization[7].

Results

- Baseline HRQoL data were collected for 123/127 patients; the mean health utility score was 0.66 (SE=0.02).
- In the pooled analysis of all study visits, the mean utility score was 0.79 (SE=0.01) for all patients, 0.80 (SE=0.01) for 114 patients with unilateral disease, and 0.74 (SE=0.02) for 13 patients with bilateral disease suggesting that patients with bilateral disease have a lower HRQoL (table 2). The estimated mean EQ-5D-5L utility is 0.90 (UK general population) considering the mean baseline age and percentage of males from ODAK trial.
- By the end-of-study, where most patients had achieved a cure[4], the mean utility value has increased compared to the mean utility value at baseline and month 3 (Table 2).
- The MMRM suggests that patients with poor vision and severe vision loss have worse HRQoL than patients with good vision (Table 3).

Table 2. EQ-5D UK by visit all subjects, patients with unilateral disease and patients with bilateral disease

	Mean (SE)		
EQ-5D UK	**All patients (N=127)**	**Patients with unilateral disease (N=114)**	**Patients with bilateral disease (N=13)**
All visits	0.7929 (0.01)	0.7990 (0.01)	0.7437 (0.02)
By visit			
Baseline	0.6575 (0.02)	0.6663 (0.02)	0.5829 (0.08)
Month 3	0.8622 (0.01)	0.8638 (0.01)	0.8471 (0.07)
End-of-study visit	0.9024 (0.01)	0.9094 (0.01)	0.8508 (0.07)

the EQ-5D-5L index scale (range, 0 [death] to 1 [full health])

Table 3. Mixed model repeated measures – actual BCVA levels

Repeated MMRM model	Estimate	Standard Error	Pr > |t|
Good vision	0.9060	0.0116	<.0001
Poor vision	-0.1060	0.0292	0.0004
Severe vision loss	-0.1225	0.0831	0.1432

Conclusions

These results emphasize that Acanthamoeba keratitis, particularly in case of a bilateral disease, may affect patient's vision and their HRQoL.

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