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Real-world experience at a Scottish university teaching hospital regarding the tolerability and persistence with topical Ciclosporin 0.1% (Ikervis) treatment in patients with dry eye disease

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Introduction

The recent DEWS II report has recognised the inflammatory component of dry eye disease (DED), and highlighted the use of topical ciclosporin as a management option [1]. Ciclosporin A (1 mg/ml) in a cationic emulsion (Ikervis, Santen) was approved for once daily use by the Scottish Medical Consortium for the treatment of severe keratitis in adult patients with DED that has not improved despite treatment with tear substitutes in October 2015. The key published studies (SANSIKA [2] and SICCANOVE [3]) both reported issues with drop instillation pain (29.2–54.5%) and subsequent discontinuation of treatment (9.9–10.4%) [2, 3]. We wished to evaluate our initial real-world experiences with Ikervis in terms of patient tolerability and persistence of therapy.

Methods

All patients prescribed topical Ikervis by two consultant ophthalmologists from October 2015 to May 2018 were identified from the NHS Greater Glasgow and Clyde pharmacy database. Their electronic patient record was reviewed to identify patient demographics, indication, concurrent topical medication, adverse events and whether Ikervis was tolerated or discontinued.

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Results

A total of 52 patients were identified (13 male, 39 female). The mean age was 58 years (range 19–91). The underlying aetiology for keratitis and DED in this patient group is outlined in Table 1. Mean duration of treatment with Ikervis was 11 months (median 8.5; range 2–30). Sixty three percent of patients (33/52) were also treated with a tapering dose of topical steroids for the first month during the initiation phase of Ikervis use. All patients remained on long-term topical lubrication treatment at least 4 times per day. At last casenote review in September 2018, Ikervis was well tolerated and treatment persisted successfully in 88% (46/52) of patients. Only 6 patients discontinued Ikervis due to intolerance in the time period identified, although 2 were able to restart and persist (intolerant of treatment 4/52; 7.7%). The reason stated for lack of persistence was local irritation, burning, or stinging in all 6 cases (11.5%). These symptoms were manifested despite initial concurrent treatment with 1 month of topical steroids in 5 out of the 6 patients.

Table 1 Table detailing underlying aetiology for keratitis and dry eye disease in this patient group prior to starting Ikervis treatment

Other associated conditions contributing to dry eye symptoms	*N* (%)
Sjogrens/Rheumatoid Arthritis	21 (40.4)
Blepharitis/lid margin disease	11 (21.6)
Allergy/atopic eye disease	6 (11.5)
Exposure/neurotrophic cornea/thyroid eye disease	3 (5.8)
Salzmann nodules	2 (3.8)
Pterygium	2 (3.8)
Previous penetrating keratoplasty	1 (1.9)
Vitamin A deficiency	1 (1.9)
Chemotherapy-related dry eye	1 (1.9)
Thygeson's keratitis	1 (1.9)
Other (zoster, ectodermal dysplasia, unknown)	3 (5.8)

Conclusion

Ikervis has been marketed as a dry eye product with less tolerance issues than other forms of topical ciclosporin (predominantly due to vehicle differences) and effective as a once daily dose (reducing instillation frequency and associated discomfort) [4]. In our study, Ikervis was tolerated in the majority of these DED patients with reasonable treatment duration (mean 11 months). However, local ocular irritation led to intolerance of treatment in a small number of patients (7.7%). It has been suggested that concurrent use of topical steroids during the initiation of topical ciclosporin use can improve tolerance by reducing local ocular side effects [5]. This appeared to be the experience for most of our patients, but was not universal, reflecting the severity and complexity of DED. The SANSIKA and SICCANOVE studies suggested that initial ocular irritation decreased with longterm Ikervis use [2, 3, 6, 7]. Our small study provides real-world experience data regarding the use, persistence and tolerability of topical Ikervis outside the controlled confines of these key clinical trials.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Unique presentation of congenital cataract concurrent with microcornea, microphthalmia plus posterior capsule defect in monozygotic twins caused by a novel *GJA8* mutation

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Congenital cataracts are the most common diseases which account for 10–30% of blindness in children [1]. Multiple genetic mutations contribute to the progression of this genetically heterogeneous and complex disease. Among the reported causative congenital cataract mutations, approximately one quarter are connexin genes, including Connexin 46 which is encoded by *GJA3* and Connexin 50 which is encoded by *GJA8* [2].

In this study, we encountered four generations of a Chinese family with bilateral congenital cataracts at the Eye Hospital of Wenzhou Medical University. Among the four affected

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