Clinical Response of Dexamethasone 0.1% Formulated in DuraSite on Blepharoconjunctivitis Patients

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Background

- **Dexamethasone** is a potent synthetic member of the glucocorticoid class of steroid drugs. It acts as an anti-inflammatory and immunosuppressant. It is 20 to 30 times more potent than the naturally occurring hormone cortisol and 4 to 5 times more potent than prednisone.
- Like other corticosteroids, dexamethasone exerts its manifold effects on cells involved in immune and inflammatory responses primarily by modulating the transcription of a large number of genes. However it is also able to influence the translational and post-translational mechanisms by which proteins are synthesized, processed and exported from cells.
- Ophthalmic formulations containing 0.025% to 0.1% dexamethasone formulated in DuraSite have been developed containing BAK (benzalkonium chloride) and buffers.
- DuraSite is a polymeric drug delivery system that prolongs drug residence time on the eye.
- DuraSite formulations of dexamethasone have been used in Phase II and Phase III clinical trials with excellent safety and efficacy profiles.

Purpose

- The purpose of this study was to investigate the efficacy and safety of 0.1% Dexamethasone suspension in DuraSite at b.i.d. dosing for patients with signs & symptoms of blepharoconjunctivitis.

Methods

- As a part of a Phase III study, 136 male and female subjects with signs & symptoms of blepharoconjunctivitis were treated with dexamethasone 0.1% in DuraSite at b.i.d. dosing for 14 days. The average age was 60.63, for 58 males (42.6%) and 78 females (57.4%). In total, 126 patients completed the study.
- Other therapeutic formulations were also included in this Phase III study such as a fixed combination of azithromycin 1% and dexamethasone 0.1% in DuraSite formulation, and a third study arm where patients received a 1% azithromycin in DuraSite formulation only. Comparable groups of patients received these other study formulations according to the same regimen.
- The primary endpoint of the study was clinical resolution, defined as the absence of all study clinical signs and symptoms.
- The secondary efficacy endpoint was bacterial eradication of baseline bacterial species at day 15. Eradication was assessed for the conjunctiva and lid separately as well as combined.

Results

- Clinical resolution was defined as the absence of all clinical signs and symptoms at day 15. The "intent-to-treat" (ITT) population with "last observation carried forward" (LOCF) data was used in the analyses for the last visit clinical resolution. 23.5% of the patients showed complete clinical resolution from all signs and symptoms of blepharoconjunctivitis. Another efficacy endpoint was bacterial eradication of baseline bacterial species at the last clinical visit (day 15). Eradication was assessed for the conjunctiva and lid separately as well as combined. The "modified intent-to-treat" (mITT) population with LOCF data was used in these analyses for the last visit clinical resolution. 40.2% of the patients showed bacterial eradication for the conjunctiva and eyelids combined. 40.9% showed bacterial eradications for eyelids only, and 64.3% showed bacterial eradication for conjunctiva only. 4 patients showed elevated intraocular pressure (IOP) of which only 1 had to discontinue the study. There was no serious adverse event recorded for this arm of the study.

Conclusion

- Ocular instillation of the DuraSite eye drop formulation with dexamethasone 0.1% in patients with clinical signs and symptoms of blepharoconjunctivitis seem to be a safe and efficacious therapy at b.i.d. regimen.
- An appreciable level of bacterial eradication was achieved with this formulation on both eyelids and the conjunctiva.
- Bacterial eradication is most likely the result of BAK (0.003%) effect.
- The level of intraocular pressure rise (IOP) is in line (or better than) other commercial ophthalmic corticosteroid formulations.

Author Disclosure Information

- All authors are employees of InSite Vision Incorporated.