

Innovative cyclosporine solution shows excellent safety, tolerability in study

Novel carrier platform delivers immunomodulatory agent without blurring, stinging, or preservatives

By Cheryl Guttman Krader; Reviewed by Philipp Steven, MD, PhD

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A NOVEL, PATENTED, non-aqueous and preservative-free formulation containing cyclosporine A 0.05% (CyclASol, Novaliq) demonstrated positive results in a phase I clinical trial.

The product formulates cyclosporine in perfluorobutylpentane (F4H5), a member of Novaliq's proprietary semi-fluorinated alkanes (SFA) technology (EyeSol), and it is the first clear cyclosporine A solution. Now, additional studies are being planned to further investigate its use in the treatment of dry eye syndrome (DES).



Dr. Steven

Philipp Steven, MD, PhD, Department of Ophthalmology, Director Ocular Surface Group and Ocular GvHD Competence Center, University of Cologne, Germany, has been involved in the development

of the cyclosporine product. He said that the SFA technology has a unique combination of physico-chemical properties that make it an exciting vehicle for formulating ophthalmic products that may overcome most of the challenges facing the ocular drug delivery industry today.

ABOUT THE SFA

The SFAs have excellent spreading behavior, are physically and chemically inert, enable solubility of poorly water-soluble medications, and do not support microbial growth, thus allowing for preservative-free multi-dose units for increased patient convenience. In addition, SFA-based products have a reduced drop volume, which minimizes blinking, contain no surfactants, and unlike emulsions, do not cause blurry vision.

These features would be expected to improve tolerability, and in fact, results of the phase I clinical trial, along with findings from an observational study with the company's SFA-based ocular lubricant (NovaTears) [See online exclusive], showed the SFAs are ex-

remely well tolerated when applied topically to the eye. In addition, there is also evidence (data on file) indicating that the SFA vehicle enhances cyclosporine bioavailability.

"There is strong rationale for using cyclosporine in the treatment of dry eye disease, and ophthalmologists using the commercially available product (Restasis, Allergan), which is a single unit dose emulsion, or compounded preparations of cyclosporine are familiar with its efficacy," Dr. Steven said. "However, many patients discontinue treatment with those agents, which are formulated with peanut or mineral oil, for reasons of intolerable stinging, hypersensitivity, or inadequate response."

Research so far using this cyclosporine preparation with F4H5 as a vehicle suggests that it has potential to overcome the limitations of existing formulations and supports additional studies, he noted.

STUDY RESULTS

Dr. Steven and colleagues have been involved in the development of the SFA-based formulation of cyclosporine, demonstrating initially that it was an excellent vehicle for dissolving cyclosporine, allowing for the formulation of stable preparations containing higher concentrations of the active ingredient.

After initial successful testing in an animal model, a phase I clinical study was initiated to demonstrate safety, local tolerability, and systemic exposure. The study was conducted using a double-blind, randomized, crossover design. In it, 18 subjects without dry eye were assigned to treatment with the cyclosporine 0.05% solution or placebo and then crossed over to the alternate agent.

The phase I results clearly demonstrated that use of the cyclosporine solution caused no signs or symptoms of ocular discomfort or irritation. Nor were there any changes in visual acuity, IOP, or adverse findings on slit-lamp examination. In addition, using

take-home

► **The first clear formulation of cyclosporine A 0.05% (CyclASol, Novaliq) demonstrated excellent safety and tolerability in a phase I study.**

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AGENT PROMISING FOR PATIENTS USING ARTIFICIAL TEARS

RESULTS OF AN OBSERVATIONAL study support the efficacy and safety of a novel ocular lubricant (NovaTears, Novaliq) for providing objective and subjective improvement in patients with mild-to-moderate evaporative dry eye disease (DES).

The F6H8 based product is commercially available in Europe. It is a preservative-free solution provided in a multidose container and is non-blurring.

Go to <http://bit.ly/116SZ50>.

a highly sensitive assay to detect cyclosporine in the blood, there was no evidence of systemic absorption.

Dr. Steven noted that results from bioavailability studies in animal eyes demonstrated that cyclosporine concentrations achieved in ocular tissues of interest for dry eye treatment are 5- to 10-fold higher using cyclosporine 0.05% in F4H5 compared with the commercially available cyclosporine 0.05% emulsion.

"Even if it is possible to create a stable topical formulation containing a higher concentration of cyclosporine, efficacy depends on the concentrations achieved in the target tissues," Dr. Steven said. "The data from bioavailability studies suggest a potential advantage of the SFA-based product, but it remains to be seen if that translates into improved clinical outcomes in terms of faster onset and/or better results." ■

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