NovaTears® as new Therapy in Dry Eye

Results from three prospective, multicenter, non-interventional studies in different patient populations

Poster Session II
Poster # 60

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Introduction:

Dry eye disease (DED) is one of the most common pathological conditions of the eye, affecting millions of patients. DED is categorized as either aqueous-deficient or evaporative.

Evaporative DED is mainly a result from increased evaporation of the tears, which can occur if the lipid layer of the tear film is affected. Meibomian Gland Dysfunction (MGD) is one of the main causes / accompanying syndromes of evaporative DED.

Graft-versus-Host Disease (GvHD) is a disease related to allogeneic hematopoetic stem cell transplantation (allo-SCT). Ocular GvHD develops in 40% - 60% of patients with allo-SCT. DED is reported to be the most frequent complication and documented to be found in 40% to 76% of GvHD patients [1].

The eye lubricant NovaTears® containing 100% perfluorohexyloctane has been certified as a medical device (marketed as EvoTears®). These preservative-free lipophilic eye drops support the lipid layer of the tear film, thereby stabilizing it, and prevent evaporation.

Three post-market clinical follow-up (PMCF) studies in different patient populations with different forms of DED (evaporative DED, MGD, GvHD) were conducted to evaluate the efficacy and safety of NovaTears® in these populations.

Methods:

Three different patient populations participated in three observational PMCF studies:

- **NT-001:** 30 patients (25 female, 5 male) with mild to moderate evaporative DED; Mean age: 63.8 years (± 16.4 SD); Treatment duration: 5-7 weeks
- **NT-002:** 72 patients (53 female, 19 male) with DED due to mild to moderate Meibomian Gland Dysfunction (MGD); Mean age: 59.7 years (± 16.6 SD); Treatment duration: 6-8 weeks
- **NT-003:** 25 patients (11 female, 14 male) with DED due to chronic ocular Graft-versus-Host Disease (ocular cGvHD); Mean age: 49.7 years (± 10.7 SD); Treatment duration: 11-13 weeks

Main Inclusion Criteria	NT-001	NT-002	NT-003
TFBUT	< 10 s	≤ 10 s	≤ 10 s
OSDI©-like questionnaire	> 20	≥ 16 and ≤ 55	> 20
CFS/CCFS (Oxford)	≤ 2 (CFS)	≤ 10 (CCFS)	≥ 1 and ≤ 3 (CFS)
Schirmer I test	< 15 mm/5min	≥ 2 mm/5min	≥ 1 and ≤ 15 mm/5min

Male and female patients >18 years old were included. After providing informed consent, patients were advised to apply NovaTears® 4 times daily in both eyes.

The following parameters were evaluated before (baseline) and after the treatment period (follow-up):

Best-corrected visual acuity (BCVA), intraocular pressure (IOP), Schirmer I test without anesthesia, tear film break-up time (TFBUT) and corneal fluorescein staining (CFS) according to the Oxford grading scale (in NT-002, corneal and conjunctival fluorescein staining (CCFS) was assessed). Additionally, patients were asked to fill out a symptom questionnaire similar to the Ocular Surface Disease Index© (OSDI©) and were questioned by the physician whether DED-related symptoms are present (e.g. itching, burning, etc.).

Statistics:

For all parameters except corneal staining, a two-sided paired t-test was performed. For corneal staining, a Wilcoxon rank sum test was performed. Two populations were defined for the analysis:

- Safety Analysis Population (SAP): All patients participating in the study(ies)
- Per-Protocol Population (PPP): All patients who used NovaTears® throughout the study period

Results:

BCVA and IOP

No changes were seen in either BCVA or IOP in all three studies in the safety analysis population.

Schirmer I Test

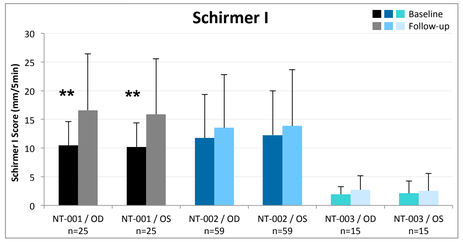

Figure 1: Schirmer I test, PPP
OD= Right Eye; OS= Left Eye;
(**)= p< 0.05

Tear volume measured via the Schirmer I test was significantly increased in patients participating in NT-001 (OD p= 0.004; OS p= 0.0013) but did not change in patients participating in NT-002 and NT-003.

TFBUT

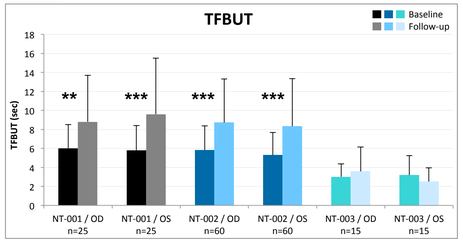

Figure 2: TFBUT, PPP
OD= Right Eye; OS= Left Eye;
(**)= p< 0.05; (***)= p< 0.001

Tear film stability measured via tear film break-up time was significantly increased in patients participating in NT-001 (OD p= 0.0026 OS p= 0.0006) and NT-002 (OD& OS p< 0.0001) but did not change in patients participating in NT-003.

Corneal (+Conjunctival) Staining

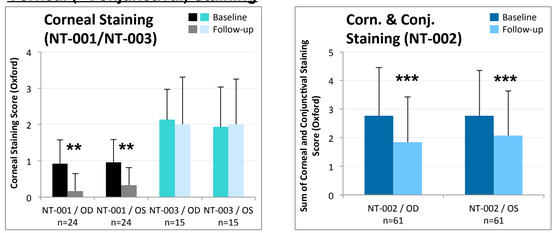

Figure 3: Corneal Staining (NT-001/ NT-003) and Sum of Corneal and Conjunctival Staining (NT-002), PPP
OD= Right Eye; OS= Left Eye;
(**)= p< 0.05; (***)= p< 0.001

Ocular surface damage as measured via corneal fluorescein staining (NT-001/ NT-003) or sum of corneal (central) and conjunctival (nasal and temporal) fluorescein staining (NT-002) showed significantly decreased scores in patients participating in NT-001 (OD p= 0.0013, OS p= 0.0041) and NT-002 (OD& OS p< 0.0001) but did not change in patients participating in NT-003. The theoretical possible range for these scales is 0-5 for corneal staining (NT-001/ NT-003) and 0-15 for the sum of corneal and conjunctival staining (NT-002).

OSDI©-like Questionnaire

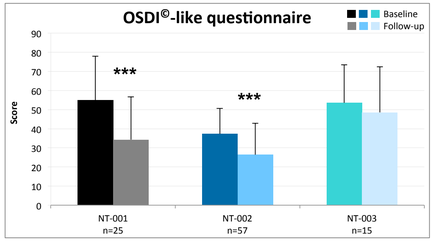

Figure 4: OSDI©-like questionnaire, PPP
(***)= p< 0.001

The severity of objective DED-related symptoms as assessed via a question-naire similar to the OSDI© decreased in patients participating in NT-001 and NT-002 but did not improve in patients participating in NT-003.

Symptom Assessment

Patients participating in NT-001 and NT-002 reported less DED-related symptoms at the follow-up visit (results are shown for the PPP).

Symptom	NT-001 (BL/FU)	NT-002 (BL/FU)	NT-003 (BL/FU)
Red eyes	22 / 9	31 / 17	14 / 11
Itching	18 / 7	25 / 12	9 / 7
Clotted eyes	9 / 1	18 / 13	8 / 5
Headache	2 / 1	10 / 5	5 / 3
Stringy mucous	2 / 0	8 / 7	6 / 7

Symptom	NT-001 (BL/FU)	NT-002 (BL/FU)	NT-003 (BL/FU)
Burning	N/A	41 / 19	13 / 11
Foreign body sensation	N/A	31 / 22	15 / 13
Tired eyes	N/A	29 / 10	11 / 10
Blurred vision	N/A	22 / 12	14 / 11
Other	N/A	9 / 6	0 / 1

Safety

In all three studies, 14 adverse events were reported (NT-001 35.7%/ NT-002 42.9%/ NT-003 21.4%). Eight of these events were definitely, probably or possibly related to NovaTears® and were mainly symptoms of mild to moderate ocular irritation, which disappeared quickly after treatment stop.

Conclusion:

The parameters measured in the three observational PMCF studies with NovaTears® show a coherent picture of the efficacy of the treatment. Patients with mild to moderate evaporative DED and MGD benefited from NovaTears®, whereas patients with severe DED due to ocular cGvHD did not receive additional benefit from treatment with NovaTears® to their existing therapy. Safety and tolerability was excellent in all three studies.

References / Financial Disclosure / Ethics / Acknowledgements:

- [1] Nair et al. (2016) Ocular GvHD: A Review of Clinical Manifestations, Diagnostic Approaches and Treatment. OJOph, 6, 20-33.
- The studies were supported by Novaliq GmbH, Heidelberg, Germany.
- The positive opinion of the ethics committees of all participating sites was present prior to study start at each site.
- The studies were registered at www.clinicaltrials.gov: NCT02111928 (NT-001), NCT02356341 (NT-002), NCT02356328 (NT-003).
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