

**Effectiveness of a new active tear substitute containing 0.2% hyaluronic acid and 0.001% hydrocortisone on signs and symptoms of Dry Eye Disease by means of low- and high-tech assessments**

Paolo Fogagnolo\*<sup>1</sup>, Giuseppe Giannaccare<sup>2</sup>, Rita Mencucci<sup>3</sup>, Edoardo Villani<sup>4</sup>, Vincenzo Orfeo<sup>5</sup>, Pasquale Aragona<sup>6</sup> and the Italian Dry Eye Study Group (listed below)

*Italian Dry Eye Study Group*: Valentino De Ruvo, Alfonso Strianese, Chiara Quisisana – Università degli Studi di Milano; Massimiliano Borselli, Costanza Rossi, Giovanna Carnovale Scalzo – University Magna Graecia of Catanzaro; Elisa Imelde Postorino, Claudia Azzaro - Dept of Biomedical Sciences, Eye Clinic, University of Messina, Messina, Italy; Stefano Mercuri, Flavia Lucarelli, Chiara De Vitto – Department of Neurosciences, Psychology, Drug Research, and Child Health, Eye Clinic, University of Florence, AOU Careggi, Florence; Eleonora Ferioli, Luca Marelli – University of Milan and Eye Clinic San Giuseppe Hospital, IRCCS Multimedica, Milan; Pasquale Napolitano, Mario Cristian Gianni – Clinica Mediterranea, Naples; Simona Parise – Ophthalmology Unit, Sant’Eugenio Hospital, Rome.

**Affiliations**

<sup>1</sup>Health Sciences Department, Università degli Studi di Milano, Milan, Italy

<sup>2</sup>Department of Ophthalmology, University Magna Graecia of Catanzaro, Catanzaro, Italy

<sup>3</sup>Department of Neurosciences, Psychology, Drug Research, and Child Health, Eye Clinic, University of Florence, AOU Careggi, 50139 Florence, Italy

<sup>4</sup>Department of Clinical Science and Community Health, University of Milan. Eye Clinic San Giuseppe Hospital, IRCCS Multimedica, Milan, Italy

<sup>5</sup>Unità Operativa di Oculistica Clinica Mediterranea, Naples, Italy

<sup>6</sup>Department of Biomedical Sciences, Eye Clinic, University of Messina, Messina, Italy

**\*Corresponding Author details:**

Paolo Fogagnolo, MD, fogagnolopaolo@gmail.com

**Supplementary Table 1.** TMH assessment with Keratograph® and Schirmer test in patients with lacrimal dysfunction after cataract surgery by follow-up visits

|   | HALH group, median (IQR) | STS group, median (IQR) | p-value**    |
|---|--------------------------|-------------------------|--------------|
| <b>TMH assessment with Keratograph®</b> |                          |                         |              |
| Baseline                                | 0.3 (0.2–0.3)            | 0.3 (0.2–0.3)           | 0.311        |
| 15 days                                 | 0.3 (0.2–0.3)            | 0.3 (0.2–0.3)           | 0.581        |
| <b>p-value*</b>                         | 0.872                    | 0.213                   | –            |
| 45 days                                 | 0.3 (0.3–0.4)            | 0.2 (0.2–0.3)           | <b>0.002</b> |
| <b>p-value*</b>                         | <b>0.002</b>             | 0.371                   | –            |
| <b>Schirmer test</b>                    |                          |                         |              |
| Baseline                                | 8.0 (6.0–10.0)           | 9.0 (6.0–12.0)          | 0.187        |
| 15 days                                 | 9.0 (8.0–12.5)           | 9.0 (7.0–10.0)          | 0.600        |
| <b>p-value*</b>                         | <b>0.023</b>             | 0.384                   |              |
| 45 days                                 | 11.0 (9.0–12.5)          | 10.0 (7.0–13.0)         | 0.187        |
| <b>p-value*</b>                         | <b>&lt;0.001</b>         | 0.253                   |              |

\*Wilcoxon signed-rank test; \*\*Mann-Whitney test. Statistically significant differences were reported in bold. TMH: tear meniscus height; HALH: hyaluronic acid and low-hydrocortisone eye drops; STS: standard tear substitute; IQR: interquartile range.

**Supplementary Table 2.** Automated assessment of conjunctival hyperemia in patients with post-cataract lacrimal dysfunction by follow-up visits

|  | HALH group, median (IQR) | STS group, median (IQR) |
|--|--------------------------|-------------------------|
| Baseline   | 1.5 (1.4–1.9)            | 1.6 (1.2–2.2)           |
| 15 days  | 1.3 (1.2–1.5)            | 1.5 (1.2–1.8)           |
| p-value*   | <b>0.008</b>             | 0.310                   |
| 45 days  | 1.3 (1.2–1.5)            | 1.4 (1.1–2.0)           |
| p-value*   | <b>&lt;0.001</b>         | 0.067                   |
| HALH: hyaluronic acid and low-hydrocortisone eye drops; STS: standard tear substitute; IQR: interquartile range. |                          |                         |

| <b>Supplementary Table 3.</b> Automated assessment of conjunctival hyperemia in patients according to treatments by follow-up visits  |  |                                    |                                    |                                    |
|---|--|------------------------------------|------------------------------------|------------------------------------|
|   | <b>HALH group<br/>(n=68), median<br/>(IQR)</b> | <b>OF (n=22),<br/>median (IQR)</b> | <b>Su (n=21),<br/>median (IQR)</b> | <b>TD (n=30),<br/>median (IQR)</b> |
| Baseline  | 1.5 (1.1–1.9)                                  | 1.8 (1.0–2.0)                      | 1.6 (1.0–1.9)                      | 1.5 (1.1–2.0)                      |
| 15 days   | 1.3 (1.1–1.5)                                  | 1.3 (0.8–1.8)                      | 1.4 (1.0–1.7)                      | 1.4 (1.2–1.7)                      |
| p-value*  | <b>&lt;0.001</b>                               | 0.107                              | 0.822                              | 0.078                              |
| 45 days   | 1.3 (1.1–1.5)                                  | 1.3 (1.0–1.8)                      | 1.3 (0.8–2.2)                      | 1.4 (1.1–1.6)                      |
| p-value*  | <b>&lt;0.001</b>                               | <b>0.023</b>                       | 0.465                              | 0.070                              |
| *Statistically significant p-values are reported in bold. HALH: hyaluronic acid and low-hydrocortisone eye drops; OF: Optive Fusion®; Su: Systane® ultra; TD: Thealoz® Duo; IQR: interquartile range. |  |                                    |                                    |                                    |

**Supplementary Table 4.** OSDI score in patients with post-cataract lacrimal dysfunction; comparison between groups

|                | HALH group (n=37), mean±SD | STS group (n=37), mean±SD | p-value      |
|----------------|----------------------------|---------------------------|--------------|
| Baseline       | 19.7±7.5                   | 21.4±8.2                  | 0.509        |
| 15 days        | 17.6±6.4                   | 20.2±6.0                  | 0.071        |
| <b>45 days</b> | <b>15.7±6.6</b>            | <b>18.1±6.4</b>           | <b>0.048</b> |

OSDI: Ocular Surface Disease Index; HALH: hyaluronic acid and low-hydrocortisone eye drops; STS: standard tear substitute; SD: standard deviation. Statistically significant differences were reported in bold.