Creating vision beyond what we see

Lissamine Green Staining

At Ora, the use of Lissamine Green (LG) helps illuminate the entire story of the anterior segment, providing crucial insight into the health and integrity of the conjunctiva.

- LG staining exhibits greater consistency than the Sodium Fluorescein across multiple visits, suggesting it can serve as a reliable primary indicator for assessing Dry Eye Disease.
- LG diagnostic staining has been validated by Ora as a primary/secondary endpoint in the US and as a secondary endpoint in Europe and Latin America.
- Ora R&D is creating a new and more insightful grading scale for LG in the conjunctiva.

Dry Eye Disease (DED) is a chronic and debilitating condition of the ocular surface that affects millions worldwide. Clinical trials involving therapeutics for Dry Eye Disease (DED) often use endpoints utilizing vital dyes, like Sodium Fluorescein (SF), to assess ocular surface damage. Currently, Lissamine Green (LG) is a vital dye that is underutilized in clinical trials.

LG is a water-soluble dye that is applied topically to the ocular surface with an application strip. After application, LG selectively illuminates damaged or compromised cells, providing crucial insights into conditions like DED. Through its precise staining properties, LG unveils subtle irregularities that might otherwise go unnoticed, guiding clinicians towards early and accurate diagnoses.

Over the last 40+ years, Ora has been at the forefront of supporting our customers in developing innovative products for the treatment of ocular surface disease, including DED. With our own in-house Research and Development (R&D) team, Ora believes in our continual evolution to match the best endpoints for each potential therapy.

Historically, used endpoints and clinical designs often lack precise control of confounders. As a result, such studies are subject to more “noise” which increases sample size requirements or have low sensitivity to changes within early stages of the disease. Ora R&D is on a quest for constant improvement of clinical endpoints and approaches to ensure we:

1. **Accurately measure product efficacy.**
2. **Fully understand the therapeutic impact.**
3. **Streamline clinical designs and sample requirements.**

Left: *Lissamine Green Stain application and a positively stained nasal conjunctival region.*

Efficacy in clinical trial design requires minimizing screen failures and utilizing endpoints with high-level consistency and repeatability. Although widely used, Schirmer's Test (ST) has been found to have high variability and limited repeatability. The Ora R&D team has recently shown that LG may present an appealing alternative to ST and serve as a complement of Sodium Fluorescein (SF) staining of the cornea[1].

In the comparative study of LG staining versus ST in a Dry Eye subject population, the Ora R&D concluded:

1. LG staining exhibits greater consistency than the ST across multiple visits, suggesting it can serve as a reliable primary indicator for assessing DED.
2. While 10 mm on ST has been historically accepted as the standard for normality of tear volume, the current data from the study suggests lowering the metric to 8 mm would be more suitable.
3. LG staining in the nasal region appears to be the appropriate clinical metric for defining dry eye related ocular surface perturbation.

Additionally, this study by Ora R&D provided insight into the need for a new LG grading scale. LG staining analysis is currently graded under the same conditions as SF. However, SF is used to assess corneal surface integrity. While LG staining provides essential insights into the health and integrity of conjunctiva.

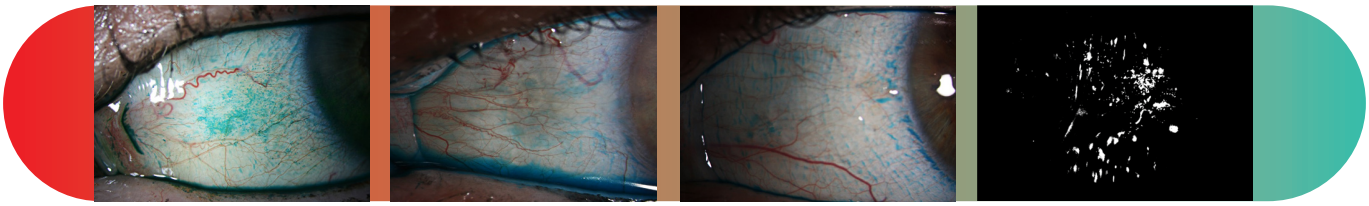
As a result, the Ora R&D team is working to develop a new LG scale based on the three staining patterns observed in hundreds of LG images. The three staining patterns include:

1. Small, dark, and distinct areas of LG staining that clump together in areas of intense staining.
2. Light and disperse cloud-like appearance of LG staining with indistinct borders.
3. Reticular structure of LG staining with long vertical strips.

Ora R&D has provided crucial insight into the benefits of utilizing LG staining in clinical studies. Unlike SF, LG illuminates ocular surface damage present in the conjunctiva and allows a more thorough assessment of the entire anterior segment. Amazingly, an R&D analysis of previous DED clinical studies showed that only 1.8% of DED test subjects screen failed due to the LG staining-based inclusion criteria (out of 1049 subjects)[1]. By using LG staining in future Ora clinical trials, we will reduce the number of subject screen failures and increase the chance of novel therapeutic approval for our sponsors.

References

O'Dell L, Kerti S, Abelson MB, Ousler G. A comparison of Lissamine Green Staining vs Shirmer Test in a Dry Eye Subject Population. The Association for Research in Vision and Ophthalmology (ARVO); 2024.



Above: *3 different Lissamine Green staining patterns: left > right=clumping, cloud, and reticular. LG image thresholding and pattern analysis allows the detailed grading of the ocular surface.*

Ora

Ora is a global full-service ophthalmic drug and device development firm with vast capabilities through all steps of clinical research, including preclinical, clinical, CMC & regulatory, and patient and site evaluations. Through Ora's 40+ years of experience, the company has assisted in bringing more than 80 products to market. Ora's team of experts utilizes global regulatory strategies, integrated research operations, and extensive site and patient engagement to accelerate product development in anterior and posterior segment, as well as ophthalmic devices.