**Purpose**

- **Dry eye disease (DED)** is a multifactorial and inflammatory tear deficient disorder affecting the cornea and conjunctiva, characterized by ocular discomfort, tear film instability, and loss of tear film stability.
- The efficacy and tolerability of PL9643 was examined in a subpopulation of patients with moderate to severe DED.

**Methods**

- This was a 12-week, phase 2, multicenter, 1:1 randomized, double-masked, placebo-controlled study of subjects with DED (NCT 04308809).
- Efficacy end points included improvement in clinical signs and symptoms of DED.
- Subjects received placebo solution during a 2-week run-in period and were randomized to either placebo or PL9643 topical ocular solution 3 times daily for 12 weeks.

**Results**

- **Overall Safety**
  - 160 subjects were randomized to the PL9643 group and 160 to the placebo group.
  - A total of 156 subjects (97.5%) completed the study: 78 (93.9%) in the PL9643 group and 78 (93.9%) in the placebo group.
  - 4 subjects (2.5%) discontinued from the study: 1 (1.3%) in the PL9643 group and 3 (3.8%) in the placebo group.

- **Subjective Symptoms**
  - The VAS assessed burning/stinging, itching, foreign body sensation, and pain.
  - Significant improvement over placebo was demonstrated for grittiness at week 12.

- **Ocular Signs**
  - PL9643 had a safety profile comparable to placebo in the moderate or severe DED population.
  - The 2 serious AEs in the placebo group were classified as a severe dry eye population.

**Conjunctival Redness and Ocular Discomfort (Symptoms)**

- PL9643 treatment showed non-significant improvement over placebo at weeks 2 and 12 for conjunctival redness (week 12 treatment difference –0.73, p=0.50; Figure 4).

**Summary and Conclusions**

- In subjects with moderate or severe DED (duration of dry eye ≥5 years), inferior corneal staining >1, and eye discomfort on a visual analog scale (VAS) ≥25 (on a scale of 0–100).
- **Significant treatment differences** were observed at week 2 and week 12 for conjunctival redness.
- PL9643 demonstrated improved ocular comfort and subjective symptoms in subjects with moderate to severe DED.
- PL9643 had a safety profile comparable to placebo.

**Safety and Tolerability (Safety Population)**

- In the overall safety population (moderate and severe dry eye) there were no AEs and one treatment-emergent AEs (TEAEs) in the placebo group (lung adenocarcinoma) vs 2 (3.8%) in the PL9643 group and 3 (4.8%) in the placebo group.
- No serious TEAEs were considered related to study drug, no effects on visual acuity, slit-lamp biomicroscopy, intraocular pressure, or stabilized funduscopy were observed.
- The Ora Calibra ocular discomfort and pain scale was comparable for the placebo and PL9643 groups, and there were no reported AEs of pain on initiation.

**References**