Post-operative ocular inflammation: A single sub-conjunctival injection of XG-102 compared to dexamethasone drops in a randomized trial

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Background:
Despite the advances in both surgical techniques and modern day technologies, inflammation following complex ocular surgery continues to be a burden for patients and physicians. XG-102 which is dextrogyre configurated protease-resistant peptide selectively **inhibits c-Jun N-terminal Kinase (JNK) activity**. Since JNK activation leads to the phosphorylation and activation of the activator protein-1 (AP-1) transcription factor family and other cellular factors implicated in autoimmune and inflammatory diseases, JNK pathway inhibitors may have an anti-inflammatory therapeutic value.

We present the results of a **Phase II randomized, double-blind, parallel group, controlled, multi-center, non-inferiority trial**. The primary objective was to evaluate the efficiency of a single sub-conjunctival injection of XG-102 900 µg, when administered after the end of the ocular surgery, compared to dexamethasone eye drops administered 4 times/ day for 21 days, on the evolution of post-operative intraocular inflammation 28 days after the ocular surgery.

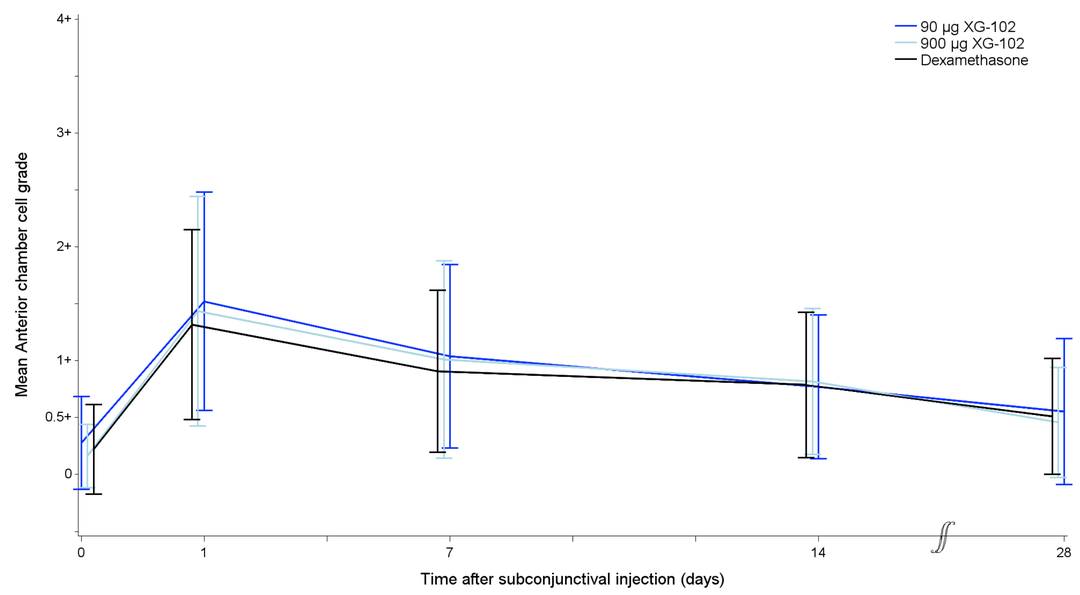
Patients & Methods: A **single sub-conjunctival injection** of 250 µl XG-102 90 µg (N=47) or 900 µg (N=48) or placebo (N=50) was administered to patients **at the end of ocular surgery** followed by eye drops instilled 4 times/day for 21 days. Patients allocated to XG-102 instilled placebo eye drops and patients who received a placebo sub-conjunctival injection instilled dexamethasone eye drops. The primary outcome measure was anterior chamber cells grade at day 28 comparing XG-102 900 µg with dexamethasone. Secondary outcomes, comparing XG-102 900 µg and 90 µg with dexamethasone included anterior chamber cells grade and flare at days 7, 14 and 28, cleared ocular inflammation, introduction of open-label anti-inflammatory therapy and occurrence of adverse events. Surgery was performed for **retinal detachment, epiretinal membrane or macular hole + cataract, filtering surgery**. Follow-up was 98% complete.

Results: At day 28, the anterior cells grade for the XG-102 groups was non-inferior to dexamethasone (-0.054 anterior cell grade, 95% Confidence Interval (CI) -0.350 - 0.242, p for non-inferiority <0.001) for XG-102 900 µg and -0.086 anterior cell grade, 95% CI -0.214 - 0.385, p for non-inferiority=0.003 for XG-102 90 µg.

The proportion with cleared ocular inflammation at day 28 was 42%, 44% and 39% for XG-102 90 µg, 900 µg and dexamethasone respectively – the difference between treatment groups did not reach statistical significance.

Rescue medication was introduced for 10 (21%), 7 (15%) and 2 (4%) patients allocated to XG-102 90 µg, XG-102 900 µg and dexamethasone respectively. The difference between XG-102 90 µg and dexamethasone was statistically significant (p=0.013). There was a similarity between the number of events reported as well as the nature of events reported between the three groups.

The quantification of XG-102 was performed in a sub-set of 32 patients. For all samples obtained and irrespective for the assigned XG-102 dose group, the XG-102 concentration was below the Lower Limit of Quantification (LLOQ) of < 10 ng/ml.



The vertical line represents the standard deviation (SD).

Figure 1: Anterior chamber cell grade up to 28 days for the PP analysis set

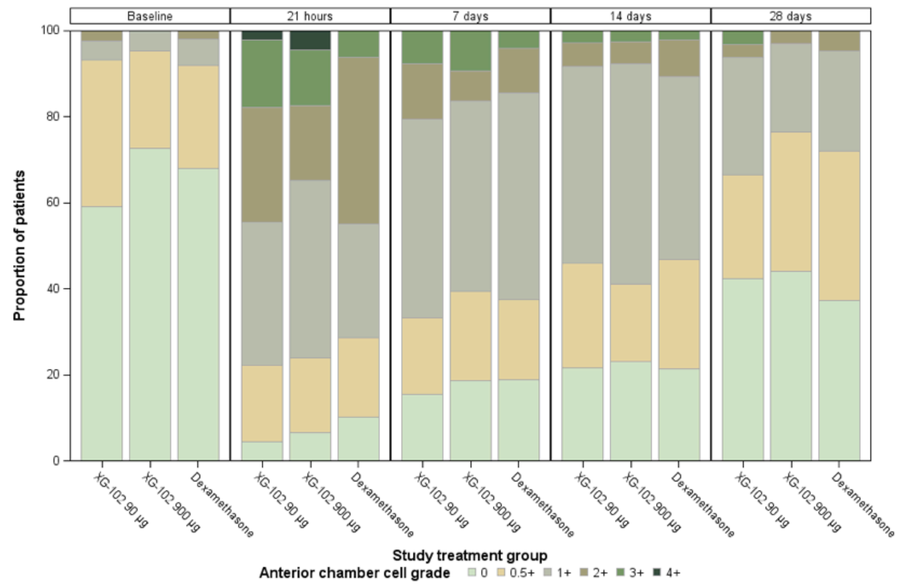


Figure 2: Anterior cell grade measured over time: proportion of patients with any grade

Conclusions: A single sub-conjunctival injection of XG-102 at the end of ocular surgery is non-inferior to dexamethasone eye drops in the treatment of post-operative ocular inflammation. XG-102 was well tolerated.