CLT-28643, an α5β1-integrin-inhibitor, in a trabeculectomy rabbit model

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Purpose: Bleb failure after glaucoma filtering surgery (GFS) is mainly caused by wound healing and scarring with myofibroblasts playing a crucial role. There is still a high medical need for a product with less toxicity compared to Mitomycin-C (MMC). α5β1-integrin plays a pivotal role in angiogenesis, inflammation and the activation of residing fibroblasts to myofibroblasts. CLT-28643, an integrin-inhibitor targeting α5β1-integrin, is expected to inhibit scarring after GFS thereby enhancing bleb survival. This is the first study investigating the effect of CLT-28643 in GFS.

Methods: We conducted a double-blinded trabeculectomy-study with 24 rabbits. The right eyes were divided in three groups: 8 eyes received intraoperative MMC (sponge application, 0.04%, for 2 minutes) and placebo eye drops postoperatively (A); 8 eye received subconjunctival CLT-28643 intraoperatively and placebo eye drops postoperatively (B); and in 8 eyes CLT-28643 was applied intraoperatively and as eye drops postoperatively 4 times a day (C). Trabeculectomy was performed on the left eyes of 12 rabbits without any adjunctive treatment (D) and 12 left eye were not operated (E). Clinical assessment included IOP-measurement by Schiötz tonometry, slit lamp examination (bleb survival and Würzburg bleb score) and photographs of the blebs. Four weeks after trabeculectomy the rabbits were sacrificed and processed for histology.

Results: CLT-28643 (groups B and C) resulted in a significantly prolonged bleb survival (p < 0.05) and a better bleb score compared to group D. IOP was significantly lowered in all trabeculectomy groups. IOP and bleb survival were comparable for CLT-28643 and MMC treated groups and superior to vehicle treated control eyes (p < 0.05) for the duration of the study. Clinically and histologically CLT-28643 was non-toxic and very well tolerated.

Conclusions: The data of this pilot study suggest that the integrin-inhibitor CLT-28643 may improve the outcome of trabeculectomy.

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