Rho kinase inhibitor AMA0526 improves surgical outcome in a rabbit model of glaucoma filtration surgery
Sarah Van de Velde1, Tine Van Bergen1, Evelien Vandewalle1, Karolien Castermans2, Nele Kindt2, Lieve Moons3, Ingeborg Stalmans1
1Lab of Ophthalmology, 2Department of Biology, KU Leuven, Leuven - Belgium
3Amakem NV, Diepenbeek - Belgium

Purpose: To elucidate the effect of a locally acting, selective ROCK inhibitor on the wound healing process and surgical outcome of glaucoma filtration surgery.

Methods: The in vitro effect of ROCK inhibitor AMA0526 (0.1-25 µM) on human brain microvascular endothelial cells (HBMEC) and human Tenon fibroblasts (HTF) was determined using a proliferation assay. Secondly the in vivo effect of topical AMA0526 0.3% TID was investigated in a rabbit model of glaucoma filtration surgery (n = 5/time point). Treatment outcome was studied by clinical investigation of the bleb area as well as immunohistological analyses for inflammation (CD45), angiogenesis (CD31) and collagen deposition (Sirius Red) at day 8, 14 and 30 after surgery. Contralateral eyes were used as control and were treated with vehicle.

Results: A dose-dependent reduction (0.1-25 µM) of HBMEC and HTF proliferation was measured after incubation with AMA0526 (p < 0.05). Incubation with the highest concentration of AMA0526 reduced proliferation of HBMEC and HTF to 22 and 35%. In the surgery model, AMA0526 significantly improved bleb area and survival compared to vehicle treated eyes (p < 0.05). Immunohistological analyses showed significant reduction of inflammation, angiogenesis and collagen deposition after treatment with the ROCK inhibitor. Compared to vehicle, inflammation was decreased by 33% at 8 days (p < 0.05), angiogenesis was reduced by 52% on day 8 and by 29% at 14 days (p < 0.01), and collagen deposition by 30% on surgical day 30 (p < 0.01).

Conclusions: This study shows that AMA0526 is able to inhibit proliferation of microvascular endothelial cells and Tenon fibroblasts in vitro, and to improve glaucoma surgery outcome in rabbits. In addition to improved bleb area, AMA0526 led to decreased inflammation, angiogenesis and fibrosis. This study can open new perspectives for a safer and more efficient glaucoma surgery.

This abstract is submitted for the 2014 ARVO meeting.