

Complementary effects of PIGF inhibition and MMC in the improvement of surgical outcome after glaucoma filtration surgery

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Abstract

PURPOSE. We previously showed that inhibition of placental growth factor (PIGF) was more effective than anti-VEGF-R2 treatment in improving surgical outcome of glaucoma filtration surgery (GFS; Figure 1). In this study, we investigated the complementary effects of mitomycin-C (MMC) and anti-PIGF therapy and compared it to the combined administration of MMC with aflibercept.

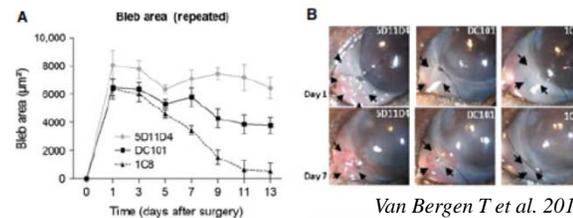
METHODS. The effect of PIGF inhibitor (5D11D4; ThromboGenics NV) and MMC on surgical outcome was investigated in a mouse model of GFS. The 1st group was treated during surgery with MMC 0.02% for 2 minutes; the 2nd group received a combination of MMC and an intracameral (IC) injection of 5D11D4 (1 µl; 5.4 µg). MMC together with IC administration of aflibercept (1µl; 3.4 µg; Eylea) was given to the 3rd group. Treatment outcome was studied by clinical investigation of the bleb every other day. Fibrosis was investigated on postoperative day 52 by performing a Sirius Red staining.

RESULTS. The combination of MMC and 5D11D4 was able to significantly improve bleb area as compared to MMC (n=15; p<0.001) by an additional reduction of fibrosis with 10 % at day 52 (n=15; p<0.001). Moreover, all blebs from the combination group survived until day 52, whereas blebs treated with MMC were failed at postoperative day 34 (n=15; p<0.001). As compared to MMC together with aflibercept, the combined administration of MMC and 5D11D4 was equally effective in improving surgical outcome (n=15; p=0.88) and reducing the postoperative fibrotic process in the bleb (n=15; p=0.49).

CONCLUSIONS. We know that inhibition of PIGF is more effective than anti-VEGF treatment. These data suggest that MMC together with PIGF inhibition may even have complementary effects in the improvement of surgical outcome and might be equally effective as the combined treatment of MMC and aflibercept.

Background

1. PIGF-inhibition is more effective in improving surgical outcome compared to anti-VEGF-R2

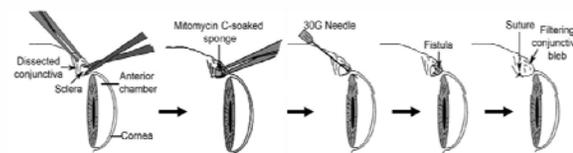


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Figure 1. Direct comparison between the two antibodies showed that administration of anti-PIGF antibody significantly improved surgical outcome, whereas anti-VEGF-R2 administration only resulted in a small effect on bleb area until post-operative day 14. Macroscopic post-operative photographs of the bleb on days 1 and 7 after surgery. Arrows: edges of the blebs.

Methods

Mouse model of glaucoma surgery



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Results

2. Combination of MMC and PIGF-inhibition is more effective in improving surgical outcome compared to monotherapy of MMC

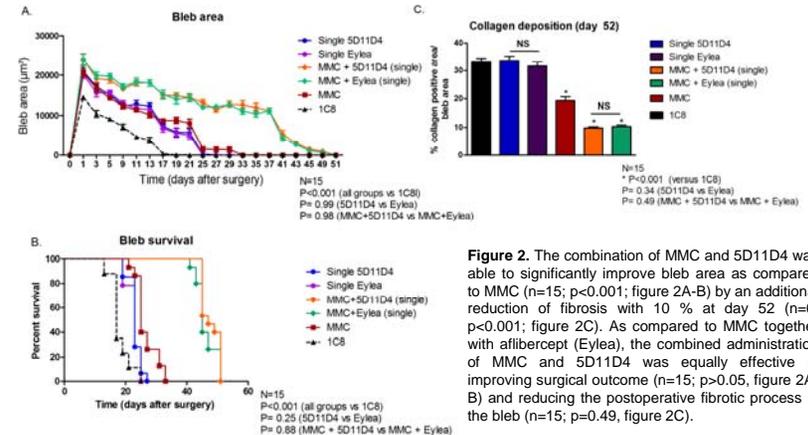


Figure 2. The combination of MMC and 5D11D4 was able to significantly improve bleb area as compared to MMC (n=15; p<0.001; figure 2A-B) by an additional reduction of fibrosis with 10 % at day 52 (n=6; p<0.001; figure 2C). As compared to MMC together with aflibercept (Eylea), the combined administration of MMC and 5D11D4 was equally effective in improving surgical outcome (n=15; p>0.05, figure 2A-B) and reducing the postoperative fibrotic process in the bleb (n=15; p=0.49, figure 2C).

Conclusion

In conclusion, this study indicates that PIGF-inhibition can enhance the beneficial effects of MMC on scarring after glaucoma surgery and that it is equally effective as the combined treatment of MMC and aflibercept. These results might open new perspectives for the future to investigate whether combination therapy can lower the dose of MMC and anti-PIGF and whether this can improve the safety profile of MMC.