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# Corneal Neovascularization: A Combined Approach of Bevacizumab and Suramin Showed Increased Antiangiogenic Effect Through Downregulation of BFGF and P<sub>2</sub>X<sub>2</sub>

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## ABSTRACT

*Purpose:* The objective is to analyze the antiangiogenic mechanism of suramab, a pharmaceutical compound of bevacizumab and suramin, in a rabbit model of corneal angiogenesis.

*Material and Methods:* Corneal neovascularization was induced in four groups of six New Zealand White rabbits by applying a filter paper disk

soaked in 1 M Na (OH) on the central cornea. Group one was treated after injury with intravenous suramab at a dose equivalent to 3 mg/kg of bevacizumab and 10 mg/kg of suramin. Group two was treated with intravenous bevacizumab (5 mg/kg). Group three was treated with 10 mg/kg of suramin while the control group received no treatment. Digital photographs were taken at days 9, 15, 21, and 35. Neovessel formation was quantified giving a 0–4 score to each quadrant according to the centripetal growth of the longest vessel (neovessel index, NVI). Animals were sacrificed at day 35. Corneas were processed for histology, immunohistochemistry, and Western-blot using primary antibodies against P<sub>2</sub>X<sub>2</sub>, basic fibroblast growth factor (bFGF), LYVE-1, PECAM-1, and vascular endothelial growth factor-A (VEGF-A).

*Results:* Suramab significantly reduced neovessel growth (mean NVI: 4.2) compared to bevacizumab (8.4), suramin (7.22), and control animals (12.2) at 35 days post-injury ( $p < 0.01$ ). A lower protein expression of P<sub>2</sub>X<sub>2</sub>, bFGF, LYVE-1, PECAM-1, and VEGF-A was found in the cornea of suramab animals than in the other groups of animals.

*Conclusions:* Joint downregulation of bFGF, P<sub>2</sub>X<sub>2</sub>, bFGF, and LYVE-1 constitutes a mechanism that induces greater and longer inhibition of corneal angiogenesis. Results might be relevant to ophthalmic care. Ocular administration of suramab is currently being investigated.

Keywords: Corneal Neovascularization, Angiogenesis, Bevacizumab, Suramin, Fibroblast Growth Factor

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## Declaration of interest

The authors alone are responsible for the content and writing of the paper. Dr Lopez, Dr Croxatto, Mr. Ortiz, and Ms. Potilinski report no conflicts of interest. Dr Gallo is the inventor of the suramab patent (EP 2186529; US 9,023,350).

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