Safety and Efficacy of Bevacizumab in High-Risk Corneal Transplant Survival

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PUBLIC ABSTRACT

Rationale and Objective: There is an increasing divide between basic and preclinical science on the one hand, and clinical care on the other. Indeed, the vast majority of important discoveries in science over the past decade that could have therapeutic benefits are not close to clinical application, or even clinical trials. Translational efforts are absolutely necessary to test "proof-of-concept" discoveries that have undergone considerable preclinical investigation and achieved toxicity/safety milestones. This study will propel the field forward considerably and at the same time provide the military and the public with better and safer treatments as a result of collaborative effort between academia and the Department of Defense.

This study proposes to evaluate whether survival in high-risk corneal transplantation can be improved with local blockade of vascular endothelial growth factor (VEGF). Recently, there has been a growing interest in using anti-VEGF agents, particularly topical bevacizumab, for the treatment of corneal neovascularization (NV). Although a few animal studies and a small number of human case studies on using topical bevacizumab for the treatment of corneal NV have demonstrated some efficacy, no systematic studies have been performed on the use of bevacizumab for promoting corneal transplant (the most common form of grafting) survival. There are good reasons to anticipate that this approach may be successful: (1) Our data in a prospective clinical study have demonstrated a significant and sustained reduction in the severity of corneal NV in response to topical bevacizumab therapy. (2) In an animal model of vascularized high-risk corneal transplantation, we have shown that local, in particular subconjunctival, bevacizumab can significantly suppress corneal NV and promote graft survival. These data suggest that treatment with topical or locally injected anti-VEGF can potentially offer an adjunctive measure to conventional therapies (e.g., corticosteroids) in the setting of vascularized high-risk corneal transplantation.

Herein we propose a randomized, multicenter study testing the efficacy and safety of subconjunctival injection followed by compounded eye drops of bevacizumab (Avastin) in patients undergoing corneal transplants that are considered at high-risk of rejection. This trial will allow us to answer the important questions that bear on this vital area of unmet medical need in ophthalmology.

Applicability: Corneal disease is the second leading cause of blindness worldwide and the most common type of ocular pathology experienced by deployed military personnel. Therefore, this trial will benefit both civilian and military populations. There are significant potential benefits to developing an effective and safe treatment for the corneal inflammatory and scarring conditions that afflict so many of the deployed military personnel (as well as cause blindness worldwide). Current treatments are largely limited to topical corticosteroids, which not only have variable efficacy, but are also fraught with many undesirable side effects such as glaucoma, cataracts, and secondary infection. A novel therapy, such as topical Avastin, will offer patients a safe and effective treatment for new blood vessel growth and prevention of graft rejection with high-risk corneal transplants, ultimately saving vision in civilian and military patients who may otherwise have no other options following trauma, infection, and scarring of the cornea.