Expert Ophthalmology Panel Releases Consensus Statement on the Management of Corneal Diseases associated with Neovascularisation

Leading Ophthalmologists Publish Statement in the British Journal of Ophthalmology

Cologne, Germany, July 7th, 2011 – Acting like a window screen, the cornea protects the eye from damage caused by trauma and is the main refractive surface of the eye. The transparency of the cornea is essential for clear vision. Therefore the normal cornea is devoid of blood vessels.

Corneal neovascularisation (CN) is abnormal new blood vessel growth into the normally avascular cornea. This causes a reduction in visual acuity and often leads to tissue scarring, oedema, loss of immune privilege, lipid deposition and persistent inflammation (keratitis) that may significantly alter vision and if left untreated, cause blindness. In addition, CN significantly impairs graft survival after corneal transplantation.

An expert panel of world renowned ophthalmologists and cornea specialists recently convened in Berlin to discuss the growing need to manage the effects of corneal neovascularisation more effectively and propose a consensual approach for the development of new drugs to treat this disorder in terms of clinical trial inclusion criteria and endpoints considered to be clinically relevant. A consensus statement resulting from the panel discussion was published online in the British Journal of Ophthalmology.

Unmet Need

"There is a significant unmet need in the treatment of corneal neovascularisation. We believe that this could be met by using novel antiangiogenic therapies, which will eventually become an integral part of our treatment strategy," explained Dr. Claus Cursiefen, Chairman and Professor Dept. of Ophthalmology, University of Cologne, Germany, a panel participant and lead author for the consensus statement while at Friedrich-Alexander University Erlangen-Nürnberg. "The panel believes that a framework for clinical evaluation and agreement on clinically relevant end points will assist future drug development and support regulatory authorities during their review of clinical trial data. This consensus statement provides an initial step in proposing this new framework."

Currently, pathological CN is treated with corticosteroids to control the inflammation associated with the disorder. However, steroids have only limited effects against new blood vessel growth and long-term steroid use has significant side-effects. It can cause increased intra-ocular pressure (with risk of damage to the optic nerves and resultant defects in visual fields) and cataract formation. Therefore, steroid-sparing treatment approaches are needed urgently.

Future drug intervention will only come from additional drug development and clinical evaluation. Several novel antiangiogenic compounds are already on the horizon such as Aganirsen, an antisense oligonucleotide directed against insulin receptor substrate 1 (IRS-1), which is currently being evaluated in Phase III clinical trials by Gene Signal. An alternative approach could emerge from anti-VEGF biologicals (Bevacizumab, Ranibizumab, Pegaptanib) but these types of compounds have so far only been licensed for use in oncology or vitreoretinal diseases. Hence, there is only limited experience in the cornea and only in an off-label setting.

Due to the significant unmet medical needs, the panel believes a consensus on clear inclusion criteria and clinically meaningful endpoints in clinical development of new therapies will help determine the safety and efficacy of novel antiangiogenic drugs specifically aimed at CN treatment and/or prevention.

Clinical Trial Endpoints

In corneal transplantation, the most common type of tissue transplantation in patients, pathological corneal neovascularisation endangers graft survival. The main goal is to maintain the viability of the graft and avoid its rejection. However, experts agree, clinical studies with anti-angiogenic compounds that set out to demonstrate increased corneal graft survival, even if theoretically desirable, are simply not practical. In the corneal transplant setting, there are too many variables that have an effect on the graft. However, clear graft survival as a secondary endpoint is highly recommended, possibly studied in an open label follow-up context.

The panel agree that inhibition of CN is the most relevant clinical primary endpoint to demonstrate the efficacy of any novel antiangiogenic treatment and can be used as a measure of corneal graft rejection (CGR), as the causal relationship of pre- and post-graft CN and CGR is well established. Other relevant endpoints to include in clinical development should also include regression of CN and improvement of visual acuity.

Similarly, these endpoints can be used to determine the effectiveness of antiangiogenic treatments on CN in keratitis from infectious origin. Evaluation of regression of CN is also a desirable clinical outcome that should be considered as a clinically useful endpoint. The effect of a novel antiangiogenic treatment on visual acuity is expected to be derived from its direct effect on CN therefore considered only as a relevant secondary endpoint in this setting.

In summary, novel specific antiangiogenic compounds will greatly enhance the therapeutic armamentarium for ophthalmologists to treat blinding diseases of the eye at the cornea.

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