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Pilot study

GS-101 aids post-graft healing

Novel topical drops target corneal neovascularization

By Cheryl Guttman Krader
Reviewed by Salvador Garcia-Delpech, MD

Valencia, Spain—Results from a prospective pilot study suggest that topical treatment with the ribonucleotide GS-101 (Gene Signal) is safe and effective for reducing corneal neovascularization in eyes that have undergone penetrating keratoplasty, said Salvador Garcia-Delpech, MD.


Dr. Garcia-Delpech

The investigation included nine eyes of nine patients seen at Hospital Universitario La Fe, Valencia, Spain, for corneal neovascularization associated with penetrating keratoplasty graft rejection. They were treated with the GS-101 drops twice daily for 3 months.

Follow-up with serial anterior segment photography during treatment showed nearly all patients had evidence of regression of the existing neovascularization beginning at 3 weeks into treatment. Over time, further improvement was noted in all eyes, and complete resolution of the corneal vessels occurred in five eyes.

There was no evidence of recurrence during ongoing monitoring of at least 2 months after the topical therapy was concluded, and no eyes developed any treatment-related adverse events.

"Corneal neovascularization is a significant problem that reduces corneal transparency and is an important risk factor for immune rejection in eyes with a corneal graft," said Dr. Garcia-Delpech, who is on the staff of the hospital. "Corneal neovascularization develops as a result of inflammation and hypoxia, and recent interest in treating ocular neovascularization has focused on the use of anti-VEGF agents. GS-101 represents a novel agent that targets expression of insulin receptor substrate-1 (IRS-1).

"Our experience with GS-101 is promising," he said. "More studies in larger patient populations and with longer follow-up are needed."

GS-101 is an antisense oligonucleotide that specifically blocks the synthesis of IRS-1 by selectively binding to IRS-1 mRNA. The IRS-1 gene is overexpressed in pathological angiogenesis, and IRS-1 acts as an upstream regulator of new vessel formation by inducing production of various proangiogenic compounds, including VEGF and interleukin-1-beta. GS-101 prevents the expression of IRS-1 to interrupt the pathologic IRS-1 mediated signaling.

Take-Home Message

Experience with the topical ribonucleotide GS-101 (Gene Signal), an antisense oligonucleotide targeting expression of insulin receptor substrate-1, indicates it is a safe and effective treatment for inducing regression of corneal neovascularization in eyes after penetrating keratoplasty.

> **'GS-101 interferes with the angiogenic pathway by modulating protein production upstream.'**
> Salvador Garcia-Delpech, MD

"In contrast to currently available antiangiogenic agents that act by binding to VEGF to prevent VEGF binding to its receptor, GS-101 interferes with the angiogenic pathway by modulating protein production upstream," Dr. Garcia-Delpech said.

"Research conducted in an animal model with experimentally induced corneal neovascularization has shown that GS-101 modulation of IRS-1 expression inhibited new vessel formation and was associated with a 42% decrease in interleukin-1 and a 50% reduction in VEGF expression," he said. **OT**

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Salvador Garcia-Delpech, MD
E-mail: Garcia@iova.es
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