Rescuing a Suspended Gene Therapy Progam

Emmes Applied Advanced Data Visualizations to Enable Robust Safety Monitoring

When the US Food and Drug Administration (FDA) put a clinical hold on further development of an intravitreal gene therapy, it was a serious setback not only for the Sponsor, but for hopeful patients as well. An independent Data Monitoring Committee for the program recommended Emmes to the biotech company as an expert resource for the biostatistical support the company needed to create a more robust monitoring system for ensuring patient safety. An Emmes team of SAS programmers and biostatisticians stepped in to quickly streamline the data transfers and create the data visualizations needed to rescue the study.

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Case Study

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The Challenge: Insufficient Patient Monitoring Program from Delayed and Incomplete Data

After a suspected, unexpected serious adverse reaction (SUSAR) was discovered in a patient being treated with an investigational, intravitreal gene therapy, the FDA placed a hold on the clinical program in which it was being tested. The Sponsor, an emerging biotech company, had been developing the treatment in two indications (neovascular age-related macular degeneration (AMD) and diabetic macular edema (DME) and was in the midst of a Phase II study.

The company aimed to investigate the root cause of the SUSAR and pursue corrective actions that would meet the FDA's requirements for reactivating the trial.

Unfortunately, the company was not able to monitor the trial data in real time, and its existing data visualizations and patient profiles were not comprehensive enough to support the type of detailed analyses that were warranted.

Acting on a recommendation from several members of an independent Data Monitoring Committee who were familiar with Emmes' specialized capabilities in ophthalmology and biostatistics, the Sponsor's Chief Medical Officer appealed to Emmes. Could Emmes revise the company's statistical analysis plan so that the company could satisfy the FDA's requirements for ongoing safety monitoring?

The Solution: Utilizing Timely and Comprehensive Patient Data Visualizations

Emmes rapidly assembled a core team of experienced programmers and biostatisticians to collaborate with the biotech's leadership in finding and implementing a solution to minimize the length of time the trial was suspended.

- We utilized our existing patient data visualization platform, Advantage eClinical, to provide patient reported outcomes to the biotech's medical monitors.
- Once the Sponsor's data was transferred over, our biostatisticians worked to clean, automate and expand the data visualizations to provide full access to the patient's data in a timely matter.
- Our biostatisticians collaborated with the Sponsor's scientific and medical experts to determine what clinical measures would serve as relevant safety signals.

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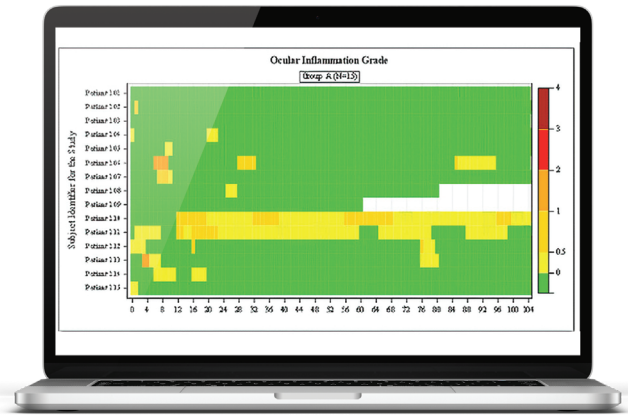
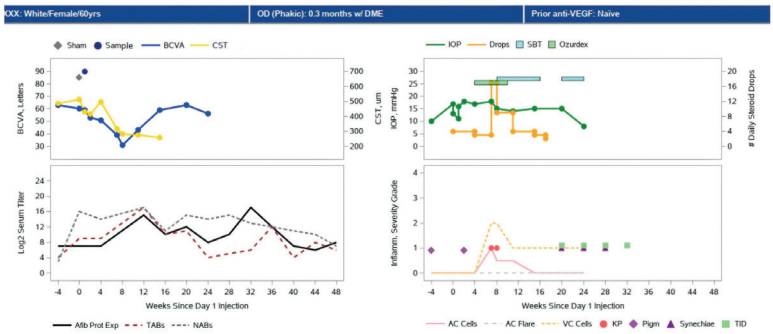
The fact that Emmes' statisticians have such a deep background in ophthalmology meant that they readily understood what data would be needed and how best to collect and display it for analysis. Consequently, the resulting list of clinical measures displayed in a variety of dashboards and patient profiles was far more comprehensive and meaningful than what the Sponsor had previously relied upon.

The data visualizations covered such critical outcomes as intraocular pressure, medication use, various types of intraocular inflammation, changes in various vision measures, and adverse events.

This allowed the Sponsor's medical monitors a more rigorous monitoring program to view patient data more effectively and resond to any safety signals that might arise.



This heat map example displays the severity and trend of intraocular inflflammation (e.g., Vitreous Cells) for individual subjects over the entire study period. The severity is on a scale of 0 to 4, where 0 = no inflflammation (green) and 4 = the most severe inflflammation (red).



The profile example indicates the pa patient's demographic and disease information to show trends over time for key safety measurements. **Graph A:** indicates the change in Best Corrected Visual Acuity (BCVA) and Central Subfifield Thickness (CST) over time after injection of loading dose and drug. **Graph B:** shows change in intraocular pressure (IOP) with the diffffferent types of prophylactic regimens received **Graph C:** change in Aflflibercept protein expression, Total Anti-body and Neutralizing Anti-body over time. **Graph D:** indicates severity (scale from 0 to 4 where Grade 4 is the most severe inflflammation) of intraocular inflflammation indicators.

The Results: Detecting the Root Cause of Patient Safety and Efficacy through Data-Driven Decisions

Once the Sponsor began receiving the right clinical measures in a meaningful format and a timely manner, they were able to detect the root cause of the safety issue and respond appropriately with protocol changes that included prophylactic regimens and treatments. Thus, within three months of enacting the hold, the FDA lifted its hold after an independent data monitoring committee voted to proceed with dose escalation per the protocol for the neovascular age-related macular degeneration study.

Emmes' data visualizations and patient profile platform was a critical factor in the biotech company's ability to confidently make a rapid no-go decision to suspend developing further trials for the treatment in DME but also to confidently continue the clinical trial in AMD.

> "We express our gratitude for Emmes' "support, experience, accountability, and dedication" to the program. In speaking of the project lead at Emmes, he said, "His work ethic and empathy has not gone unrecognized and is one of the major deciding factors in our continuing to expand services with Emmes."
>
> The Sponsor's VP of Clinical Operations

After rescuing the biotech's suspended ophthalmic gene therapy clinical trial, the project was expanded to included data management and full-service statistical support on two existing and three subsequent protocols – a true reflection of the value that Emmes has provided to the company.

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