

P076 - From Signals to Insight: Integrated Approaches for Improved IDMC Safety Evaluation

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Motivation

Patients' safety during trials is essential and is the Independent Data Monitoring Committees' (IDMCs) key responsibility.

This case study shows how close collaboration between multiple experts and integration of multiple datapoints addresses this mission.

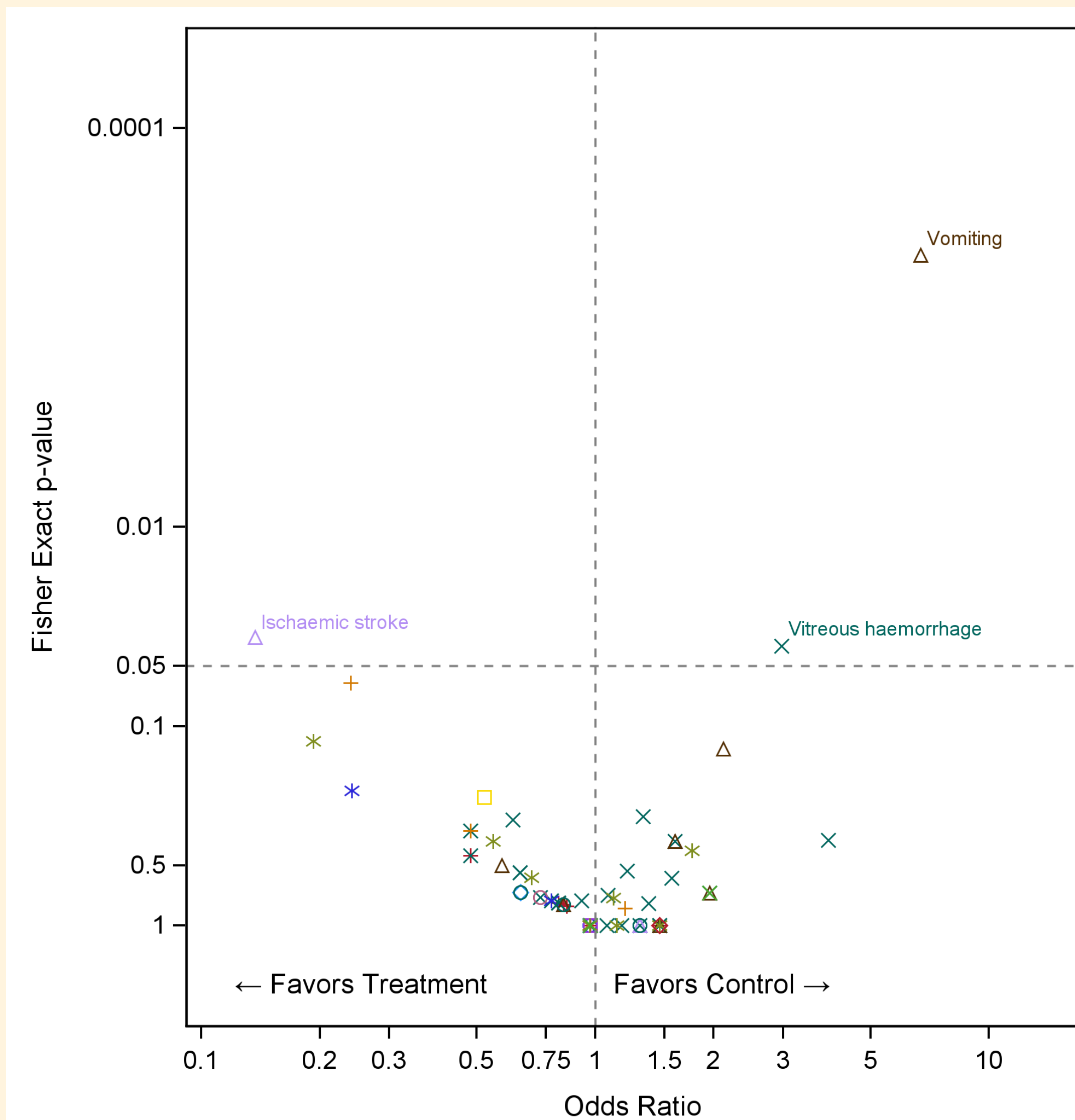
Case study

- A program composed of 4 studies investigating the same compound, in similar indications
- Two IDMCs: A in charge of 3 studies jointly, B in charge of 1 study
- Stakeholders: Statistical Data Analysis Center (SDAC), IDMC medical and biostatistical experts, Sponsor's study teams including Pharmacovigilance (PV) experts

Statistical signal detection

IDMC experts, in collaboration with the SDAC, identified safety endpoints relevant for detection of potential safety signals, such as adverse events, at individual study level.

For each study, SDAC highlighted potential meaningful imbalances by means of statistical significance testing.



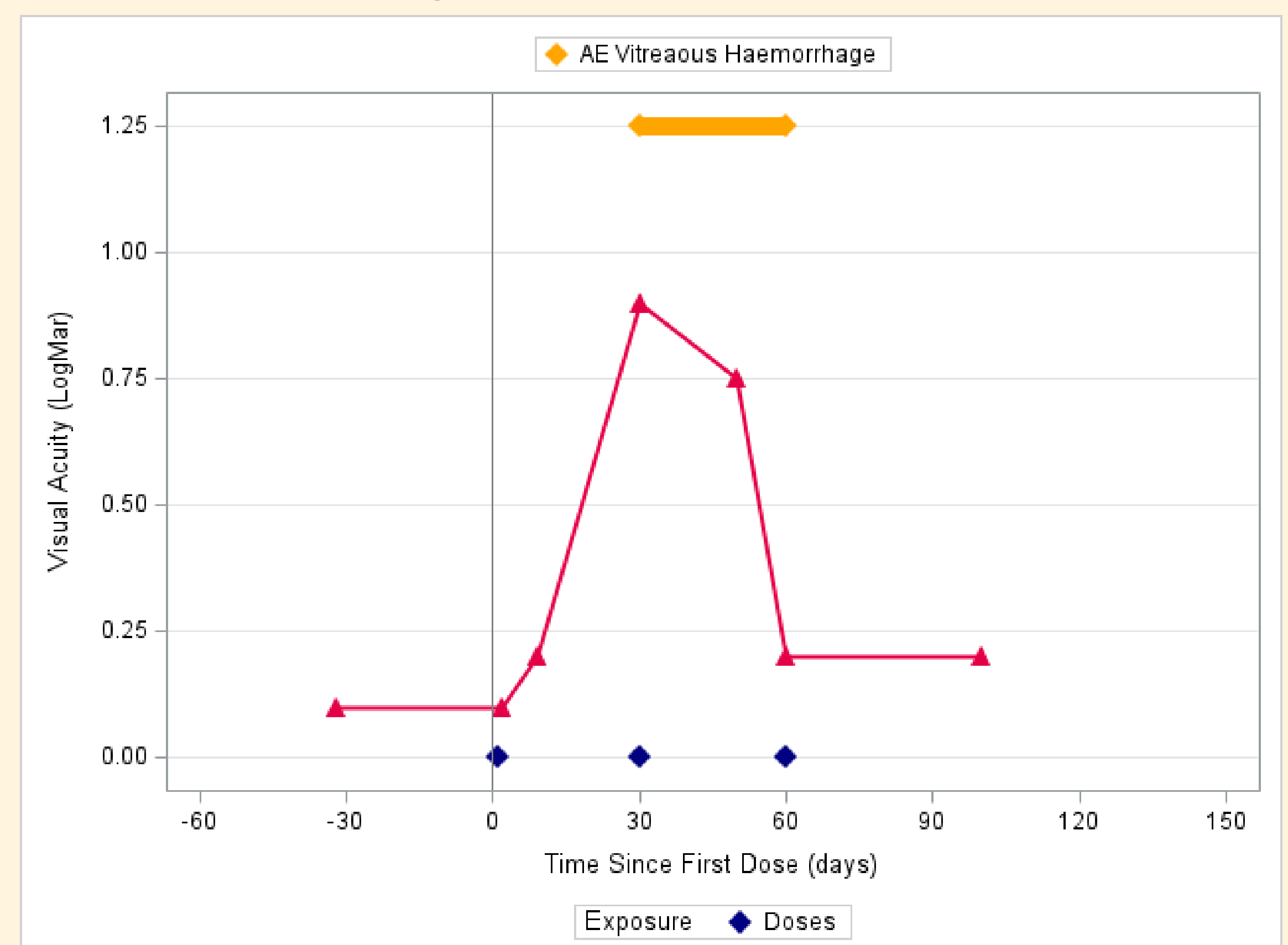
Volcano plot showing the statistical significance, p-value, against the odds ratio of the event.

- ✓ Rapid identification of potential safety signals for discussion with IDMC experts
- ⊖ Low statistical power and multiplicity issues should be considered during interpretation

In-depth clinical exploration

The IDMC, supported by the SDAC, reviewed targeted patients presenting suspicious safety patterns via:

- Case Narratives provided by PV experts
- Subgroup analyses
- Patient-level listings and visualisations



Swimlane plot combining visual acuity, exposure and AE of interest over time.

External contextual evidence

The IDMC enriched their assessment with:

- Investigator's brochure (IB)
- Historical and real-world data
- Blinded trial and safety updates provided by Sponsor's study team

Within the joint IDMC A, a combined analysis of targeted suspicious safety patterns across sister studies evaluated the signal on a broader population. In our context, it showed that 'Vitreous haemorrhage' was specific to a single study.

IDMC A recommended to communicate selected information at study and combined level with IDMC B to support their assessment of sister study. Sponsor supported this action in a blinded manner by setting the legal documents in place, and SDAC facilitated the sharing of selected information. IDMC B included additional analyses to monitor this signal in sister study.

Insight

The combination of these approaches and the collaboration between all stakeholders strengthened the IDMCs' ability to interpret and monitor the safety signals and formulate relevant recommendations.

Related work: Poster P078 – "Beyond Tables: Visualization as a Decision-Support Tool for IDMCs"

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