Podcast Summary: OCEANICSTROKE Trial – M. Sharma

Welcome to today's audio overview, where we'll be discussing the key findings from the late-breaking OCEANIC-STROKE phase 3 trial, presented by Dr. Sharma. This was a pivotal study focusing on the risks and benefits of asundexian, a factor XIa inhibitor, in acute non-cardioembolic ischemic stroke and high-risk transient ischemic attack (TIA).

That's right. The second goal was to see whether adding asundexian 50 milligrams daily to standard antiplatelet therapy could reduce recurrent ischemic strokes without increasing major bleeding events. We'll also be covering the trial's rationale, design, and clinical implications.

To begin, let's look at the scientific rationale. Genetic deficiency of factor XI is rare but has been shown to lower the risk of ischemic stroke without raising the risk of intracerebral hemorrhage. This suggests that inhibiting factor XI, it could help break the link between pathological thrombosis and normal hemostasis.

The concept here is to target the part of the clotting cascade that promotes dangerous clots inside blood vessels, without interfering significantly with essential clotting after tissue injury. That's precisely why factor XIa inhibition has attracted attention in secondary stroke prevention.

Asundexian itself is a direct, oral inhibitor of factor XIa, taken once daily. Earlier phase 2 trials showed it achieves over 90% inhibition—both at peak and trough—yet did not significantly increase major bleeding compared to placebo, even when used with antiplatelets.

Right, and those phase 2 results directly shaped the dosage and methods used in this phase 3 trial. Now, for design specifics: it was a large, double-blind, placebo-controlled study at more than 700 sites in 37 countries, enrolling adults with recent noncardioembolic stroke or high-risk transient ischemic attack, all on antiplatelet therapy.

Participants were randomized 1:1, receiving asundexian or matching placebo, with planned treatment ranging from 3-31 months. The primary efficacy endpoint was time to first ischemic stroke, while the key safety endpoint was major bleeding as defined by the International Society on Thrombosis and Haemostasis (ISTH).

Let's turn to the results. Asundexian reduced ischemic stroke events from 8.4% down to 6.2%, with a cause-specific hazard ratio of 0.74 and a one-year number needed to treat of 53. Crucially, there was no statistically significant increase in major bleeding, minor bleeding, or intracranial hemorrhage between drug and placebo groups.

The effects were consistent across demographics, vascular risk factors, stroke subtypes, and different antiplatelet strategies. So, the evidence supports asundexian as an effective and safe adjunct in secondary stroke prevention for these patients.

In summary, the OCEANICSTROKE trial demonstrates that asundexian offers significant protection against recurrent ischemic stroke without increasing major or intracranial bleeding risk, pointing toward a promising future for targeted antithrombotic therapy.