Abstract TMP15: Penumbral Rescue by Normobaric O2 in Ischemic Stroke With Target Mismatch ProFile (PROOF)

Sven Poli, Jean-Claude Baron, Robin Lemmens, Patrik Michel, Robert Mikulik, Carlos Molina, Daniel Strbian, Turgut Tatlisumak, Guillaume Turc, Jens Fiehler, Holm Graessner, Johannes Hüsing, Joan Montaner, Susanne Siemonsen, Eivind Berge, Gary Randall, Peter Rosenberger, Heinrich J Audebert, Martin Dichgans, Aneesh Singhal, Roland Veltkamp, and Florian Härtig

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Abstract

Introduction/Hypothesis: Despite effective reperfusion therapies, outcome following ischemic stroke (IS) often remains poor. Shortly after IS onset, the already necrotic area is surrounded by the severely hypoperfused but still viable penumbra. Sustaining the latter may widen treatment time windows and improve outcomes. As tissue damage in IS is primarily mediated by hypoxia, increasing penumbral oxygen (O2) supply seems a logical approach. Normobaric hyperoxygenation (NBHO) increased penumbral O2 and attenuated brain injury when initiated early in animal models of transient vessel occlusion. The few clinical trials conducted so far did not adapt these insights: NBHO initiation was late (treatment windows of more than 9 hours) and patients eligible for intravenous thrombolysis and endovascular treatment were excluded.

Methods: Multi-center, randomized phase-II proof-of-concept trial studying NBHO adjunct to standard IS treatment; adaptive patient sample size of 180 to 460 depending on interim analysis.

Eligibility: Patients with an acute large vessel occlusion in the anterior circulation (terminal ICA plus M1, proximal M1, or distal M1) and an Alberta Stroke Program Early CT Score of 7 or higher. Study treatment must be initiated prior to recanalization therapy and within 3 hours after IS onset. NBHO is achieved by administration of high-flow O2 (40 L/min) via non-rebreather face mask with reservoir or FiO2 of 1.0 during mechanical ventilation. NBHO will be stopped after endovascular treatment or applied for a maximum of four hours in case of not-attempted endovascular

treatment. Controls will receive standard O2 supplementation whenever required.

Primary Endpoint: Infarct growth from baseline to 24 hours; key secondary endpoint: Δ24h-NIHSS.

Conclusion: PROOF is the first clinical trial to incorporate two cornerstones of effective experimental NBHO: early initiation and fast reperfusion. If proven beneficial, phase-III trials may be undertaken. Considering its low cost, NBHO may impact stroke care worldwide.

Footnotes

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