Title: **A randomised, double-blind, sham-controlled study of percutaneous transluminal angioplasty for extracranial vein stenoses (CCSVI) in patients with multiple sclerosis**

Abstract

Introduction

Following controversy about CCSVI, an ethics approved randomised, double-blind, sham-controlled cross-over study with two-year follow-up to assess the safety and efficacy of venoplasty for the treatment of extracranial vein stenosis in MS-patients.

Methods

Patients were randomised 1:1 to balloon or sham venoplasty. Imaging (US,MRV,DSA) was used to assess the extracranial veins. Outcomes were measured at 1,3,6,12,18 and 24mths. Crossover occurred at 12mths. Venoplasty was repeated if restenosis was noted. The primary safety-endpoint was number of AEs and the primary efficacy-endpoint was change in the EDSS. Other measures included MS-QoL-54, CogState, PASAT, Fatigue-Score, MRI-brain.

Results

36 patients consented. 4(11%) had normal DSA, two were MRI ineligible and two withdrew. 28 patients completed the study. There was no difference between the groups for gender, age, MS-type, disease-duration or types of abnormalities. More patients were on immunomodulators in the sham-arm (12:7). 12/62 AEs were trial related (2-haematoma, 4-neck/groin/cannulation pain, 2-thrombus, 2-headache. Two patients relapsed, one at 6mths after a sham-procedure and the other 3mths after venoplasty. At 12 and 24mths, no significant difference was found for PASAT, FS, Cogstate or MRI lesion-volume. 26/28 patients had enlarged perivascular spaces (scores 1-4). At 12mths there was no significant difference in EDSS ($p=0.229$). There was a significant difference in the EDSS at 24mths ($p=0.025$).

Conclusion

This study suggests improvement in EDSS occurs only after 24mths. RCTs by other groups were for ≤1yr and did not include EDSS as a primary-endpoint. A vascular/endothelial cell component in the pathogenesis of MS warrants further investigation.