Background Experimental studies have demonstrated that granulocyte-colony stimulating factor (G-CSF) stimulates neovascularization and confers cardiomyocyte protection. Limited data exist for the safety and efficacy of G-CSF in patients with severe ischemic heart disease (IHD). We hypothesized that repeated low dose G-CSF administration in conjunction with exercise would mobilize bone marrow derived endothelial progenitor cells (EPC) and improve ischemia in patients with severe IHD.

Methods Eighteen patients (89% males, mean age 62 ± 7 years) with Canadian Cardiovascular Society Class III-IV angina were randomized into a double-blind crossover study of G-CSF (4.5 μg/kg sc) versus placebo, with exercise that was commenced 6 weeks prior. G-CSF or placebo was administered daily for 5 consecutive days at fortnightly intervals for a total of 3 cycles, before a 6-week washout period and crossover. The primary outcome was myocardial perfusion by cardiac magnetic resonance imaging (CMR). Secondary outcome measures included a Seattle Angina and Utility Based Health Questionnaire, exercise stress test (EST) and quantification of peripheral EPCs by flow cytometry, and stromal cell-derived factor-1 (SDF-1) and angiopoietin-1 (Ang-1) by enzyme linked immunosorbent assay.

Results Compared to placebo, G-CSF had no effect on myocardial ischemia by CMR, EST or angina measures despite effective EPC mobilization (up to 19 fold increase, peak levels: CD34+ = 61; CD34+CD133+ = 37; CD34+VEGFR-2+ = 4.5; CD34+CD133+VEGFR-2+ = 1.5, x 10⁶ cells/L (p < 0.05 vs. placebo for all)). Plasma SDF-1 and Ang-1 levels remained unchanged. Seven Troponin I-positive events (≥0.6 μg/L) occurred during G-CSF, compared to two events during placebo (p = 0.45). Other biomarkers that increased with G-CSF compared to placebo include: high sensitivity C-reactive protein, 5.9 ± 9.3 mg/L vs. 2.8 ± 0.4 mg/L (p = 0.01); N-terminal pro-brain natriuretic peptide (median and inter-quartile range), 343 ng/L (217 - 599 ng/L) vs.178 ng/L (110 - 348 ng/L) (p < 0.01).

Conclusion In patients with severe IHD, G-CSF therapy mobilizes EPCs but does not improve myocardial perfusion or angina, and may increase adverse prognostic cardiac biomarkers.