AUTOLOGOUS CD34 CELL THERAPY FOR TREATMENT OF CORONARY MICROVASCULAR DYSFUNCTION IN PATIENTS WITH ANGINA AND NON-OBSTRUCTIVE CORONARY ARTERIES

(ESCaPE-CMD)

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SCAI
Society for Cardiovascular
Angiography & Interventions

DISCLOSURES

ESCaPE CMD – **E**xploratory **S**tudy of **C**LBS16 in **P**ati**e**nts with **CMD**

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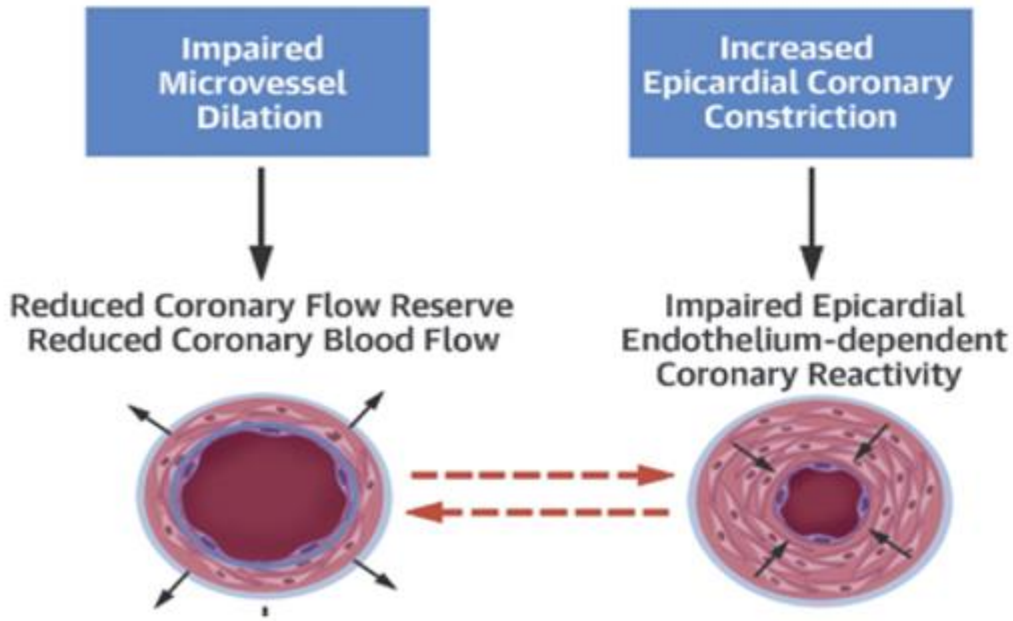
INOCA (ISCHEMIA & NON-OBSTRUCTIVE CORONARY ARTERY DISEASE) & CORONARY MICROVASCULAR DYSFUNCTION (CMD)



Impaired Microvessel Dilation

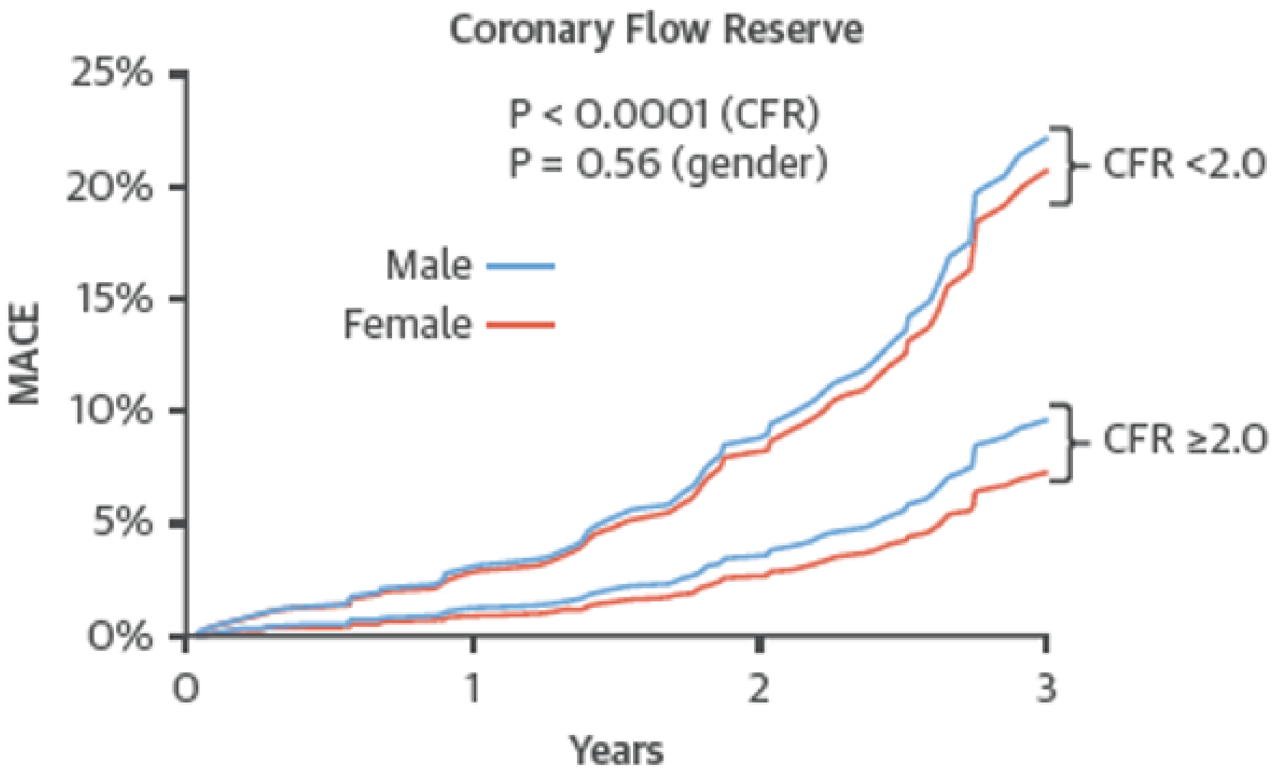
Reduced Coronary Flow Reserve
Reduced Coronary Blood Flow

Increased Epicardial Coronary Constriction

Impaired Epicardial Endothelium-dependent Coronary Reactivity

- INOCA is increasingly recognized
  - Estimated prevalence of 3 to 4 million
  - Women make up about 70% of INOCA population in the US
- CMD is present in ~50% INOCA

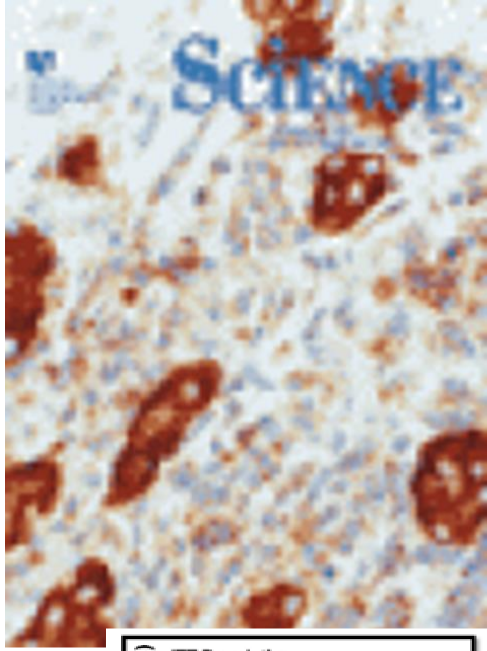
BACKGROUD: REDUCED CORONARY FLOW RESERVE IS ASSOCIATED WITH SIGNIFICANTLY INCREASE RISK OF MACE

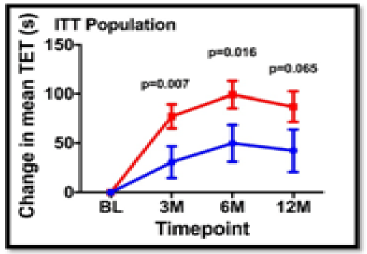


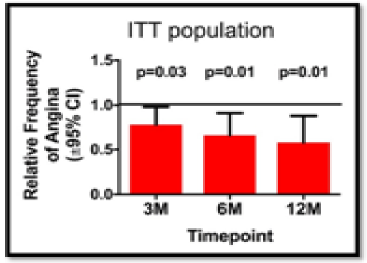
Murthy et al, Circulation, 2014

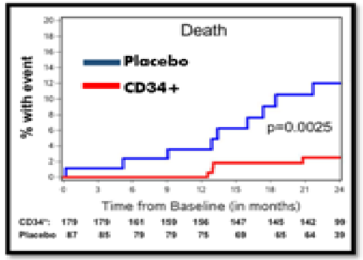
CD34+ BACKGROUND

- Therapeutic potential of CD34 cell as naturally occurring endothelial progenitor discovered in 1997
- Preclinical models document natural ability of CD34 to stimulate microvascular angiogenesis in ischemic tissue
- Clinical studies in *No Option Refractory Disabling Angina, Critical Limb Ischemia* and *Dilated Cardiomyopathy* reveal consistent therapeutic effects including improved LV function, reduced angina, reduced mortality and reduced amputation
- No prior studies in coronary microvascular dysfunction









CLBS16 PROOF OF CONCEPT STUDY (ESCAPE-CMD)

Design	▪ Interventional, open label, proof-of-concept study in patients with coronary microvascular dysfunction (CMD) defined as CFR ≤ 2.5
Endpoints	▪ Safety and the evaluation of adverse events ▪ Changes from baseline to 6 months for CFR, coronary blood flow (CBF), time to angina; other cardiovascular metrics
Study Size	▪ 20 subjects at 2 centers in the USA (Cedars-Sinai, Los Angeles & Mayo Clinic, Rochester)
Dose	▪ 300 x 10^6 CD34+ cells administered by intracoronary infusion (CLBS 16)

NCT03508609

ESCAPE-CMD INCLUSION AND EXCLUSION CRITERIA

- Angina ≥ 3 times per week
- No obstructive disease on coronary angiogram
- Invasive intracoronary adenosine CFR ≤ 2.5
- Exclusions:
    - ACS/Myocardial infarction < 90 days
    - Significant valvular heart disease
    - LVEF < 40%
    - Requiring anticoagulation

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ESCAPE-CMD CLBS16 MANUFACTURING

- GCSF-mobilized autologous CD34 cells in a formulation that maximizes function:

  - 5 days of GCSF 5 µg/kg
  - Apheresis
  - Selection CD34 cells (central processing)
  - Proprietary formulation for intracoronary infusion in 10 mL volume
  - Return to investigator within 48 hrs
  - Administered by intracoronary infusion

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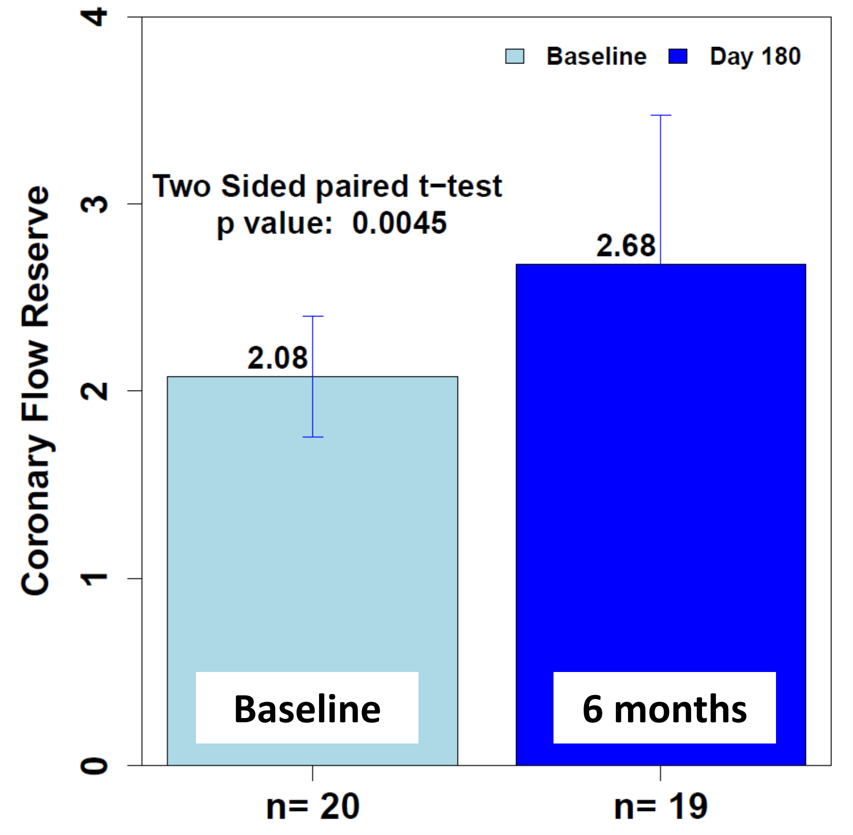
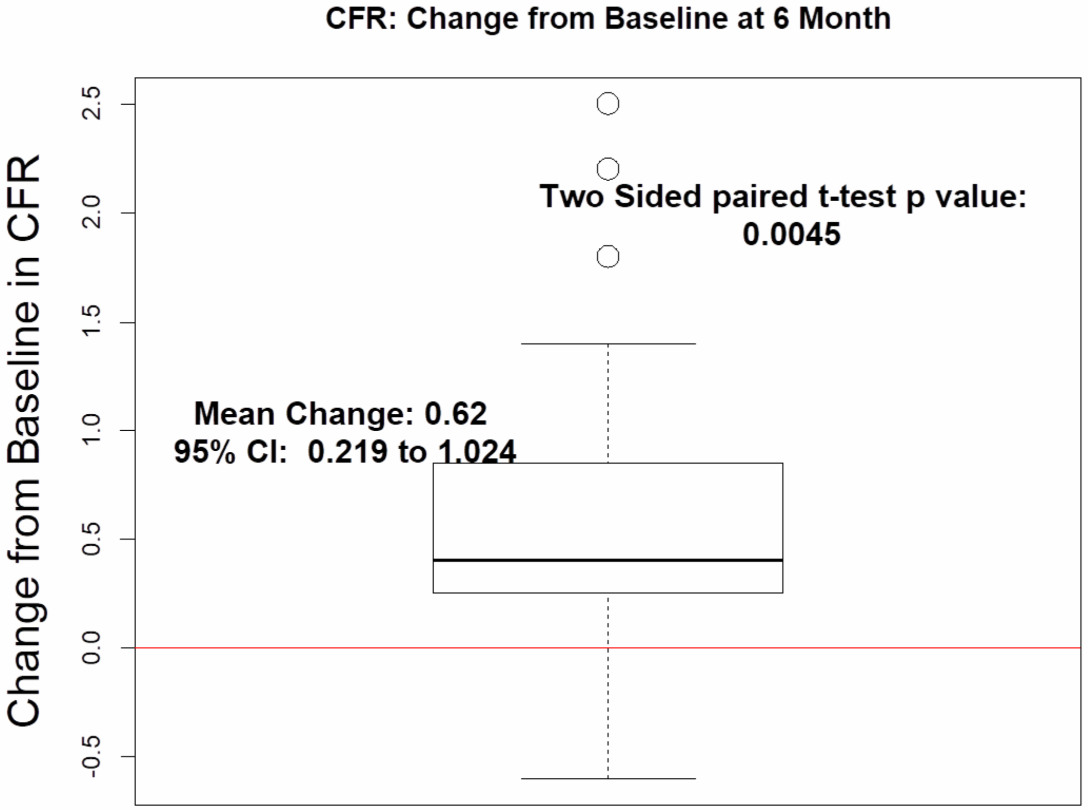
ESCaPE-CMD Subject Demographics

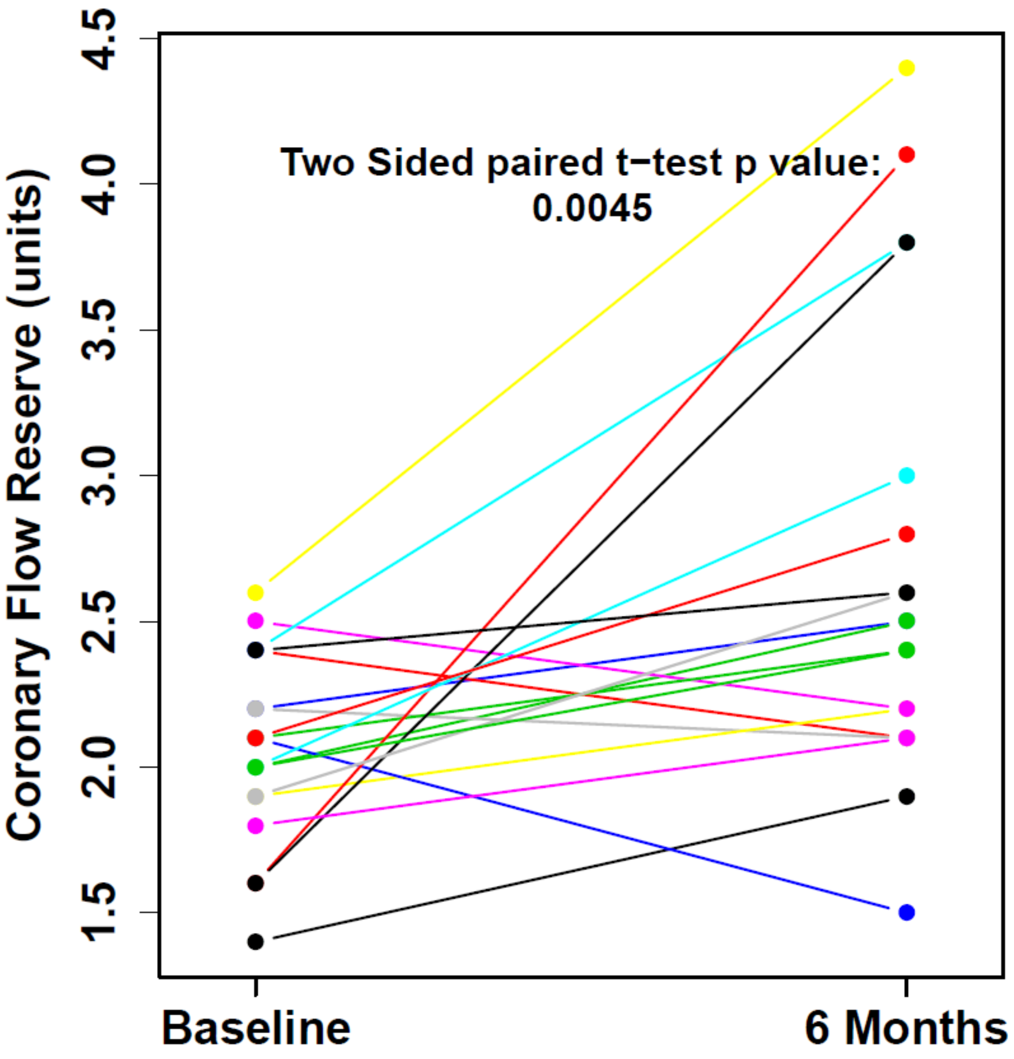
Variable		CLBS16 (n=20)
Age (years), Mean ± SD		54.3 ± 12.7
< 65, n (%)		14 (70%)
≥ 65, n (%)		6 (30%)
BMI (kg/m^2), Mean ± SD		29.5 ± 7.3
Gender, n (%)	Female	17 (85%)
	Male	3 (15%)
Race, n (%)		
White		16 (80%)
American Indian/Alaskan Native		1 (5%)
Asian		2 (10%)
Ethnicity, n (%)		
Hispanic		1 (5%)
Blood Pressure (mm Hg), Mean ± SD	Systolic	126.8 ± 19.0
	Diastolic	76.9 ± 13.2
Angina Medications, n (%)		
Beta Blockers		11 (55%)
Nitrates		16 (80%)
Calcium Channel Blockers		10 (50%)
Ranolazine		5 (25%)

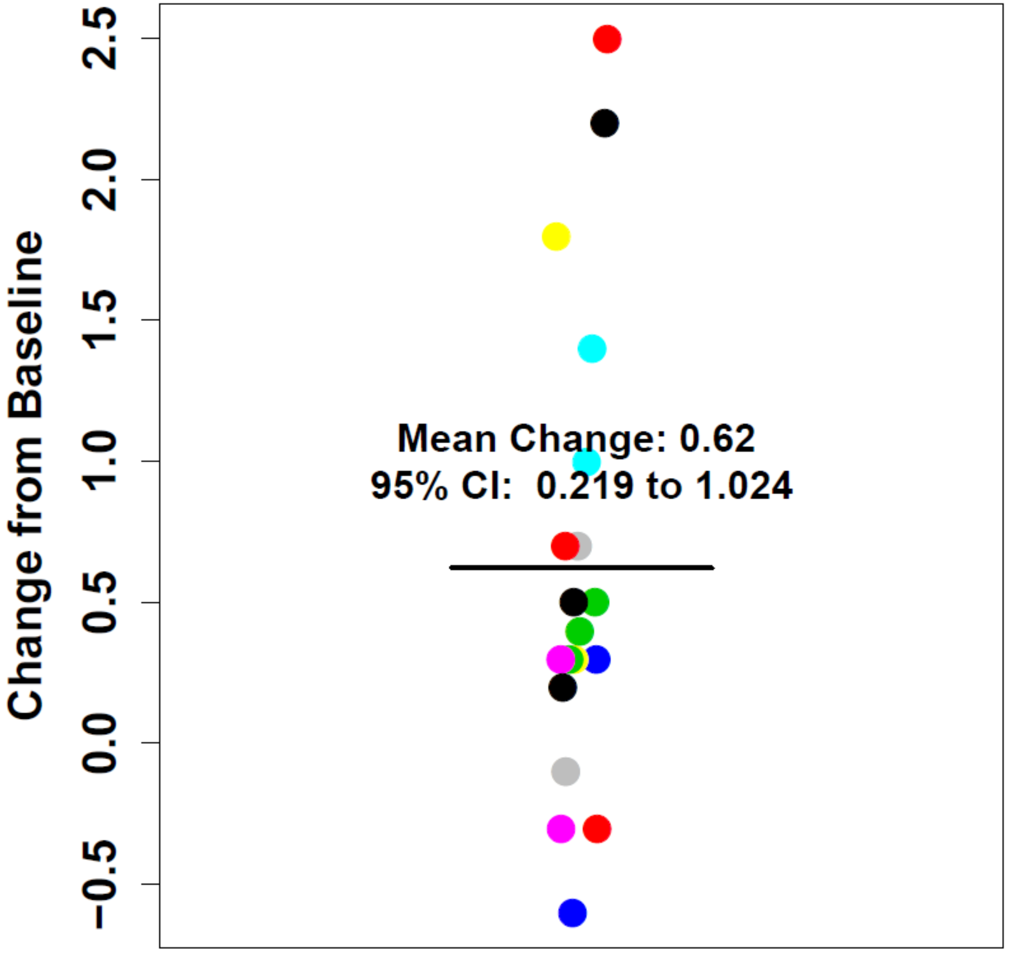
ESCaPE-CMD Increases CFR at 6 months in CMD



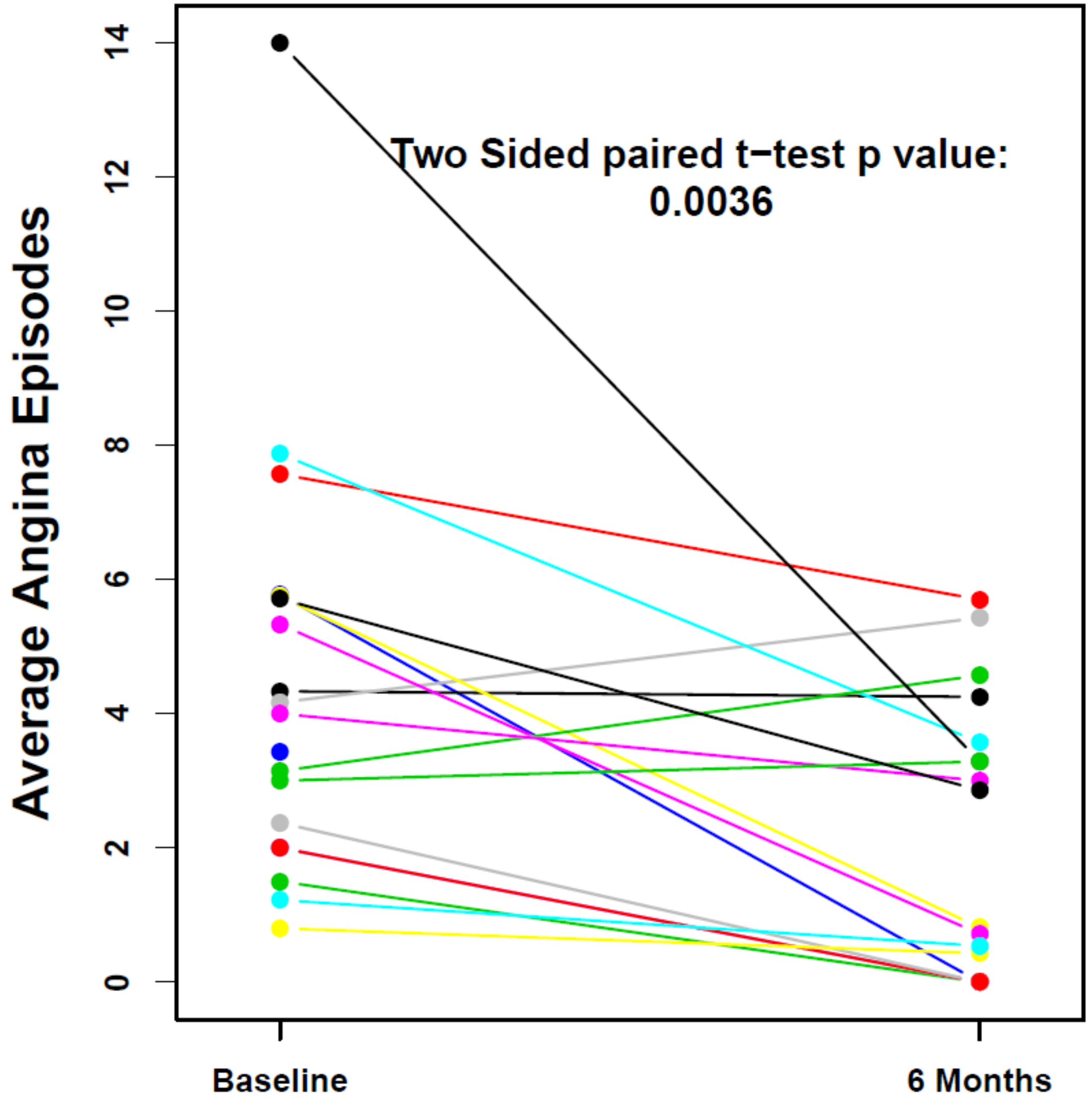


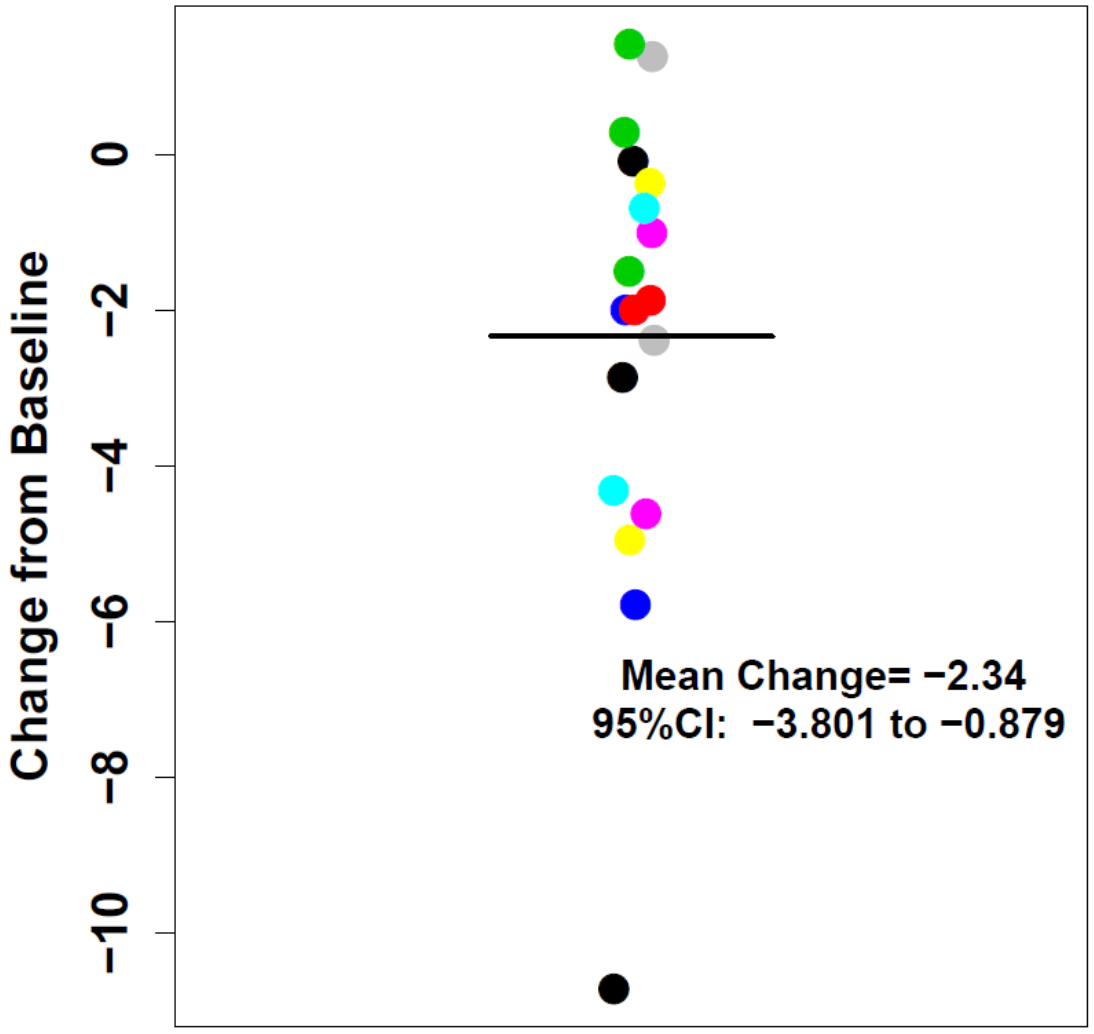
ESCAPE-CMD INCREASES CFR AT 6 MONTHS IN CMD



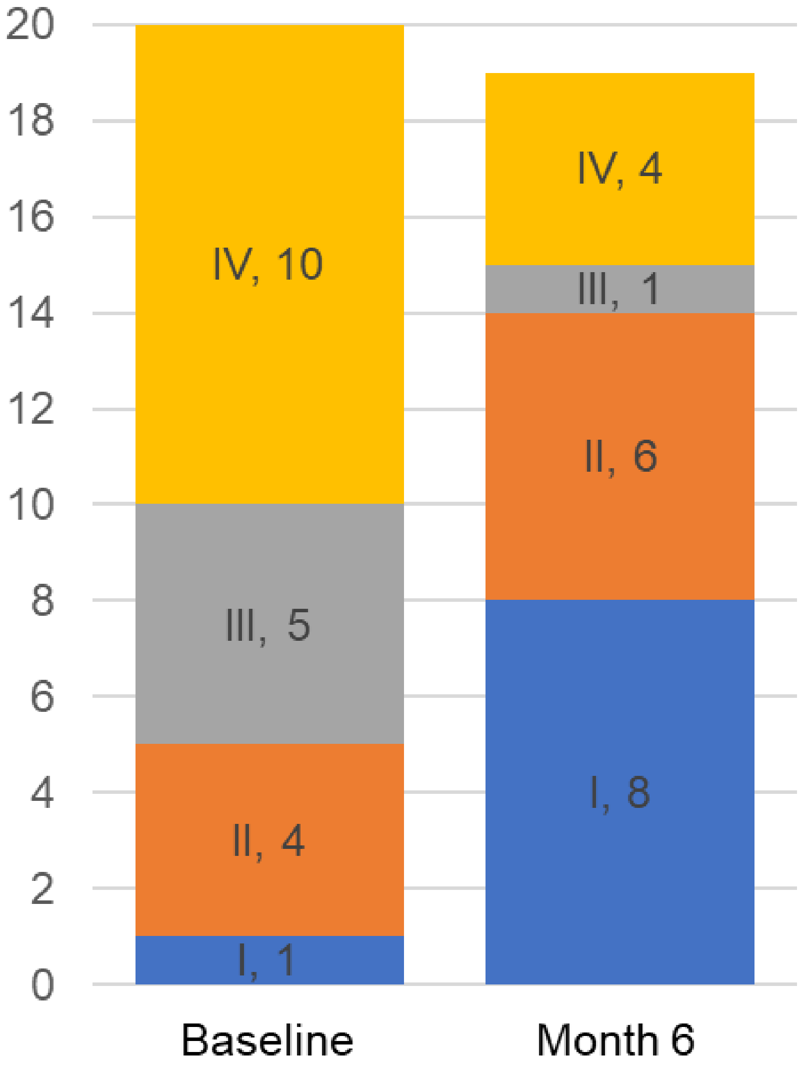


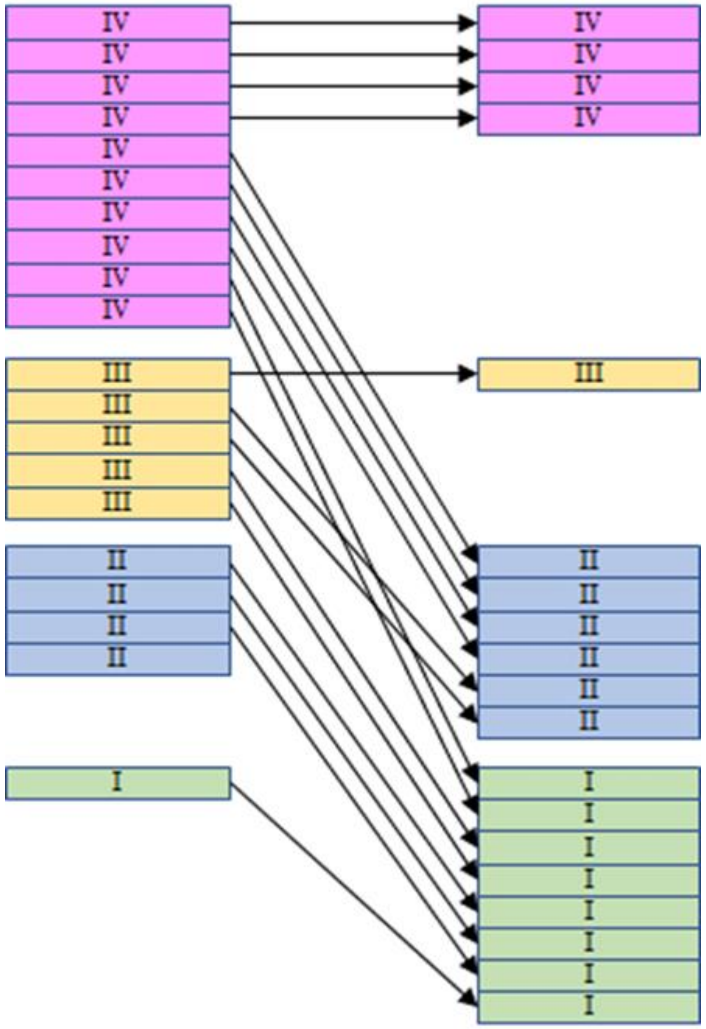
ESCAPE-CMD DECREASES ANGINA FREQUENCY AT 6 MONTHS





ESCAPE-CMD IMPROVES CCS ANGINA CLASS AT 6 MONTHS

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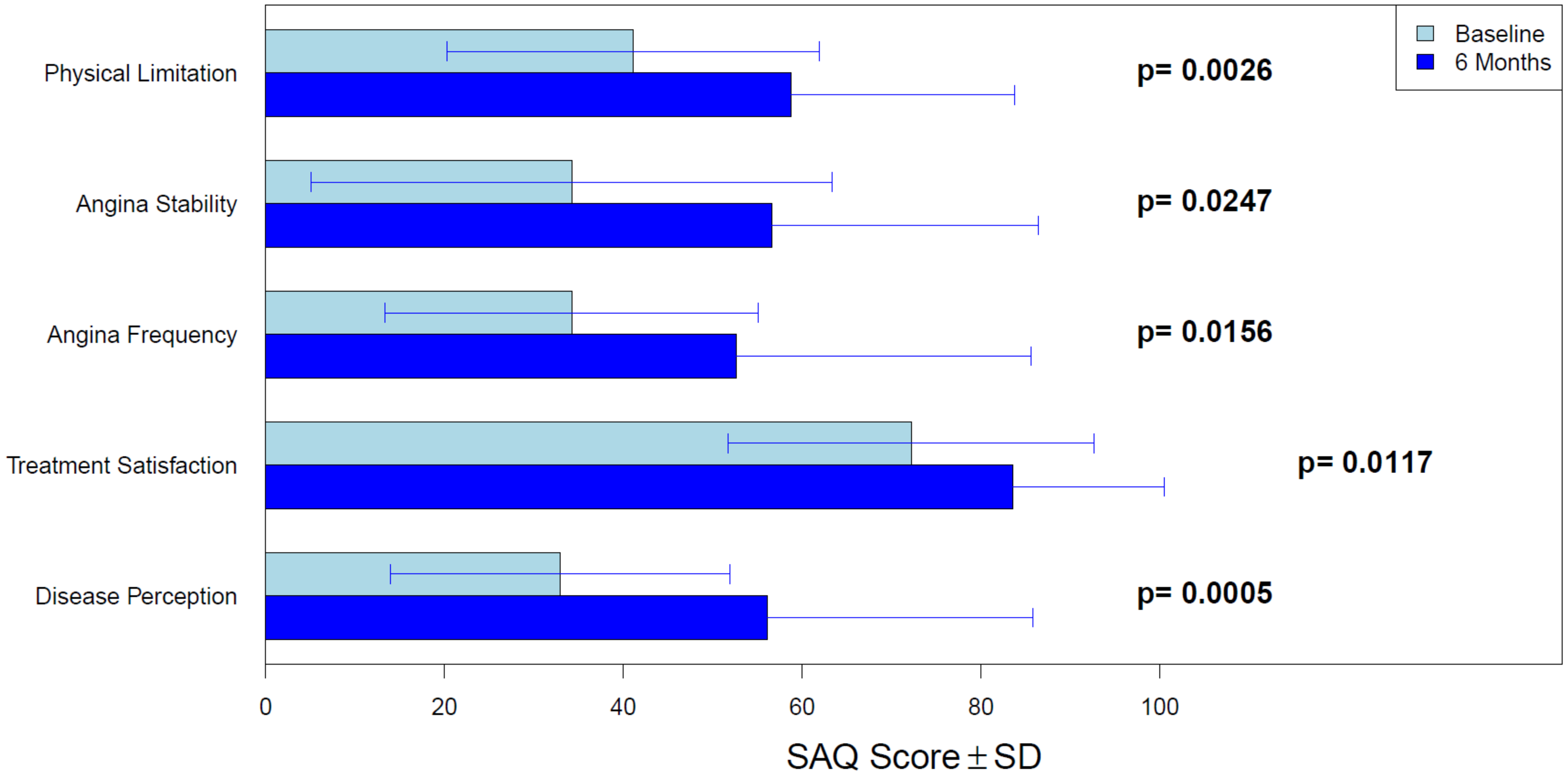
CCS angina class changes from baseline to month 6.

ESCAPE-CMD IMPROVES SEATTLE ANGINA QUESTIONNAIRE SCORES AT 6 MONTHS



SERIOUS ADVERSE EVENTS

- Procedure related focal dissection with stent placement
- No myocardial infarction or repeat revascularization
- No cell related adverse events
- No Mortality

ESCAPE-CMD CONCLUSIONS

- First study of CD34 cell therapy for CMD
- No evidence for cell related adverse events
- We demonstrate significant:
  - Improvement in invasive Coronary Flow Reduction
  - Reduction in Angina frequency
  - Improvement in Angina Class
  - Improvement in all domains of the SAQ
  - Based on these preliminary results a randomized, blinded clinical trial is being planned