Safety and Efficacy of Ixmyelocel-T, A Patient-Specific Expanded Multicellular Therapy, in Dilated Cardiomyopathy

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Minneapolis Heart Institute Foundation
Creating a world without heart disease™

Disclosure

- Trial was sponsored by Aastrom
- Research support for other cell therapy trials from NIH, Baxter, and Angioblast

Introduction

- Increasing number of patients have ongoing failure (HF) symptoms despite optimal medical and device therapy
- Current options include LV assist device and cardiac transplantation
- Cell therapy is an attractive alternative

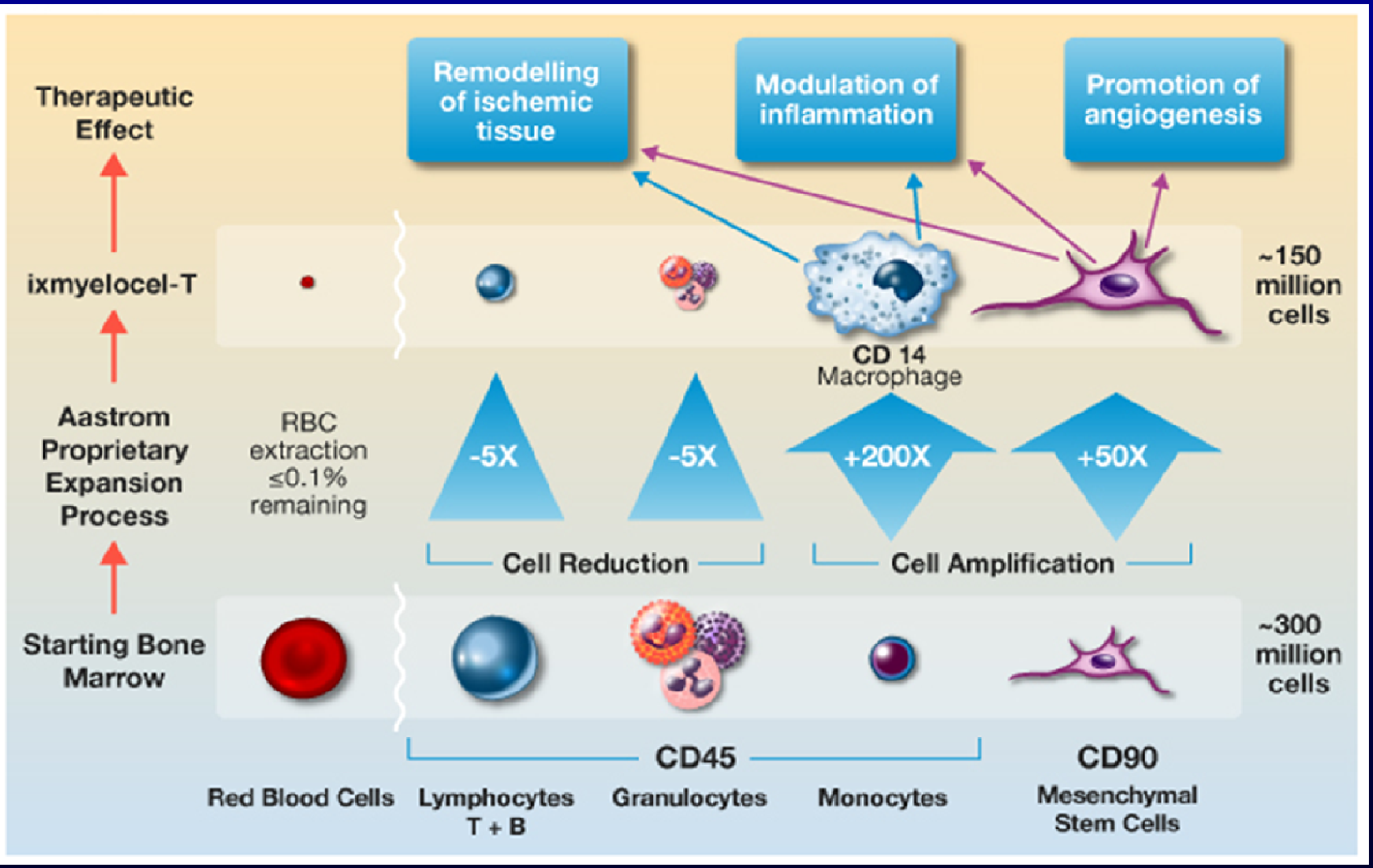
Cardiovascular Cell Therapy for HF

- Strong preclinical data with multiple cell types
- Excellent safety and positive signals from phase 1 unselected bone marrow mononuclear cells
- Number and potency of autologous stem cells from unselected bone marrow decrease with age and risk factors
- FOCUS trial (JAMA 2012;307:1717-1726):
  - Overall no improvement in MVO_2 or ESV
  - Significant improvement in LVEF (+2.9%)
  - Clinical benefits directly related to cell function and type

Strategies to Enhance Cell Therapy

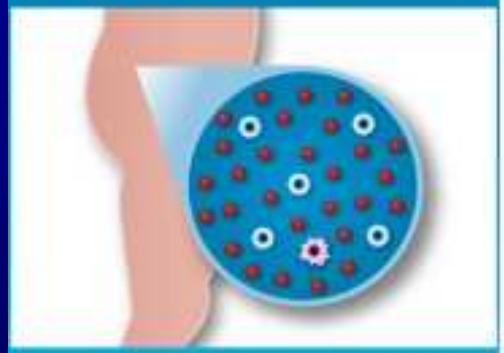
1. Increase the number of cells (autologous)
   - Whole bone marrow (Harvest)
2. Selected cells (autologous)
   - Adipose derived cells (Cytori)
   - CD34+ cells (Baxter)
   - ALD-bright (Aldagen)
3. Expand and/or enhanced cells (autologous)
   - Aastrom Biosciences
   - C-Cure
4. Allogeneic
   - MPC (Mesoblast-Teva)
   - MSC (Osiris)
   - MAPC (Athersys)
5. Cardiac derived
   - Caduceus (Capricor)
   - SCIPIO

A Unique Multicellular Therapy: Ixmyelocel-T



Ixmyelocel-T
Automated 14 Day Process

EXTRACT BONE MARROW



Day 1

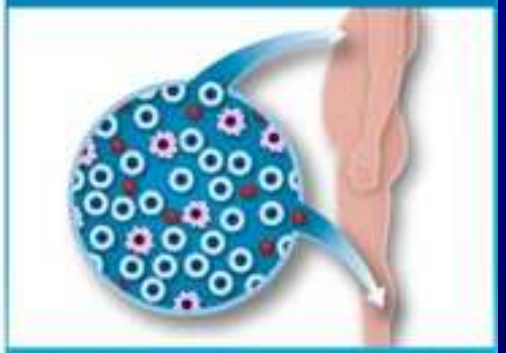
- Bone marrow (approx. 50ml/3 tablespoons) is taken from patient's hip
- 15 minute outpatient procedure

EXPAND CELL POPULATION

Days 2-13

- Aastrom's proprietary automated system expands key beneficial cell types

ADMINISTER TO PATIENT



Day 14

- Expanded multicellular therapy is administered to the same patient
- 20 minute in-office procedure for CLI patients
- Endocardial catheter injections for DCM patients

Ixmyelocel-T
Final Product

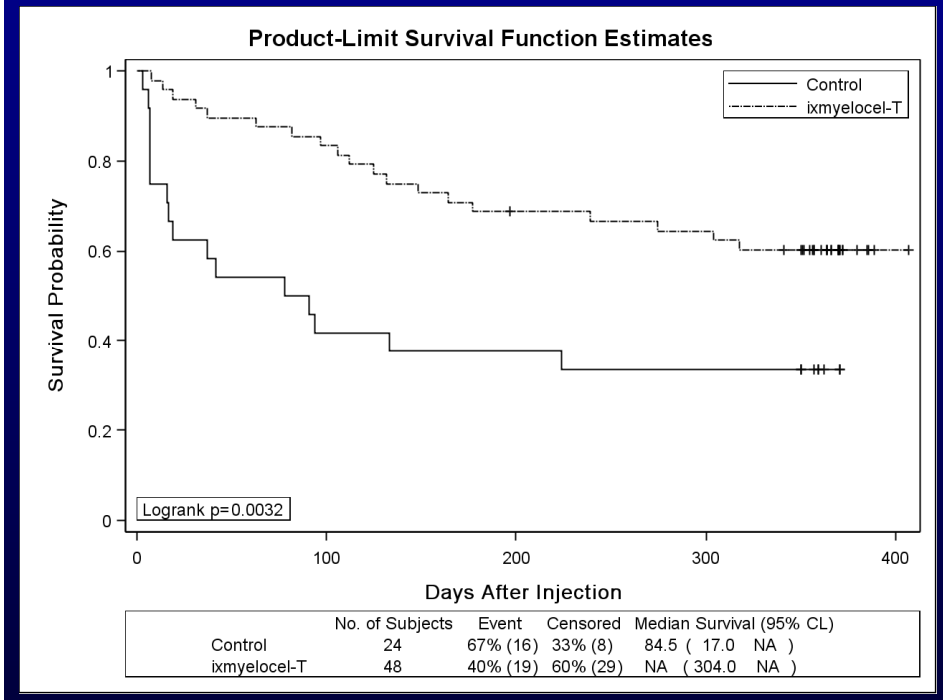
- **Safe**
- **Easy to use**
- **Ready to use:**
  - **No freezing or refrigeration**
  - **No thawing**
  - **No reconstitution**

Ixmyelocel-T Clinical Trials

- CLI
  - RESTORE-CLI (Phase 2b completed)
  - REVIVE-CLI (Phase 3 initiated in early 2012) http://www.revivecli.com/
- Dilated cardiomyopathy
  - Impact-DCM (Phase 2a completed)
  - Catheter-DCM (Phase 2a completed 12-month)
  - RENEW-DCM (Phase 2b will be initiated in June this year)

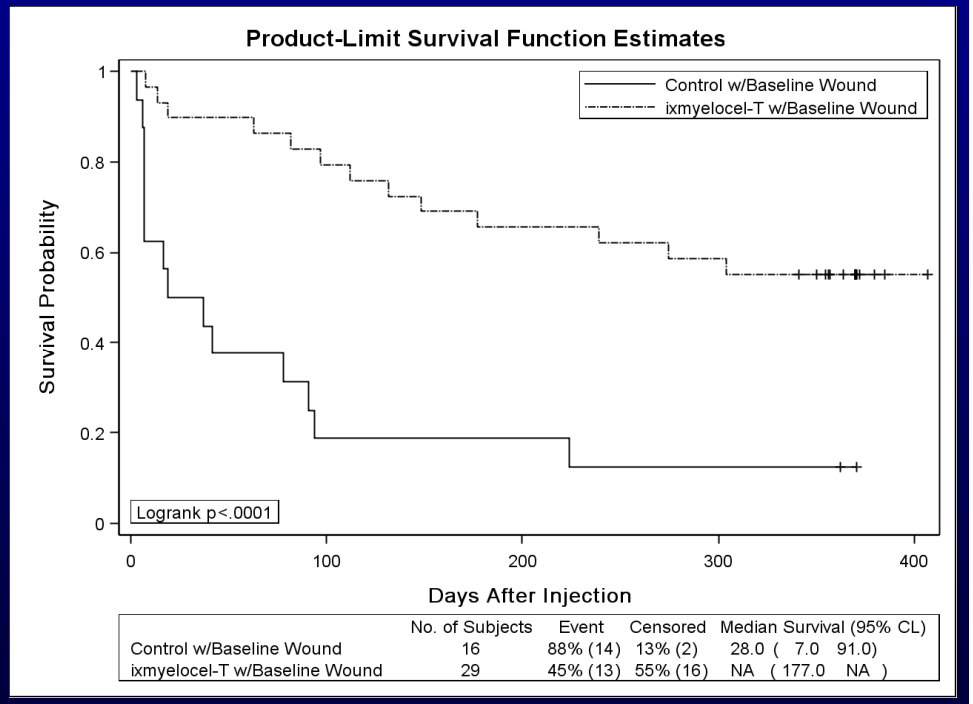
RESTORE CLI: Time to First Occurrence of Treatment Failure

All Treated Patients (N=72)



62% risk reduction: HR 0.38, 95%CI = (0.20-0.74)

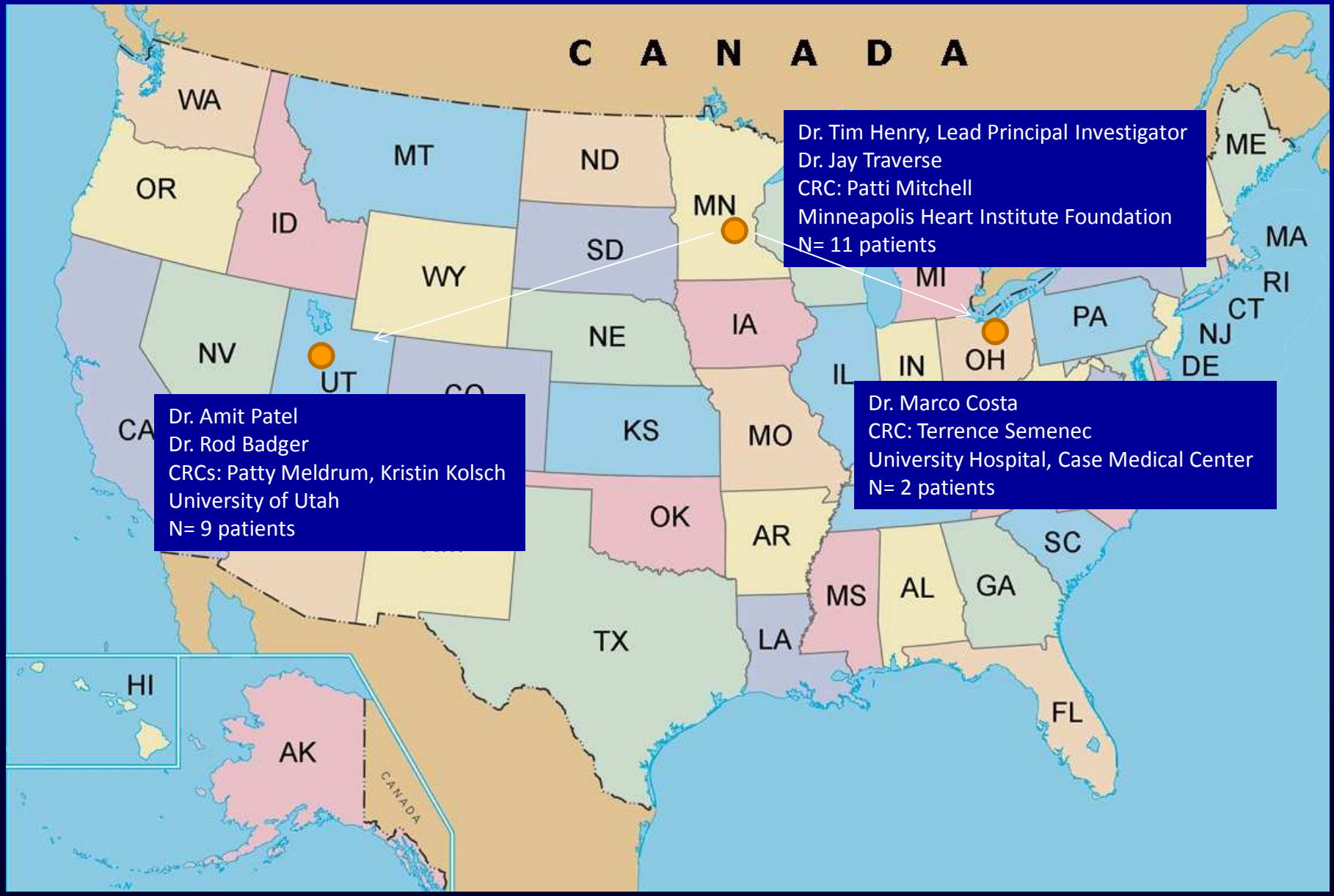
Baseline Wound Patients (N=45)



77% risk reduction: HR = 0.225, 95% CI = (0.103, 0.490)
Cox PH p-value for treatment = 0.0002


Catheter DCM
AASTROM

Catheter-DCM: Participating Centers



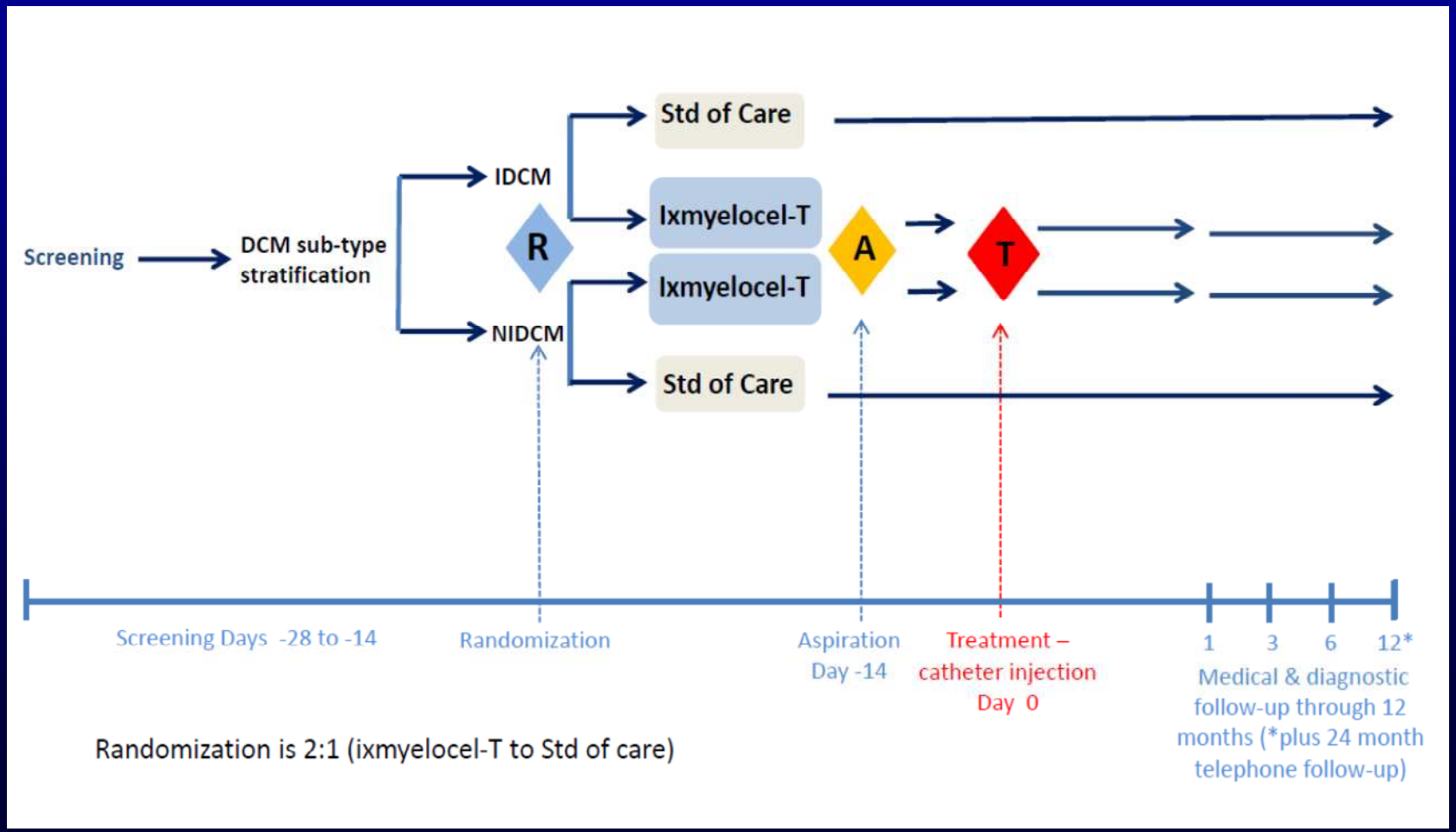
Study Objectives

- Primary objective: safety
  - Planned interim analysis conducted when all subjects completed 6 months
  - Planned final analysis conducted when all subjects completed 12 months
- Secondary objective: investigate efficacy endpoints
  - Clinical (MACE events)
  - Functional endpoints (cardiopulmonary stress, 6 min walk)
  - Structural Endpoints (ECHO, LVEF/volume)
  - QOL/Subjective endpoints (NYHA, MLWHF)

Study Design

- Randomized 2: 1 (ixmyelocel-T: standard of care)
- Stratified by ischemic (IDCM) or non-ischemic DCM (NIDCM)
- Catheter-based transendocardial injections into left ventricle (NOGA®/MYOSTAR™)
- Control subjects received standard of care/no additional intervention
- Both groups had maximal care throughout the study
- Control patients allowed to crossover to ixmyelocel-T treatment after a minimum of 6 months of follow-up

Study Schematic



Key Inclusion/Exclusion Criteria

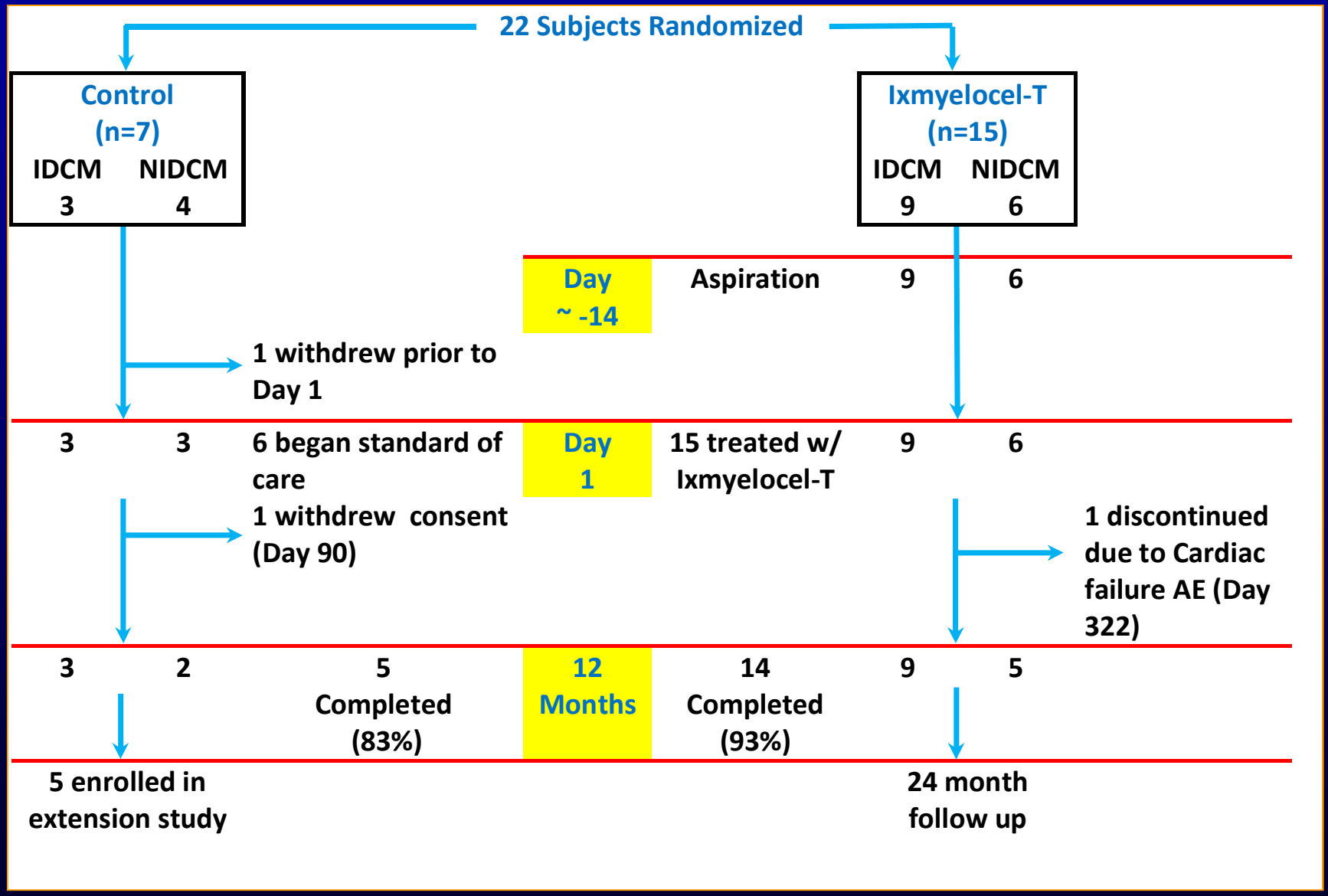
Inclusion Criteria

- Age 18-86yrs
- Ischemic or non-ischemic DCM
- NHYA Class III /IV
- EF≤ 30% (echo)
- No other revascularization options
- Appropriate, stable medical therapy for DCM
- AICD in place ≥3 mos (unless contraindicated)

Exclusion Criteria

- Severe valvular heart disease
- History of COPD
- BMI ≥40 Kg/m^2
- Unstable angina
- Complication risk from cardiac catheterization/injection procedure
- End stage renal disease (requiring dialysis)

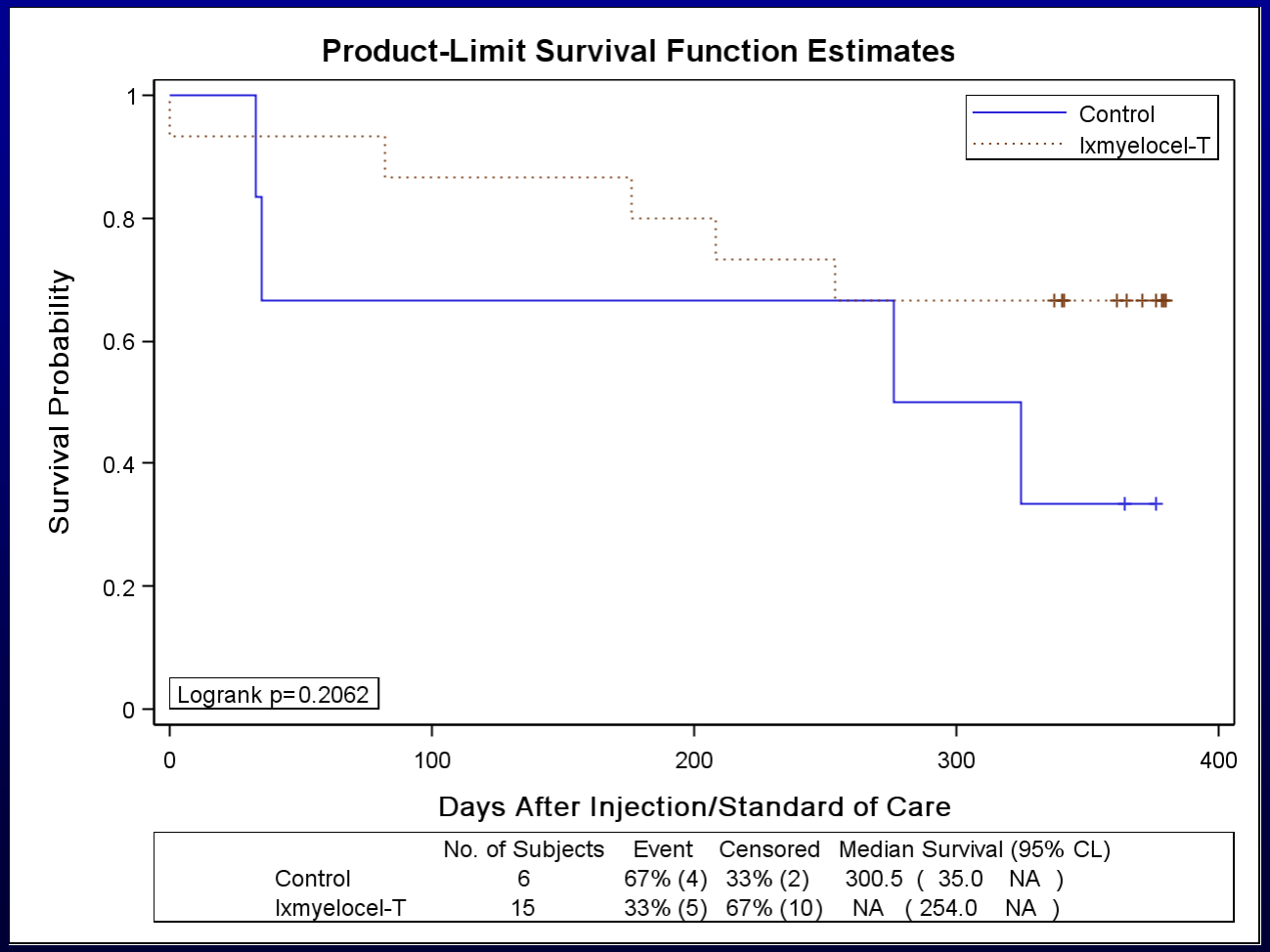
Subject Disposition



Demographics

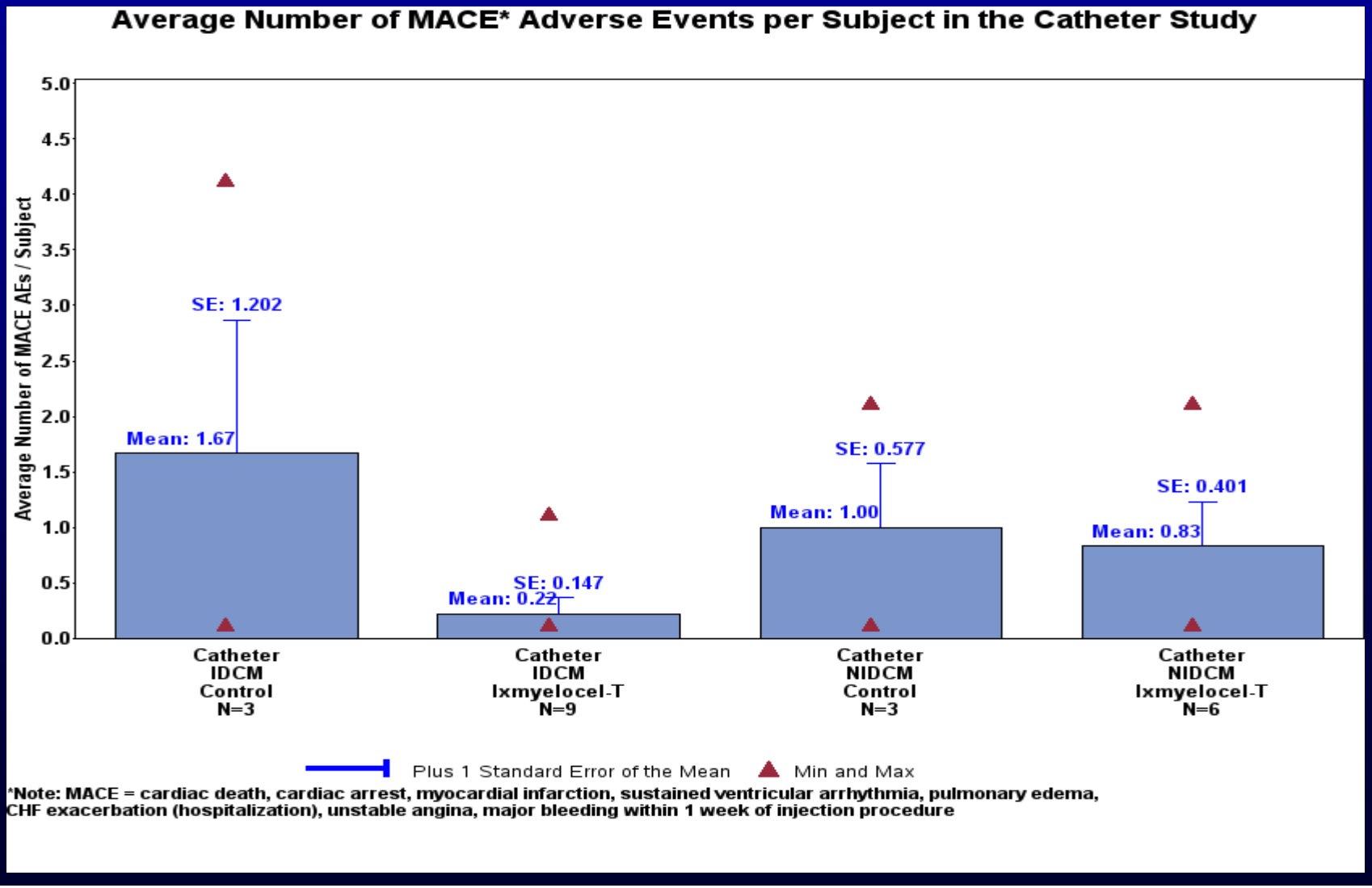
Category	Ixmyelocel-T N=15	Control N=6
Male N (%)	14 (93.3)	6 (100)
Age (years) mean min,max	 64.0 29, 83	 56.8 29, 79
BMI mean min,max	 28.8 22, 39	 27.5 20, 36
EF% (from echo) Mean	 23.9	 22.3
NYHA III/IV	 14/1	 6/0

Time to Occurrence of First MACE Event (by Treatment)



	No. of Subjects	Event	Censored	Median Survival (95% CL)
Control	6	67% (4)	33% (2)	300.5 (35.0 NA)
Ixmyelocel-T	15	33% (5)	67% (10)	NA (254.0 NA)

Average # of MACE/Patient



Efficacy
Functional: NHYA

Improvement NYHA >1 from Baseline	Ixmyelocel-T n / N (%)		Controls n / N (%)
	IDCM	NIDCM	(Controls combined)
At 3 Months	7 / 9 (78)	3 / 6 (50)	0 / 5 (0)
At 6 Months	7 / 9 (78)	3 / 6 (50)	1 / 5 (20)
At 12 Months	9 / 9 (100)	2 / 5 (40)	0 / 5 (0)

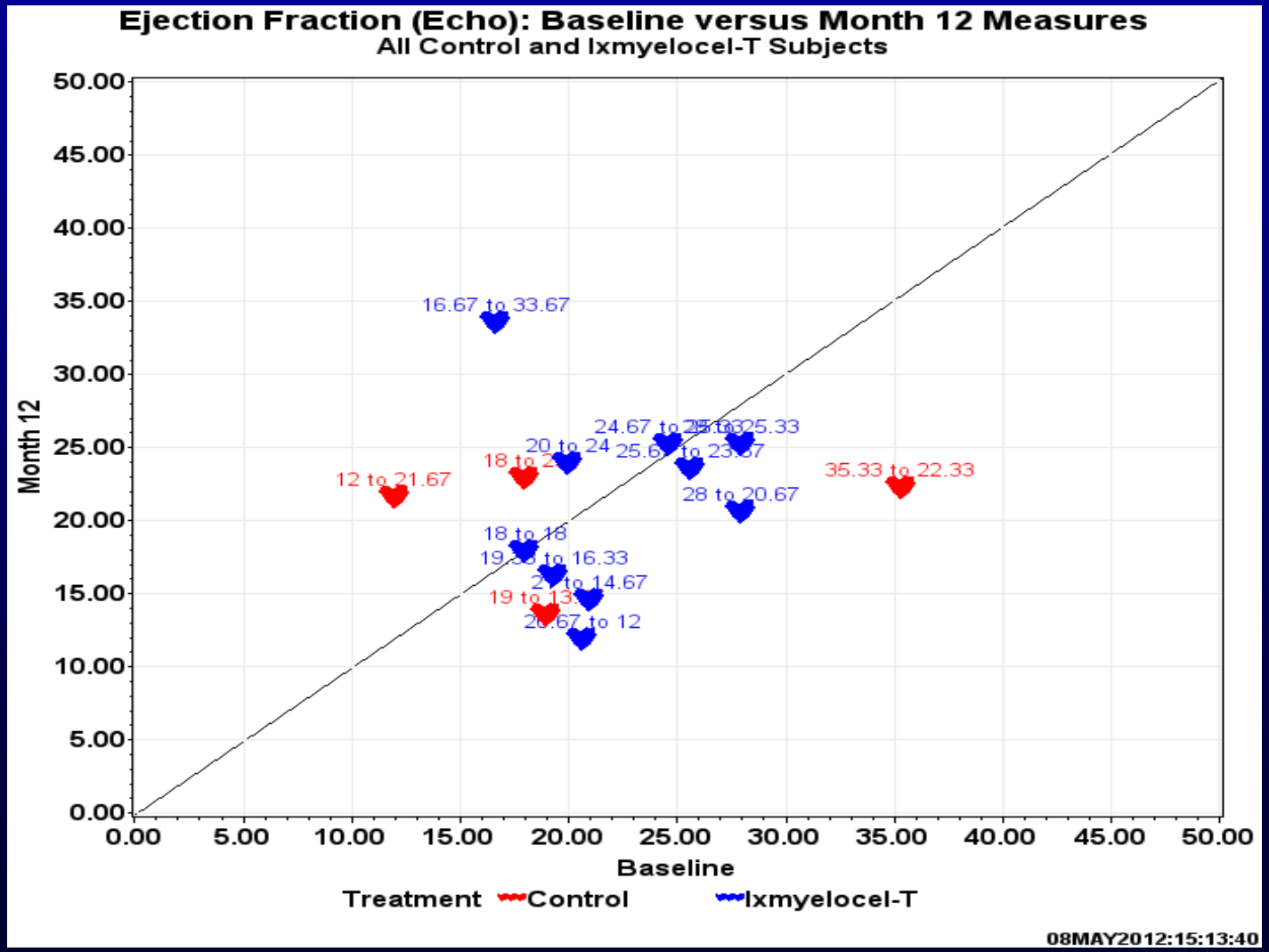
Efficacy
Functional: 6 Minute Walk

Improvement from Baseline	Ixmyelocel-T n / N (%)		Controls n / N (%)
	IDCM	NIDCM	(Controls combined)
At 3 Months	8 / 9 (89)	4 / 6 (67)	0 / 5 (0)
At 6 Months	7 / 9 (78)	5 / 5 (100)	4 / 5 (80)
At 12 Months	6 / 9 (67)	2 / 4 (50)	1 / 5 (20)

Efficacy
Structural: Ejection Fraction (ECHO)

Improved EF (ECHO) from Baseline	Ixmyelocel-T n / N (%)		Controls n / N (%)
	IDCM	NIDCM	(Controls combined)
At 3 Months	4 / 7 (57)	1/6 (17)	1 / 4 (25)
At 6 Months	5 / 7 (71)	2/6 (33)	1 / 4 (25)
At 12 Months	1 / 5 (20)	2/5 (40)	2 / 4 (50)

Ejection Fraction – All Patients at 12 months



Conclusions

- Transendocardial injection of ixmyelocel-T was well tolerated in patients with DCM
- AE incidence was comparable between the ixmyelocel-T group and the control standard of care group
- Despite small patient numbers, trends toward improvement were observed in IDCM patients:
  - MACE events
  - NYHA
  - 6 minute walk
- Large phase 2b will begin this summer with IDCM patients with EF ≤30%