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

Timothy D. Henry, Jay H. Traverse, Rod Badger, Marco Costa, Patricia Mitchell, Kristen Kolsch, Ronnda L. Bartel, Sharon Watling, Amit N. Patel

Minneapolis Heart Institute Foundation™
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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

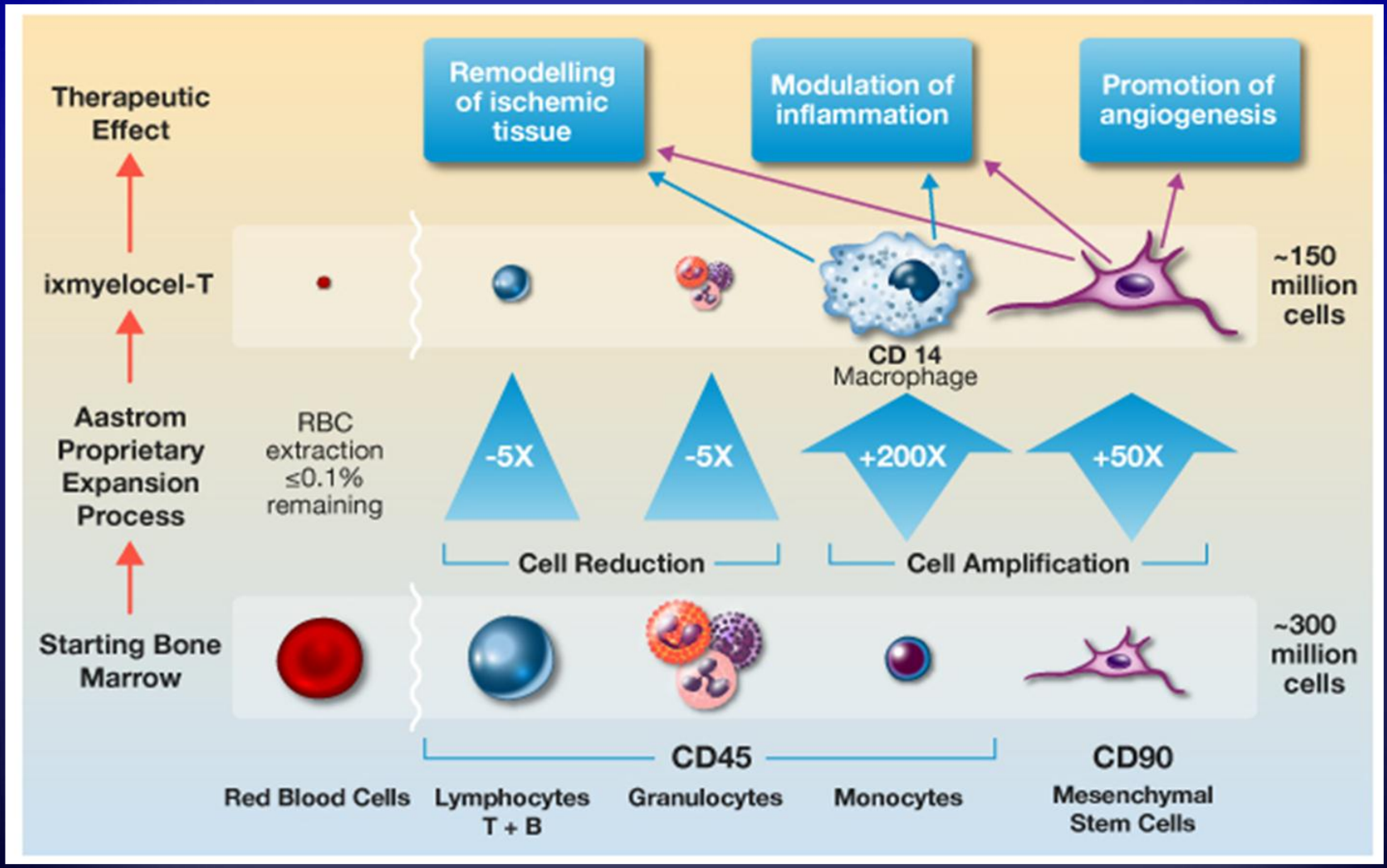
Cardiovascular Cell Therapy for HF

- 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

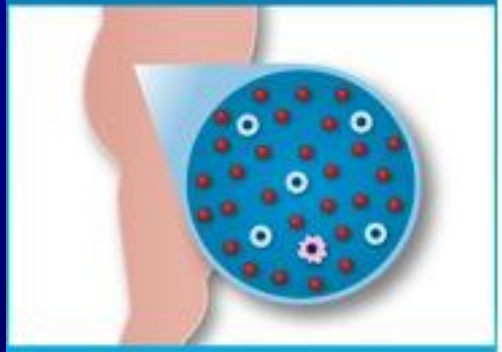
1. Increase the number of cells (autologous)
   - Whole bone marrow (Harvest)
2. Selected cells (autologous)
   - Adipose derived cells (Cytori)
   - CD34+ cells (Baxter)
   - ALD-bright (Aldagen)
3. Expand and/or enhanced cells (autologous)
   - Aastrom Biosciences
   - C-Cure
4. Allogeneic
   - MPC (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

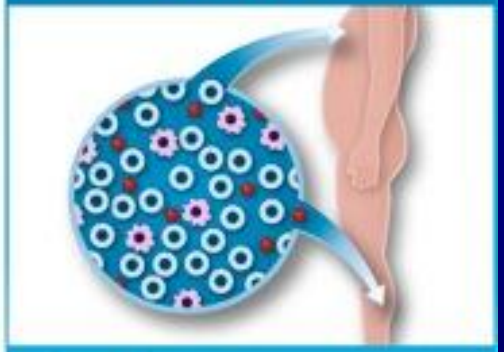
- Bone marrow (approx. 50ml/3 tablespoons) is taken from patient's hip
- 15 minute outpatient procedure

EXPAND CELL POPULATION

Days 2-13

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

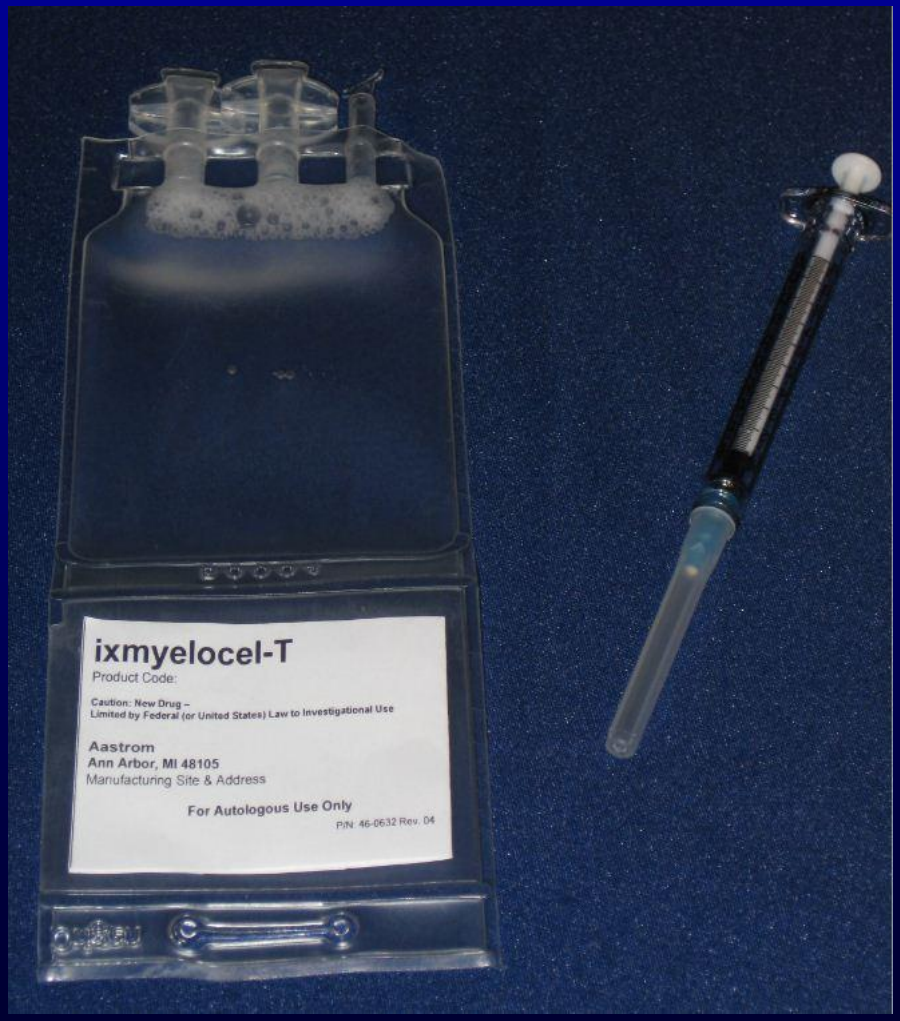
ADMINISTER TO PATIENT



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



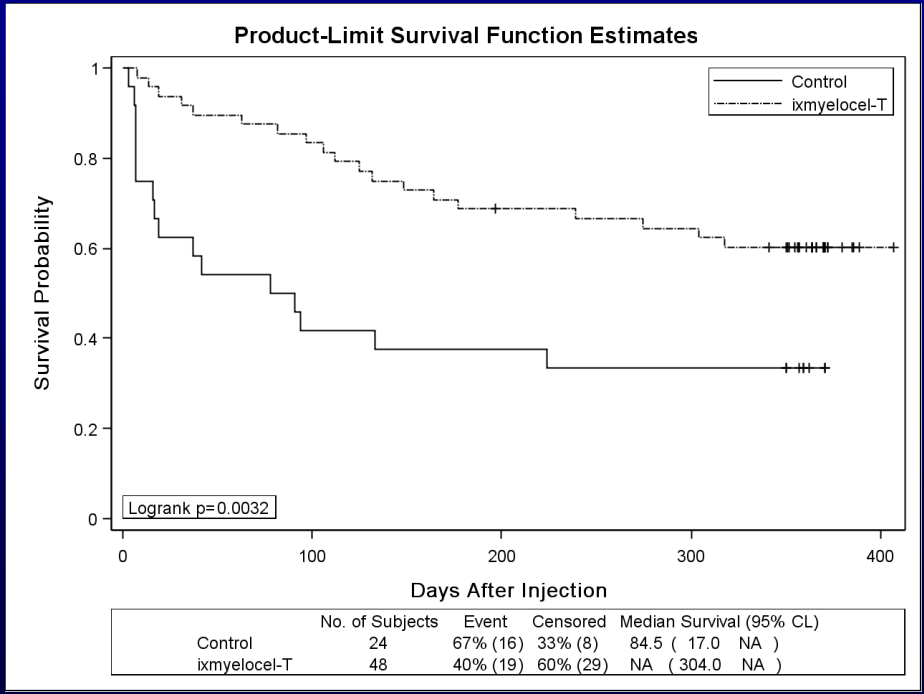
- **Safe**
- **Easy to use**
- **Ready to use:**
  - **No freezing or refrigeration**
  - **No thawing**
  - **No reconstitution**

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)

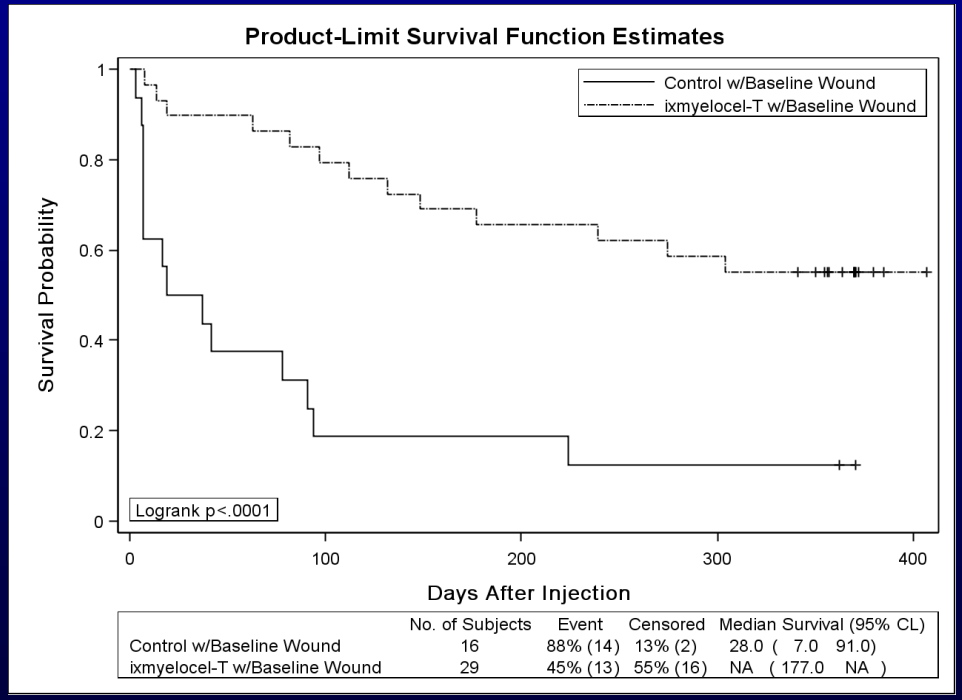
RESTORE CLI: Time to First Occurrence of Treatment Failure

All Treated Patients (N=72)



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

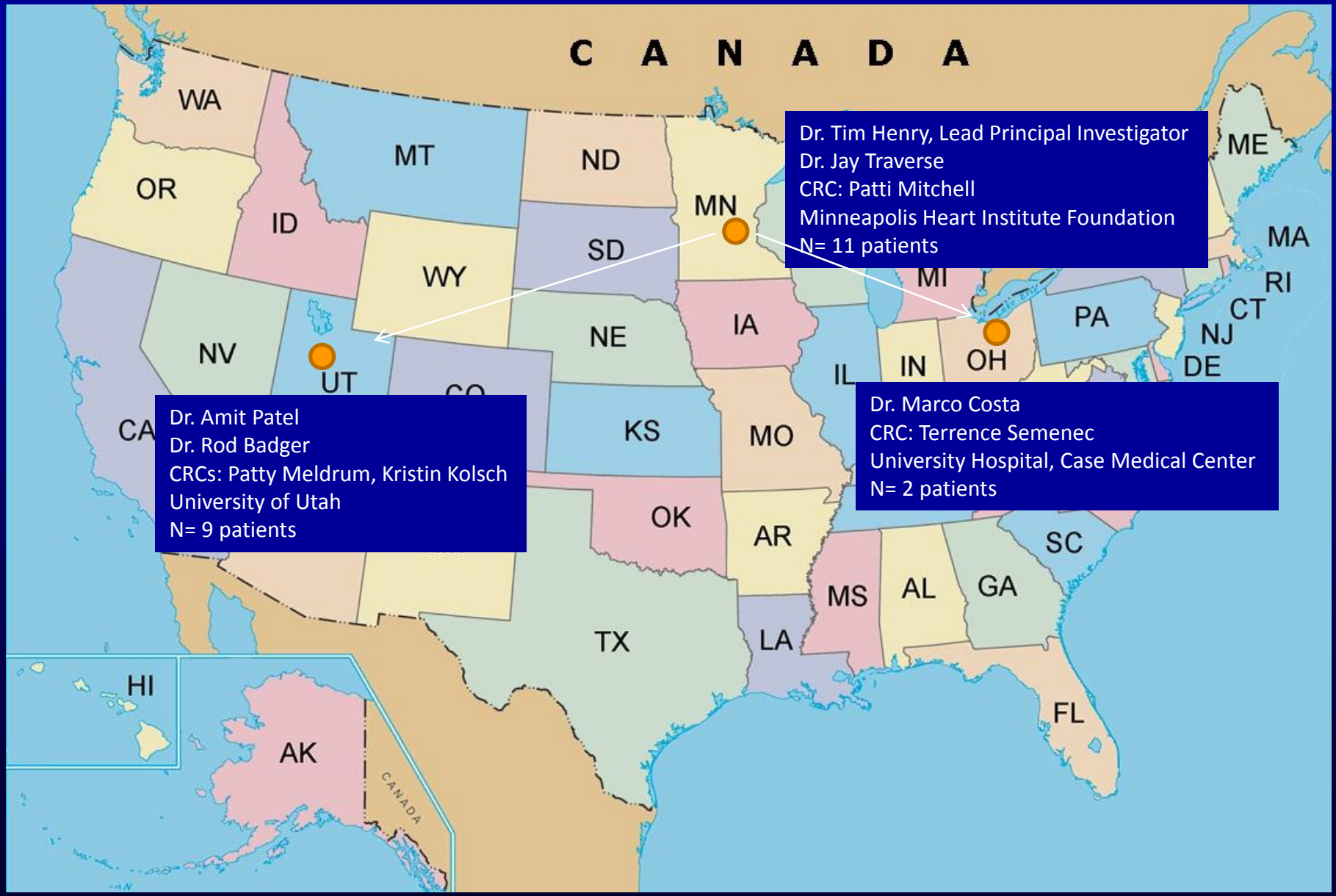
Baseline Wound Patients (N=45)



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



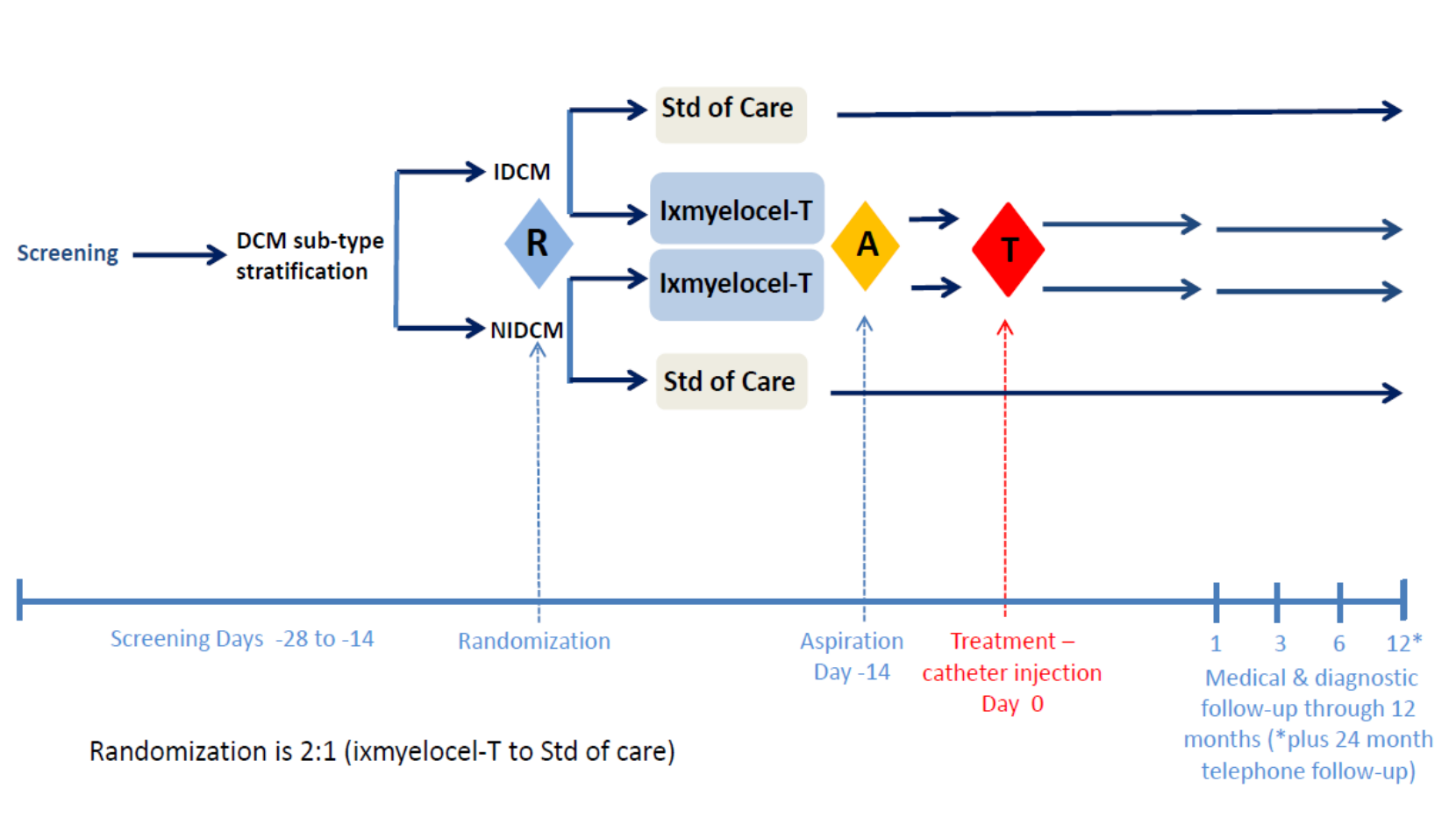
Study Objectives

- 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

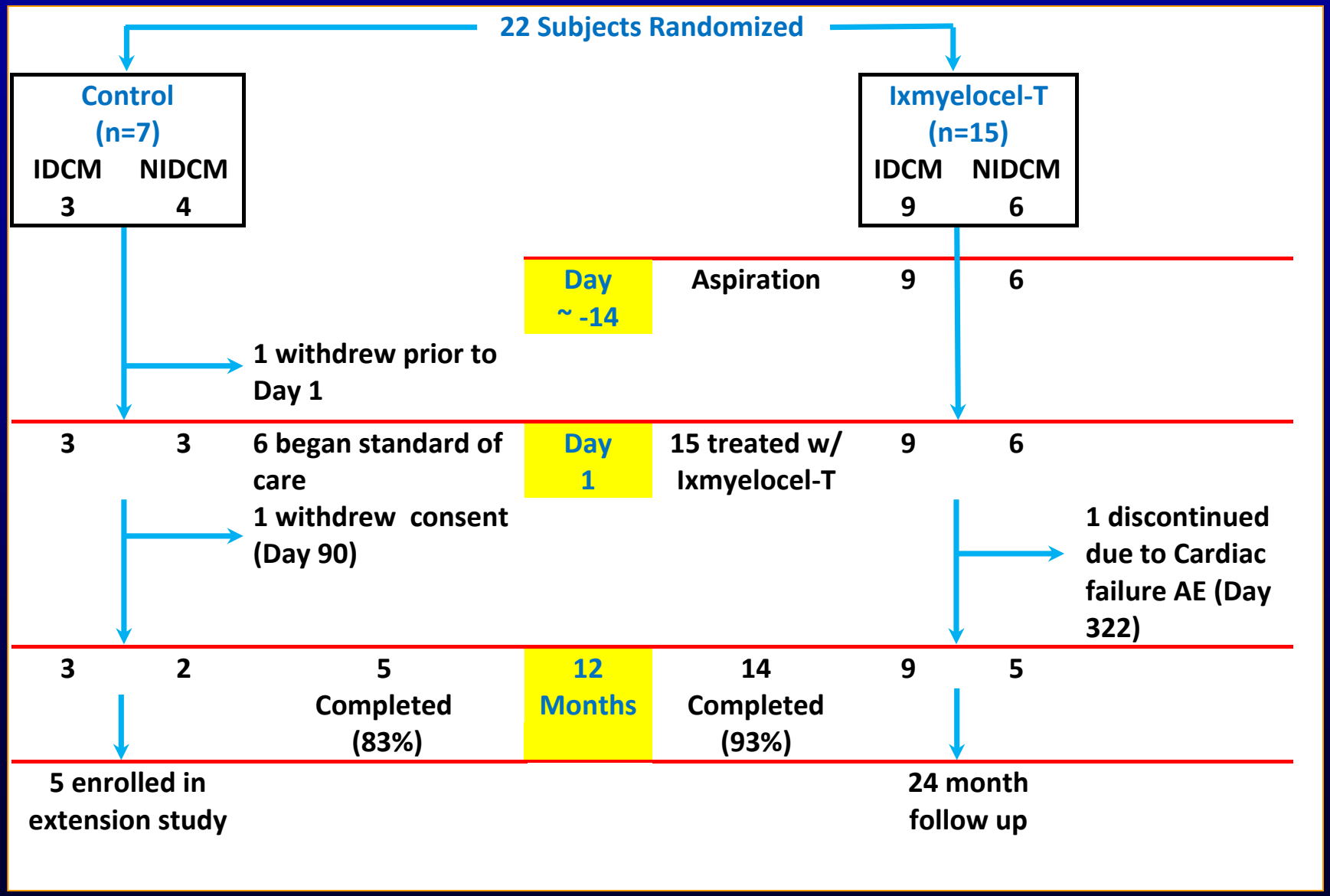
Inclusion Criteria

- 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)

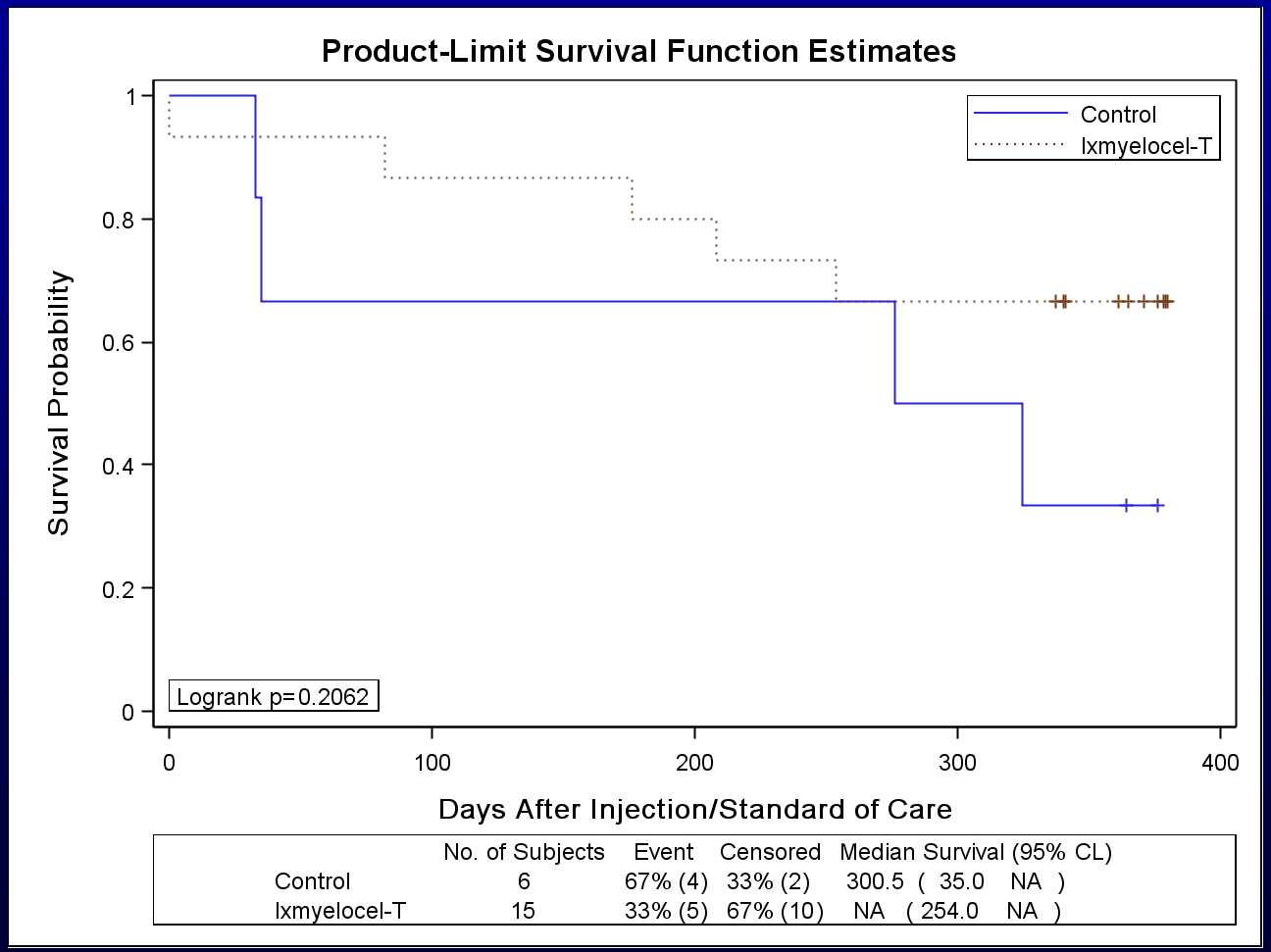
Subject Disposition



Demographics

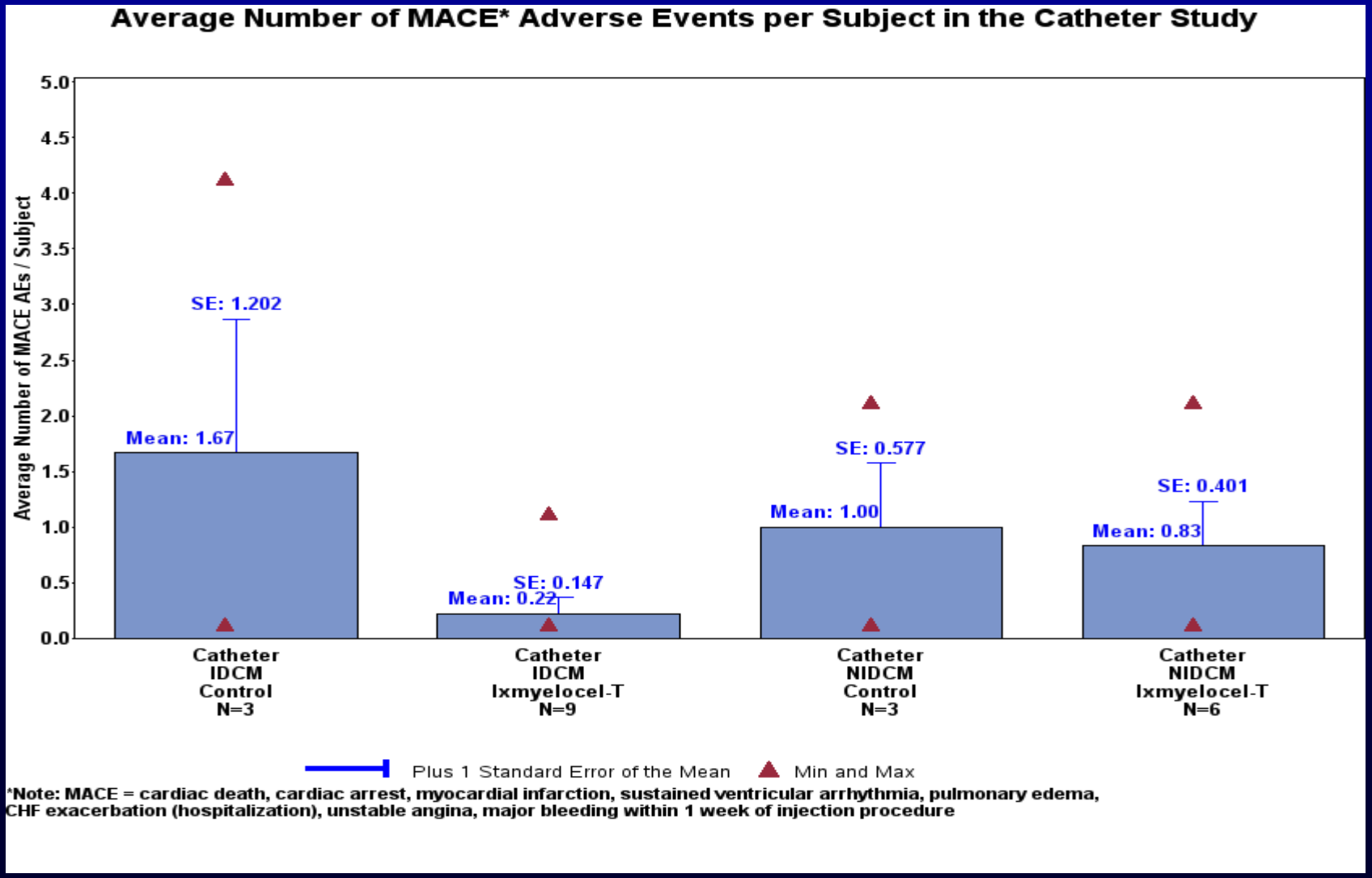
Category	Ixmyelocel-T N=15	Control N=6
Male N (%)	14 (93.3)	6 (100)
Age (years) mean min,max	 64.0 29, 83	 56.8 29, 79
BMI mean min,max	 28.8 22, 39	 27.5 20, 36
EF% (from echo) Mean	 23.9	 22.3
NYHA III/IV	 14/1	 6/0

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)

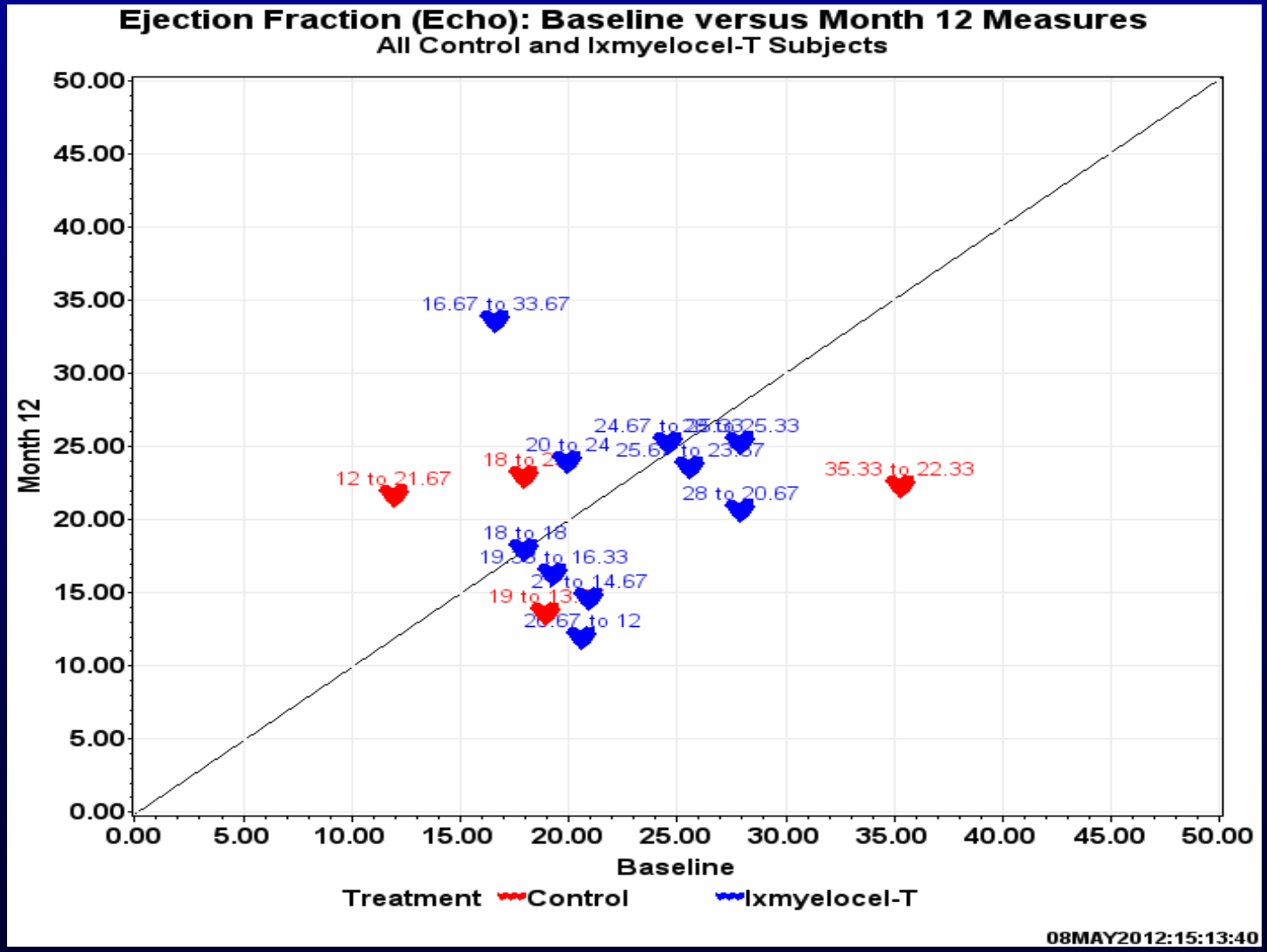
Efficacy
Functional: 6 Minute Walk

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%