

Title:

Safety and Efficacy of Ixmyelocel-T, An Expanded Patient-Specific Mixed Cell Product, in Dilated Cardiomyopathy (IMPACT-DCM)

Authors:

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Objectives:

Intramyocardial injection of ixmyelocel-T was assessed in patients with ischemic dilated cardiomyopathy (IDCM) and non-ischemic dilated cardiomyopathy (NIDCM) in IMPACT-DCM, a Phase 2 trial. The objectives included: (1) safety and tolerance of ixmyelocel-T; and (2) preliminary signals of efficacy via symptomatic, functional and structural assessments.

Methods:

Forty patients diagnosed with IDCM or NIDCM, NYHA Class III/IV heart failure and an overall mean left ventricular ejection fraction (LVEF) of  $\leq 30\%$  and with no treatment options were enrolled. Patients were randomized to either a single administration of ixmyelocel-T or standard of care (control group) and followed for 12 months. Autologous bone marrow cells were cultured for 12 days in a closed, automated bioreactor, expanding the number of mesenchymal stromal cells, monocytes and macrophages while retaining many of the mononuclear cells from the original bone marrow. This combination has been associated with biological activities that promote tissue remodeling and immunomodulation, which may promote and support angiogenesis. Only the ixmyelocel-T patients underwent mini-thoracotomy or thoracoscopy for product injection into the LV.

Results:

Twenty-eight patients completed the 12 month study. Five control patients left the study after 6 months to enter the treatment extension study. Post thoracotomy hospital discharge, there was no difference in the incidence of adverse events in the treated and control patients. Ixmyelocel-T showed greater effect in the IDCM stratum. IDCM patients treated with ixmyelocel-T had better outcomes (major adverse cardiovascular events [MACE], NYHA class and 6 minute walk distance) compared to control (table below). In addition, there was an increase in septal thickening although cells were not injected into the septum.

Conclusions:

Treatment with ixmyelocel-T was well tolerated. Efficacy observations in IDCM were consistent with improved function of impaired myocardium and support reverse remodeling of the LV chamber.

Preliminary Efficacy in IMPACT-DCM

		<b>IDCM</b>	
		<b>Ixmyelocel- T</b>	<b>Control</b>
<b>Percent of Patients with MACE Adverse Events</b>			
Enrolled Subjects		12	7
All MACE Events (n/%)		6 / 50.0	5 / 71.4
<b>Number of Patients with Improvements from Baseline in Efficacy /Total Patients in Group</b>			
Decrease in NYHA Score	- 1 mo	9 / 10	1 / 6
	- 3 mos	9 / 10	0 / 4
	- 6 mos	8 / 10	0 / 3
	-12 mos	9 / 10	1 / 3
Increase in six minute walk test	- 1 mo	8 / 10	1 / 5
	- 6 mos	6 / 10	1 / 3
	-12 mos	6 / 10	0 / 3
Increase in MRI/CT septal thickness	- 6 mos	7 / 10	1 / 3