



Heart Failure

SAFETY AND TOLERABILITY OF GLIAL GROWTH FACTOR 2 IN PATIENTS WITH CHRONIC HEART FAILURE: A PHASE I SINGLE DOSE ESCALATION STUDY

Poster Contributions

Poster Sessions, Expo North

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Authors: *Daniel J. Lenihan, Sarah Anderson, Carrie Geisberg, Anthony Caggiano, Andrew Eisen, Evan Brittain, James A.S. Muldowney, III, Lisa Mendes, Douglas Sawyer, Vanderbilt University, Nashville, TN, USA, Acorda Therapeutics, Inc., Hawthorne, NY, USA*

Background: Glial Growth Factor 2 (GGF2) is a neuregulin peptide critical for cardiac function. GGF2 enhances myocardial function and repair in animal models of cardiac injury. A first-in-human, double-blind, placebo-controlled, single escalating dose study was conducted to begin examining safety and tolerability of GGF2 in patients with systolic heart failure (HF).

Methods: After informed consent, 40 patients with symptomatic HF were randomized (4:2) to GGF2 or placebo in 7 ascending dose cohorts from 0.007 to 1.5 mg/kg. Patients were observed in hospital for 30 hours, then evaluated for adverse events (AEs) at 1, 2, 4, 12, and 24 weeks after infusion. AEs were graded using the Combined Toxicity Criteria.

Results: There were no notable effects of treatment on hematologic or electrical parameters and no AEs leading to withdrawal. Treatment Emergent AEs are shown in Table 1. A dose-limiting toxicity meeting Hy's Law criteria (ALT, AST, bilirubin) and one case of superficial uroepithelial carcinoma occurred in the seventh cohort (1.5 mg/kg).

Conclusions: A single dose of GGF2 in patients with HF was generally well tolerated up to 0.75 mg/kg. Higher doses may be associated with reversible hepatotoxic events. Further studies are needed to assess safety and tolerability GGF2 therapy in symptomatic HF.

Table 1: Treatment Emergent Adverse Events (TEAEs) (at time of drafting)

GGF2 (mg/kg) Dose	Placebo (n = 13)	0.007 (n=4)	0.021 (n=4)	0.063 (n=4)	0.189 (n=4)	0.378 (n=4)	0.756 (n=4)	1.512 (n=3)
Patients with Any TEAEs	5	4	4	2	4	4	4	3
Total TEAEs	6	12	7	4	16	13	13	10
Nervous System - headache		2	2	1		2	2	
Nervous System - other					3			2
GI	3	2		1	2	2	3	2
Administration Site	2	1		1	1	2	2	2
Respiratory, Thoracic		3			1	2	1	
Investigations and Bilirubin		1			2	2	1	0*
Vascular		1	1		1		2	1
Infections		1			2	1		
Musculoskeletal			2		1			1
Cardiac - Angina pectoris			1		1			
Cardiac - HF					1			
Cardiac - flutter						1		
Metabolism/Nutrition	1						2	1
Renal and Urinary				1				1**
Dermal		1			1			
Ear and Labyrinth								1
Eye			1					
Hepatobiliary - Hy's Law								1*
Procedural						1		

*Defined Dose Limiting Toxicity: reversible elevation in AST, ALT, Bilirubin

**Uroepithelial carcinoma in situ: investigation on-going