Dystrophinopathy in ACTION; Analysis of the first 500 males enrolled in the *Advanced Cardiac Therapies Improving Outcomes Network* prospective dystrophinopathy registry.

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A lack of functional dystrophin leads to fibro-fatty replacement of cardiac myocytes and clinically, to progressive cardiomyopathy (CM) that is a leading cause of death. We seek to improve cardiac care by understanding current care practices and outcomes for patients with dystrophinopathy.

Males with dystrophinopathy and at least one of the following; age ≥ 10 years, evidence of CM, or receipt of gene therapy, are eligible for enrollment in the ACTION registry. Data collection occurs at the time of enrollment and every 6 months thereafter. Data points include demographics, genetics, neuromuscular, cardiac, and pulmonary function endpoints, medication use, use of advanced cardiac therapies, and outcomes, including hospitalization and death.

500 males with dystrophinopathy from 20 North American Centers have been enrolled in the ACTION registry from launch in 2021; mean age 18.0 (± 5.5) years, the majority white (81.2%) with Duchenne Muscular Dystrophy (91.4%), on steroids (80.6%), non-ambulatory (67.2%), and with 46.0 % requiring respiratory support. Left ventricular ejection fraction at enrollment was 51.6% (± 11.8%), 113 (22.6%) had an arrhythmia, 8 (1.6%) had an implantable cardioverter defibrillator, 6 (1.2%) had a ventricular assist device, and 4 (0.8%) had a heart transplant. Cardiac medication use was common; 458 (91.6%) on an angiotensin-converting enzyme inhibitor (ACE-I) or equivalent, 346 (69.2%) on a mineralocorticoid receptor antagonist, and 264 (52.8%) on a beta-blocker. Of the 428 males > 10 years at enrollment, 400 (93.5%) were on an ACE-I or equivalent; most commonly lisinopril 10 mg daily.

The ACTION dystrophinopathy registry is the first known cardiac-specific data registry in this population. This prospectively followed cohort will help define cardiac outcomes and disease progression in an era of rapidly evolving cardiac and neuromuscular therapies. This registry data will help inform future cardiac clinical trial design in dystrophinopathy.

Figure 1. ACTION Dystrophinopathy Registry Enrollment.