ACT DMD (Ataluren Confirmatory Trial in Duchenne Muscular Dystrophy): effect of Ataluren on timed function tests (TFT) in nonsense mutation (nm) DMD

N Goemans (Leuven) C Campbell (London)* CM McDonald (Sacramento) T Voit (London) X Luo (South Plainfield) G Elfring (South Plainfield) H Kroger (South Plainfield) P Riebling (South Plainfield) T Ong (South Plainfield) R Spiegel (South Plainfield) SW Peliz (South Plainfield) K Bushby (Newcastle upon Tyne)
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Background: Ataluren is the first drug to treat the underlying cause of nmDMD. Methods: ACT DMD is a Phase 3, randomized, double-blind study. Males 7-16 years with nmDMD and a screening six-minute walk distance (6MWD) ≥150m and <80%-predicted were randomized to ataluren 40 mg/kg/day or placebo for 48 weeks. A pre-specified subgroup included patients with baseline 6MWD 300-400m. A meta-analysis of the overall ACT DMD population and the ‘ambulatory decline phase’ subgroup of the Phase 2b study (those patients meeting ACT DMD entry criteria) was pre-specified in the statistical plan. Results: In the overall ACT DMD population (N=228), changes in TFTs favored ataluren over placebo: 10-meter walk/run, -1.2s (p=0.117); 4-stair climb, -1.8s (p=0.058); 4-stair descend, -1.8s (p=0.012). In the pre-specified subgroup (n=99), these differences increased to -2.1s, -3.6s, and -4.3s, respectively, and were statistically significant (p<0.01) for 4-stair climb and descend. Results are supported by the meta-analysis (N=291), which demonstrated significant differences (p<0.05) in 10-meter walk/run, 4-stair climb, 4-stair descend. Conclusions: TFT results showed a benefit for ataluren in ACT DMD, and a larger treatment effect in the pre-specified baseline 6MWD 300-400m subgroup as well as the pre-specified meta-analysis of ACT DMD and the Phase 2b study decline subgroup.

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D.09 Pharmacological therapy for the prevention and management of cardiomyopathy in Duchenne muscular dystrophy: a systematic review

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Background: Improved respiratory care of Duchenne muscular dystrophy (DMD) patients has unmasked cardiomyopathy as a major source of morbidity and mortality. There is currently no consensus regarding the management of DMD-associated cardiomyopathy (DMD-CM). The objective of this systematic review was to evaluate the efficacy of pharmacological therapies for prevention and management of DMD-CM, and determine the optimal timing to commence these interventions. Methods: A systematic search was conducted in October 2015 and updated in January 2016 using MEDLINE, EMBASE and CINAHL databases and 9 grey literature sources for studies evaluating the use of angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), beta-blockers (BB) or aldosterone antagonists (AA) in DMD patients. References of retrieved records were searched. Quality assessment was conducted using the Downs and Black Quality Assessment Checklist. PRISMA reporting guidelines were used. Results: The 11 included studies were of low methodological quality. However, the use of an ACEi, ARB, BB and AA tended to improve or preserve left ventricular systolic function and delay the progression of cardiomyopathy. Conclusions: While there is evidence supporting the use of heart failure medication in patients with DMD-CM, data regarding these interventions for delaying the onset of DMD-CM and when to initiate therapy is lacking.

D.10 Acute flaccid paralysis in Canadian youth, 1996 to 2014

J Rotondo (Ottawa)* S Desai (Hamilton) M Beaulieu (Ottawa) TF Booth (Winnipeg)
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Background: Acute flaccid paralysis (AFP) is notifiable in Canada with a differential diagnosis that includes a number of conditions. This analysis describes the epidemiology of AFP in Canadian youth less than 15 years old. Methods: Monthly active surveillance for AFP was conducted as part of the Canadian AFP Surveillance System. Results: From 1996 to 2014, 850 cases of AFP were reported, representing an average annual crude incidence rate of 0.77 cases per 100,000 youth less than 15 years old. The mean age of cases was 6.8 years (median 5.9 years). Nine percent had an abnormal neurological history and 53% had an acute respiratory illness within 30 days of onset. Fever occurred in 23% of cases, 96% experienced bilateral weakness, 21% had respiratory muscle involvement, and 26% had cranial nerve involvement. The average hospital length of stay was 13.5 days. The most common diagnoses were Guillain-Barré Syndrome (GBS) or a variant (70%), and transverse myelitis (TM, 14%). At the time of the initial report, 14% had fully recovered. Conclusions: Our AFP surveillance system provides a baseline for AFP and its causes in the Canadian paediatric population. While rare, AFP is associated with