in individuals with DMD, however biomarkers to measure the efficacy of these interventions are needed. The purpose of this study was to develop magnetic resonance imaging (MRI) biomarkers of bone quality in DMD. 32 individuals with DMD (12.9 ± 3.8 years old) and 18 unaffected control participants (11.9 ± 2.8 years old) provided informed consent to participate in the study. The DMD group was 100% corticosteroid treated (63% deflazacort, 15% prednisone, 22% prednisolone), with 23% of participants treated with bisphosphonates. 27% of unaffected control participants and 56% of participants with DMD reported a history of fracture. An MR examination including high resolution imaging and Dixon imaging was performed in the distal femur, and MR images were analyzed to extract trabecular and cortical bone parameters and bone marrow fat fraction. Boys with DMD had significantly worse bone quality than unaffected boys as measured by bone marrow fat fraction (0.85 ± 0.10 vs. 0.77 ± 0.08, p=0.03), cortical thickness (1.6 ± 0.7 vs 2.3 ± 0.3 mm, p=0.0006), trabecular bone volume fraction (0.08 ± 0.03 vs 0.14 ± 0.03, p<0.0001), and finite element analysis-estimated bone stiffness (1.5 ± 0.5 vs 2.4 ± 0.4, p<0.001). Additionally, these variables were significantly correlated with both age and duration of corticosteroid use in individuals with DMD. MRI can noninvasively measure trabecular and cortical bone alterations in DMD at the distal femur, a common fracture site in boys with DMD. These measurements may offer a way to track the effects of bone-targeted interventions for DMD and other neuromuscular disorders.

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399P

MRI assessment of microdystrophin gene therapy in DMD: a five year longitudinal study

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Microdystrophin gene therapy (GT) shows promise for treating Duchenne muscular dystrophy (DMD), but the results of clinical trials have had mixed results. Magnetic resonance imaging (MRI) data collected 6-24 months after delandistrogene moxeparvovec administration showed preservation of muscle quality in 3 boys with DMD, however the persistence and generalizability of this effect is unknown. The objective of this ongoing longitudinal study is to evaluate MRI-determined muscle fat infiltration in microdystrophin GT-treated boys with DMD relative to an untreated natural history cohort. Muscle fat fraction (FF) was measured using chemical shift-based imaging acquired using a 3T MRI scanner in 6 muscles of the upper and lower legs of 3 microdystrophin GT treated boys with DMD and group age-matched steroid-treated boys with DMD. The longitudinal study included 3 delandistrogene moxeparvovec treated boys with DMD (10.0, 10.6, and 12.1 years) and 71 corticosteroid-treated boys with DMD (11.0 ± 0.9 years). For each GT treated subject, an individual comparator cohort was generated comprising all untreated subjects whose age was ± 0.5 years. 5- or 6-years post-GT administration (range 4.8-6.0 years), muscle FF remained low in GT treated boys, with FF less than 0.20 across all muscles measured including the proximal vastus lateralis (VL) and biceps femoris long head (BFLH) muscles. By contrast, the age-matched comparator cohorts had group mean FF of 0.40 to 0.47 in the VL and 0.60 to 0.63 in the BFLH. Boys treated with delandistrogene moxeparvovec were initially reported to have low fat infiltration 6-24 months after GT administration. More than five years after GT administration, these boys continue to show markedly slowed muscle fat accumulation compared with age-matched non-GT treated boys with DMD.

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400P

Longitudinal evaluation of ambulatory function with ankle wearable technology in ambulant DMD

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Assessing the efficacy of investigational drugs in ambulant patients with Duchenne muscular dystrophy (DMD) is challenging due to a lack of objective, reliable, and sensitive outcome measures, especially in patients <4 years old (yo). Using the ActiMyo/Syde wearable device to accurately measure ambulation in the daily life, we recently secured primary endpoint qualification of SV95C (95th centile of stride velocity, the 5% most rapid strides) by the European Medicines Agency, in ambulant DMD from the age of 4. The multicentre ActiLiège-Next study aims to determine the feasibility, robustness & sensitivity of SV95C in children 1-14yo and to gather 3-year longitudinal data from ambulant DMD patients and healthy controls. ActiMyo/Syde sensors are worn on the ankle by patients daily for the first 3 months and then for 1 month daily every 3 months, and by controls for 1 month daily every 6 to 12 months. 116 DMD patients aged 1 to 14 yo (median±SD: 7.0±3.0yo) and 43 controls (8.8±3.7yo) were enrolled, of which 26 patients and 10 controls were younger than 4yo. SV95C reliability at baseline was excellent, with an ICC of 0.97 (patients ≥4yo) and 0.92 (patients <4yo). SV95C was statistically different between DMD and controls, including in patients <4yo. The Spearman correlation with North Star Ambulatory Assessment, 6-Minute Walk Test, 4-stair climbing test and time to rise from floor was 0.72, 0.60, -0.73 and -0.70 respectively (n=76-84; p<0.001). In patients ≥4yo, median SV95C relative change from baseline at 6 and 12 months was 0.3% (n=56) and -8.4% (n=48) respectively, with a marked decline in patients ≥8yo. All available longitudinal data will be shared (6-month and 18-month data for <4yo and 4-14yo patients, respectively). If these promising results and good metric properties are confirmed, SV95C could be the first functional assessment that can be used in all ambulant DMD including those below the age of 4 and enable development and approval of new treatments. 88 ambulant DMD patients aged 4 to 14 years old (median ± SD: 7.9 ± 2.4yo) and 33 age-matched healthy controls (9.8 ± 2.6yo) were enrolled. SV95C reliability at baseline was excellent, with an age-independent intraclass correlation greater than 0.97. The Spearman correlation with North Star Ambulatory Assessment, 6-Minute Walk Test, 4-stair climbing test and time to rise from floor was 0.70, 0.55, -0.74 and -0.70 respectively (n=75-79; p<0.001). Median SV95C relative change from baseline at 6 and 12 months was 0.3% (n=56) and -8.4% (n=48) respectively, with a marked decline in patients ≥8 years old (-3.6% and -11.9% respectively, n=27 and 23). These data confirm the excellent reliability, external validity and responsiveness of SV95C in ambulant DMD patients above 4 years of age. The available 18-month follow-up data will be presented.

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538P

Muscle haptoglobin biomarks cachexia induced by anti-acute myeloid leukemia chemotherapy

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Cancer-associated cachexia is an acquired multifactorial wasting syndrome involving loss of body and lean tissue mass that may also include fat loss. Common hallmarks of cachexia are skeletal muscle wasting and dysfunction, systemic inflammation, dysregulated metabolism, and reduced food intake. Cancer cachexia has been historically associated with tumour-host signalling interactions that drive muscle wasting. However, anti-cancer chemotherapy treatment has gathered traction as a critical cachexia-promoting factor. Patients with haematological cancers such as acute myeloid leukemia (AML) are prone to cachexia, which may be driven by the intensity of initial treatment. Universally, this comprises the '7+3' chemotherapy induction regimen (CIR) involving delivery of the anti-metabolite, cytarabine, over 7-days, concomitant with 3-days of an anthracycline, typically daunorubicin, on days 1-3. Since skeletal muscle mass has emerged as a key prognostic factor for survival in AML, preventing muscle cachexia is critical for improving survival in a disease that already has grim mortality statistics. In this study we sought to identify putative protein biomarkers of muscle cachexia induced by the AML CIR for future targeting. Three-month-old male Balb/C mice underwent 7 days of treatment with either a vehicle (0.9% saline administered daily, VEH) or