Enzyme replacement therapy in juvenile glycogenosis type II: a longitudinal study

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INTRODUCTION and AIM

Glycogenosis type II (GSDII) is a lysosomal storage disorder, resulting in a spectrum of clinical phenotypes. Enzyme replacement therapy (ERT) seems to be effective in the infantile form of the disease, while little is known about its effectiveness in late-onset disease, especially in juvenile patients. The purpose of this retrospective cohort study was to assess the long-term effects of ERT in juvenile GSDII.

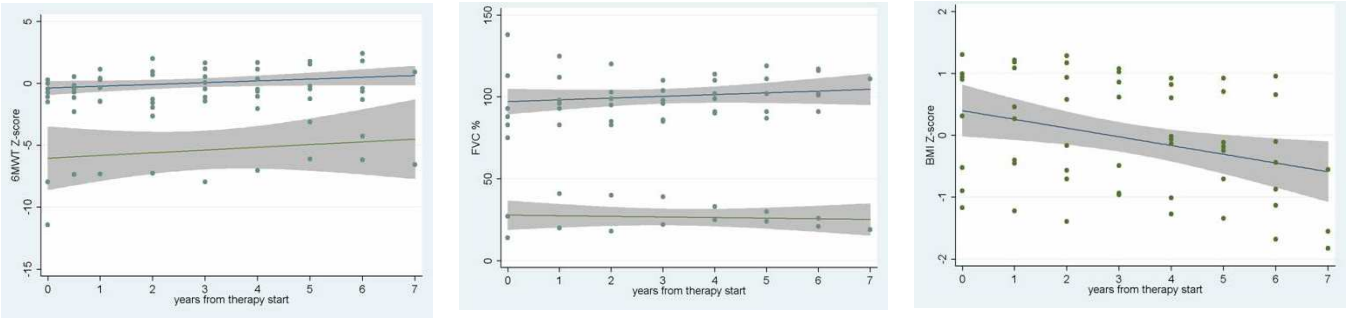
METHODS

Eight Italian juvenile GSDII patients, receiving bi-weekly infusions of 20mg/Kg recombinant human α-glucosidase for at least 72 months, were enrolled (median age at therapy start: 11.8 years). Six-minute walk test (6MWT) and forced vital capacity (FVC), measured in upright position, were chosen as the principal outcome measures. Global motor disability (modified Walton Scale, WS), muscle enzymes levels (CK, LDH, AST, ALT) and body mass index (BMI) were also analyzed both at baseline (therapy start) and annually afterwards. Both 6MWT and BMI measurements were standardized on age and gender using pediatric reference values (Geiger et al, 2007; CDC, 2000).

RESULTS

At baseline, most patients (6/8) did not show muscle function impairment (WS≤2). When the performance at 6MWT was examined, two subgroups were identified, according to disease severity. A slight improvement was clear in both, irrespective of their performance at therapy start, although only in three patients Z-scores were normal at the end of follow up. The same two groups could be identified when the FVC was studied. In both, a similar trend was seen, patients being quite stable in time, irrespective of their baseline pulmonary function.

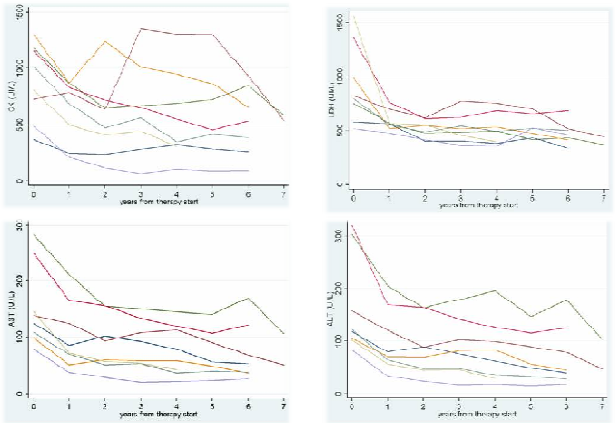
Trend of 6MWT Z-score, FVC, and BMI Z-score from baseline (therapy start) to the end of follow up



An overall decrease in BMI was also observed during follow-up, although at the individual level trends were very different.

Muscle enzymes levels showed a clear decrease after the first year of treatment, while remained stable afterwards.

Trend of muscle enzymes levels from baseline (therapy start) to the end of follow up



CONCLUSION

ERT is effective in stabilizing both motor and lung functions in juvenile patients with GSDII, slowing down significantly the rate of disease progression. Randomized controlled trials are needed to understand whether early treatment allows juvenile patients to reach adulthood with a more beneficial residual muscular function than untreated patients.

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