A Single Center, Retrospective Chart Review Evaluating the Safety and Efficacy of Eteplirsen (EXONDYS 51) in Patients with Duchenne Muscular Dystrophy Post Heart Transplantation

Stephanie Salabarria, BHSc, Norane Shehab, MD, Kara Godwin, APRN, Renata Shih, MD.

INTRODUCTION

Duchenne muscular dystrophy (DMD) is a neuromuscular disorder characterized by progressive muscle wasting due to mutations in the *Dystrophin* gene. Heart problems arise as a result of little to no dystrophin in the heart muscle expressing as irregular heart beats, dilated cardiomyopathy, and heart failure. Imaging shows scar tissue beneath the outer layer and within the middle layer of the heart muscle, fat infiltration, and muscle atrophy. There is some evidence that these heart symptoms can be delayed by early initiation of medications that decrease the structural remodeling of the heart however, a subset of DMD patients continue to have a more rapid progression resulting in heart failure.

Here, we present data on three patients who underwent heart transplantation. In all three patients, eteplirsen infusions were initiated following commercialization in 2017. Eteplirsen (EXONDYS 51) is the first FDA approved DMD treatment for patients who have a confirmed genetic mutation in the dystrophin gene that can be treated by skipping exon 51. In some patients, it helps make a shorter form of the dystrophin protein. There is currently no literature available regarding eteplirsen's safety and efficacy in heart transplant patients.

METHODS

Data collection for primary outcomes:

- Patient demographics (age, race, gender, etc.)
- Medical History, including confirmatory genetic report
- Vital signs
- Cardiac biomarkers (BNP, CRP, EF), endomyocardial biopsy results
- Hematological biomarkers (WBC, Hb, Platelet)
- Hepatic biomarkers (AST, ALT)
- Renal biomarkers (Creatinine)

Secondary outcomes:

- Pulmonary function testing (FVC, MIP, MEP)
- Upper and lower extremity testing (Brooks scale, Vignos scale)

ANALYSIS

The average for all three patients at each time point was graphed for relevant laboratory values (BNP, CRP, EF, WBC, Hb, Platelet).

Forced Vital Capacity (FVC), the total amount of air exhaled during a forced breath, was graphed for each patient.

CONCLUSION

In all three patients eteplirsen proved to be safe to use post-heart transplant. Additionally, all patients displayed a slower predicted rate of decline when compared to age matched DMD natural history controls.

FUTURE DIRECTIONS

In the future, we'd like to analyze the heart muscle biopsy samples from each patient's heart prior to and after the initiation of eteplirsen to see if any exon skipping is occurring within cardiac muscle.

Eteplirsen is safe to use post-heart transplantation and provides the same clinical benefit to transplanted exon 51-skip amenable patients as it does to all non-transplanted patients.

SCAN ME

https://raredisease.powellcenter.med.ufl.edu

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RESULTS

Primary Outcomes:

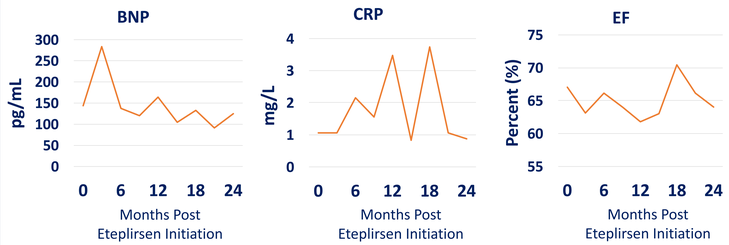
- All three patients had stable kidney and liver safety biomarkers throughout the duration of eteplirsen treatment.

Patient 01 started weekly eteplirsen infusions 183 weeks post heart transplant. He displayed no signs of infusion reactions or inflammation and no episodes of significant heart transplant rejection or complications to date (6 years after heart transplant).

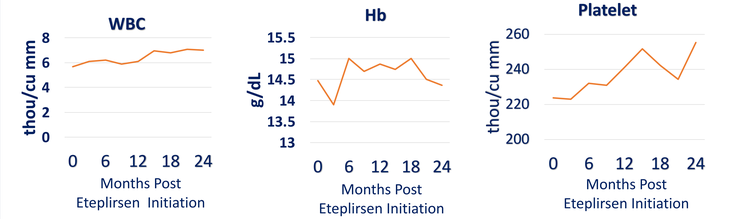
Patient 02 started weekly eteplirsen infusions 88 weeks post heart transplant. He displayed no signs of infusion reactions or inflammation and no episodes of significant heart transplant rejection or complications to date (5 years after heart transplant).

Patient 03 started weekly eteplirsen infusions 295 weeks post heart transplant. He had no episodes of significant heart transplant rejection. Unlike the others, Patient 03 developed a common long-term complication called coronary artery vasculopathy and antibodies to his new heart 6 years post transplant. Sirolimus and rituximab were added to his regimen and he is 9 years post transplant with no further complications.

CARDIAC & RENAL MARKERS

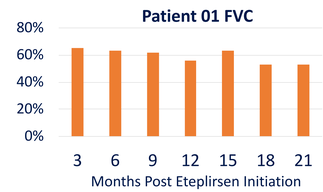


HEMATOLOGICAL MARKERS

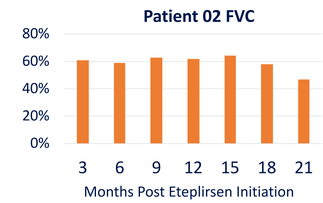


Secondary Outcomes:

Patient 01 maintained his Brooke and Vignos score. His FVC was stable during the first two years (62%-63%) with a slight decline the third year (53%).



Patient 02 maintained his Brooke score. He had a slight decline on the Vignos scale, which may have been related to non-adherence to his daily stretches and worsening contractures. His FVC was stable during the first two years (64%-63%) with a slight decline in his third year (58%) .



Patient 03 maintained his Brooke score. His Vignos scores are not documented for the first year of infusions; however, he was non-ambulatory and was able to bear weight with assistive transfers post-transplant. His FVC is stable (79%-85).