

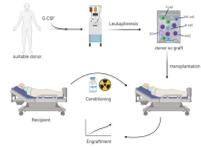
Outcomes of Allogeneic HSCT in Individuals with MPS II (Hunter Syndrome)

Leigh Anne Weisenfeld¹, Kristin Clinard¹, Nitya Yerraguntla¹, Tisha Ulak¹, Lindsay Torrice¹, Claudia Greenberg², Kim Stephens¹, Elizabeth R Jalazo¹, Joseph Muenzer¹

¹University of North Carolina Chapel Hill, Chapel Hill, NC, USA; ²University of North Carolina Greensboro, Greensboro, NC

OVERVIEW

- Mucopolysaccharidosis II (MPS II, Hunter syndrome) is an X-linked lysosomal disorder caused by deficiency of iduronate-2-sulfatase (IDS) enzyme which causes the accumulation of glycosaminoglycans (GAGs)
- Variants in the *IDS* gene cause enzyme deficiency
- Disease spectrum ranges from non-neuronopathic (progressive physical disease, minimal cognitive impact) to neuronopathic (severe form, progressive physical disease and neurologic impairment, premature death)
- Hematopoietic stem cell transplantation (HSCT) is one treatment available to individuals diagnosed with MPS II
- HSCT has proven successful for patients with neuronopathic MPS I (Hurler syndrome); although not a cure, it works to preserve cognitive function if performed early in disease course and alleviates need for weekly ERT.



CURRENT TREATMENTS

Enzyme Replacement Therapy (ERT) involves weekly intravenous infusions of idursulfase. ERT is not a cure, but can slow the progression of physical disease

- Currently available ERT does not cross the blood brain barrier into the central nervous system (CNS)
- Limitations include need for lifelong weekly infusions and lack of impact on brain/neurologic disease

Allogeneic hematopoietic stem cell transplant (HSCT) is a one-time procedure in which patients receive healthy stem cells (bone marrow or cord blood) from a donor that can produce the missing enzyme

- HSCT improves neurologic outcomes in severe MPS I (Hurler Syndrome) if performed early, but the outcomes for MPS II are unclear
- HSCT carries significant risk

CNS-penetrating ERT for MPS II are in clinical trials but are not yet approved for commercial use in the United States

SCOPE & PURPOSE

To date, there has been no systematic evaluation of the prevalence, safety, and long-term efficacy of HSCT in MPS II. Due to the significant risks and limited evidence of efficacy, HSCT has not been regularly recommended as a therapeutic intervention for individuals with MPS II. Its use in this patient population remains limited. This study aims to further evaluate real-world outcomes of transplant in the MPS II population. It is important to understand the factors that families consider when selecting a treatment method as it can inform future recommendations for HSCT in this population. As study recruitment is ongoing, these results focus primarily on reported complications following HSCT in MPS II as well as preliminary review of adaptive behavior outcomes in transplanted individuals.

METHODS

Caregiver Questionnaire

- Gathers in-depth information regarding the HSCT procedure and patient status prior to and following transplant

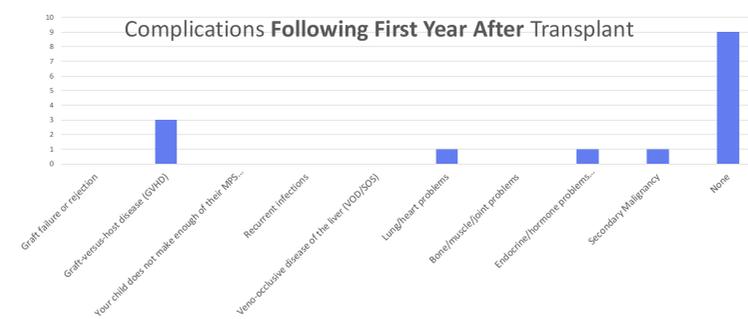
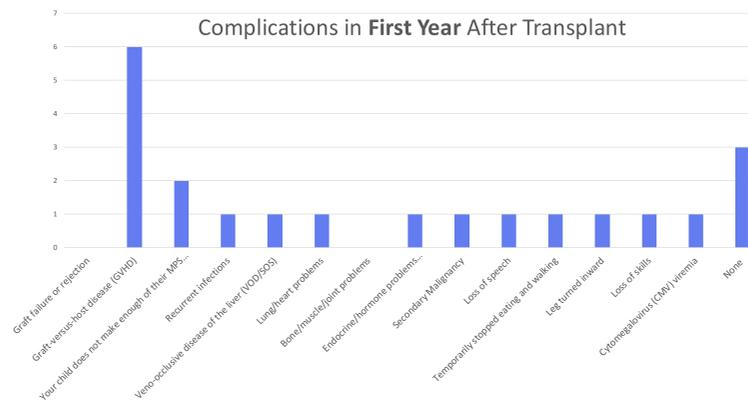
Semi-Structured Interview

- Conducted to explore family experiences with HSCT
- Questions focus on topics such as:
 - Factors considered when choosing transplant
 - Expectations for outcomes after transplant
 - Perceived advantages and disadvantages of HSCT in MPS II
 - Thoughts on child's development following transplant
 - Impact of choosing HSCT on family and child

Vineland Adaptive Behavior Scales (VABS-3)

- Individually administered measure of adaptive behavior
- Adaptive behavior is the performance of daily activities required for personal and social sufficiency (i.e., skills for everyday life)
- Vineland interviews were conducted with the primary caregiver of MPS II transplanted individuals

COMPLICATIONS AFTER HSCT IN MPS II



FUTURE DIRECTIONS

This study aims to investigate family decision-making processes and clinical outcomes for patients with MPS II who have undergone HSCT. Some limitations in our study may include:

- Small population of transplanted patients, resulting in data that cannot be generalized for all patients.
- Current data is only inclusive of US-based individuals

Additional data from the semi-structured interviews has not yet been analyzed, but it is anticipated to provide insight into caregiver attitudes toward the decision to proceed with HSCT

Deeper analysis of the nuances of patient outcomes and caregiver attitudes can help inform future families facing similar decisions.

VINELAND-3 RESULTS

Age at First Transplant	Adaptive Behavior Composite Score
3 months	59
3 months	90*
3 months	73
4 months	36
18 months	20
21 months	68
22 months	81
23 months	20
37 months	31
58 months	40

The Vineland-3 ABC score has a mean of 100, standard deviation of 15. Scores between 85-115 are considered average

*The preliminary Vineland-3 (VABS-3) results indicate that **only one individual out of 10 surveyed is functioning in the average range.** That individual was diagnosed with MPS II at birth and was transplanted at 3 months of age.

CONCLUSIONS

The purpose of this study is to evaluate outcomes of HSCT in individuals with MPS II as well as family satisfaction with the choice of treatment. In the future, data from this study can be utilized by families to aid in making an informed decision regarding treatment choice for an individual with MPS II.

- Preliminary VABS-3 data indicates that outcomes of individuals who have undergone HSCT include:
 - Varying results depending on patient
 - Earlier age of transplant does not guarantee average adaptive skill levels
 - The majority of transplanted patients are not functioning in the average range for adaptive skills
- While many patients experienced complications within the first year after transplant, these complications were not typically long-lasting
- Additionally, early data from the interviews indicates that caregivers who opted for HSCT may *not* have chosen the same if current alternatives were an option at the time (various clinical trials as well as treatments approved in other countries)
- While compilation of data from the semi-structured interviews is ongoing, early trends show that motives for choosing HSCT include:
 - Avoiding the burden of weekly infusions
 - Hoping for skill preservation and cognitive growth
 - Lack of alternative treatments that cross the blood-brain barrier and address CNS involvement

ACKNOWLEDGEMENTS



PROJECT ALIVE

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