Costs of Episodes of Care for Allogeneic Transplant for the Treatment of Cerebral Adrenoleukodystrophy in the U.S.

Clark Paramore[1], Andrew Dietz[1], Luke Boulanger[2]

[1]bluebird bio, Inc., Cambridge, MA, USA; [2]IBM Watson Health, Cambridge, MA USA

PND48

INTRODUCTION

- Cerebral adrenoleukodystrophy (CALD) is a rare, X-linked, metabolic disease characterized by rapidly progressive inflammatory cerebral demyelination leading to progressive, irreversible loss of neurologic function and death, if left untreated.[1]
  - The incidence of adrenoleukodystrophy among newborn males is 1 in 21,000 and the cerebral form (i.e. CALD) develops in approximately 40% of affected boys.[2]
  - Patients with CALD experience critical deficits across multiple neurologic domains within a short period after onset of clinical symptoms.[3]
- Allogeneic hematopoietic stem cell transplantation (allo-HSCT) has been shown to have a beneficial effect on clinical indices of disease and long-term survival, especially if performed at the early stages of cerebral involvement.[4-7]
- However, allo-HSCT in CALD has significant associated risks, such as transplant-related mortality, graft failure or rejection, and graft-versus-host disease (GVHD).
  - Reported rates of grades II to IV acute GVHD and chronic GVHD in patients with CALD range from 18% to 39% and 7% to 31.6%, respectively.[8-16]
- Given complete lack of published data on the costs of care for allo-HSCT specific to CALD, here we analyze the one-year costs per allo-HSCT episode in the treatment of CALD. The one-year timeframe was chosen to better ensure capture of sequelae of allo-HSCT (e.g. GVHD) that can occur after the initial transplant hospitalization.

METHODS

Data source

- This study utilized patient-level, de-identified U.S. administrative claims data from the IBM MarketScan Commercial and Medicaid Multi-State databases for the period from January 1, 2012 to December 31, 2018.
- These databases include medical encounter and outpatient pharmacy data covering roughly 43 million enrollees per year linked by a unique blinded identifier across the continuum of care.
- The MarketScan Research Databases are de-identified, fully compliant with the Health Insurance Portability and Accountability Act of 1996 and are representative of the U.S. managed-care population.

Patient Identification

- Initial search included manual review, by a stem cell transplant physician, of patient-level claims history for any patient with evidence of ≥ 1 medical claim with a specific CALD diagnosis code (ICD-10-CM E71.520: became available as a code in the U.S. starting October 1, 2015). The reviewer raised concerns about 1) ability to confirm receipt of an allo-HSCT, and 2) potential to not identify some relevant cases.
- The refined (and final) approach required evidence of ≥ 1 medical claim for allo-HSCT (based on relevant set of ICD-9-CM procedure codes) AND ≥ 1 medical claim with a specific CALD diagnosis code OR ≥ 1 medical claim of either peroxisomal disorder (ICD-9-CM 277.86/ICD-10-CM E71.50) or glucocorticoid deficiency (ICD-9-CM 255.41/ICD-10-CM E27.1).

Study Variables and Outcomes

- An index date was defined as the date of the initial allo-HSCT during the claims period.
- Episode costs (i.e. amounts reimbursed by insurer) included all costs incurred by the patient in the one-year period after the index date (including the initial transplant stay costs).
- Occurrence of GVHD based on relevant ICD-9-CM or ICD-10-CM diagnosis codes.
- Systemic steroid use included prescription claims for either prednisone or methylprednisolone.

RESULTS

Sample Sizes and Baseline Characteristics

- There were 14 episodes of allo-HSCT for CALD identified during the study period.
- At transplant, median age was 8 years, mean age 10 years, minimum age 2 years (13/14 patients <16 years old).
- Available follow-up time in the claims database for the identified allo-HSCT episodes ranged from 6.3 to 56.7 months.

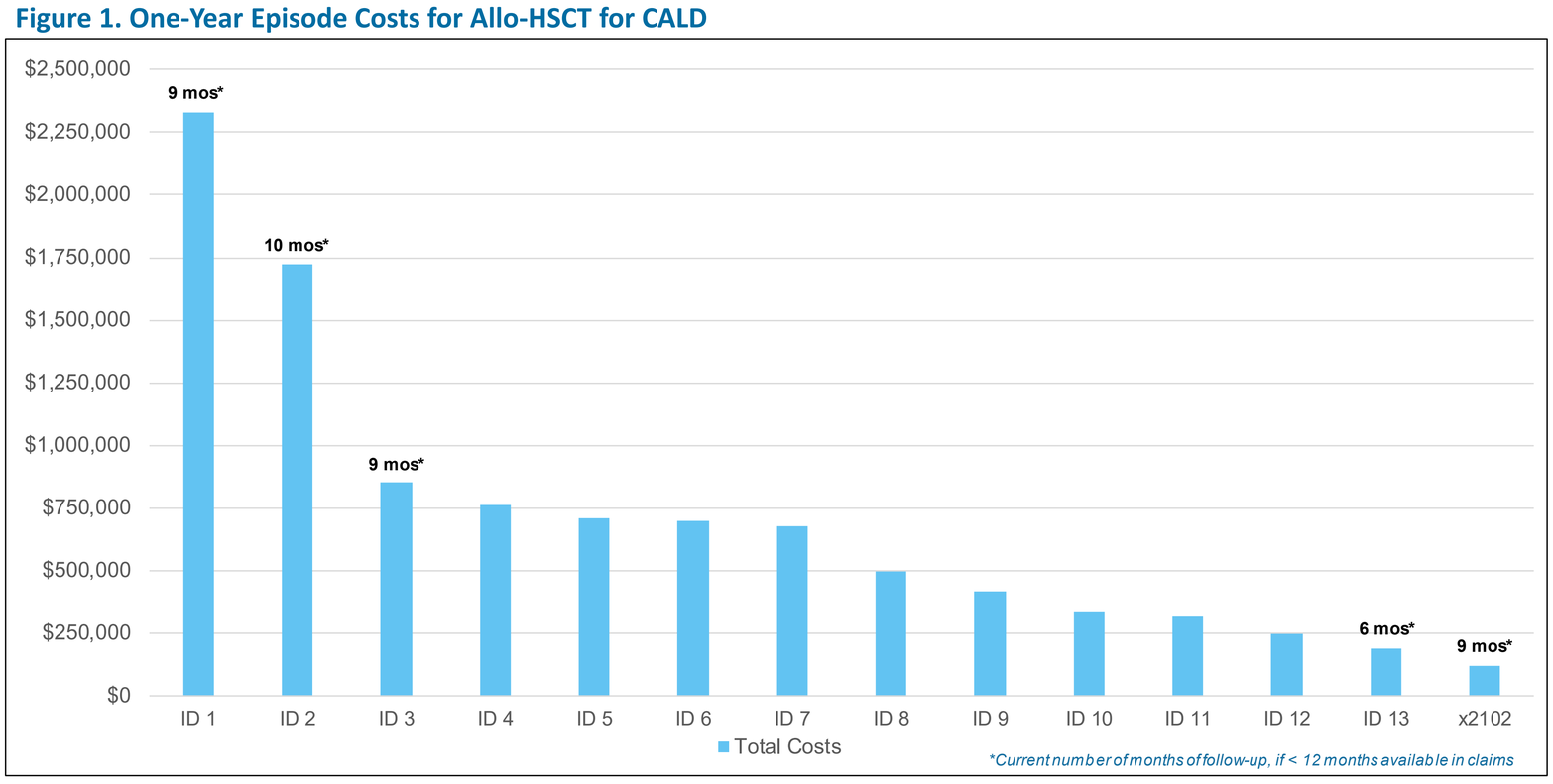
Outcomes

- GVHD was identified in 85.7% (12/14) episodes [see Table 1]. There were:
  - 2 episodes with acute GVHD specified
  - 2 episodes with chronic GVHD specified
  - 4 episodes with both acute & chronic GVHD
  - 4 episodes with unspecified GVHD type
- Systemic steroids were utilized in 7/11 episodes (prescription claims data files were not available for 3 patients) [See Table 1].
- Median total episode costs were $588,233 (mean $704,812; range $118,912 - $2,327,603) [see Figure 1].

Table 1. GVHD and Systemic Steroids Following Allo-HSCT for CALD

ID Number	GVHD?	Use of Systemic Steroids?
1	Acute & Chronic	Yes
2	Chronic	No prescription claims available
3	Acute	Yes
4	None	No prescription claims available
5	Unspecified GVHD type	No
6	Unspecified GVHD type	No
7	None	No prescription claims available
8	Acute & Chronic	Yes
9	Acute & Chronic	Yes
10	Acute	No
11	Unspecified GVHD type	Yes
12	Acute & Chronic	Yes
13	Chronic	Yes
14	Unspecified GVHD type	No

Figure 1. One-Year Episode Costs for Allo-HSCT for CALD



- The initial allo-HSCT inpatient stay (i.e. index event) accounted for a mean 60.3% of total episode costs, ranging from 13.1% to 89.6%.
- Many rehospitalizations during the one-year follow-up period included diagnoses of GVHD, with some of these rehospitalization stays costing in excess of $300,000.

STUDY LIMITATIONS

- The algorithm utilized in this study to identify cases of CALD allo-HSCT has not been clinically validated and additional research is warranted.
- Some patients may have received an allo-HSCT prior to the study period (i.e. before January 1, 2012).
- This study was limited to only those individuals in the U.S. with commercial health insurance, Medicare coverage, or Medicaid coverage; therefore, the results may not be generalizable to patients with other insurance or without health insurance coverage.
- The misclassification of patients is possible due to coding error or gaps such as under-coding because some claims do not affect reimbursement.

CONCLUSIONS

- Total episode costs for allo-HSCT for the treatment of CALD are substantial, and there is wide variation in costs depending upon the need for rehospitalization (e.g. additional transplant, management of GVHD).
- When considering the economic impact of allo-HSCT for CALD, it is important to factor in subsequent medical care and healthcare resource use beyond the initial allo-HSCT hospital stay.

REFERENCES

1. Moser HW. Adrenoleukodystrophy: phenotype, genetics, pathogenesis and therapy. *Brain* 1997;120(Pt 8):1485-508.
2. Bezman L, Moser AB, Raymond GV, et al. Adrenoleukodystrophy: incidence, new mutation rate, and results of extended family screening. *Ann Neurol* 2001;49:512-7.
3. Suzuki Y, Takemoto Y, Shimozawa N, et al. Natural history of X-linked adrenoleukodystrophy in Japan. *Brain Dev* 2005;27:353-7.
4. Mahmood A, Raymond GV, Dubey P, et al. Survival analysis of haematopoietic cell transplantation for childhood cerebral X-linked adrenoleukodystrophy: a comparison study. *Lancet Neurol* 2007;6(8):687-2.
5. Miller WP, Rothman SM, Nascene D, et al. Outcomes after allogeneic hematopoietic cell transplantation for childhood cerebral adrenoleukodystrophy: the largest single-institution cohort report. *Blood* 2011;118(7):1971-8.
6. Peters C, Charnas LR, Tan Y, et al. Cerebral X-linked adrenoleukodystrophy: the international hematopoietic cell transplantation experience from 1982 to 1999. *Blood* 2004;104(3):881-8.
7. Raymond GV, Aubourg P, Paker A, et al. Survival and functional outcomes in boys with cerebral adrenoleukodystrophy with and without hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant* 2019;25:538-48.
8. Moser HW, Mahmood A, Raymond GV. X-linked adrenoleukodystrophy. *Nature Clin Pract Neurol* 2007;3(3):140-51.
9. Raymond GV, Aubourg P, Paker A, et al. Survival and functional outcomes in boys with cerebral adrenoleukodystrophy with and without hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant* 2019;25:538-48.
10. Miller WP, Rothman SM, Nascene D, et al. Outcomes after allogeneic hematopoietic cell transplantation for childhood cerebral adrenoleukodystrophy: the largest single-institution cohort report. *Blood* 2011;118(7):1971-8.
11. Kuhl JS, Kupper J, Baque H, et al. Potential risks to stable long-term outcome of allogeneic hematopoietic stem cell transplantation for children with cerebral X-linked adrenoleukodystrophy. *JAMA Netw Open* 2018;1(3):e180769.
12. Chiesa R. An observational study of patients with cerebral adrenoleukodystrophy (CALD) treated with allogeneic hematopoietic stem cell transplant. *Society for the Study of Inborn Errors of Metabolism 2018 Annual Meeting.* Abstract O-010.
13. Mitchell R, Nivison-Smith I, Anazodo A, et al. Outcomes of haematopoietic stem cell transplantation for inherited metabolic disorders: a report from the Australian and New Zealand Children's Haematology Oncology Group and the Australasian Bone Marrow Transplant Recipient Registry. *Pediatr Transplant* 2013;17(6):582-8.
14. Beam D, Poe MD, Provenzale JM, et al. Outcomes of unrelated umbilical cord blood transplantation for X-linked adrenoleukodystrophy. *Biol Blood Marrow Transplant* 2007;13:665-74.
15. Tsai SB, Liu H, Shore T, et al. Frequency and risk factors associated with cord graft failure after transplant with single-unit umbilical cord cells supplemented by haploidentical cells with reduced-intensity conditioning. *Biol Blood Marrow Transplant* 2016;22:1065-72.
16. Reinfjell T, Tremolada M, Zeltzer LK. A review of demographic, medical, and treatment variables associated with health-related quality of life (HRQOL) in survivors of hematopoietic stem cell (HSCT) and bone marrow transplantation (BMT) during childhood. *Front Psychol* 2018;8:253.
17. Eissa HM, Lu L, Baassiri M, et al. Chronic disease burden and frailty in survivors of childhood HSCT: a report from the St. Jude Lifetime Cohort Study. *Blood Adv* 2017;1:2243-6.

DISCLOSURES

CP and AD are employees of bluebird bio and own stock in the company. LB is an employee of IBM Watson and conducted analyses under contract between IBM Watson and bluebird bio.

ACKNOWLEDGEMENTS

This study was sponsored by bluebird bio. IBM Watson supported bluebird bio and the authors in the conduct of this research and analysis of the data.

Presented as Poster at Virtual ISPOR 2020, May 18-20

This study is sponsored by bluebird bio