Cost-Equalization Approach to Estimate the Minimum Duration of Effect of Cell and Gene Therapies to Demonstrate Cost Savings to Payers: A Methodological Approach Using Late-Onset Pompe Disease

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Objectives

- While the upfront costs of cell and gene therapies can be high, they have the potential to replace costly standard of care treatments that often require lifelong management.
- Durability of effect of cell and gene therapies is a clinical value attribute and a driver of cost-offsets in chronic diseases where the standard of care is costly.
- In this case study of late-onset Pompe disease (LOPD), we demonstrate cost-equalization analysis, a health economic modeling method that can be applied to the evaluation of cell and gene therapies to estimate the minimum duration of effect to yield cost-savings.

Background to Pompe disease

- LOPD was chosen for this study because it is representative of other indications with new, and potentially expensive, gene therapies that may displace expensive standard of care treatments in market.
- Pompe disease is a rare, genetic autosomal recessive glycogen storage disorder and affects around one in 40,000 people.[1]
- It is caused by over 300 different mutations in the gene encoding lysosomal acid alpha-glucosidase (GAA), resulting in progressive accumulation and storage of glycogen within cells.[1]
- LOPD is associated with partial insufficiency of GAA and has a chronic course, characterized by progressive myopathy, which can progress to loss of mobility and respiratory insufficiency requiring assisted ventilation.[2]
- The primary treatment for LOPD is enzyme replacement therapy (ERT) with alglucosidase alfa or avalglucosidase alfa. However, ERT is not curative, and patients have been reported to return to their pre-treatment decline after 2–3 years of treatment.[1]
- Furthermore, ERT can be time-consuming to administer, requires high-volume infusions and is associated with adverse infusion reactions.[3]

Methods

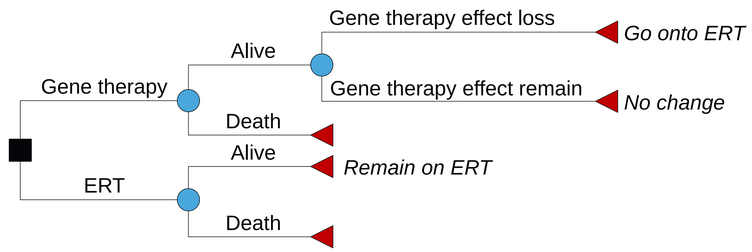
Modeling approach

- The advantage of modeling is the capability to tie together predicted patient survival and time on treatment to estimate the time of cost-equalization.
- Individual simulation was developed in TreeAge Pro® to evaluate the total costs associated with gene therapy versus ERT alone (**Figure 1**).
  - Population: patients with LOPD
  - Time horizon: patient lifetime
  - Perspective: US payer
  - Costs modeled: drug associated costs (drug and administration costs).
- The model calculated likelihood of cost-savings with gene therapy over a range of gene therapy durability of effect thresholds.
  - 10,000 model iterations were run per gene therapy durability of effect scenario
  - The likelihood of cost-savings is equal to the proportion of iterations in which total costs associated with gene therapy are less than ERT only
  - Time of cost-equalization is when there is at least a 50% likelihood of gene therapy being cost-saving.

Model assumptions

- Following gene therapy loss of effect, patients were placed on ERT, and accrued costs associated with ERT.
- Gene therapy was assumed to have a similar treatment effect on survival and safety as ERT.
- Survival was predicted using a published Cox regression model based on the International Pompe Association/Erasmus MC Pompe Survey (**Figure 2**).
  - Baseline population characteristics fed into the survival model were: age 49 years, 52% male, 31% requiring ambulatory support, and 27% on ventilation.[4]
- The cost of gene therapy was $2,450,000, based on one-time gene therapy costs in other conditions (**Table 1**).[5]
- The cost of ERT was $637,000 per year, equal to the average cost of alglucosidase alfa or avalglucosidase alfa.[6]
- The ERT maintenance dose was 20 mg/kg every 2 weeks for a patient weighing 70 kg and no dose increase over time.
- No ERT discontinuation was assumed, as ERT discontinuation in LOPD is rare.[7]

Figure 1. Model diagram



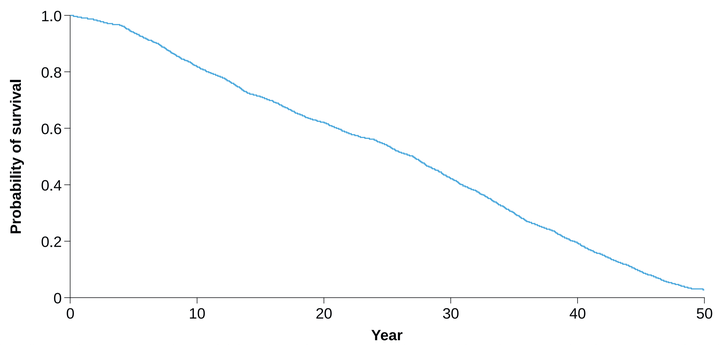
ERT, enzyme replacement therapy.
The model had two health states: alive and death. Simulated patients in the gene therapy arm were assumed to resume ERT upon loss of effect.

Table 1. Cost inputs

Costs	Input	Source
Gene therapy one-time costs	$2,450,000	Average list price of gene therapies in other indications from NAVLIN 2023[5]
ERT annual drug cost	$637,000	Average list price of alglucosidase alfa or avalglucosidase alfa from NAVLIN 2023[6]
ERT administration costs		
Hospital outpatient administrations	$75	HCPCS Code 96365
Proportion of administrations at home	79%	Assumptions from Kanters et al[4]

ERT, enzyme replacement therapy; HCPCS, Healthcare Common Procedure Coding System.

Figure 2. Model predicted survival

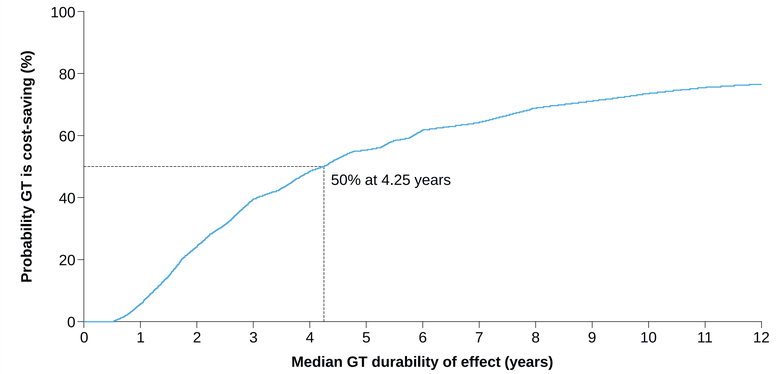


Survival predicted using Cox regression model time-dependent Cox regression model based on International Pompe Association/Erasmus MC Pompe Survey.[4]

Results

- The model predicted that a patient with LOPD on ERT alone will accrue $10.6 million in drug associated costs over their lifetime.
- The minimum duration of effect of gene therapy to result in equal lifetime drug associated costs as ERT was calculated as 4.25 years (**Figure 3**).

Figure 3. Likelihood gene therapy is cost-saving versus durability of effect



GT, gene therapy.

Conclusions

- Cost-equalization analysis is a simple and data-inexpensive modeling method that can be applied to cell and gene therapies to predict the minimum durability of effect to be economically advantageous to standard of care.
- Information from this analysis can be used in commercial and pricing development, and payer negotiations.

References

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Disclosures

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