Comparing Predicted vs Real-World Spending in the United States for Single-Administration Cell and Gene Therapies

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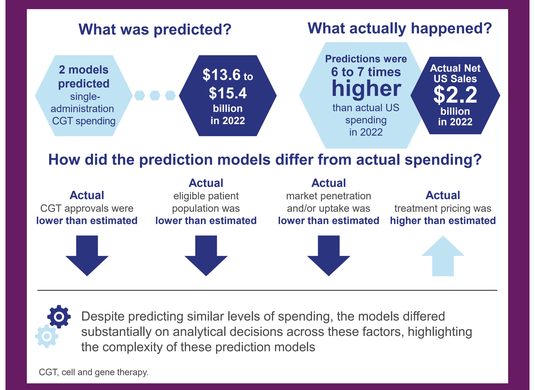
Key Findings

Predicted spending for single-administration CGTs was 6 to 7 times higher than actual spending. Main factors impacting overestimation were fewer/delayed approvals, smaller eligible patient populations, lower market penetration and/or slower uptake, and discrepancies in treatment price



CGT, cell and gene therapy.

Background

- Cell and gene therapies (CGTs) are emerging therapies that offer the potential for significant treatment benefits with a single administration
- Prices for single-administration CGTs reflect benefits over an extended number of years, and 2024 United States (US) list prices range from close to $400,000 to over $4 million per treatment course[1]
- These list prices have been notably higher than the list price per dose of traditional chronic therapies, leading to “sticker shock” reactions and affordability concerns for the US healthcare system[2-6]
- Researchers have estimated substantial US national spending for single-administration CGTs through 2030 and beyond using analytical prediction models[7-9]
- However, no published analyses have assessed whether these predictions have aligned with real-world spending on CGTs to date

Objective

- This study identified published predictions of US spending across CGTs and compared them with real-world spending to date

Methods

- All single-administration CGTs approved by the US Food and Drug Administration (FDA) as of December 2022 were identified (**Table 1**)
- A targeted literature review (TLR) was conducted between May 2023 and July 2023 to identify analytical predictions of US national spending across all single-administration CGTs
  - The TLR was limited to published research, conference abstracts, posters, reports/white papers, press releases, and trade press
  - Structured searches were supplemented by additional hand searching and gray literature review
- Annual US net sales data were gathered from public financial records from pharmaceutical manufacturers for all approved single-administration CGTs
  - For years in which net sales data were not disclosed for a given therapy, net sales were estimated based on best-available data

Results

- There were 11 single-administration CGTs approved by the US FDA as of December 2022

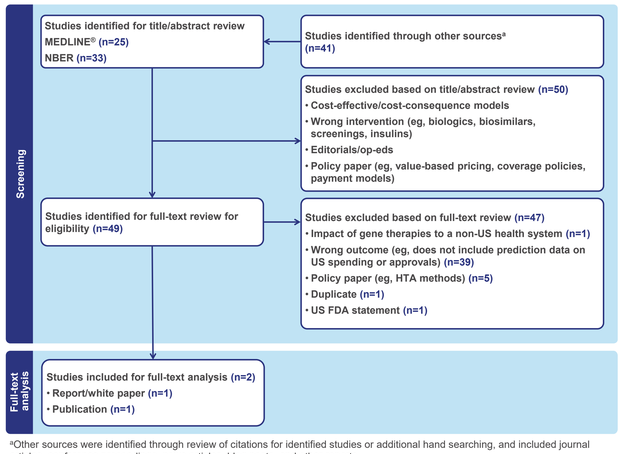
Table 1 *Single-administration CGTs approved by the US FDA as of December 2022*

Brand name	Generic name	First BLA approval date
ABECMA	Idecabtagene vicleucel[a,c]	March 2021
BREYANZI	Lisocabtagene maraleucel[a,c]	February 2021
CARVYKTI	Ciltacabtagene autoleucel[a,c]	February 2022
HEMGENIX	Etranacogene dezaparvovec-drlb[b,d]	November 2022
KYMRIAH	Tisagenlecleucel[a,c]	August 2017
LUXTURNA	Voretigene neparvovec-rzyl[b,d]	December 2017
SKYSONA	Elivaldogene autotemcel[b,d]	September 2022
TECARTUS	Brexucabtagene autoleucel[a,c]	July 2020
YESCARTA	Axicabtagene ciloleucel[a,c]	October 2017
ZOLGENSMA	Onasemnogene abeparvovec[b,d]	May 2019
ZYNTEGLO	Betibeglogene autotemcel[b,d]	August 2022

[a]CGT indicated for oncology; [b]CGT indicated for non-oncology rare disease; [c]Cell therapy; [d]Gene therapy.
BLA, Biologics License Application; CGT, cell and gene therapy; US FDA, US Food and Drug Administration.

- Of the 99 publications identified for title and abstract review, 2 studies were included for full-text analysis (**Figure 1**)

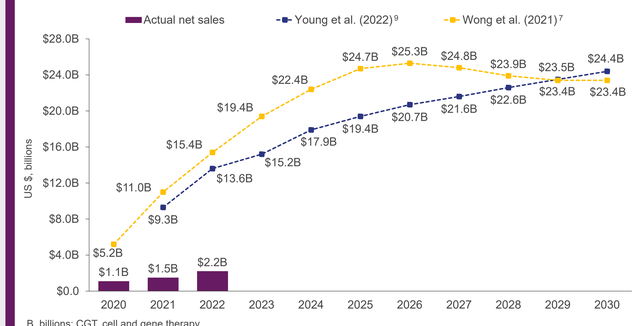
Figure 1 *PRISMA diagram for the TLR*



[a]Other sources were identified through review of citations for identified studies or additional hand searching, and included journal articles, conference proceedings, news articles, blog posts, and other reports.
HTA, health technology assessment; NBER, National Bureau of Economic Research; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; TLR, targeted literature review; US FDA, US Food and Drug Administration.

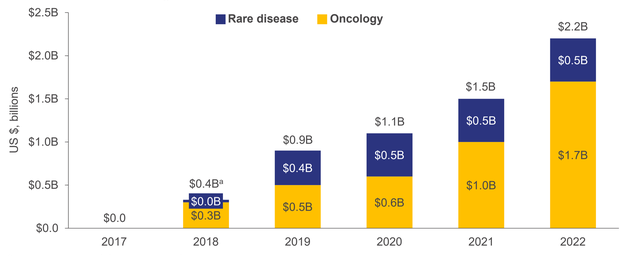
- Prediction models estimated similar spending amounts: between $13.6 billion and $15.4 billion in 2022, and between $23.4 billion and $24.4 billion annually by 2030, for all single-administration CGTs (**Figure 2**)[7,9]
- US net sales for the 11 therapies approved by the US FDA as of December in 2022 alone were $2.2 billion, equating to approximately 15% of predicted levels
  - Real-world net sales in 2022 also fell below predicted confidence intervals and ranges presented in the studies
- Differences between predictions and real-world spending were primarily driven by oncology therapies, where net sales of $1.7 billion in 2022 were significantly lower than predicted (range, $8.0 billion to $12.8 billion in 2022; **Figure 3**)[7,9]
- Given these differences, prediction model methods were reviewed, and 4 key factors were identified that may have contributed to an overestimation of real-world spending:
  1) Fewer/delayed CGT approvals per year
  2) Smaller eligible patient populations
  3) Lower market penetration and uptake
  4) Discrepancies in treatment price

Figure 2 *Predicted vs real-world annual US spending for single-administration CGTs*[7,9]



B, billions; CGT, cell and gene therapy.

Figure 3 *Real-world US net sales for single-administration CGTs by rare disease and oncology treatment categories*[7,9]



[a]The discrepancy in total value is due to rounding.
B, billions; CGT, cell and gene therapy.

1. Treatment approvals and timing

- Although details on approval predictions are limited in the identified studies, the estimated number of approvals for single-administration CGTs through 2022 (13-13.6 disease areas or treatments with approvals) was slightly higher than the real-world 11 CGTs approved by the US FDA across 10 disease areas

2. Treatment eligibility

- CGT approvals span multiple diseases, and not everyone with a given disease may be included in the FDA label
- Especially for rare diseases, estimates on prevalence and incidence may be limited or have a wide range of uncertainty
- This challenge is highlighted by the substantial differences in treatment-eligible population estimates across the prediction models

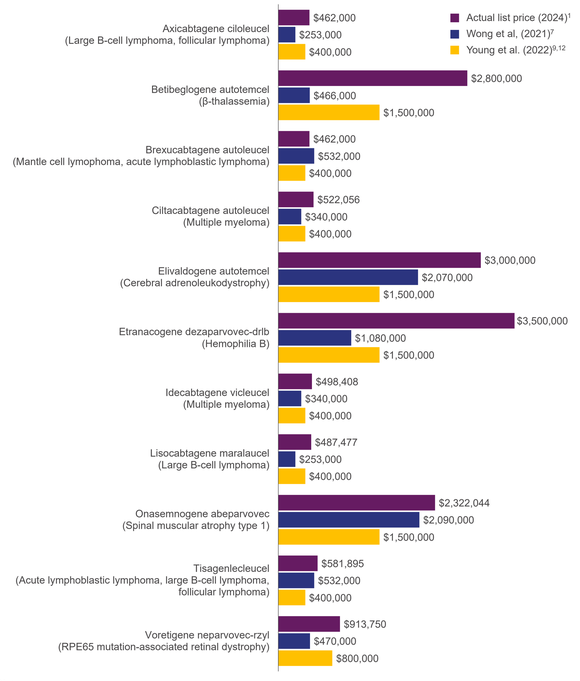
3. Market penetration and uptake

- Market penetration and uptake assumptions across the prediction models varied considerably
- For Wong et al. (2021)[7], peak market penetration and time to peak market penetration was 10% and 12 months for oncology, 40% and 6 months for rare disease, and 1% and 60 months for general conditions, respectively[7]
- For Young et al. (2022)[9], peak market penetration and time to peak market penetration was 75% and 2 years for oncology (modeling restricted to incident patients), 74% (average, range 0-90%) and 4 years (average, range 1-7 years) for rare disease, and 44% (average, range 1-90%) and 5 years (average, range 3-7 years) for general conditions, respectively[9]
- For the 3 CGTs approved in 2022 to treat rare diseases, low numbers for treated patients from approval through 2023 (betibeglogene autotemcel, 20; elivaldogene autotemcel, 6; etranacogene dezaparvovec-drlb, “a handful”) suggest that true market penetration and uptake in rare disease indications may be lower than predicted[10,11]

4. Treatment price

- For the 6 cell therapies approved by the US FDA as of December 2022, list prices assumed in prediction models were generally comparable to 2024 US list prices set by the manufacturers (**Figure 4**)[1,7,9,12]
- For the 5 gene therapies approved by the US FDA as of December 2022, 2024 list prices were generally higher than assumed in the prediction models

Figure 4 *2024 list prices[1,a] for approved single-administration CGTs compared with price assumptions in prediction models[9,12,b,c]*



Notes:
[a]All 2024 list prices are derived from the Merative Micromedex® RED BOOK®.[1]
[b]For each treatment, comparable prices were derived from those reported in Wong et al. (2021)[7] based on estimated quality-adjusted life year gains in each modeled treatment area.
[c]For each treatment, comparable prices were derived from those reported in Young et al. (2022)[9,12] based on analogue list prices for approved CGTs.
CGT, cell and gene therapy; RPE65, retinal pigment epithelium-specific 65.

- Lack of public reporting on US net prices makes it difficult to determine how modeled prices may have differed from real-world net prices

Conclusions

- Prediction models are important tools to estimate the potential budget impact of therapies on future healthcare spending
- This analysis highlights model assumptions that were most likely to result in substantial differences between predicted and actual spending for CGTs and the challenges with forecasting national spending across CGTs spanning a range of diseases

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NK, **ACK**, and **KLG** are employees of Sarepta Therapeutics, Inc., and may own stock and/or stock options in the company. **JJ**, **CS**, **LT**, and **MC** are employed by Medicus Economics, which received consulting fees from Sarepta Therapeutics, Inc.

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