Finding a Way for Patients to Access Gene Therapies

HPR175

Lasota K[1], Soltysiak E[1], DeOcampo GA[2], Junghahn M[3], Stanisic S[4], Vargas M[3], Casciano R[5]
[1]Certara Evidence and Access, Kraków, Poland, [2]Certara Evidence and Access, Manila, Philippines, [3]Certara, Princeton, NJ, USA, [4]Certara Evidence and Access, Milan, MI, Italy, [5]Certara, Mamaroneck, NY, USA

CERTARA

Risk-sharing agreements provide a solution to manage the uncertainty around long-term treatment outcomes and the cost-effectiveness of gene therapies. Outcome-based agreements offer the opportunity to link payment for treatment to the benefits received by the patient

Objectives

Gene therapies (GTx) show high potential in many rare diseases, often in treating patients with the highest unmet medical need.
From 2012 to June 2024, 12 single-administration non-oncological GTx were approved in the US and Europe, and the number of new therapies is expected to increase (58 ongoing phase 3 clinical trials listed on clinicaltrials.gov with expected completion in the next five years).
This research aimed to investigate risk-sharing agreements (RSA) used to manage GTx costs and increase patient access.

Methods

We conducted a targeted search to identify publicly available information on implemented RSAs for non-oncological single-administration GTx in the UK, Canada, Australia, and the US.
In June 2024, we searched health technology assessment (HTA) reports, and reimbursement decisions for 12 available therapies as well as conducted free web searches (e.g., manufacturer websites, ministry of health reports)

Results

- RSA were identified for nine of 12 single-administration GTx: onasemnogene abeparvovec (n=4), voretigene neparvovec (n=4), etranacogene dezaparvovec (n=2), betibeglogene autotemcel (n=2), atidarsagene autotemcel (n=1), eladocagene exuparvovec (n=1), exagamglogene autotemcel (n=1), lovotibeglogene autotemcel (n=1), valoctocogene roxaparvovec (n=1) (Table 1). No information on RSAs was identified for alipogene tiparvovec, delandistrogene moxeparvovec-rokl and elivaldogene autotemcel.
- Seven RSAs were identified in the US, five in the UK, three in Canada, and two in Australia (Table 1). Among them RSAs for onasemnogene abeparvovec and voretigene neparvovec were identified in all four countries.
- Published details about implemented and/or planned RSAs for available GTx are limited and vary across the countries.
- Identified RSAs include financial-based (n=7, in Canada and UK), outcome-based (n=8, in the US and Australia), and mixed schemes (n=1, in Australia).
- **Financial-based RSAs (UK and Canada):**
  - UK: patient access scheme with simple confidential discount[1-6]
  - Canada: price reduction is listed as one of the reimbursement conditions for all evaluated GTx; additionally, in their reports, the Canadian Drug Agency (CDA, ex- CADTH) encourages jurisdictions to consider establishing product listing agreements that mitigate the long-term financial risk to public payers[7-9]
- **Outcome-based RSAs (US and Australia)** (Table 2)**:**
  - These RSAs are linked to the treatment outcomes in patients treated in clinical practice such as reduced mortality or improved clinically relevant outcomes (e.g. achieved performance on motor milestones in Spinal Muscular Atrophy (SMA); absence of need to return to treatment with prophylactic factor IX in hemophilia), to reduced drug cost[10-22]
  - The time horizon for the outcomes assessment varies depending on GTx and indication: from 30-60 days (e.g., voretigene neparvovec) to five years (e.g., onasemnogene abeparvovec).[10-22]
  - In case of treatment failure, outcome-based RSAs include provisions for additional rebates or payback. The payback to payers can reach up to 100% of GTx cost.[10-22]

Table 1. Risk Sharing Agreements Identified in TLR (June 2024)

	UK	US	Canada	Australia
Atidarsagene autotemcel	💰	⊕*		
Betibeglogene autotemcel	✓#	⊕		
Eladocagene exuparvovec	💰			
Etranacogene dezaparvovec		⊕	💰	
Exagamglogene autotemcel		✓^		
Lovotibeglogene autotemcel		⊕		
Onasemnogene abeparvovec	💰	⊕	💰	💰/⊕
Valoctocogene roxaparvovec-rvox		⊕		
Voretigene neparvovec	💰	⊕	💰	⊕

💰 - financial-based; ⊕ - outcome-based; ✓ - no details
*information about the plan to establish outcome-based and value-based agreement , but no information about RSA details and whether it was implemented
#not recommended by NICE; however, information available on potential commercial arrangement, which would have been applied if the technology had been recommended.
^RSA details not available.

Conclusions

GTx may prevent further progression of severe genetic diseases and potentially may have “curative” effect. Seeking to address the uncertainties around the long-term treatment effect, cost-effectiveness and to manage financial impacts related to GTx high cost, local decision-makers implement RSAs:

- In Australia and in the US, the payers aim at implementing schemes which ensure that treatment costs borne by payers correspond to the expected health outcome for a particular patient.
- The US Centers for Medicare and Medicaid Services are developing a Cell and Gene Therapy Access Model which will negotiate outcomes-based agreements with gene therapy manufacturers on behalf of state Medicaid agencies to improve access to gene therapies for their patients; the program is prioritizing access to sickle cell disease gene therapies exagamglogene autotemcel and lovotibeglogene autotemcel and initial details of negotiated agreements are expected in late 2024.
- In Canada and in the UK, the payers mainly use financial-based schemes built on simple price discounts. However, the recent NICE recommendation on etranacogene dezaparvovec (July 2024)[23,] is the first example of an outcome-based payment model in England, indicating potential NICE shift towards outcome-based RSAs

Abbreviations: CADTH, Canadian Agency for Drugs and Technologies in Health; CDA, Canada's Drug Agency; FST, Full-field light sensitivity threshold; GTx, gene therapies; MSAG, Medical & Scientific Advisory Group; NICE, National Institute for Health and Care Excellence; PBAC, Pharmaceutical Benefits Advisory Committee; RSA, risk-sharing agreements; SMA, Spinal Muscular Atrophy; UK, United Kingdom; US, United States;

Table 2. Summary of identified outcome-based agreements for GTx in Australia and the US

Drug	Indication	Agreement description
Atidarsagene autotemcel	Metachromatic leukodystrophy	Manufacturer has stated its intention to work with both private and public payers to establish outcomes and value-based agreements for GTx, but remains unclear whether such agreements have been enacted.[10]
Betibeglogene autotemcel	β-thalassemia	Guaranteed **payback to** payer of **up to 80% of GTx cost** if patients do not achieve or maintain **transfusion independence** for **two years post treatment.**[11-12]
Etranacogene dezaparvovec	Severe hemophilia B	**Price discounts** if patient is required to **return to prophylactic factor IX treatment** within **3.5 to four years** of treatment.[13,14]
Exagamglogene autotemcel	β-thalassemia Sickle cell disease	**Flexible payment arrangements**; RSA details have not been identified[15]
Lovotibeglogene autotemcel	Sickle cell disease	**Potential rebates** if **hospitalization due to vaso-occlusive crisis** occurs within **three years** post treatment [15, 16]
Onasemnogene abeparvovec	SMA	Pay-over-time options and patient program to support affordability and access. **Rebates and state payments** are dependent on **performance over five years**. [17, 18]
Valoctocogene roxaparvovec-rvox	Severe hemophilia A	**Potential payback of up to 100% of GTx cost** for patients who do not achieve specified performance metrics **within four years of treatment**; RSA details are confidential.[19]
Voretigene neparvovec	Retinal dystrophy	**Rebates** based on **short-term (30–90 days) and long-term (30 months) improvement of outcomes on Full-field light sensitivity threshold (FST) testing** when compared with individual patient baseline (pre-GTx treatment)[20]
Drug	**Indication**	**Agreement description**
Onasemnogene abeparvovec	SMA	**During 1st assessment in 2021**: outcomes-based RSA with a **rebate** for GTx cost over at least **five years post-listing**, in case of **patient death, invasive permanent ventilation**; and the need for **subsequent treatment with nusinersen or risdiplam**. PBAC recommended **total cap on expenditures** to manage the total financial impact. **At resubmission in the 2023:** the previously agreed outcomes-based RSA was recommended for implementation in the extended population; it included a **full refund** if patients **die within two years**, or a **refund equivalent to the difference in cost between onasemnogene and risdiplam or nusinersen for years two-five**.[20, 21]
Voretigene neparvovec	Retinal dystrophy	**Significantly reduced GTx price (or no payment)** in case the **improvement on FST testing is below the threshold of 0.3 log10 (cd.s/m2) 60 days** after administration.[22]

Want to learn more?
<< Scan Here

References: 1. NICE 2022. Atidarsagene autotemcel. Guidance; 2. NICE 2022. Betibeglogene autotemcel. Draft guidance; 3. NICE 2023. Eladocagene exuparvovec. Guidance; 4. NICE 2021. Onasemnogene abeparvovec. Guidance; 5. NICE 2023. Onasemnogene abeparvovec. Guidance; 6. NICE 2019. Voretigene neparvovec. Guidance; 7. CADTH 2024. Etranacogene dezaparvovec; 8. CADTH 2021. Onasemnogene abeparvovec; 9. CADTH 2020. Voretigene neparvovec; 10. Orchard Therapeutics 2024. Orchard Therapeutics Outlines U.S. Launch Plans for Lenmeldy™ (atidarsagene autotemcel), the Only Approved Therapy for Children with Early-onset Metachromatic Leukodystrophy; 11. Bluebirdbio 2022. bluebird bio Announces U.S. Commercial Infrastructure to Enable Patient Access to ZYNTEGLO®, the First and Only FDA-Approved Gene Therapy for People with Beta-Thalassemia Who Require Regular Red Blood Cell Transfusions; 12. Managed Healthcare 2023. Value-based Outcomes Contracts Can Address High-Cost Gene Therapies; 13. Managed Healthcare 2023. Manufacturers Adopt ‘No Cure, No Pay’ Pricing for Hemophilia Gene Therapy; 14. Pharmaceutical technology 2023. Are haemophilia gene therapies truly “one and done”?; 15. Navlin Daily 2024. BCBS Will Cover Lyfgenia and Casgevy in 2024; 16. Managed Healthcare 2024. Are Value-Based Contracts the Answer to Ultra-High-Priced Gene Therapies?; 17. Novartis 2019. AveXis Announces Innovative Zolgensma® Gene Therapy Access Programs for US Payers and Families; 18. wbur 2020. Mass. Outlines Deal For A $2 Million Drug: Pay Only If It Works; 19. Managed Healthcare 2023. Manufacturers Adopt ‘No Cure, No Pay’ Pricing for Hemophilia Gene Therapy; 20. Pharmacy Times 2020. Payment Models for Pricey Transformative Pharmaceuticals; 21. PBAC 2021. Onasemnogene abeparvovec. Public Summary Document. PBAC meeting; 21. PBAC 2023. Onasemnogene abeparvovec. Public Summary Document. PBAC meeting; 22. MSAG 2020. Voretigene neparvovec. Public Summary Document. 23. NICE 2024. Etranacogene dezaparvovec. Guidance.