EE830

Exploring Long-Term Durability Assumptions In Cost-Effectiveness Models Of Cell And Gene Therapies

A Study Of 39 Health Technology Assessments

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Rare genetic diseases pose a global challenge, with a high burden and few effective, long-term therapies. Cell and Gene Therapies (CGTs) offer a potentially durable solution, but immature data from small trials complicate Health Technology Assessments (HTAs). Long-term durability is a key driver of CGT value. An analysis of current HTA assumptions provides valuable benchmarks for assessing the long-term value of CGTs.

7 HTA bodies from the UK, France, Germany, Italy, Spain, Canada, and USA

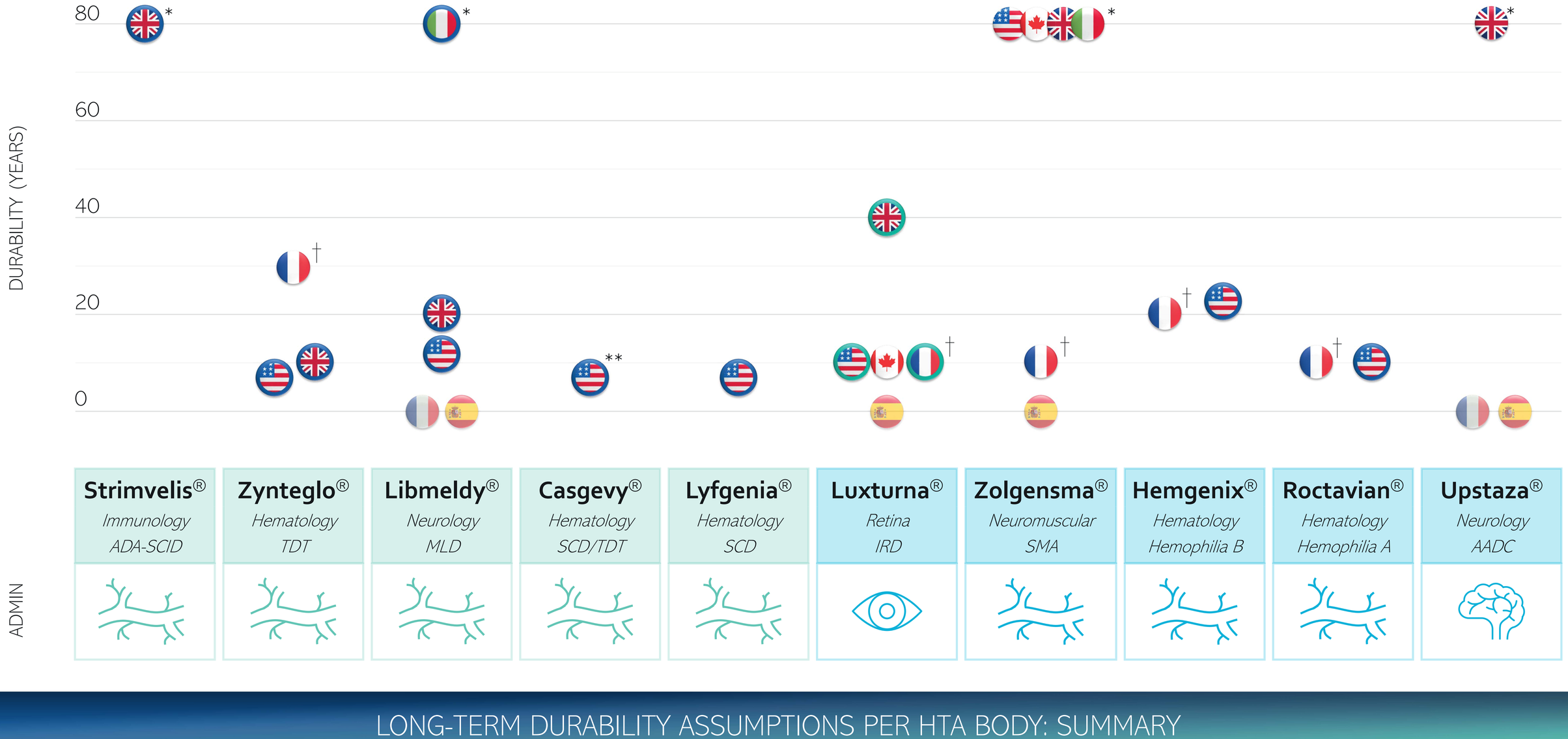
10 Strimvelis®, Zynteglo®, Libmeldy®, Casgevy®, Lyfgenia®, Luxturna®, Zolgensma®, Hemgenix®, Roctavian®, Upstaza®

39 Health Technology Assessments reviewed

LONG-TERM DURABILITY ASSUMPTIONS OF RARE DISEASE CELL & GENE THERAPY IN HTAs

LEGEND

- *Ex vivo* delivery
- *In vivo* delivery
- Base-case durability assumed by HTA
- Durability highly uncertain
- Treatment waning applied
- Cure proportion applied
- Systemic infusion
- Intraputaminal infusion
- Intravitreal injection



LONG-TERM DURABILITY ASSUMPTIONS PER HTA BODY: SUMMARY

HTA	AIFA	NICE	CADTH	ICER	HAS§	G-BA	AEMPS
Number of assessments	4	6	2	9**	7	7	4
Mean durability assumed (yrs)	80* (n=2)	52 (n=6)	45 (n=2)	18 (n=8)	16 (n=5)	‡	‡

Notable variability exists in the long-term durability assumptions of rare disease CGTs across HTAs. Yet, among 23 HTAs, the mean durability assumed was around 35 years. Further analysis is needed to unearth the key factors influencing these assumptions.

*Lifetime durability - 80 years used as maximum to calculate means; **Assessment of Casgevy in SCD and TDT considered as two indications; † End of model horizon; ‡ Germany & Spain did not perform formal cost-effectiveness analysis on any of the rare CGTs; § HAS issued economic analyses for two HTAs after data collection for this abstract. This data is included in the poster.

Note: Strimvelis® (autologous CD34+ enriched cell fraction), Zynteglo® (betibeglogene autotemcel), Libmeldy®/Lenmeldy™ (atidarsagene autotemcel), Casgevy® (exagamglogene autotemcel), Lyfgenia® (lovotibeglogene autotemcel), Luxturna® (voretigene neparvovec), Zolgensma® (onasemnogene abeparvovec), Hemgenix® (etranacogene dezaparvovec), Roctavian® (valoctocogene roxaparvovec), Upstaza® (Eladocagene exuparvovec); **Abbreviations**: AADC: Aromatic L-Amino Acid Decarboxylase, ADA-SCID: Adenosine Deaminase Deficiency Severe Combined Immunodeficiency, AEMPS: Agencia Española de Medicamentos y Productos Sanitarios, AIFA: Agenzia Italiana del Farmaco, CADTH: Canadian Agency for Drugs and Technologies in Health, G-BA: Gemeinsamer bundesausschuss, HAS: Haute Autorité de Santé, ICER: Institute for Clinical and Economic Review, IRD: inherited retinal dystrophy, MLD: metachromatic leukodystrophy, NICE: National Institute for Health and Care Excellence, SCD: sickle cell disease, SMA: spinal muscular atrophy, TDT: Transfusion-dependent beta-thalassemia; **References**: **1.** NICE. Strimvelis for treating adenosine deaminase deficiency–severe combined immunodeficiency: Highly specialised technology guidance. London: NICE; 2018 Feb 07. **2.** NICE. Betibeglogene autotemcel for treating transfusion-dependent beta-thalassaemia: Appraisal consultation document. London: NICE; 2021 Feb. **3.** ICER. Betibeglogene Autotemcel for Beta Thalassemia: Effectiveness and Value: Final evidence report. Boston: ICER; 2022 Jul 19. **4.** Avis d'efficience. Zynteglo Bluebird bio). Paris: HAS. 2020 Feb 11. **5.** Benefit assessment of medicinal products with new active ingredients according to section 35a SGB V: Betibeglogene Autotemcel. G-BA. 2020 Dec 3. **6.** NICE. Atidarsagene autotemcel for treating metachromatic leukodystrophy: Highly specialised technology guidance. London: NICE; 2023 Mar 28. **7.** ICER. Atidarsagene Autotemcel for Metachromatic Leukodystrophy: Final Evidence report. Boston: ICER; 2023 Oct 30. **8.** Transparency Committee Summary. Autologous CD34+ cell enriched population that contains haematopoietic stem and progenitor cells (HSPC) transduced ex vivo using a lentiviral vector encoding the human arylsulfatase A (ARSA) gene LIBMELDY, 2-10 x 106 cells/mL dispersion for infusion. Paris: HAS. 2021 Apr 21. **9.** Bewertung von Arzneimitteln für seltene Leiden nach § 35a Absatz 1 Satz 11 i. V. m. Kapitel 5 § 12 Nr. 1 Satz 2 VerfO Wirkstoff: Atidarsagene autotemcel/OTL-200. 2021 Aug 2. **10.** Scientific Report. Libmeldy (Atidarsagene autotemcel): AIFA. 2022 May 20. **11.** Informe de Posicionamiento Terapéutico de Atidarsagene autotemcel (Libmeldy) en de la leucodistrofia metacromatica: AEMPS. 2023 Sep 01. **12-14.** ICER. Gene therapies for sickle cell disease: Evidence report. Boston: ICER; 2023 Jul 13. **15.** NICE. Voretigene neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations: Highly specialised technology guidance. London: NICE; 2019 Oct 9. **16.** ICER. Voretigene Neparvovec for Biallelic RPE65-Mediated Retinal Disease: Effectiveness and Value. Final evidence report. Boston: ICER; 2018 Feb 14. **17.** Pharmacoeconomic Report for voretigene neparvovec (Luxturna). Ottawa (ON): CADTH; 2021 Jan. **18.** Transparency Committee Summary. Luxturna (voretigene neparvovec). Paris: HAS. 2019 Apr. **19.** Benefit assessment of medicinal products with new active ingredients according to section 35a SGB V: Voretigene neparvovec. G-BA. 2019 Oct 17. **20.** Informe de Posicionamiento Terapéutico de Voretigene neparvovec (Luxturna) para distrofia retiniana asociada a la mutacion RPE65 bialelica: AEMPS. 2021 Jun 25. **21.** NICE. Onasemnogene abeparvovec for treating spinal muscular atrophy: Highly specialised technology guidance. London: NICE; 2021 Jul 7. **22.** ICER. Spinraza® and Zolgensma® for Spinal Muscular Atrophy: Effectiveness and Value: Evidence report. Boston: ICER; 2019 May 24. **23.** Pharmacoeconomic Report for Onasemnogene abeparvovec (Zolgensma). Ottawa (ON): CADTH; 2021 May. **24.** Avis economique. Zolgensma (Onasemnogene abeparvovec). Paris: HAS. 2020 Dec 15. **25.** Bewertung von Arzneimitteln für seltene Leiden nach § 35a Absatz 1 Satz 11 i. V. m. Kapitel 5 § 12 Nr. 1 Satz 2 VerfO Wirkstoff: Onasemnogene abeparvovec. 2020 Oct 1. **26.** Technical Report. Zolgensma (Onasemnogene abeparvovec): AIFA. 2021 Jul 12. **27.** Informe de Posicionamiento Terapéutico de Onasemnogene abeparvovec (Zolgensma®) en Atrofia Muscular Espinal: AEMPS. 2022 Feb 01. **28 & 31.** ICER. Gene Therapy for Hemophilia B and An Update on Gene Therapy for Hemophilia A: Effectiveness and Value: Final evidence report. Boston: ICER; 2022 Dec 22. **29.** Advice on medications. Etranacogene dezaparvovec. Paris: HAS. 2023 Aug 30. **30.** Bewertung von Arzneimitteln für seltene Leiden nach § 35a Absatz 1 Satz 11 i. V. m. Kapitel 5 § 12 Nr. 1 Satz 2 VerfO Wirkstoff: Etranacogen Dezaparvovec. 2023 Aug 1. **32.** Advice on medications. Valoctocogene roxaparvovec. Paris: HAS. 2023 Sep 06. **33.** Benefit assessment of medicinal products with new active ingredients according to section 35a SGB V: valoctocogen roxaparvovec /BMN 270 (ROCTAVIAN). G-BA. 2022 Dec 15. **34.** VALUTAZIONE DELL'INNOVATIVITA. Roctavian (valoctocogen roxaparvovec): AIFA. 2023 Feb. **35.** NICE. Eladocagene exuparvovec for treating aromatic L-amino acid decarboxylase deficiency: Highly specialised technology guidance. London: NICE; 2023 Apr 19. **36.** Opinion on medicinal products. Eladocagene exuparvovec. Paris: HAS. 2022 Dec 7. **37.** Benefit assessment of medicinal products with new active ingredients according to section 35a SGB V: Eladocagene exuparvovec AADC deficiency, >18 months. G-BA. 2023 Feb 02. **38.** VALUTAZIONE DELL'INNOVATIVITA. Upstaza (Eladocagene exuparvovec): AIFA. 2023 May. **39.** Informe de Posicionamiento Terapéutico de eladocagen exuparvovec (Upstaza®) en pacientes con defciencia de L-aminoacido descarboxilasa con fenotipo grave: AEMPS. 2023 Aug 10.

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