Gene Therapy: Is Europe Ready to Value and Reimburse the Next Medical Frontier?

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Outline of Presentation

- How do we currently value therapies in Europe?
- What value do gene therapies offer?
- Are there any important characteristics of gene therapy?
- How can Europe assess and pay for gene therapy?

Common approaches used to assess value in Europe

Calculation of the quality-adjusted life years (QALYs) gained

- The QALY is used as a global measure of health gain[1]
- Cost per QALY is compared with a formal or informal 'threshold' of willingness-to-pay for QALY[2]
- QALYs are used in the UK[1] and several other Northern European countries[3], and in Australia[4], New Zealand[5] and Canada[6]

Global ratings[3]

- An assessment of '(clinical) added value' is made
  - This is then used in price negotiations
  - Used in France and Germany

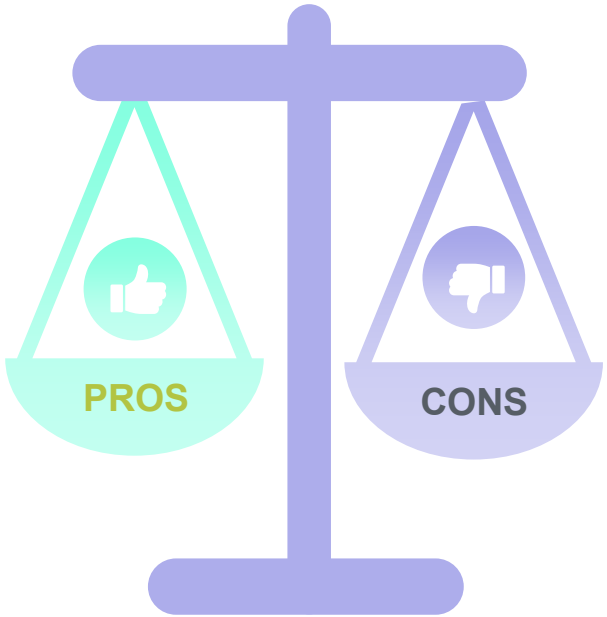
QALY, quality-adjusted life year.

1. Whitehead SJ and Ali S. *Br Med Bull*. 2010;96:5-21; 2. Cameron D, *et al. Glob. Health Action*. 2018;11:1447828; 3. Drummond M, *et al. Pharmacoeconomics*. 2014;32(5):509-20; 4. Taylor C and Jan S. *Aust Prescr*. 2017;40:76-8; 5. PHARMAC (2020). Estimating Health Benefits. Available at: https://www.pharmac.govt.nz/assets/_generated_pdfs/6-estimating-health-benefits-2062.pdf. Last accessed: November 2020; 6. Lipscomb J, *et al. Value Health*. 2009; 12:S18-S26.

Pros and Cons of the Global Scoring Approach[1]

Flexible

Can potentially consider all aspects of value



Lacking in transparency

Does not consider the opportunity cost under the budget constraint

Does not normally consider sub-groups (useful for targeting therapy)

1. Speaker opinion

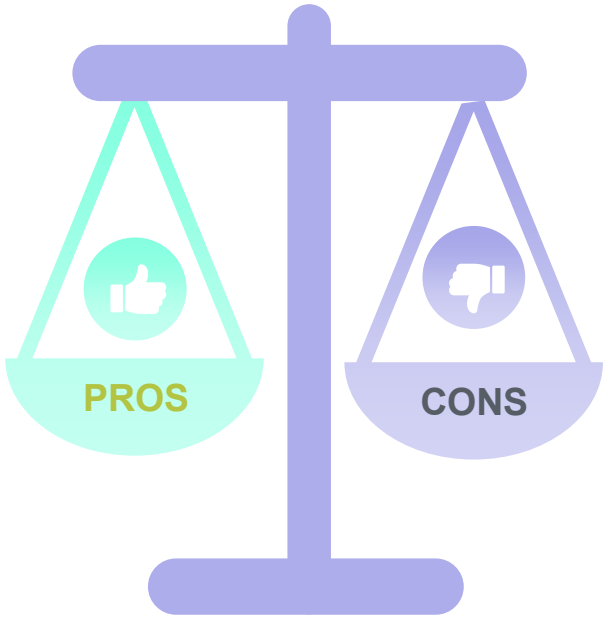
Pros and Cons of the Cost per QALY Approach[1]

Relatively transparent

Encourages consistency in decision-making

Can consider the opportunity cost under the budget constraint

Can consider sub-groups and target therapy



May not reflect all aspects of value

Relatively inflexible

Discriminates against the elderly and disabled when life-extending therapies are being assessed

- QALY, Quality-adjusted life year.
- 1. Speaker opinion.

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A Health Economics Approach to US Value Assessment Frameworks—Summary and Recommendations of the ISPOR Special Task Force Report [7]

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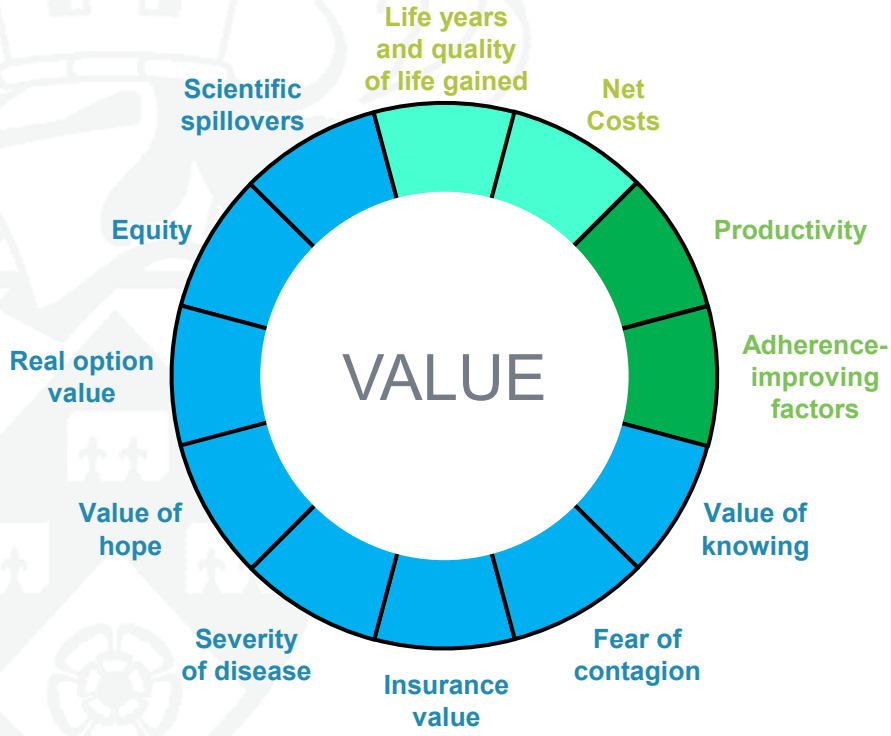
ABSTRACT

Potential Elements of Value to Consider[1]



- Core elements of value
- Common but inconsistently used elements of value
- Potential novel elements of value

- Figure adapted from Lakdawalla DN, *et al. Value Health* 2018;21:131–139.

1. Drummond M, *et al. Value Health.* 2019;22(6):661–668.

Estimates of QALYS gained from the literature for a selection of cell and gene therapies

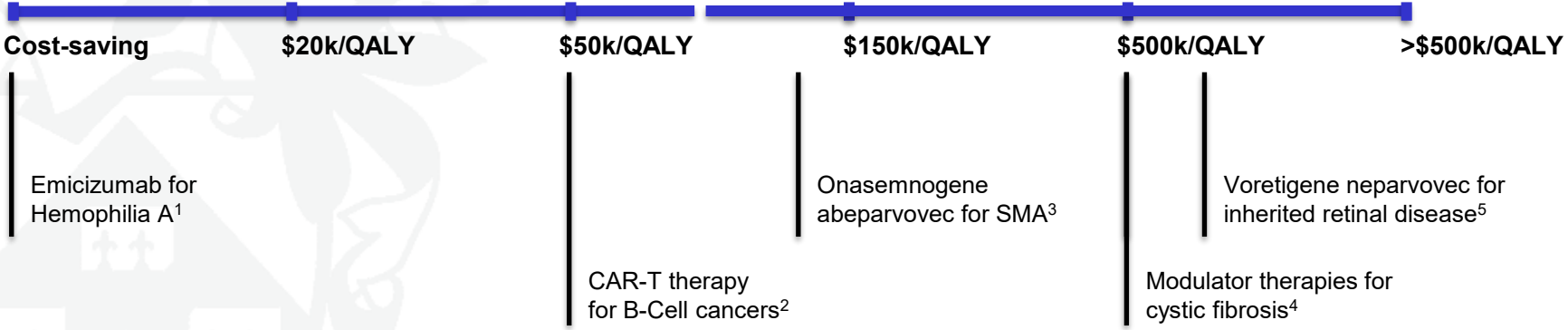
Treatment name	Indication	Incremental QALY gain estimate
Onasemnogene abeparvovec (Zolgensma®)	Spinal muscular atrophy	11.77[1]
GSK2696273 (Strimvelis®)	Adenosine deaminase deficiency	11.7[2]
Experimental gene therapy for hemophilia A	Hemophilia A	8.33[3]
Tisagenlecleucel (Kymriah®)	Refractory B-cell acute lymphoblastic leukemia	8.18[4]
Axicabtagene ciloleucel (Yescarta®)	Refractory B-cell acute lymphoblastic leukemia	3.19[5]
Voretigene neparvovec (Luxturna®)	RPE65-mediated inherited retinal disease	1.3[6]
ChondroCelect®	Knee cartilage lesions	1.28[7]
Talimogene laherparepvec (Imlygic®)	Melanoma	0.16[8]

QALY, quality-adjusted life year.

1. ICER (2019). Value Assessment Methods and Pricing Recommendations for Potential Cures: A Technical Brief. Available at: https://icer-review.org/wp-content/uploads/2019/08/ICER_TechnicalBrief_SSTs_080619.pdf. Last accessed November 2020; 2. NICE (2017). Evaluation consultation document: Strimvelis for treating adenosine deaminase deficiency–severe combined immunodeficiency. Available at: https://www.nice.org.uk/guidance/hst7/documents/evaluation-consultation-document. Last accessed November 2020; 3. Machin N, *et al. Blood Adv*. 2018;2(14):1792–8; 4. Whittington MD, *et al. JAMA Ped*. 2018;172(12):1161–8;
5. Whittington MD, *et al. JAMA Netw Open*. 2019;2(2):e190035; 6. Zimmermann M, *et al. Value Health Reg Issues*. 2019;22(2):161–7; 7. Gerlier L, *et al. Pharmacoeconomics*. 2010;28(12):1129–46 [ABSTRACT]; 8. Almutairi AR, *et al. JAMA Dermatol*. 2019;155(1):22–28.

Are Cell and Gene Therapies Cost-Effective?

Evidence from ICER reviews in the US



ICER, Institute for Clinical and Economic Review; QALY, Quality-adjusted life year.

1. ICER (2018). Emicizumab for Hemophilia A: Effectiveness and Value. Available at: https://icer-review.org/wp-content/uploads/2017/08/ICER_Hemophilia_A_Draft_Report_012618.pdf. Last accessed November 2020; 2. ICER (2018). Chimeric Antigen Receptor T-Cell Therapy for BCell Cancers: Effectiveness and Value. Available at: https://icer-review.org/wp-content/uploads/2017/07/ICER_CAR_T_Final_Evidence_Report_032318.pdf. Last accessed November 2020; 3. ICER (2019). Spinraza® and Zolgensma® for Spinal Muscular Atrophy: Effectiveness and Value. Available at: https://icer-review.org/wp-content/uploads/2018/07/ICER_SMA_Final_Evidence_Report_052419.pdf. Last accessed November 2020; 4. ICER (2020. Modulator Treatments for Cystic Fibrosis: Effectiveness and Value. Available at: https://icer-review.org/wp-content/uploads/2019/09/ICER_CF_Draft_Report_022020.pdf. Last accessed November 2020; 5. ICER (2018). Voretigene Neparvovec for Biallelic RPE65- Mediated Retinal Disease: Effectiveness and Value. Available at: https://icer-review.org/wp-content/uploads/2017/06/MWCEPAC_VORETIGENE_EVIDENCE_REPORT_01122018-1.pdf. Last accessed November 2020.

The economic case for a higher cost-effectiveness threshold for innovative therapies[1]

Several organizations assessing the value of health technologies have a higher cost-effectiveness threshold for treatments for ultra-rare or health-catastrophic conditions[1]

Some of the broader concepts of value are particularly relevant, such as:[1]

Severity of disease

Insurance value

Real option value

Value of hope

Equity

1. Garrison LP, *et al. J Manag Care Spec Pharm*. 2019;25(7):793-799.

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Analytic Considerations in Applying a General Economic Evaluation Reference Case to Gene Therapy

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ABSTRACT

The concept of a reference case, first proposed by the US Panel on Cost-Effectiveness in Health and Medicine, has been used to

Important characteristics of gene therapy

Rare conditions

Single-arm trials

Pediatric populations

More uncertainty about long-term effects

Large caregiver impacts

Role of discounting

Scientific spillovers

1. Drummond M, *et al. Value Health*. 2019;22(6):661–668.

Checklist for assessing gene therapies[1]

Item	Yes	No	Notes
Clinical effectiveness			
Surrogate endpoint used	☐	☐	Validation given?
Rare disease	☐	☐	Prevalence _____
Serious condition	☐	☐	
Single-arm trial	☐	☐	Matched historical cohort used?
Pediatric population	☐	☐	Age range _____
Reporting of adverse consequences and risks	☐	☐	
Size of clinical trial	_____ number of patients		
Length of clinical trial	_____ duration in months		
Extrapolation to long-term outcomes	_____ duration in months		
	Yes	No	Quantification
Elements of value			
Severe disease	☐	☐	
Value to caregivers	☐	☐	
Insurance value	☐	☐	
Scientific spillovers	☐	☐	
Lack of alternatives	☐	☐	
Substantial improvement in life expectancy	☐	☐	
	Yes	No	Notes
Other considerations			
Discounting			
Different discount rates explored	☐	☐	
Uncertainty			
Alternative payment models explored	☐	☐	

1. Drummond M, *et al. Value Health*. 2019;22(6):661–668.

Experience from the National Institute for Health and Care Excellence (NICE) in England

No special treatment of gene therapy *per se*

Some gene therapies for rare conditions may qualify for the "Highly Specialised Technologies' (HST) programme[1]

The HST programme provides for a higher cost-effectiveness threshold of £100,000 per QALY, with the possibility of rising to £300,000 per QALY if 30 QALYs are gained over the patient's lifetime[1]

HST, Highly Specialised Technologies; QALY, quality-adjusted life year.

1. NICE (2017). NICE and NHS England consultation on changes to the arrangements for evaluating and funding drugs and other health technologies assessed through NICE's technology appraisal and highly specialised technologies programmes. Available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/board-paper-TA-HST-consultation-mar-17-HST-only.pdf. Last accessed: November 2020

Modifiers* used by the Scottish Medicines Consortium (SMC)[1]

Evidence of a substantial increase in life expectancy (>3 months)

Evidence of a substantial improvement in quality of life

Evidence that a sub-group may derive specific or extra benefit

Absence of other therapeutic options of proven benefit

Possible bridging to another proven therapy

Emergence of a licensed medicine as the only therapeutic option for a specific indication

*Modifiers represent situations where a higher cost per quality-adjusted life year threshold may be accepted.
SMC, Scottish Medicines Consortium.

1. SMC (2012). SMC modifiers used in appraising new medicines. Available at: https://www.scottishmedicines.org.uk/media/3565/modifiers.pdf. Last accessed: November 2020.

Dealing with Uncertainty in Long-term Benefits

Gene therapy poses uncertainty concerning both long-term efficacy and durability and therefore requires a novel financing approach[1]

Devising a performance-based risk-sharing arrangement, linking payment with the accumulated knowledge about the effectiveness of the therapy to be evaluated

Payment for therapy over a long-term set period rather than up front

Partial payments for less than full efficacy treatments with overall payment commensurate to results

1. Drummond M, *et al*. *Value Health*. 2019;22(6):661–668.

Conclusions

Cost/QALY analyses provide a starting point for discussions of value

A completely new approach for assessing gene therapies is not required, but a tailored checklist for analysts and decision makers can be helpful

Health Technology Assessment organizations need to consider carefully how they cover and reimburse gene therapies for rare diseases

QALY, quality-adjusted life year.