Key Features and Challenges of Cell and Gene Therapies Highlighted in Health Technology Assessment Submissions

Poster #HTA12

Jessica Tu-Anh Tran[1], Bach Khoa Vu[1*], Rhiannon Campden[2], Mengqi Chloe Zhou[3], Mihaela Musat[4], Deepika Thakur[3]

[1]Cytel Inc., Montréal, QC, Canada, [2]Cytel Inc., Vancouver, BC, Canada, [3]Cytel Inc., Toronto, ON, Canada, [4]Cytel Inc., Waltham, MA, US

Background

- Cell and gene therapies aim to manipulate genetic materials for the treatment of inherited or acquired diseases. They are a promising solution for managing diseases with few or no alternative therapies but are often associated with potential risks and high costs.

Objective

- The research aimed to highlight the positive aspects and limitations cited by health technology assessment (HTA) agencies in submissions for cell and gene therapies.

Methods

- Completed HTA submissions for cell and gene therapies were searched in the following HTA agencies (cut-off date November 5, 2022): National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), and Gemeinsamer Bundesausschuss/ Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (G-BA/IQWiG).
- Positive remarks, uncertainties, and limitations highlighted by the HTA committees were identified and summarized.

Discussion

- Despite the limitations identified in the clinical and economic aspects, all HTA submissions deemed evaluable received a positive recommendation.
- The limitations highlighted by the HTA bodies are known obstacles within this field such as difficulties surrounding the modeling of long-term efficacy.
- The majority of economic evaluations identified limitations regarding utility elicitation. Among these, only one targeted an oncology indication; the others were in rare diseases. Robust utility values were a constant challenge in rare diseases given the lack of consensus on the preferred method to generate them.
- As expected, single-arm studies were largely used in rare disease indications and require the use of a historical cohort to demonstrate the clinical effectiveness. However, patient characteristics and treatment landscapes change, causing limited comparability between real-life cohorts and clinical studies. Comparing with a similar cohort is essential to demonstrate an accurate differential clinical benefit. The use of modern techniques such as matched-adjusted indirect comparison, simulated treatment comparison, or synthetic control arms could be a possible solution to address these limitations. Bayesian methods can also be used as solutions for some clinical trial challenges, such as adopting historical and external data.

Conclusion

- The uncertainties related to long-term outcomes and the high costs associated with cell and gene therapies are often surpassed by the significant benefits demonstrated in populations with high unmet need.
- The robustness of comparative effectiveness assessments is highly influenced by the choice of RWE data in the absence of RCTs.

Results

- In total, 17 HTA submissions were reviewed (Figure 1), of which 11 incorporated an economic assessment (Figure 2). Six HTA submissions were in oncology indications (four of 11 economic assessments) and the remainder targeted rare diseases.
- Most submissions received a positive recommendation (15 of 17). Two submissions were rejected by IQWiG because comparative effectiveness could not be established.

Figure 1. Number of clinical evaluations per HTA body

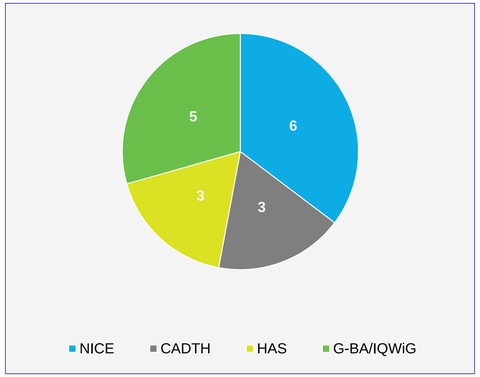


Figure 2. Number of economic evaluations per HTA body

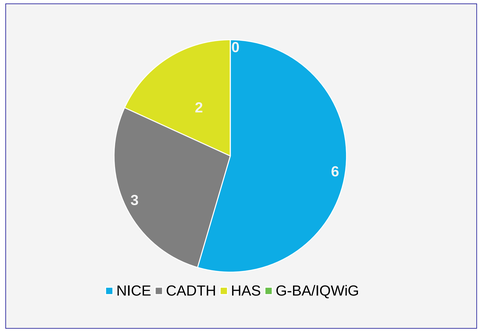
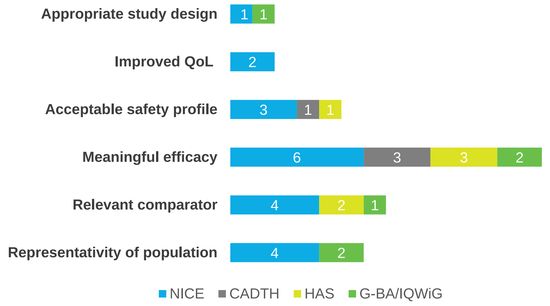


Figure abbreviations: CADTH, Canadian Agency for Drugs and Technologies in Health; G-BA, Gemeinsamer Bundesausschuss; HAS, Haute Autorité de Santé; ICER, incremental cost-effectiveness ratio; IQWiG, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen; QoL, quality of life

Clinical evaluations of HTA submissions

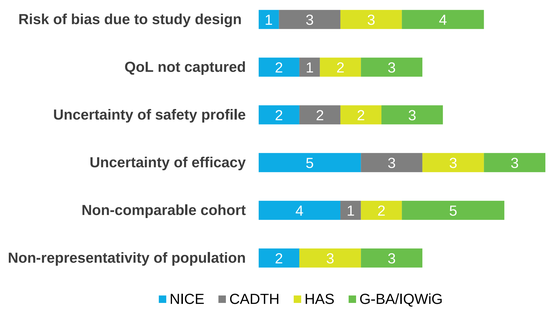
- Fifteen of 17 HTA submissions reported meaningful clinical efficacy, despite some results derived from single-arm trials (Figure 3).

Figure 3. Positive aspects reported by clinical categories



- Regarding the design of the investigational therapy trial:
  - 12 of 17 HTA submissions reported the use of indirect comparison with real-world evidence (RWE) data as a limitation in assessing comparative effectiveness since single-arm studies were used to assess the clinical efficacy (Figure 4).
  - The use of historical cohorts with incomplete patient characteristics or cohorts that did not fully match the population was among the most common critiques of the evidence.
- Fourteen of 17 HTA submissions reported uncertainties surrounding the duration of clinical effect and surrounding the generalization of the observed benefit considering the small sample sizes (Figure 4).

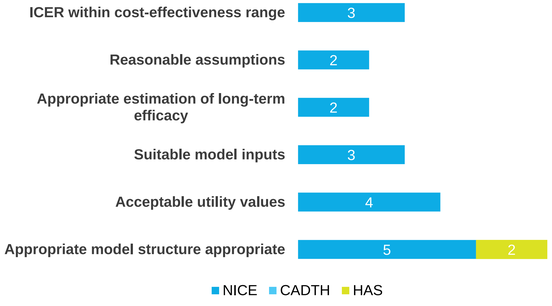
Figure 4. Limitations reported by clinical categories



Economic evaluations of HTA submissions

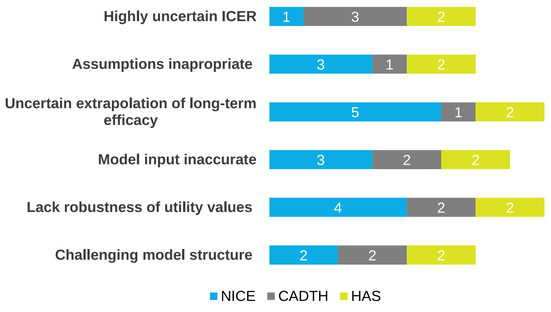
- Seven of 11 economic models were deemed appropriate for decision-making despite their complexity (Figure 5).

Figure 5. Positive aspects reported by economic categories



- Economic evaluations were largely criticized for the use of utility values (eight of 11) (Figure 6):
  - Lack of robustness (e.g., values from another population, source of data not robust, lack of face validity)
  - Methodological limitations in the approach used to derive utility values (e.g., elicitation based on small sample size, problems with valuation study)
- Eight of 11 HTA submissions identified the approach and assumptions for estimating long-term efficacy as important sources of uncertainty due to insufficient data and which had an impact on cost-effectiveness (Figure 6).

Figure 6. Limitations reported by economic categories



*Affiliation at the time of study conduct and completion

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Contact information: www.cytel.com