Challenges for Economic Evaluations of Advanced Therapy Medicinal Products: A Systematic Review

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Background and objective

Advanced therapy medicinal products (ATMPs) are drugs for human use for the treatment of chronic, degenerative and/ or life-threatening diseases that are based on genes, tissues or cells. There are currently more than 2500 active clinical trials of ATMP, of those 250 are Phase III (ref). Over 50% of these are for treatments of cancer, although investigation is underway in almost all clinical specialities. Many ATMPs are for very specific, rare, or highly debilitating conditions and have curative intent, but others have much wider application, such as treatments for repair of knee cartilage or stress urinary incontinence.

The aim of this poster is to identify and critically review published economic analyses of Advanced therapy medicinal products.

Methods

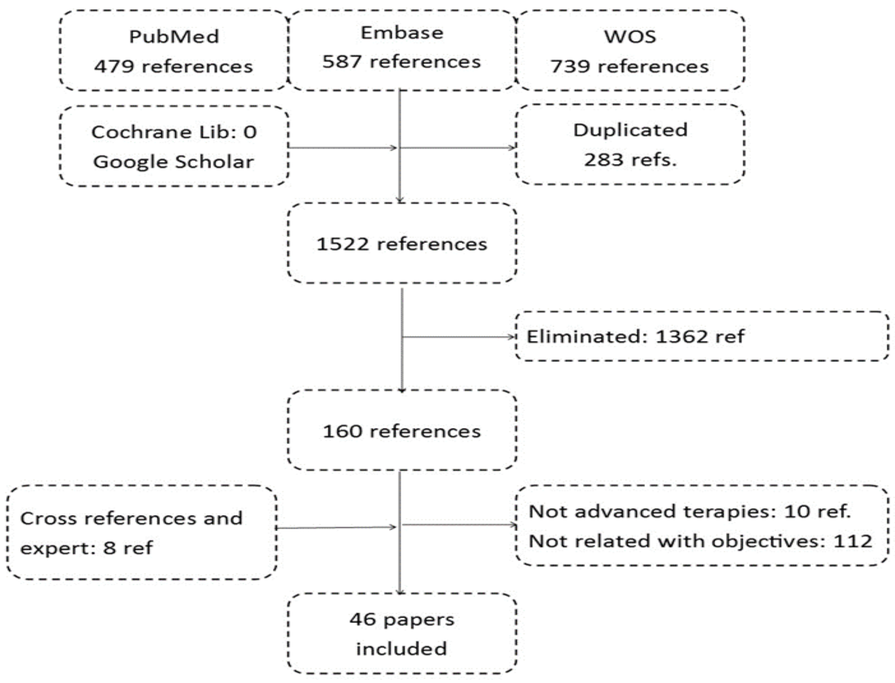

Fig 1. PRISMA flow diagram

A **systematic review of economic analyses** of ATMPs was undertaken. The search strategy includes commercial names and INN of ATMPs with marketing authorization and “tissue-engineered,” “somatic-cell therapy,” and “gene therapy” as general terms. A checklist was used to evaluate the methodological quality and risk of bias of each article. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42021233727).

The authors worked together to elaborate recommendations for HTA evidence, procedure and criteria of relevance for ATMP, based on the evidence extracted from the review. However, all conclusions are exclusively those of the authors.

Results

A total of **46 economic analyses of ATMP were included** [(gene therapy (71,7%), cell therapy (8,7%) and tissue-engineered (19,5%)]. A total of 39 studies were Cost-Utility Analysis and 2 were cost only studies. 23 predicted that the ATMP offered a step-change in the management of the condition and 6 studies estimated that the ATMP would offer a lower mean cost. In cost-utility studies, most of them (34/39) used mathematical models to extrapolate clinical effectiveness from trial data in the intervention and control group to longer term outcomes, using time horizons of 40 years or more.

Recommendations

- **Appropriate length of follow up** and endpoints are crucial. Sources of between-study heterogeneity must be explored
- Analyses should take account of **baseline differences** between intervention and control groups
- Use of **statistical models** such as mixture cure fraction models should be undertaken cautiously and results compared against clinical measures of freedom from remission
- Clinical studies should include **generic quality of life instruments**
- Economic evaluations should conduct **sensitivity analyses and threshold analyses** for a plausible range of prices
- Payers should aim for **consistency and clarity**. Routine HTA evidentiary requirements and criteria should apply unless there is a strong case otherwise. Manufacturers need to ensure they design clinical studies that align with HTA criteria
- There is a patchwork of post marketing surveillance platforms. Regulators and national payers should aim for **compatibility and interchange of data**.
- **Hospital exemption should be reviewed** to ensure transparency and best interests of patients
- Careful **critical evaluation of industry dossiers** is required, alongside comparison with non-industry funded models where possible

Reference: Olry de Labry-Lima A, Ponce-Polo A, García-Mochón L, Ortega-Ortega M, Pérez-Troncoso D, Epstein D. Challenges for Economic Evaluations of Advanced Therapy Medicinal Products: A Systematic Review. Value Health. 2022:S1098-3015(22)02100-3. doi: 10.1016/j.jval.2022.07.004.