IP13: Should gene therapies be exempt from HTA scrutiny?

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Moderator:

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Tolley Health Economics
A bespoke approach to health economics, statistics and HTA

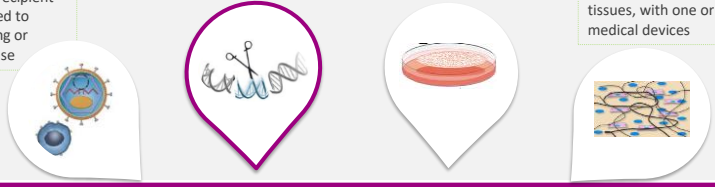
There are four different types of ATMP according to the EMA definition

Cell therapies: cells subject to substantial manipulation or not intended to be used for the same essential function(s) in the recipient and the donor, used to treating, preventing or diagnosing a disease

Gene therapies: contain recombinant nucleic acid used to regulating, repairing, replacing, adding or deleting a genetic sequence

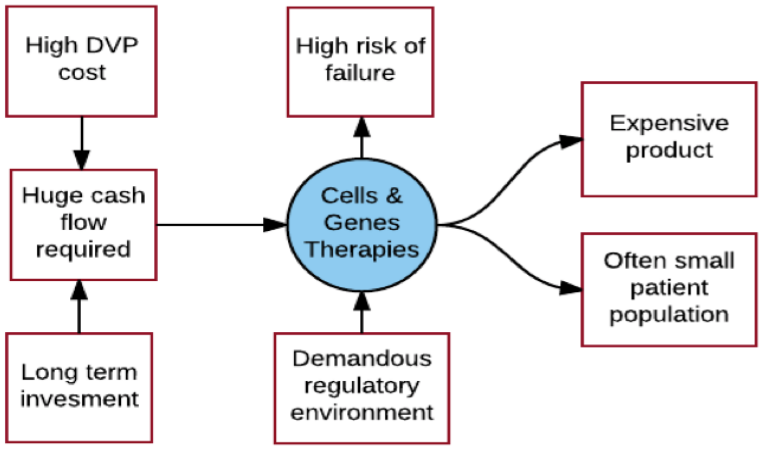
Tissue engineered products: contain engineered cells or tissues, used to regenerating, repairing or replacing a human tissue

Combined products: contain engineered cells or tissues, with one or more medical devices



Advanced Therapy Medicinal Products: ATMPs is a class of innovative biopharmaceuticals that encompass gene therapies, cell therapies, tissue engineered products and combined therapies

Gene therapies are a risky R and D investment



Source: https://www.labiotech.eu

Early struggles!

- Not a glorious start!

"Uniqure withdraws €1m drug Glybera from market"

"With treatment cost of €1m+ per patient, Glybera (the AAV-based gene therapy to treat the rare inherited disorder lipoprotein lipase deficiency (LPLD)) **was the most expensive therapy ever approved in Europe. Now, Uniqure has decided to terminate post-marketing studies required for prolongation of its existing EU conditional market approval".**

Licensed in 2012 with EMA, withdrawn in 2017 due to limited sales

The Three P's

- **The potential:**
  - A cure or transformation of the condition with a single shot of the drug
  - Often (but not always) in rare severely debilitating, life threatening conditions without any currently effective treatment
  - Potential for substantial patient/caregiver benefit, disease modification or cure

- **The price:**
  - CAR-T therapies (Kymriah, Yescarta) are priced at €300,000 (Launched in Europe 2018)
  - Strimvelis is priced at around €600,000 (Launched in Europe 2018)
  - voretigene neparvovec (Luxterna) for treatment of adult/paediatric patients with vision loss due to inherited retinal dystrophy with price of ~€650,000
  - New gene therapies about to hit the European markets soon, include:
    - Zyntelgo for thalassaemia and sickle cell (aims to reduce the need/use of blood transfusions) recently approved under the EMA Priority Medicines (PRIME) process
    - Onasemnogene abeparvovec (Zolgensma) for treating SMA type 1.....positive phase III results.... but more focus on the expected ~€2 million price tag

5

The third P.....

The payer nightmare!

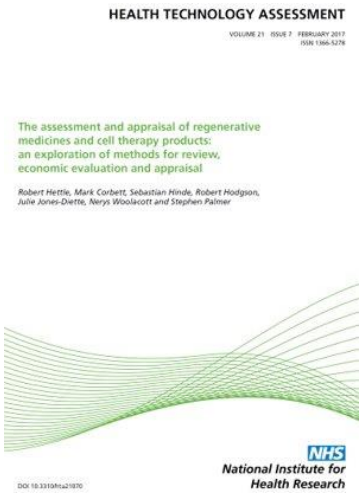
1. Uncertainty over the durability of the cure or transformation!
2. Affordability - high up front cost
3. Poor or at least highly uncertain cost-effectiveness
4. Lots more coming....at least 25 gene therapies in phase III (or registrational trials) mainly in rare diseases, but also in less rare diseases such as haemophilia A, cancer, heart failure...

But is it perceived or real?

6

The HTA and payer challenge!

- HTA is a tool that should be of value to payers to help them determine which are the best value new therapies to spend health care funds and resources on.
- NICE in the UK and ICER in the US haven't shirked performing conventional (cost/QALY) assessment of gene therapies to date: Car-T's, Luxterna....
  - York University report determined that the conventional cost/QALY value framework could be feasibly applied to Car-T therapies.
- Payers are typically willing to pay more for medicines for ultra-rare diseases and curative therapies than for "conventional" therapies..[higher incremental cost per QALY gained thresholds]....



7

The birth of a new HTA process model?

Healthcare Improvement Scotland | Scottish Medicines Consortium

- The **Scottish Medicines Consortium** have introduced a new ultra-orphan process whereby new eligible medicines for very rare diseases will be reimbursed without full appraisal of cost-effectiveness as long as certain conditions are met:
  - The company offers a patient access scheme (price discount)
  - The company agrees to a data collection plan to reduce clinical and economic uncertainties
- A possible model for gene therapies for ultra-rare conditions?

8

So the issue to be debated

The proposition

- Demonstrating cost-effectiveness of gene therapy is difficult and highly uncertain to the point that conventional HTA, whilst feasible to perform, is itself cumbersome and arguably of limited value for reliable decision-making.
- An alternative proposal is to bring key stakeholders together (payers, clinicians, patients, manufacturers) in order to negotiate a fair, affordable and sustainable price, and a payment plan that respects the constraints of the healthcare system
- Alternative approaches to conventional HTA need urgent discussion before more gene therapies hit the market!

Let's debate!

9

The audience view….

- The ISPOR polling facility – using your smartphones which of course you all (?) will have!

10

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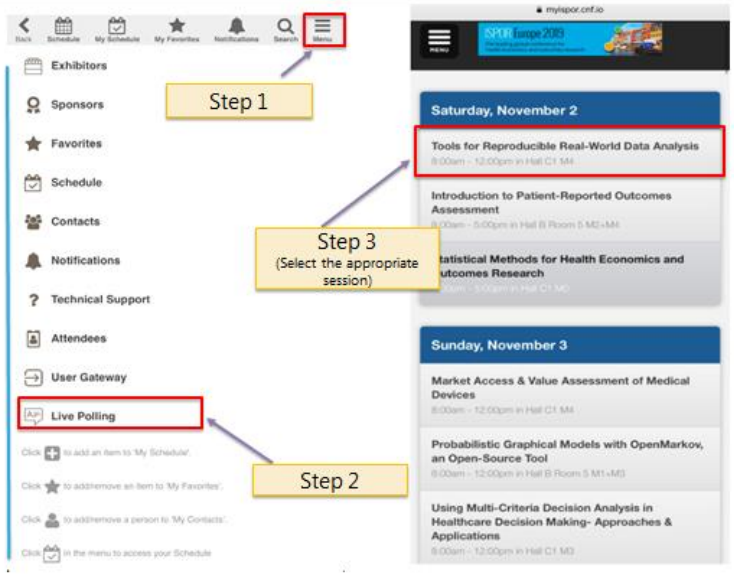

11

Live Content Slide

When playing as a slideshow, this slide will display live content

Poll: Do you agree we should move away from the application of conventional HTA (at least the cost effectiveness part) for gene therapies?

Panelists:

Maarten Postma, Prof PhD, University of Groningen, Netherlands

Takes an HTA analyst perspective on the issue

Darren Walsh, Senior Director, Market Access & Govt. Affairs EMEA , Orchard Therapeutics

Takes an industry perspective on the issue

Josie Godfrey, JG Zebra Consulting Ltd, London, UK , and Trustee at Metabolic Support UK

Takes a patient perspective on the issue

Francis Pang, Vice President, Orchard Therapeutics

Maarten as he more normally looks!