EU ATMP access study and draft consensus recommendations

Paolo Morgese
ARM - Alliance for Regenerative Medicine

Disclaimer

The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to Drug Information Association, Inc. (“DIA”), its directors, officers, employees, volunteers, members, chapters, councils, Special Interest Area Communities or affiliates, or any organisation with which the presenter is employed or affiliated.

Alliance for Regenerative Medicine

DIA

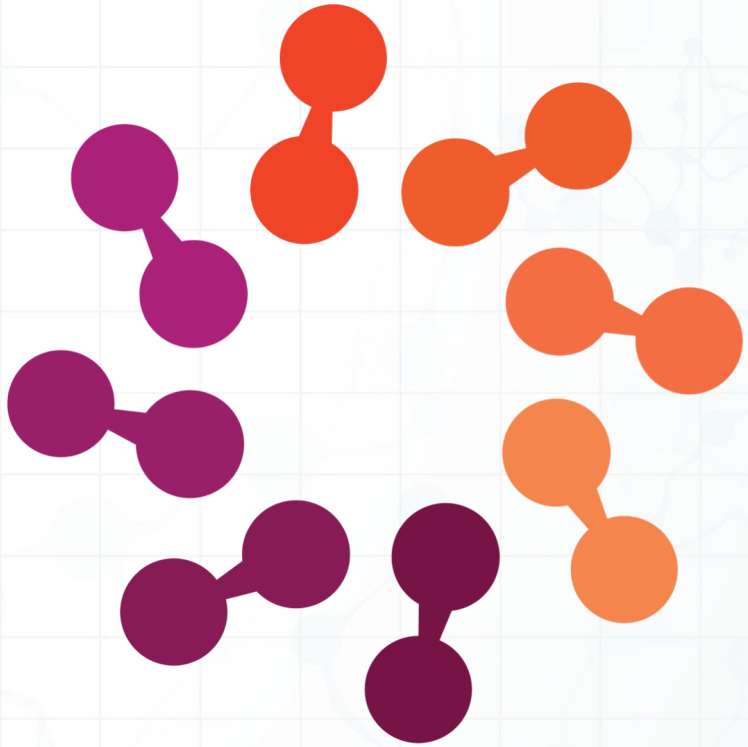
Mission Statement

The Alliance for Regenerative Medicine (ARM) is the preeminent global advocate for regenerative and advanced therapies. ARM fosters research, development, investment and commercialization of transformational treatments and cures for patients worldwide.

By leveraging the expertise of its membership, ARM empowers multiple stakeholders to promote legislative, regulatory and public understanding of, and support for, this expanding field.

About ARM

- **International advocacy organization**
  - Dedicated to realizing the promise of safe and effective regenerative medicines for patients around the world
- **320+ members**
  - Small and large companies, non-profit research institutions, patient organizations, and other sector stakeholders
- **Priorities:**
  - Clear, predictable, and harmonized **regulatory** pathways
  - Enabling market access and value-based **reimbursement** policies
  - Addressing industrialization and **manufacturing** hurdles
  - Conducting key stakeholder outreach, **communication**, and education
  - Facilitating sustainable access to **capital**



DIA

Alliance for Regenerative Medicine

Examples of ARM Member Companies & Organizations

Gene Therapy	• AGTC • Audentes Txs • BioMarin • bluebird bio • Celgene	• Caribou Biosciences • Casebia • CRISPR Txs • Editas Medicine • Intellia Txs	• Orchard Tx • LogicBio • Novartis • Pfizer • Oxford BioMedica	• REGENXBIO • Sangamo Txs • Sarepta • Shire • Spark Txs
Cell Therapy	• Akron Biotech • Atara Bio • Athersys • BlueRock Txs • CDI/Fujifilm	• Celgene • Cell Medica • EMD Millipore • GE Healthcare • GSK	• J&J • Kiadis Pharma • MolMed • Novadip Bio • PCT/Hitachi	• ReNeuron Group • Thermo Fisher • TiGenix • Tmunity Txs • ViaCyte
Tissue Eng.	• Aspect Biosystems • AxoGen • Avery Txs • Bone Txs • DiscGenics	• Fibrocell Science • Histogenics • Mesoblast • MiMedx Group • Miromatrix Medical	• Novadip Biosciences • Organovo • Orthocell • Pluristem Txs • PolarityTE	• Skingenix • StemBioSys • TERMIS - Americas • VERIGRAFT • Videregen
Non-Profits	• Baylor College • Catapult • CCRM • Chemelot Campus • CIRM	• City of Hope • Cleveland Clinic • FARA • Fondazione Telethon • Fraunhofer Institute	• Fred Hutchinson • GENETHON • Global Genes • Johns Hopkins U. • MJ Fox Foundation	• Missouri Cures • MSK • Northwestern U. • NYSCF • UPENN

DIA

The ARM EU market access study and consensus report

Market Access Landscape: EU5

Key:

- HTA Negative opinion
- HTA positive opinion
- HTA positive opinion with limitations

✓ Reimbursed

✗ Not reimbursed

X Withdrawn from market

		France (TC/CEESP)	Germany (IQWIG/ G-BA)	UK (NICE/SMC)	Italy (AIFA/ regional)	Spain (national/ regional)
Gene Therapies	Glybera X	✗	Non-quantifiable added benefit ✓	-	-	-
	Imlygic	-	No added benefit but reimbursed ✓	PAS ✓	Authorized, hospital only, Cnn	-
	Strimvelis	-	- ✓	✓	Payment by results ✓	-
	Kymriah	ASMR III	- ✓	CED scheme ✓	-	-
	Yescarta	ASMR III	- ✓	CED scheme ✓	-	-
	Luxturna	-	- ✓	-	-	-
Cell Therapies	Provenge X	-	Non-quantifiable added benefit ✓	Negative NICE Guidance ✗	-	-
	Zalmoxis	-	Non-quantifiable added benefit ✓	-	Hospital only, flat cost per patient ✓	-
	Alofisel	-	Non-quantifiable added benefit ✓	Negative NICE Guidance ✗	-	-
Tissue Therapies	Chondrocelect X	✗	Not eligible for EBA	Negative NICE Guidance ✗	-	National reimbursement ✓
	MACI X	-	Not eligible for EBA	Negative NICE Guidance ✓	- ✓	-
	Holoclar		Not eligible for EBA	PAS	Hospital only payment by results	-

As of December 2018

- Evolving market access landscape
- Evolving quality of evidence packages

Challenges in Ensuring Access to Cell and Gene Therapies in Europe

	Challenges	Advocacy areas
HTA feasibility	• Uncertainty on magnitude and duration of effect can substantially limit pricing potential • Fragmented European HTA processes at national/regional level can considerably delay access	• Early-dialogue activities • Post-approval evidence generation and conditional reimbursement • More coordinated HTA activities at European level
Financial sustainability	• Concerns related to one-off prices and financial sustainability both on developers' and payers' sides	• Design and implement new pricing and payment solutions
Innovative Pricing feasibility	• Misperception on value-based-pricing • Misperception on one-off prices • ATMPs still small market compared to traditional technologies and not deemed to justify policy changes	• Stakeholder education • Multi-stakeholder dialogue

Several reviewed papers highlight the need for adapting reimbursement pathways to these novel therapies but there is no consensus. With long-term post approval evidence development, ATMP's value proposition gets less uncertain. Therefore, HTA/reimbursement processes in the respective countries may need to be adapted to reflect this (e.g., yearly negotiations) – especially if their willingness to accept risk does not change

HTA processes are not yet adapted to the early clinical datasets and novel outcome measures of ATMPs

- ATMPs require new approaches to assessing value, and strong value stories that educate on ATMPs addressing burdensome conditions
- The focus of HTA analyses are typically on the healthcare budget efficiency, therefore often exclude implications on social care or other indirect costs
- Including validated new outcome measures into clinical trials may provide an opportunity to support more adapted health economics analyses, and early-stage advanced therapy are expected to incorporate such data points
- The reimbursement/assessment processes need to better deal with, or accept some of the risk & uncertainty associated with ATMPs

- Novel reimbursement frameworks need to be developed to fully capture the ATMPs benefits
- Cell therapy could be an ideal setting for new reimbursement models as precise tracking is more achievable than with traditional drugs and therefore patient-by-patient reimbursement more appropriate
- There is a need to develop methodologies to measure the social value of pharmaceutical products

DIA

A one-time transformational treatment for a rare or ultra-rare condition with high unmet needs is likely to have a high price tag, which is likely to generate tensions between developers and payers

- Developing gene therapies is high cost in addition to complex manufacturing procedures
- Usually the target population is small. Therefore, the short-term cost-per-patient is higher
- Developers need to be fairly compensated for their innovations and risks
- ATMPs may have the potential to cure some incurable chronic diseases therefore they have an important value. Developers are requesting fair value recognition the ATMP provide to the patients and the society, using value-based pricing
- Developers consider that payers need to accept to share some risks with developers or need to change the payment mechanisms

Developers' perspective: Fair Prices

Payers' perspective: Sustainability Issue

- Payers struggle to pay for innovation: social affordability question
- Debates on accepting high prices:
  - Some stakeholders reject the presumption that a cure needs to be costly
  - Some payers accept the high price for effective therapies with high value if industry develops sound rationales
  - Payers will want to see improvements in other outcomes like productivity and reduced care burden
  - They suggest focusing on better predictability and cost management
- ATMPs are expected by some payers to severely impact health insurance budget: High budget impact was identified for ATMP in Alzheimer disease, Parkinson disease and heart failure

DIA

Draft consensus recommendations

Potential solutions: emerging elements of consensus

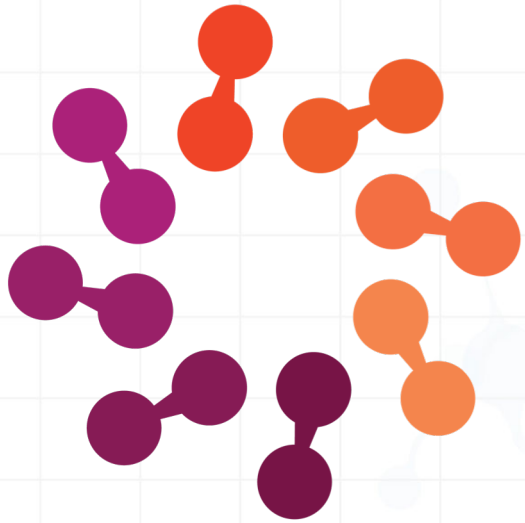
Uncertainty of effect

1. Better adapt evidence requirements and HTA frameworks
in some countries, by developing HTA methods to better adapt to lack of direct comparative data and long-term follow-up

2. Improve early dialogue activities
increasing capacity and therefore ED opportunities for all stakeholders. Engage in horizon scanning discussions with all relevant stakeholders

3. Develop RWE infrastructure
that will allow timely and efficient collection of RW data to be used by HTAs and payers

4. Set up conditional reimbursement
schemes and infrastructure as an opportunity to gain early patient access to ATMPs while developing additional evidence



Affordability and financial sustainability

7. Set up dedicated healthcare funds
e.g. for rare genetic conditions – for implementing innovative payment schemes

6. Remove barriers to annuity payments schemes
and therefore better allocate investment over patient life

5. Set up pay-per-outcome
schemes and infrastructure to improve return on healthcare investment

DIA