Global Pricing, Reimbursement and Market Access Trends for Regenerative Medicines, ATMPs, Cell/Gene Therapies

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Objective

To examine the current pricing, reimbursement, and market access (PRMA) landscape for regenerative medicines, ATMPs, cell/gene therapies across three quite different jurisdictions US, Europe, and Japan.

Methods

Reviewed all regenerative medicines, ATMPs and cell/gene therapies approved as of May 2022 and available in the US, EU4 (France, Germany, Italy, Spain), UK and Japan as of August 2022

- Also noted products that have been withdrawn

Analysed HTA, pricing, reimbursement status and time to market

- Data gathered from EMA, national Health Technology Assessment (HTA) agencies and Pricing and Reimbursement (P&R) bodies
- Sources for launch date and HTA information provided in Table 1

Table 1: Sources for HTA, pricing, reimbursement and time to market

Country	Sources
US	MediSpan, Fingertip formulary
France	Légifrance, Haute Autorité de Santé (HAS)
Germany	Lauer Taxe, Gemeinsamer Bundesausschuss (G-BA)
Italy	Agenzia Italiana del Farmaco (AIFA)
Spain	Ministerio de Sanidad
UK	NHS DMD, National Institute for Health and Care Excellence (NICE)
Japan	Ministry of Health, Labour and Welfare of Japan (MHLW)

Results

Global availability and access for regenerative medicines, ATMPs and cell/gene therapies is geographically fragmented

A total of 36 regenerative medicines, ATMPs, cell/gene therapies are approved globally and currently authorized in the US, Europe or Japan EU (Figure 1)

- Only 5 overlap across all three jurisdictions (US, Europe and Japan) and 9 across the US and Europe
- US: 21 FDA approved cell/gene therapies (8 are cord blood products) of which 13 are marketed and reimbursed (does not include 2 cell therapies that are discontinued)
- Europe: 14 EC approved ATMPs currently available on the market (does NOT include 7 ATMPs that have been withdrawn)
- Japan: 16 PMDA approved regenerative medical products are available and reimbursed

Although value of these therapies is recognized in France and Italy, this is not the case in Germany

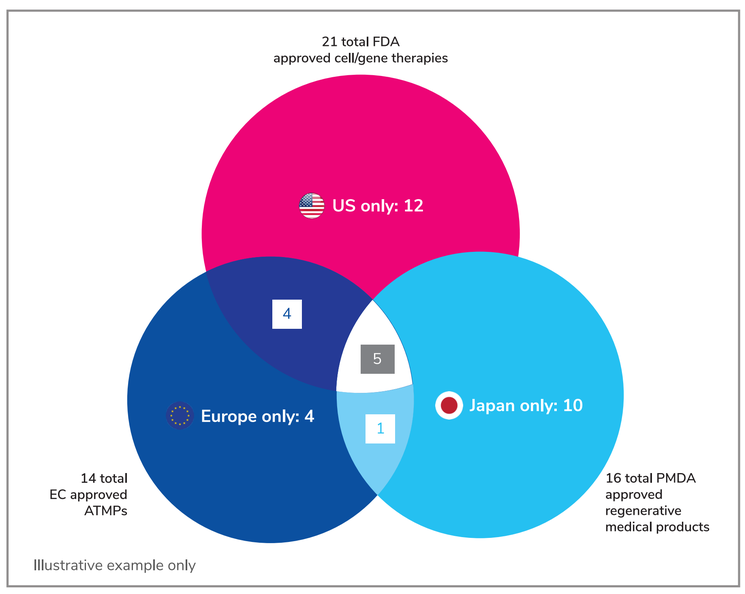
- Only 1 therapy assigned hint of considerable added benefit in Germany with majority assigned a non-quantifiable benefit
- 60% of therapies evaluated were assigned ASMR II/III in at least one group in France and 70% assigned innovative status in Italy

Cell/gene therapies with highest annual visible ex-factory price are:

- US: Rethymic (Allogeneic processed thymus tissue–agdc) at $2.7M (€2.65M)
- Europe: Libmeldy (atidarsagene autotemcel) at £2,875,000 (€3.38M)
- Japan: Zolgensma (Onasemnogene abeparvovec) at JPY 167,077,222 (€1.20M)

Generally, net cost of therapy in Europe following negotiations was 10% to 40% below visible ex-factory price

Figure 1: Regenerative medicines/ATMPs/cell/gene therapies approved and currently available across US, Europe and Japan



European Central Bank Historical Exchange rate: (June to August 2022) :
1 JPY= €0.007; 1 USD= €0.9727; ; 1 GBP= €1.1754)

Market access status of cell/gene therapies, ATMPs varies considerably across the six countries (Figure 2)

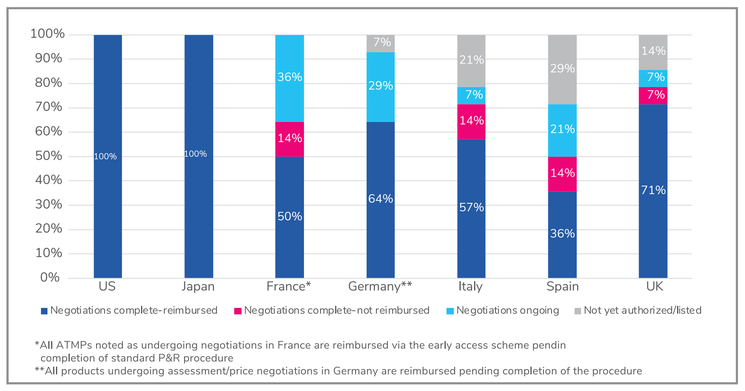
- US: cell/gene therapies are generally reimbursed under the medical benefit
- Japan: Favourable access for all PMDA approved therapies (all included on the NHI list)
- France: 86% of therapies are accessible, consisting of 50% reimbursed under the standard pathway and 36% available via the early access scheme
- Germany: 93% of ATMPs are reimbursed; 64% having completed the AMNOG procedure and additional 29% currently undergoing negotiations
- UK: 71% of ATMPs are currently recommended for reimbursement by NICE
  - Interestingly only 40% of the therapies have been assessed via the Highly Specialized (HST) Technologies pathway, which seems specifically designed for them
- Italy: 57% of ATMPs are reimbursed, all with patient registries and several with payment by results agreements
- Spain: Poor access to ATMPs, with only 36% having completed negotiations with a positive recommendation

Data above does NOT include ATMPs that have been withdrawn from these markets

- US: 2 therapies that are no longer marketed (Gintuit and Laviv)
- Europe: 7 therapies have been withdrawn post-approval for clinical/commercial reasons (Maci, Provenge, Chondrocelect, Glybera, Zalmoxis, Zynteglo, Skysona)

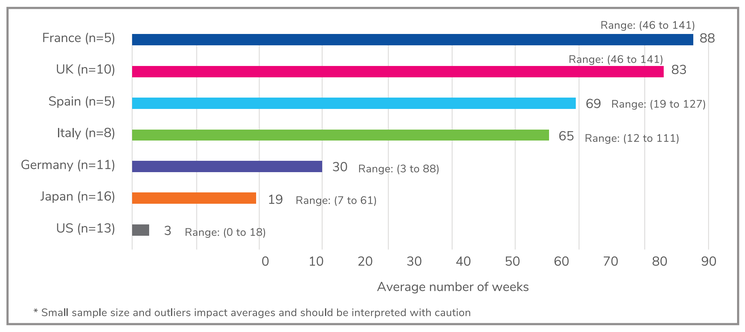
Average time to reimbursed access post regulatory approval was 3 weeks in the US and ranged from 30 weeks in Germany to 88 weeks in France (Figure 3)*

Figure 2: P&R procedural status of Regenerative medicines/ATMP/cell/gene therapies approved and currently available in the US, Japan and Europe



*All ATMPs noted as undergoing negotiations in France are reimbursed via the early access scheme pendin completion of standard P&R procedure
**All products undergoing assessment/price negotiations in Germany are reimbursed pending completion of the procedure

Figure 3: Average time to reimbursed access post regulatory approval



* Small sample size and outliers impact averages and should be interpreted with caution

Conclusions

We continue to see an evolution of the geographic fragmentation from both the regulatory and market access perspectives for cell/gene therapies

This is likely due to the fundamentally varied approaches across countries in the classification of these therapies as well as willingness to pay and reimburse

- Several cell/tissue-engineered therapies are approved only in Japan whereas many cord blood therapies are included in this classification and approved only by the FDA
- On the other hand, fewer centralized EC approved cell/tissue-engineered therapies are available in Europe, primarily due to local competition from 'home-brewed' therapeutic alternatives

Despite the market access fragmentation there are some areas of commonality:

- A greater consensus is observed across jurisdictions for CAR-T therapies and some other gene therapies which have obtained approval and reimbursement in most major geographies although timing can significantly vary
- Visible ex-factory prices continue to set new highs with gross to net differences becoming increasingly prominent

Therapeutic area and product variability, national differences in approach and timing are crucial for manufacturers to consider in planning for the fragmented global cell/gene therapy landscape

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