Pricing, Reimbursement and Market Access Trends for Cell & Gene Therapies and ATMPs in the US and Europe

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OBJECTIVE

To examine the pricing, reimbursement and market access (PRMA) landscape for cell and gene therapies and ATMPs approved in the US and Europe

METHODS

- Reviewed all cell/gene therapies and ATMPs approved as of November 2021 and available in the US, EU4 (France, Germany, Italy, Spain) and the UK as of April 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  - Also noted products that have been withdrawn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 below

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

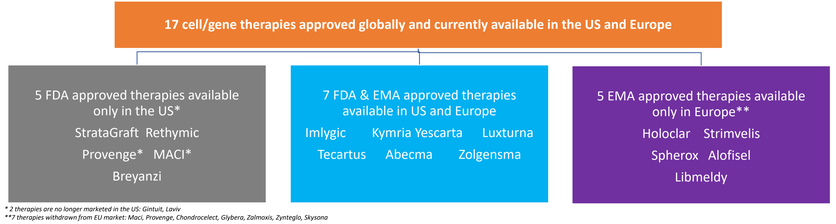
Country	Sources
US	MediSpan, Fingertip formulary
France	Légifrance, Haute Autorité de Santé (HAS)
Germany	Lauer Taxe, Gemeinsamer Bundesausschuss (G-BA)
Italy	Agenzia Italiana del Farmaco (AIFA)
Spain	Ministerio de Sanidad
UK	NHS DMD, National Institute for Health and Care Excellence (NICE)

RESULTS

- Availability and access for cell and gene therapies is not universal globally
- A total of 17 cell/gene therapies approved globally and currently available in the US and EU (Figure 1)
  - Only 7 cell/gene therapies overlap in both jurisdictions (US/EU)
  - Overall, 12 cell and gene therapies are currently authorized by the FDA and marketed
  - Overall, 12 are currently authorized by the European Commission and available on the market
  - Data above does NOT include ATMPs that have been withdrawn from these markets
- Although value of these therapies are recognized in France and Italy, this is not the case in Germany
  - Only 2 therapies assigned hint of considerable/major 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
  - Generally, net cost of therapy in Europe following negotiations was 10% to 40% below visible ex-factory price
- Cell / gene therapies with highest annual visible ex-factory price are:
  - US was Rethymic (Allogeneic processed thymus tissue–agdc) at $2.7M
  - Europe was Libmeldy (atidarsagene autotemcel) at $3.75M (£2,875,000)
  - Neither product is approved by both FDA and EMA presently

RESULTS (Continued)

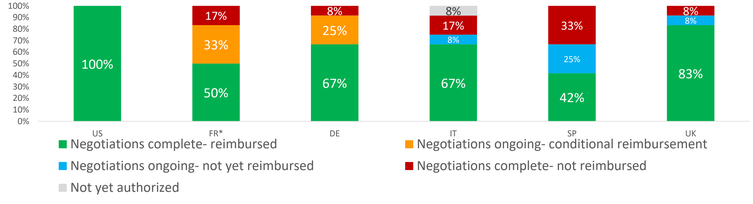
Figure 1: Approval status of cell and gene therapies in the US and Europe as of November 2021



** 2 therapies are no longer marketed in the US: Gintuit, Laviv*
***7 therapies withdrawn from EU market: Maci, Provenge, Chondrocelect, Glybera, Zalmoxis, Zynteglo, Skysona*

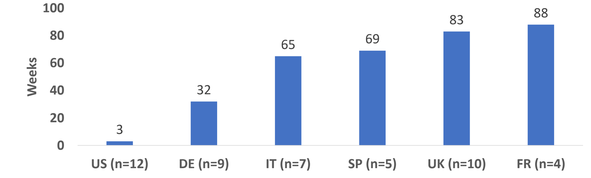
- Market access status of cell and gene therapies, ATMPs varies considerably across the six countries (Figure 2)
  - US: 100% of the cell and gene therapies are reimbursed under medical benefit
  - France: While only 50% of therapies have completed negotiations and received positive reimbursement recommendations, patients do currently have access to an additional 33% undergoing negotiations via the early access pathway (overall 83%)
  - Germany: 67% of ATMPs are reimbursed following completion of the AMNOG procedure
    - An additional 25% of therapies are currently undergoing negotiations and patients have access given reimbursement is immediate post launch (overall 92%) (Spherox is the exception despite majority being assigned non-quantifiable additional rating)
  - Italy: 67% of ATMPs are reimbursed, all with patient registries and several with Payment by Results (PbR) agreements
  - Spain: Poorest access to ATMPs in EU4, with only 42% having completed negotiations with a positive recommendation based on protocol, PbR agreement, free drug for certain patients or spending ceilings
  - UK: 83% of ATMPs are currently recommended for reimbursement by NICE
    - Interestingly only one-third have been assessed via Highly Specialized (HST) Technologies pathway, which seems specifically designed for them
- 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)*

Figure 2: Reimbursement status of cell/gene therapies and ATMPs approved and currently available in the US, EU4 and the UK



**All ATMPs currently undergoing negotiations in France are included in the early access scheme*

Figure 3: Average time to reimbursed access post regulatory approval was 3 weeks in the US and ranged from 32 weeks in Germany to 88 weeks in France



Conclusions

- Cell/gene therapy and ATMP markets are still developing as evidenced by the fragmented regulatory and market access landscape
  - Regulatory approval generally tends to be consistent across the US and EU, however this is not the case for cell/gene therapies and ATMPs
  - For manufacturers, this isn't a traditional market as evidenced by the heterogeneity in regulatory environment, HTA, acceptable prices and market access pathway(s)
- Market access remains challenging particularly in Europe where 7 therapies have been withdrawn for clinical/commercial reasons
  - Within Europe, there is a huge variation in access with UK and Germany leading the way with largest number of reimbursed therapies and Spain lagging behind, although this has improved over the past year
  - Type of therapy also impacts access with CAR-Ts and gene therapies for rare pediatric conditions more likely to be reimbursed, at least in Europe, relative to 'tissue engineered therapies'
- Visible ex-factory prices of recently introduced cell and gene therapies are still setting new highs; however, contracting (in the US) and confidential discounts / managed access agreements (in Europe) often reduce net prices
  - In general, gross to net differences in Europe are becoming increasingly important, with overall discounts for reimbursed cell and gene therapies ranging from 10% to 40%
  - Gross to net differences may grow in future, especially within more "competitive" categories (e.g. CAR-Ts,) and also as a consequence of gradual expansion into earlier lines of treatment / broader indications
- Innovative approaches to market access will continue to evolve, as more cell/gene therapies and ATMPs are launched, bringing important health benefits, but also with substantial potential impact on pharmaceutical budgets

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