ATMPs in Europe: Existing challenges and future directions

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BACKGROUND

- Advanced therapy medicinal products (ATMPs) are medicines for human use including gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines[1]
- ATMPs offer potential treatment for serious conditions where conventional therapies are considered inadequate[2]
- European Medicines Agency's (EMA) committee, The Committee for Advanced Therapies (CAT), is responsible for assessing the quality, safety and efficacy of ATMPs in Europe[1]
- Gene therapy was first conceptualized in 1970; there has been enormous progress in this research area in the last two decades

OBJECTIVE

- The current review was conducted to understand the current trends, challenges and to provide future directions for ATMPs with respect to pipeline molecules, regulatory approvals, reimbursement and market access across Europe

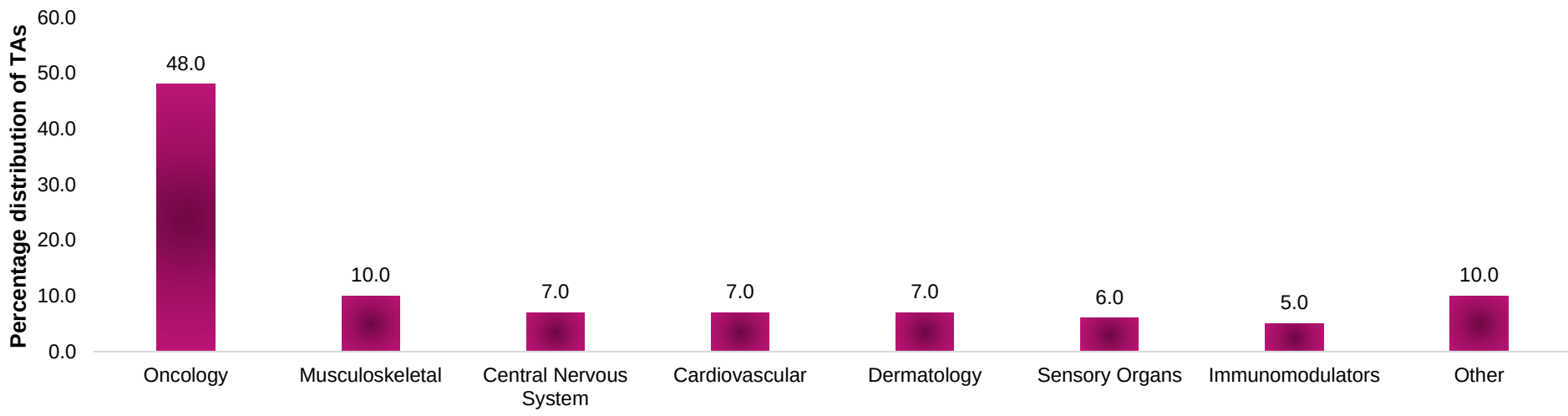
METHODS

- For the current trends in ATMPs, information regarding pipeline molecules was extracted from clinical trial websites (clinicaltrials.gov[3] and EudraCT[4]), approved molecules from European regulatory website (EMA[5]) and reimbursement-related from HTA bodies (NICE[6], SMC[7], IqWIG[8], HAS[9] and AIFA[10])
- Grey literature search was also supplemented to understand the challenges faced during marketing authorization and launch and to offer potential solutions

RESULTS

- Approximately 800 ATMPs are currently in-development in Europe[3,4]. Of which, around 50% are in Oncology, followed by ≤10% in other therapeutic areas[3,4] (Figure 1).

Figure 1: Percentage distribution of ATMPs per TAs



- However, only 10 ATMPs have yet been approved by EMA[5]. This low rate of regulatory approvals can be attributed to quality or scale-up aspects, non-clinical aspects and absence of long-term efficacy and safety data.
- Additionally, evidence from HTA bodies suggested that six ATMPs have been approved by NICE[6], three each by HAS[9], IqWIG[8] and AIFA[10], and one by SMC[7] (Table 1).

Table 1: HTA status of ATMPs

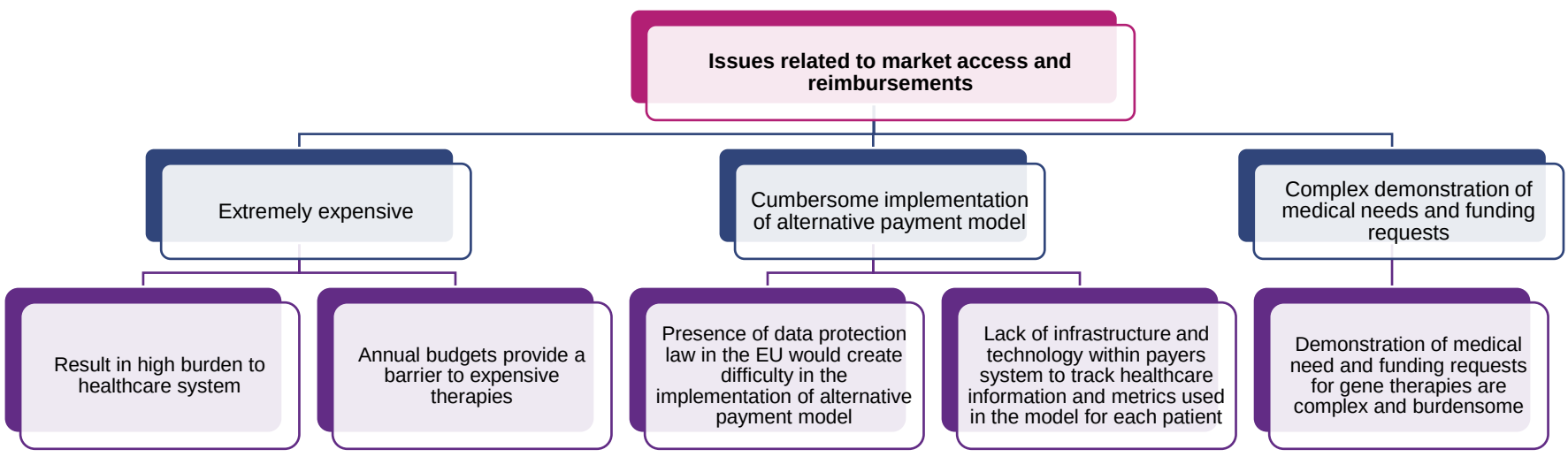
Brand name (Generic name)	Indication	NICE	IqWIG	HAS	SMC
Alofisel (Darvadstrocel)	Crohn's Disease	●	●	○	◌
Spherox (spheroids of chondrocytes, cells found in healthy cartilage)	Repair defects to the cartilage in the knee in adults	●	-		-
Holoclar (Ex vivo expanded autologous human corneal epithelial cells containing stem cells)	Replace damaged cells on surface of cornea	●	-	●	-
Imlygic (talimogene laherparepvec)	Unresectable metastatic melanoma	●		-	○
Kymriah (tisagenlecleucel-t)	B-cell ALL and DLBCL	●	●	●	○
Strimvelis (autologous CD34+ enriched cells)	Severe combined immunodeficiency due to adenosine deaminase deficiency	●	-	-	-
Yescarta (axicabtagene ciloleucel)	Non-Hodgkin lymphoma	●		-	○
Zalmoxis (allogeneic T cells genetically modified to express human low-affinity nerve growth factor receptor and the herpes simplex I virus thymidine kinase)	Add-on treatment in adults who have received a HSCT	-	●	○	-
Zynteglo (Characterized viable autologous cartilage cells expanded ex vivo expressing specific marker proteins)	Beta-thalassaemia	◌	-	-	-

● Recommended ○ Recommended with restrictions ◌ Under consideration/ In development ○ Not Approved

ALL: Acute Lymphocytic Leukemia; DLBCL: Diffuse Large B Cell Lymphoma; HAS: Haute Autorité de Santé; HSCT: Hematopoietic Stem Cell Transplantation; IQWIG: Institute for Quality and Efficiency in Health Care; NICE: National Institute for Health and Care Excellence; SMC: Scottish Medicines Consortium

- The reason of encountering substantial hurdles in market access and reimbursements can be smaller target population, high costs, lack of long-term efficacy and safety data and complexities associated with administration, dosing, and monitoring[5]. Other issues are presented in the below figure (Figure 2).

Figure 2: Issues related to market access and reimbursement of ATMPs[2]



- These challenges are likely to intensify with marketing of more ATMPs and expansion to cover wider population
- To overcome these challenges, it is recommended that manufacturers' collect long-term safety and efficacy data and consider new clinical trial methodologies, while payers should refine/restructure value demonstration and pricing strategies.

CONCLUSION AND LIMITATION

- Higher efficacy, increasing approvals and one-time treatment feature of ATMPs clearly demonstrate the shifting paradigm of healthcare. However, uncertainty of launch approval can augment burden on payers during decision-making. Thus, ATMPs may be the next source of major impact on payers' drug budgets
- However, findings of this review were limited as the review was not conducted using systematic approach. Thus, these should be interpreted with caution

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