Logistical and Financial Challenges in the Adoption of CAR-T Therapies: A Narrative Review

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BACKGROUND

Chimeric antigen receptor T cell (CAR-T) therapy is a new class of medicinal products genetically engineered from T cells, and which have transformed the paradigm of cancer treatment.[1] In 2019 the first CAR-T therapies were funded according to their marketing authorizations in key European markets under different reimbursement schemes. In France and the UK, reimbursement is subject to future reassessments based on additional long-term data collection, and outcome-based payments tied to individual patient data were employed in Italy and Spain. Both access schemes were using in Germany.[2,3] However, fulfilling the requirements of various reimbursement schemes and ensuring optimal patient access requires additional infrastructure.[2,4]

OBJECTIVES

Summarize the challenges and solutions arising in EU4 and UK due to the reimbursement of CAR-T therapy, categorized as related to:

- **Access** (brain-to-vein time, patient access to qualified centers, etc.)
- **Manufacturing and supply** (qualification of manufacturing sites, decentralized production, staff education, etc.)
- **Financial** (cost to patients, cost to institutions, cost to health systems)

METHODOLOGY

A narrative literature search in electronic databases [PubMed/MedLine, Google Scholar] and grey literature was conducted to examine the funding and policies for CAR-T therapies in the EU4 and UK. English, French, and Spanish language resources were considered. The research excluded articles written before the reimbursement of the first CAR-T therapies (2019). Clinically-focused literature was excluded, and papers examining the access, financial, and manufacturing or supply challenges of CAR-T therapy coverage were a target of the search.

RESULTS

Adopting CAR-T therapy poses financial, logistical, and access challenges (Figure 1). A complex clinical infrastructure and an experienced multidisciplinary team are required to successfully deliver therapy to patients, necessitating strict accreditation of the procuring, manufacturing, administering, and monitoring of CAR-T therapy; however, this severely limits the availability of treatment. [5]

Paired with an expanding pool of eligible patients, current capabilities and supply are insufficient.[6] Decentralized, or "in-house" production of CAR-T may provide support to current industrialized manufacturing and at a lower cost: estimated in a German setting from €33,000 to €60,000.[7]

The limited supply of CAR-T therapy has led to the use of national or institutional systems for the assignment of slots. Patient referral varies by countries, but generally follows a hub-and-spoke model where local hospitals refer to regional centers.[8] The UK and Spain have formed national panels to select patients to fill available slots.[9,10] However, those making referral and assignment decisions may interpret CAR-T eligibility differently, resulting in potentially unnecessary exclusion of patients.[11]

The financial burden of CAR-T extends beyond the drug price of the therapy. Pre- and post-treatment costs that must be negotiated separately include hospitalization, costs for apheresis, training of staff for the new treatment, quality assurance and structural costs.[12] This has been estimated in a review of available HTA and economic analyses of the EU4 and UK as approximately €50,000 per patient. In Germany the CAR-T centers shoulder both the cost of providing this innovative therapy, as well as managing financial risk if per patient costs exceed the negotiated contract.[2,11]

Financial aid to certified hospitals or systems covers a portion of the costs of establishing specialized capabilities. Since DRG payments for CAR-T therapy are currently insufficient, countries are using other forms of payments for innovative and expensive therapies, such as *liste en sus* in France or *NUB* in Germany.[2] For costs beyond the treatment itself, Innovate UK shows an example of funding of regional advanced therapy treatment centers, which promotes partnerships across academia, NHS, and the commercial sector to solve challenges of ATMP adoption.[9,13]

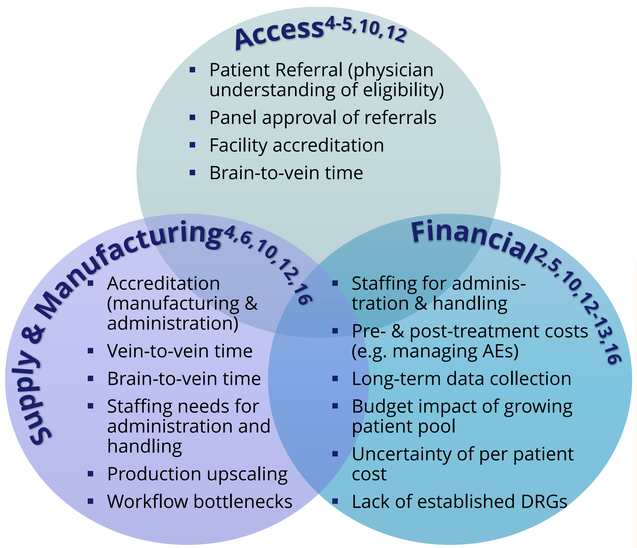

Figure 1. Challenges across EU-4 and UK in the adoption of CAR-T Therapy

Meanwhile, EBMT and EHA's GoCART Coalition was established to coordinate education, policies, registries, SoC, HTA process, and other key areas of bottleneck across EU stakeholders.[14,15] Most recently, guidelines for Pharmacies and Apheresis for ATMPs in the UK have been adapted by the GoCART Coalition to apply to other European countries.[15]

CONCLUSIONS

Thoughtfully forming solutions to the challenges today posed by CAR-T therapy provides needed structure for the expanding CAR-T space, including into new tumor locations (e.g., solid cell tumors). It also serves as a foundation for future reimbursement in the increasingly crowded ATMP space.[9] Although initiatives to unite the space are ongoing, funding and logistical gaps remain. Real-world evidence and comprehensive reviews of the circumstances faced across health systems are still needed.

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ATMP: Advanced therapy medicinal product; CAR-T: Chimeric antigen receptor T cell; DRG: Diagnosis-related group; EBMT: European society for blood and marrow transplantation; EHA: European hematology association; EU: European; HTA: Health technology assessment; NUB: *Neue Untersuchungs- und Behandlungsmethoden*; UK: United Kingdom; SmPC: Summary of product characteristics; SoC: Standard of care