Translating Innovation into access for ATMPs
3rd EU-Innovation Network multi-stakeholder meeting

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CASE STUDIES OF ACADEMIC DEVELOPMENT OF ATMP ARI0001 and ARI0002h

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Regulatory in advanced therapies

ATMPs Legal framework

ATMPs are under European regulation that states that their authorization **must follow** the centralized procedure.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

However, the regulation itself establishes a **hospital exemption (HE).**

European Regulation EC 1394/2007, directive 2001/83/EC and EC 723/2004

HE: Legal framework

- ATMPs prepared occasionally in a **hospital** and under the professional responsibility of a registered **physician** in order to comply with an individual optional prescription of a custom-made product intended for a **single patient**.

- Manufacture must be authorized by the competent authority.

- ATMPs entirely prepared, and **non-profit** used in centers linked to the National Health System and that its manufacturing is carried out in centers authorized for this purpose by the Ministry of Health and are medicines in the clinical investigation phase or medicines that the AEMPS considers that satisfy the guarantees of quality, safety, efficacy, identification and information.

European Regulation EC 1394/2007, directive 2001/83/EC and EC 723/2004

HE authorization clause - SPAIN

RD 477/2014 AUTHORIZATION OF ATMPs OF NON-INDUSTRIAL MANUFACTURE

- It allows the use of ATMPs under the conditions specified in the same authorization. Guarantees that the medicinal product satisfies the required quality, safety, efficacy, identification and information standards.

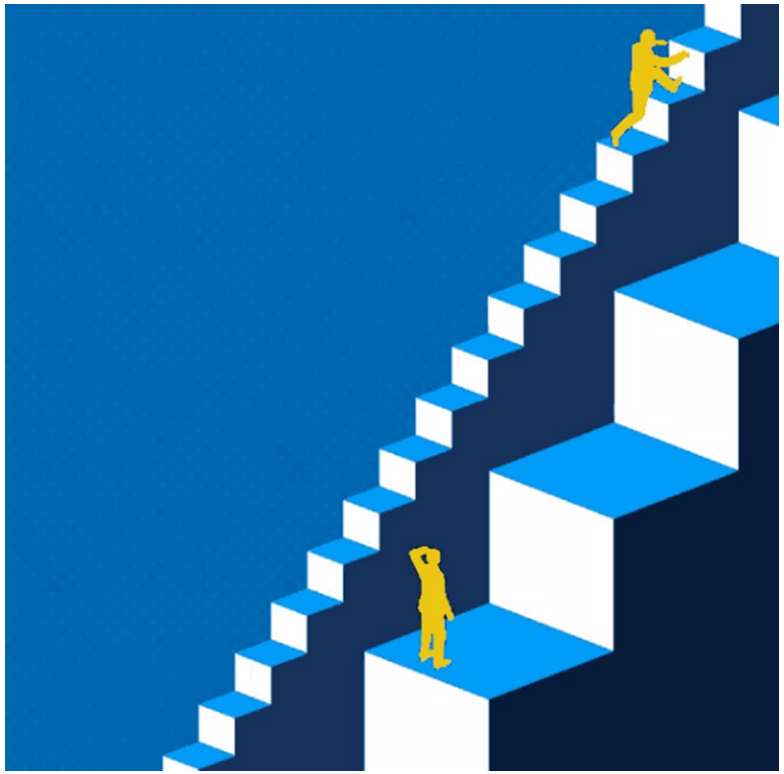
- The authorization of use may contain elements of cross-compliance which oblige the holder to submit additional data.

HE follows strict standards of traceability, pharmacovigilance, and quality.

Spanish Royal Decree 477/2014 complements EC 1394/2007, directive 2001/83/EC and EC 723/2004

HE: an opportunity for academia

- HE allows for the use of ATMPs under special conditions.
- HE is only applicable to individual patients treated in the hospital setting and it is limited to member states of the European Union (EU).
- HE is only conceded to the academic centers that developed the ATMP, being granted by the national competent authority (NCA).



What is ARI-0001?

INN: Varnimcabtagene autoleucel

- Completely developed in an academic hospital.
- Gene therapy product: Adult differentiated autologous T-cells from peripheral blood, expanded and transducted with a lentivirus to express a chimeric antigen receptor with anti-CD19 specificity [A3B1] conjugated to the 4-aBB and CD3z co-stimulatory regions.
- ARI-0001 cells (var-cel) was approved in Spain (HE) for the treatment of patients older than 25 years with acute lymphoblastic leukaemia (ALL) that are refractory or in relapse after a minimum of two lines of therapy or in relapse post-transplant.

What is ARI-0001?

INN: Varnimcabtagene autoleucel

Regulatory status:

- Use approval under hospital exemption (HE) was conceded to Hospital Clinic of Barcelona by Spanish Agency of Medicines and Medical Devices (AEMPS) for patients older than 25 years with relapsed or refractory CD19+ acute lymphoblastic leukemia (FEB 2021).
- First academic product granted with EMA PRIME designation (DEC 2021).
- PIP approved
- 2025 intent to submit a centralized MAA

What is ARI0002h?

INN: Cesnicabtagene Autoleucel

- Completely developed in an academic hospital.
- Gene therapy product: Adult differentiated autologous T-cells from peripheral blood, expanded and transducted with a lentivirus to express a chimeric antigen receptor with anti-BCMA specificity [J22.9] conjugated to 4-1BB and CD3z costimulatory regions.
- Regulatory status: ARI-0002h cells (cesni-cel) was approved in Spain (Hospital Exemption) by the Spanish Agency of Medicines and Medical Devices (AEMPS) for the treatment of multiple myeloma patients that are refractory or in relapse after a minimum of two lines of treatment (AUGUST 2024).
- Now under negotiation of price & reimbursement

Room to improve in Regulatory Agencies

Proposals to overcome the regulatory challenges on academic development

1. Risk assumption.
2. Tailored interaction with regulatory agencies (more flexibility).
3. Differences NCAs/EMA
4. Feasible requirements (limited funding capacity).
5. Regulatory fees-reduction.
6. Open-mind for innovative Point-of-Care manufacturing strategy.

Room to improve in Academia

Proposals to be taken by Academic centers

1. Need to guarantee strict quality standards.
2. Limit collaborations and external communications.
3. Real investment in staff, software and facilities.
4. Strategic regulatory-thinking