EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Highlights on the Committee for Advanced Therapies
Joint PCWP- HCPWP session, 3rd March 2023

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Committee for Advanced Therapies

CAT stands for

- Safe and efficacious first-in-class ATMPs
- Including incremental scientific-clinical knowledge in regulatory decision making
- Supporting ATMP developers
- Incorporating physician and patient perspectives in our deliverables
- Supporting patient access by analysing root causes of RWD deficiencies and by increasing interactions with HTAs
- Warning against unproven cell-based therapies
- Strengthened communication and exchange with EMA committees and working parties

What are the main differences to other medicines?

- Complex products to develop, manufacture, characterise, test
- Non-standard non-clinical & clinical development programmes
- Concomitant therapies, e.g. conditioning therapy
- Novel toxicities, risk assessment of insertional mutagenesis events
- Specific post-authorization obligations to address remaining uncertainties
- No precedent cases for regulatory decision making

CAT workplan 2023: Highlights for PCWP& HCPWP

1. ***B*enefit/Risk methodology:** Contribution to the finalisation of the reflection paper on single-arm trials

2. **Interactions with HTA bodies to enhance the access to innovative medicines for patients:** Product-specific discussions on newly approved ATMPs to present to HTA bodies the scientific grounds for the approval.

3. **Post -authorisation safety and efficacy follow-up for ATMPs.**

   CAT will prepare (a) scientific publication(s) on the follow-up of patients treated with AAV-based gene therapies and patients treated with CAR-T cells.

4. **Real World Data in regulatory decisions for ATMPs.**

   Use RWD to complement CT evidence and provide an additional perspective on the use and performance of medicines in everyday clinical use.

EMA-funded pilot study on spinal muscular atrophy (SMA)

- A severe, rare, autosomal recessive neuromuscular disease resulting from a deletion in the survival motor neuron gene 1 (SMN1) gene located on chromosome 5 (5q13.2)

Currently 3 medicinal products authorised for the treatment of SMA		
Spinraza (nusinersen) - 2017	Intrathecal bolus injection	For the treatment of pediatric and adult patients with 5q SMA
Zolgensma (onasemnogene abeparvovec) – 2020 (ATMP)	One-time IV administered, gene replacement therapy	Patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene
Evrysdi (risdiplam) - 2021	Oral solution injection	Patients with 5q SMA 2 months of age and older, with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies

EMA-funded pilot study on spinal muscular atrophy (SMA)

Procedural steps

- Detailed discussion with CAT subgroup on RWE on their needs
- Landscape of registries and informal discussions with 4 registry networks on feasibility of study

Main study objectives

- a registry-based cohort study of Spinal muscular atrophy (SMA) disease, with the aim to describe the natural history of SMA, the evolution of SMA care management over time and disease progression considering the new disease modifying therapies (including ATMPs) based on real world data from EU registries.
- Highlight the study challenges and lessons learned from performing the study within the registries.

EMA-funded pilot study on spinal muscular atrophy (SMA)

DESIGN	SOURCE	PERIOD	SIZE
Non-interventional descriptive registry-based cohort study of SMA patients	7 European registries (10 european countries) Clinical /Patient/combined Reported data	2010-2022	1200/1400 patients estimated

EMA-funded pilot study on spinal muscular atrophy (SMA)

OUTCOMES

- Natural history of SMA
- Post-diagnosis outcomes
- Assessment of DMT patterns
- Assessment of DMT safety

DESCRIPTIVE ANALYSIS

- Assessment of the hetereogenity of management of care or reporting.
- Assessment of the SMA Natural history in the untreated cohort.
- Clinical management evolution over time
- Descriptive analysis of DMT use & safety
- Descriptive analysis of DMT effectiveness

AADC deficiency

Upstaza, eladocagene exuparvovec

Disease:

- Ultra-rare genetic disease, 200 patients known/published, loss of dopamine production, no head control, sit, stand or walk, other symptoms, no approved treatments

Indication

- Patients aged 18 months and older with a clinical, molecular, and genetically confirmed diagnosis of aromatic L-amino acid decarboxylase (AADC) deficiency with a severe phenotype.

Treatment concept:

- Gene replacement based on AAV2 vector

Posology and method of administration

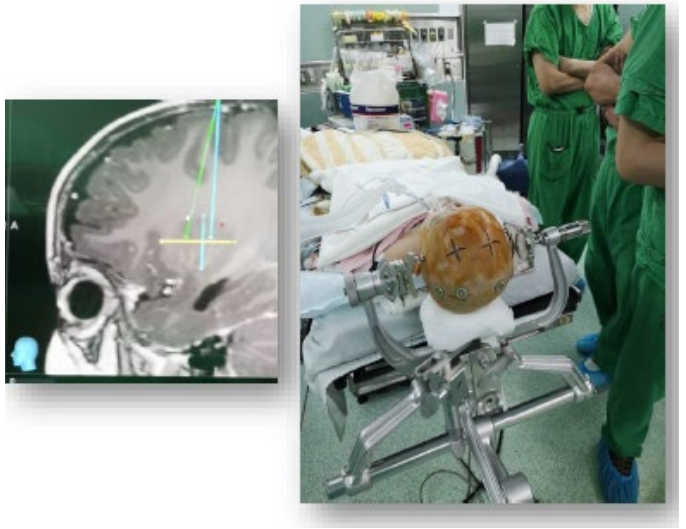
- 1.8 × 1011 vg, intraputaminal injection

AADC deficiency

Upstaza, eladocagene exuparvovec

Specific discussion points in B/R evaluation

- Comparability of manufacturing processes
- Relevance of clinical data generation in third country
- Specificities of administration procedure
- Extrapolation to younger/older patient population
- (Non-)comprehensiveness of data
- MA under exceptional circumstances
- Observational, registry-based study



By Prof. Opladen, Heidelberg University

Haemophilia A

Roctavian, valoctocogene roxaparvovec

Disease: Severe haemophilia A (congenital factor VIII deficiency)

Study: Single-armed. 104 weeks.

Indication

- Adults with severe haemophilia A who do not have inhibitors (antibodies) against factor VIII and who have no antibodies against adeno-associated virus serotype 5 (AAV5).

Treatment concept:

- Gene replacement based on AAV5 vector.

Method of administration:

- Intravenous infusion

Haemophilia A
Roctavian, valoctocogene roxaparvovec

- Orphan drug designation on 21st March 2016.
- Conditional authorisation on 24th August 2022.
- Efficacy:
  - CT demonstrated that Roctavian was effective at increasing the level of factor VIII activity and that this increase was sustained for at least 2 years.
  - 104 weeks after receiving a single dose of the medicine, 75.4% of the patients had decreased their symptoms to those of mild haemophilia.
  - The yearly number of bleeding episodes decreased by 85.5% and the need for additional factor VIII replacement treatment dropped by 97.5%.
- Safety: Hepatotoxicity treated with corticosteroids.

  Long term follow up.