EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

ATMP lifecycle support and patient access

CAT Industry Interested Parties Meeting

26th October 2021

Martina Schuessler-Lenz
Chair, Committee for Advanced Therapies
Paul-Ehrlich-Institut, German Federal Institute for Vaccines and Biomedicines

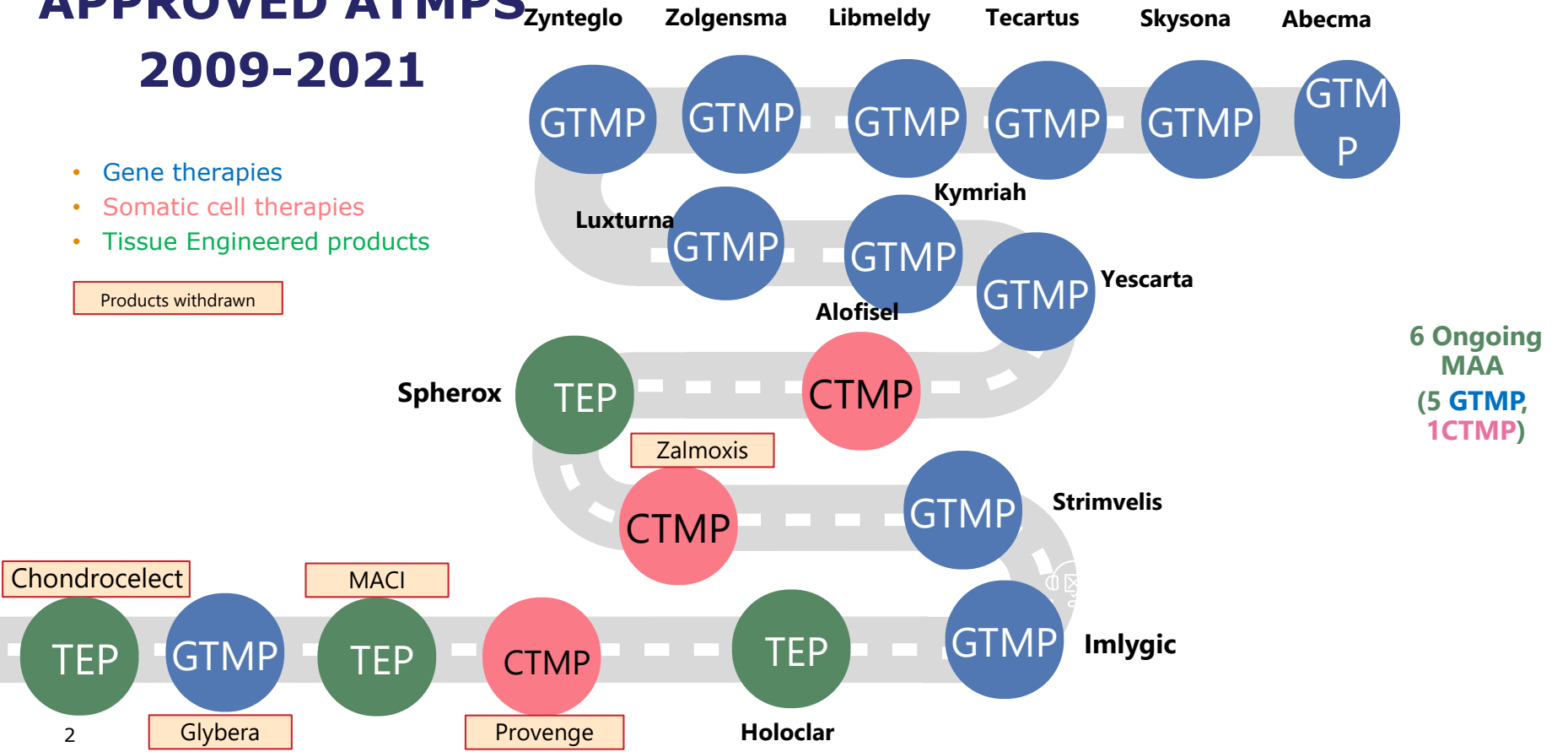
The number of EU approved ATMPs is growing.

Is this accompanied by timely and sustainable patient access to ATMPs?

APPROVED ATMPS 2009-2021

- Gene therapies
- Somatic cell therapies
- Tissue Engineered products

Products withdrawn



6 Ongoing MAA (5 GTMP, 1CTMP)

The ATMP life cycle – road to patient access

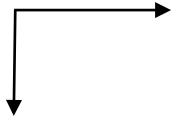
Pre-authorisation | Marketing A. | Post-authorisation

Primary evidence generation

- Single arm trials, orphan, unmet need
- Limited patient numbers
- Limited follow-up time
- Compelling efficacy data
- RW data to contextualize results

Wait for more data and delay MA?

Benefit-risk Uncertainties



Conditions/ Obligations

Post-authorisation evidence generation

- Adress uncertainties
- Follow-up safety and efficacy (ATMP regulation)
- Comply with pharmacovigilance
- Satisfy HTA and payers needs, outcomes-based reimbursement

Timely patient access to ATMPs

Review of CAT activities to support ATMP developers

Focus on pre-authorisation and authorisation phase

- Guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells. Special clinical considerations on CART cells, clinical development.
  - Includes gene editing considerations in quality and non-clinical sections. No specific GL envisaged in near future

- Guideline on core SmPC, Labelling and Package Leaflet for advanced therapy medicinal products (ATMPs) containing genetically modified cells. Draft in external consultation 31.10.2021, feedback welcome
  - Provides applicants and assessors with harmonized guidance on information to be included in the Product Information (PI) of ATMPs containing genetically modified cells.

Review of CAT activities to support ATMP developers (2)

- Questions and answers on the principles of GMP for the manufacturing of starting materials of biological origin used to transfer genetic material for the manufacturing of ATMPs. (EMA/246400/2021)
  - GMP considerations for viral vectors used as starting material

- Questions and answers on comparability considerations for advanced therapy medicinal products ATMP. (EMA/CAT/499821/2019)

- Questions and answers on use of out-of-specification batches of authorized cell/tissue-based ATMPs. (EMA/CAT/224381/2019)

Review of CAT activities to support ATMP developers (3)

- Questions and answers on the exemption from batch controls carried out on ATMPs imported into the European Union from a third country. EMA/354272/2019
  - Explains principles for exemptions from re-testing upon importation in the absence of Mutual Recognition Agreement

- Questions and answers related to the assessment of similarity for ATMPs in the context of the orphan legislation. 2018_qa_atmps_en
  - Revised/extended principles aimed to support market access of orphan ATMPs

Developed in collaboration with BWP, IWG, European Commission

CAT activities and work in progress – workplan and beyond

- Guideline on requirements for ATMPs in clinical trials
  - Current and 2022 work plan. Delayed related to BCP

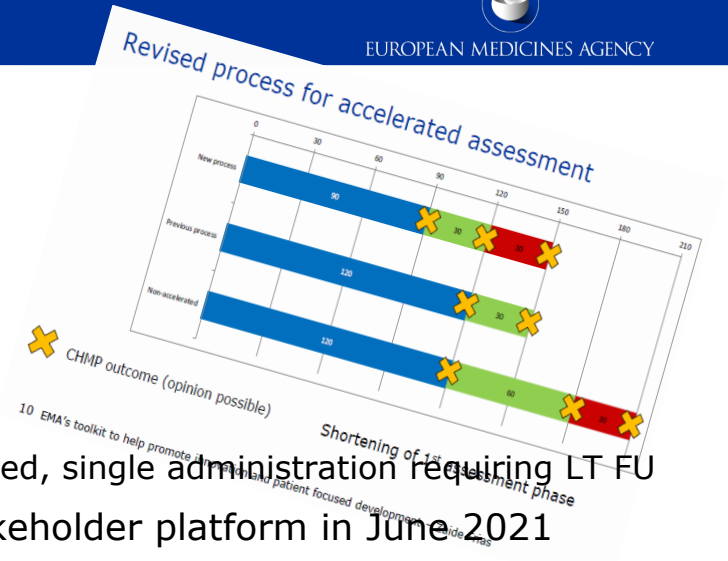
- Comprehensiveness of clinical data in marketing authorisations
  - Addresses the point „lack of consistent guidance when CMA is appropriate"
  - ➢ Presentation by Maura O`Donovan (CAT)

- ATMP specific aspects of the Clinical Trial Information System (CTIS)
  - ➢ Presentations on ERA and GMO related issues in marketing authorisations and clinical trials from Patrick Celis (EMA) and Tomas Boran (CAT). Recorded trainings and webinars, not ATMP specific, go to EMA homepage https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-training-support

CAT activities and work in progress (2)

- New Active Substance status of ATMPs
  - CAT involved, high priority, draft reflection paper planned to be published in 2021
- EU Master File for ATMPs
  - Discussed in the frame of EC pharmaceutical legislation revision
- Prime Toolbox – common themes from comments
  - Comments under review, plan to have updated toolbox published in Q1 2022, depending on FDA input. Industry encouraged to propose this topic for discussion at the BWP or QWP interested parties meeting.
- Procedure for consultation of Notified Bodies during marketing authorization of a combined ATMP, article 117 and Notified Body interaction
  - ATMPs are not subject to the requirements of article 117. CAT will look into the procedure for specific questions related to ATMPs once the overarching procedure for NB consultation is in place.

CAT activities and work in progress (3)



- Prime and Accelerated Assessment (AA) of ATMPs
  - 35%-40% of products in Prime Scheme are ATMPs
    - Small patient populations/orphans, high unmet medical need, single administration requiring LT FU
  - Analysis presented at 6th EMA meeting of industry stakeholder platform in June 2021
  - Average number of days in centralized procedure reduced, but only 1/9 in AA time frame
  - Compared to non-ATMPs more quality/CMC Major Objections, delayed GMP inspections
  - Need for robust data package at MAA
  - 5-year review of AA ongoing -> findings will be presented at Industry Platform R&D meeting 23.11.2021
  - Currently no room to revise the ATMP AA assessment schedule

Timely and sustainable patient access to ATMPs

The post-authorisation phase

The regulator`s perspective

- All authorized ATMPs are subject to post-authorisation safety and efficacy follow-up (obligations with MA) in PASS and PAES.
  - Aim: supplement available data, PhV, life cycle management, convert CMA to full MA
- Post-authorisation Real World data collection and reporting has gaps and deficiencies
  - Late planning, late engagement with registry holders, issues with implementation of ATMP specific data
  - Issues with identification of available disease registries in a fragmented EU landscape
- Call for early landscaping, feasibility analyses, planning during pre-authorsation phase
  - ➢ Presentations regarding CAT-EMA initiatives from Gianmario Candore (EMA) and Kieran Breen (CAT).

Timely and sustainable patient access to ATMPs

The post-authorisation phase (2)

The downstream decision makers perspective

- ATMPs are approved with too limited data
  - Small, uncontrolled single arm trials, uncertainty regarding duration of efficacy (treatment claimed lifelong/curative)
  - Conditional MA
- Strengthened EU HTA cooperation and joint clinical assessment of ATMPs

➢ Presentation regarding HTA initiatives from Flora Giorgio, EU-HTA cooperation office

The industry perspective

- Disharmonized post-authorisation data generation requirements vs central marketing authorisation

➢ Presentations from industry

Paul-Ehrlich-Institut, Germany

This CAT Industry Interested Parties Meeting is meant to reinforce dialogue and collaboration, while respecting our different roles.

We look forward to a fruitful meeting

Thank you for your attention

martina.schuessler-lenz@pei.de

European Medicines Agency, Amsterdam, NL

Photo: Rob Acket