Advanced Therapy Medicinal Products (ATMP)-a rapidly evolving regulatory landscape

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No affiliations to disclose
The new home of EMA!

EMA to relocate to Amsterdam, the Netherlands

Press release

20/11/2017

EMA to relocate to Amsterdam, the Netherlands

Agency to begin working immediately with Dutch government to ensure successful move by end of March 2019

The European Medicines Agency (EMA) will relocate to Amsterdam in the Netherlands. This decision was taken today by the EU 27 Member States in the margins of the General Affairs Council (Art. 50). The Agency now has just over 16 months to prepare for the move and take up its operations in Amsterdam on 30 March 2019 at the latest.

“We welcome today’s decision on the new location of EMA. Now that we finally know where our journey is taking us, we can take concrete actions for a successful move,” said EMA Executive Director Guido Rasi.
Presentation Outline

After viewing this presentation, the participant will be able to:

✓ Understand key definitions and the overarching regulatory guidelines in place for ATMPs, with a focus on Europe

✓ Recognize some of the early engagement opportunities available to interact with regulatory authorities
Definitions
Advanced therapy medicinal product (ATMP) means any of the following medicinal products for human use:

- a somatic cell therapy medicinal product (SCTMP),
- a tissue engineered product (TEP),
- a gene therapy medicinal product (GTMP)
- combined ATMP
Key Definitions in Europe

ATMPs are classified into 4 main groups:

- a somatic cell therapy medicinal product (SCTMP)
  - contain cells or tissues that have been manipulated to change their biological characteristics or cells or tissues not intended to be used for the same essential functions in the body. They can be used to cure, diagnose or prevent diseases

- a tissue engineered product (TEP)
  - contain cells or tissues that have been modified so they can be used to repair, regenerate or replace human tissue

- a gene therapy medicinal product (GTMP)
  - contain genes that lead to a therapeutic, prophylactic or diagnostic effect. They work by inserting 'recombinant' genes into the body, usually to treat a variety of diseases, including genetic disorders, cancer or long-term diseases. A recombinant gene is a stretch of DNA that is created in the laboratory, bringing together DNA from different sources

- combined ATMP
  - contain one or more medical devices as an integral part of the medicine. An example of this is cells embedded in a biodegradable matrix or scaffold
Committee for Advanced Therapies (CAT) at EMA

CAT - established in accordance with Regulation (EC) No 1394/2007 on ATMPs. Multidisciplinary committee, high level expertise - assess the quality, safety and efficacy of ATMPs, follow scientific developments in the field.

The Committee for Advanced Therapies (CAT) is the European Medicines Agency’s (EMA) committee responsible for assessing the quality, safety and efficacy of advanced therapy medicinal products (ATMPs) and following scientific developments in the field.

It was established in accordance with Regulation (EC) No 1394/2007 on ATMPs as a multidisciplinary committee, gathering some of the best available experts in Europe.

Role of the CAT:

The committee’s main responsibility is to prepare a draft opinion on each ATMP application submitted to EMA, before the Committee for Medicinal Products for Human Use (CHMP) adopts a final opinion on the marketing authorisation of the medicine concerned.

At the request of EMA’s Executive Director or the European Commission, the CAT can also draw up an opinion on any scientific matter relating to ATMPs.

The CAT also:

- participates in certifying quality and non-clinical data for small and medium-sized enterprises developing ATMPs;
- participates in providing scientific recommendations on the classification of ATMPs;
- contributes to scientific advice, in cooperation with the Scientific Advice Working Party (SAWP);
- takes part in any procedure delivering advice on the conduct of efficacy follow-up, pharmacovigilance or risk-management systems for ATMPs;
- advises the CHMP on any medicinal product that may require expertise in ATMPs for the evaluation of its quality, safety or efficacy;
- assists scientifically in developing any documents relating to the objectives of the Regulation on ATMPs;
Educational Reading Materials- EMA website


- Committee for Advanced Therapies (CAT). EMA website.  

- Guidelines Relevant for Advanced Therapy Medicinal Products. EMA website  
Opportunities for early engagement interactions with regulators
EMA’s Innovation Task Force (ITF)

+ Multidisciplinary group with scientific, regulatory and legal competences
+ Forum for very early dialogue on innovative aspects in medicines development
+ Particularly useful for SMEs, academics, researchers, to proactively identify scientific, legal and regulatory issues of emerging therapies and technologies
+ ITF briefing meeting (free of charge) intended to be much earlier than scientific advice
  + facilitate informal exchange of information
  + guidance more in development process, informing of existing formal procedures such as ATMP Classification, PRIME, Orphan Drug Designation, Scientific Advice
ATMP Classification by EMA

+ Optional but useful procedure (free of charge)
+ Scientific recommendation from CAT, after consultation with European Commission within 60 calendar days
+ Receive confirmation from EMA that product meets scientific criteria for defining an ATMP
+ Agreed public summaries published by EMA e.g.

| Autologous human adipose mesenchymal stromal cells, expanded in culture | Intended for cardiac repair | Tissue engineered product | 13/10/2016 |

+ Why do it?
  + Fee reduction (by 65%) for EMA scientific advice procedures
  + Including Classification documentation in CTA
    + Useful in navigating procedures at local level for countries with less experience and visibility of ATMPs
Interacting with Regulators through Scientific Advice

+ Obtain input from regulators on quality, non-clinical and/or clinical aspects of product development
+ Ensure development of product meets regulatory requirements for both CTAs and MAA
+ Adds value by ‘validating’ or optimizing proposed approach during development
+ Useful for potential partnering/investment discussions
+ Inclusion in CTA helps navigate through process in other countries
+ Beneficial at all stages of development
  + But, sufficient information must be provided to facilitate response
  + Purely hypothetical discussions - not usually beneficial
+ For ATMPs- requires careful planning; suggested national advice first (in ~1-3 countries) followed by EMA advice
National Scientific Advice

+ Larger agencies generally offer scientific advice procedures (e.g. UK, Germany, Denmark, Finland, Sweden etc.)
  + Other agencies offer advice only under specific conditions
+ Face-to-face meeting ~90 mins
+ Typically time for ~6-8 questions
+ Feedback early in development pre-CTA
+ Allows refinement of briefing materials and questions before taking more formal, lengthy and costly EMA advice
+ Procedures for scientific advice vary between the national agencies (as does the fee!)
  + Therefore, important to be aware of specifics of each intended procedure
EMAn Scientific Advice

+ Pan-European perspective
+ More formal than national advice
  + Written procedure (no limit to question #)
  + Template available to write into on EMA website
  + Lengthy, fixed and published timetable by EMA**
+ ATMPs typically out to Day 70 (rarely Day 40)
+ Expensive! (up to ~€ 85K) but:
  + Free, if have both orphan drug designation and SME status
  + Fee reduction with ATMP classification status
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Evolving landscape for clinical trials and ATMPs
Evolving Landscape in EU for Clinical Trials

+ Clinical Trials legislation (Regulation EU No 536/2014 adopted on 16 April 2014 and entered into force on 16 June 2014
+ Current status – pending submission EU portal readiness, anticipated in 2019

+ What does it mean for ATMPs?
  + Streamlined application procedure via a single entry point-EU portal
  + Harmonized review
  + Faster CTA approval timelines??
Evolving Landscape for ATMPs


+ One of the action points, currently planned to be completed by Q3 2018, is "To reduce discrepancies across the EU regarding the application of GMO rules (Directives on deliberate release or contained use) to ATMPs containing or consisting of GMOs. Issues relevant for both clinical trials and marketing authorisation will be addressed. The aim is to help create coherent approaches for the assessment of these novel products without changing the basic legislation."

+ Draft EMA guideline on investigational ATMPs, to create common standards for assessment, is planned for Q4 2018.
Closing Remarks

+ Regulatory environment for ATMPs is dynamic, complex and advancing fast!

+ Continual need to have current regulatory intelligence

+ Early, frequent and *appropriate* interactions with regulatory agencies is highly recommended

+ Raise awareness and understanding of ATMP development through scientific meetings such as this!
Additional Educational Textbook Reading Material


+ Textbook by Viswanathan and Hematti: “Mesenchymal Stromal Cells: Translation to Clinical Adoption” (2017)
Questions

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