EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Perspectives from EMA Scientific Committees

Committee for advanced therapy medicinal products – CAT

Regulatory challenges and opportunities

PCWP/HCPWP workshop on personalised medicines

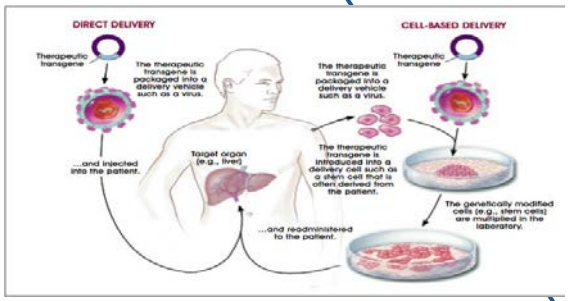
Presented by Margarida Menezes Ferreira on 14 March 2017
Senior Assessor and Scientific Advice Coordinator at INFARMED. PT Member at BWP, CAT

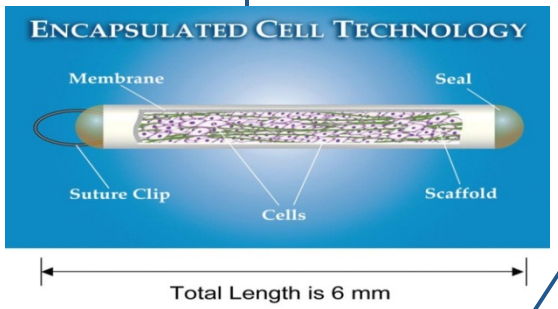
Gene Therapy Medicinal Products

Somatic Cell Therapy Medicinal Products

Tissue Engineering Products

Genetically modified cells

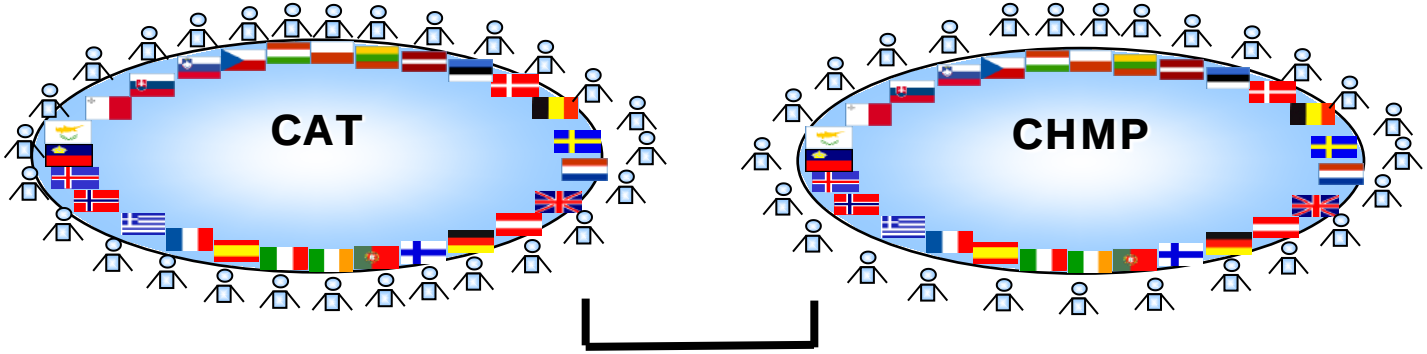





Severe burn victim before and 6 months after treatment with Dermagraft.

medical device + ATMP → combined ATMP

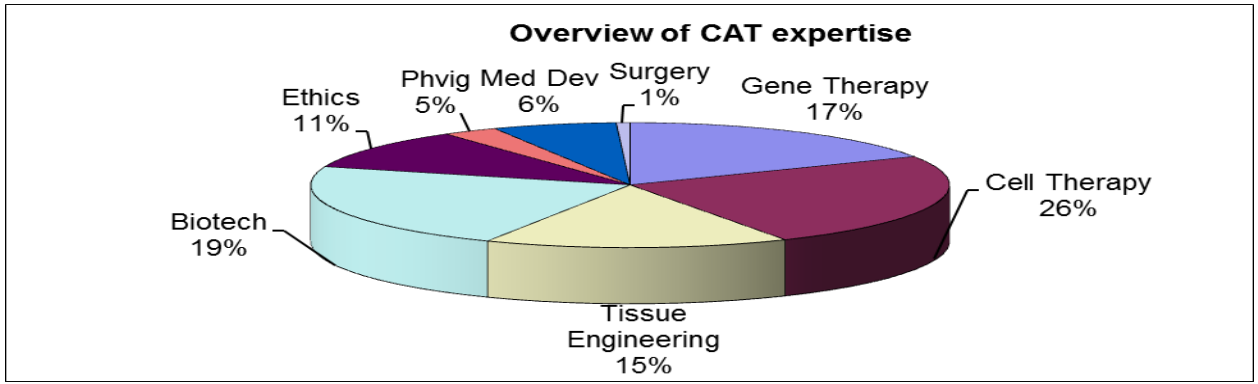
EMA Committees for ATMPs



5 „double members“

- 18 quality experts
- 12 non-clinical experts
- 21 clinical experts (including 4 members representing physicians)
- 1 inspector
- 4 patient representatives
- 8 other (scientists, heads of departments etc.)

Total **68** experts



Use favourable legal tools specific for ATMP's

COMMISSION DIRECTIVE 2009/120/EC
of 14 September 2009
amending Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use as regards advanced therapy medicinal products

→ **RISK BASED APPROACH**

REGULATION (EC) No 1394/2007 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 13 November 2007
on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004

→ **Long term safety and efficacy follow up**

Start March 2016

PRIME: in brief

Medicines eligible for PRIME must address an unmet medical need.

Preliminary data must be available showing the potential to address this need and bring a major therapeutic advantage to patients.

NON MA CAT procedures (December 2016)

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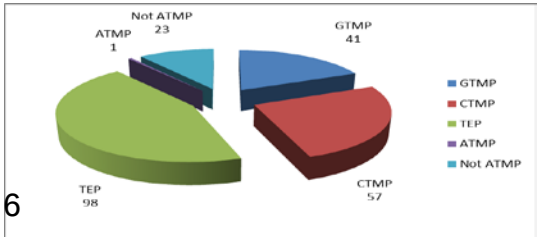

Classifications 2009-2016

Scientific recommendation on advanced therapy classification									
	2009	2010	2011	2012	2013	2014	2015	2016	Total
Submitted	22	19	12	22	20	28	61	60	244
Adopted	12	27	12	16	23	29	31	87	237

- **219** scientific advice procedures for ATMPs
- **47** PIPs
- **22** ATMP applications for PRIME, **7 granted**
- Over **300** ATMPs have been studied in clinical trials during 2011-2015 (~**200** CTs during 2004-2010)

slide provided by Paula Salmikangas

MAAs / CAT 2009-2016 (September)

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APPROVED AND LATER WITHDRAWN:

ChondroCelect for cartilage repair, 2009 *(withdrawn 06/2016)

MACI for cartilage repair, 2012 *(closure of EU manufacturing site 09/2014)

Provenge for treatment of advanced prostate cancer, 2013 *(withdrawn 05/2015)

APPROVED :

Glybera for treatment of LPL deficiency, 2013

Holoclar for treatment of limbal stem cell deficiency, 2015

Imlygic for treatment of advanced melanoma, 2015

Strimvelis for treament of ADA-SCID, 2016

Zalmoxis for treatment of high-risk haematological malignancies (adjunctive to HSCT)

✓ **2** ATMPs under evaluation, several new ones expected 2017

Embryonic stem cell trials for macular degeneration: a preliminary report

Steven D Schwartz, Jean-Pierre Hubschman, Gad Heilwell, Valentina Franco-Cardenas, Carolyn K Pan, Rosaleen M Ostrick, Edmund Mickunas, Roger Gay, Irina Klimanskaya, Robert Lanza

Summary

Background It has been 13 years since the discovery of human embryonic stem cells (hESCs). Our report provides the first description of hESC-derived cells transplanted into human patients.

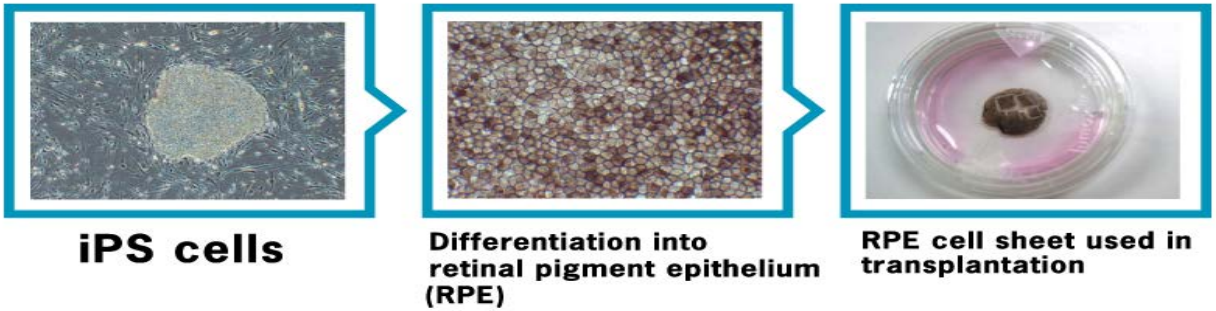
Methods We started two prospective clinical studies to establish the safety and tolerability of subretinal transplantation of hESC-derived retinal pigment epithelium (RPE) in patients with Stargardt's macular dystrophy and dry age-related macular degeneration—the leading cause of blindness in the developed world. Preoperative and postoperative ophthalmic examinations included visual acuity, fluorescein angiography, optical coherence tomography, and visual field testing. These studies are registered with ClinicalTrials.gov, numbers NCT01345006 and NCT01344993.

Interpretation The hESC-derived RPE cells showed no signs of hyperproliferation, tumorigenicity, ectopic tissue formation, or apparent rejection after 4 months. The future therapeutic goal will be to treat patients earlier in the disease processes, potentially increasing the likelihood of photoreceptor and central visual rescue.

Lancet 2012; 379: 713–20

Jules Stein Eye Institute Retina Division, Department of Ophthalmology, David Geffen School of Medicine, University of California, Los Angeles, CA, USA (Prof S D Schwartz MD, J-P Hubschman MD, G Heilwell MD, V Franco-Cardenas MD, C K Pan MD, R M Ostrick MPH); and Advanced Cell Technology, Marlborough, MA, USA (E Mickunas MS, R Gay PhD, I Klimanskaya PhD, R Lanza MD)

Pilot safety study of iPSC-based intervention for wet-type AMD



Great Ormond Street Hospital for Children NHS Foundation Trust

World first use of gene-edited immune cells to treat 'incurable' leukaemia

05 November 2015

A new treatment that uses 'molecular scissors' to edit genes and create designer immune cells programmed to hunt out and kill drug resistant leukaemia has been used at Great Ormond Street Hospital (GOSH).

The treatment, previously only tested in the laboratory, was used in one-year-old, Layla, who had relapsed acute lymphoblastic leukaemia (ALL). She is now cancer free and doing well.

This breakthrough comes from GOSH and UCL Institute of Child Health's (ICH) pioneering research teams with support from the National Institute for Health Research (NIHR) Great Ormond Street Biomedical Research Centre, who together are developing treatments and cures for some of the rarest childhood diseases.

Gene Editing – next big thing … ?

Transposons …

TALENS used in clinic …

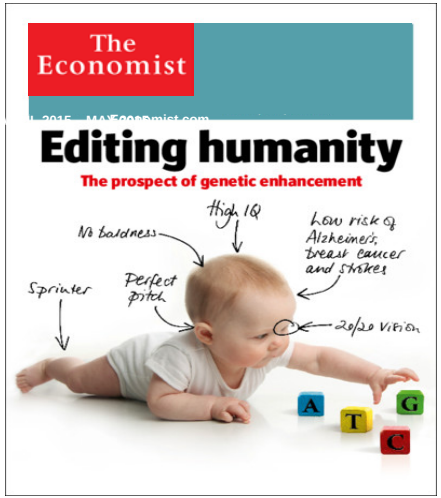
CRISPR/Cas very efficient editing … accurate?

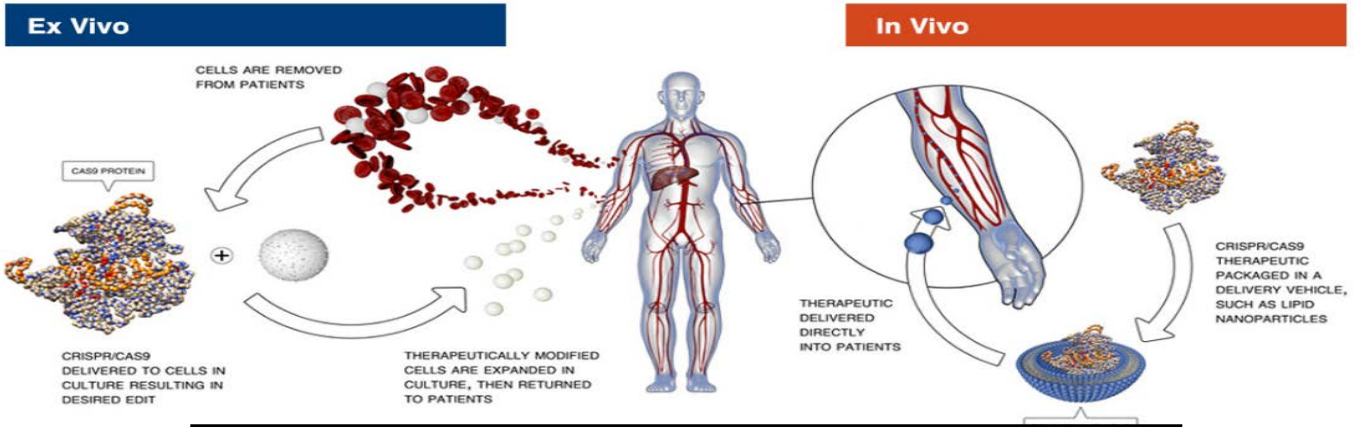
Zinc Finger Nucleases …

Briefing Meetings

CRISPR/Cas9

2012 to now!





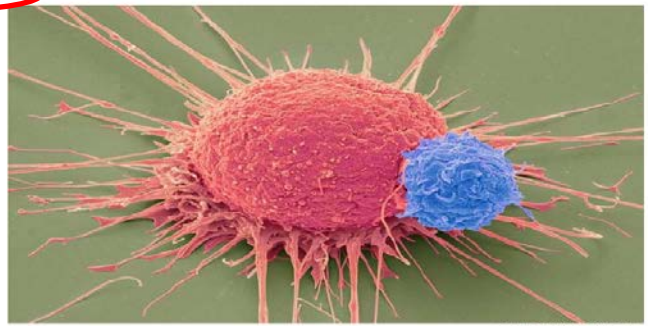
NATURE | BREAKING NEWS

First CRISPR clinical trial gets green light from US panel

The technique's first test in people could begin as early as the end of the year.

Sara Reardon

22 June 2016



STEVE GSCHMEISSNER/SPL

Human T cells (blue) will soon be modified using the CRISPR technique in a clinical trial to attack cancer cells (pink).

CRISPR, the genome-editing technology that has taken biomedical science by storm, is finally nearing human trials.

On 21 June, an advisory committee at the US National Institutes of Health (NIH) approved a proposal to use CRISPR–Cas9 to help augment cancer therapies that rely on enlisting a patient's T cells, a type of immune cell.

Advanced therapy medicines: towards increased development and patient access

News

03/02/2017

Advanced therapy medicines: towards increased development and patient access

Follow-up activities addressing stakeholder needs

The European Medicines Agency (EMA) has published today a set of ideas to better support development and expand patients' access to high quality, safe and effective advanced therapy medicinal products (ATMPs).

The existing efforts in the area of ATMPs are enriched by these ideas that were developed following a multi-stakeholder expert meeting on advanced therapy medicines organised in May 2016, at which EMA, the European Commission and representatives from the national competent authorities explored together with stakeholders ways to encourage innovation, research and development.

ATMPs, comprising gene therapies, tissue engineered products and somatic cell therapies, have the potential to reshape the treatment of a wide range of conditions. These therapies are particularly important for severe, untreatable or chronic diseases for which conventional approaches have proven to be inadequate.

Related content

- Multi-stakeholder advanced therapy medicinal products (ATMPs) expert meeting: exploring solutions to foster ATMPs' development and patient access in Europe (27/5/2016)
- Advanced therapy medicinal products

Related documents

- Issues identified by stakeholders at the workshop - Multi-stakeholder advanced therapy medicinal products (ATMPs) expert meeting: exploring solutions to foster ATMPs' development and patient access in Europe (06/02/2017)

slide provided by Paula Salmikangas

	Issues raised and on-going/planned activities	Additional details	Topic lead
	challenges within the regulatory network for awareness and best practice	provide an exchange platform for the benefit of the EU network.	
3	**GLP for ATMP (practical application of GLP to ATMPs)**	A CAT position paper on the application of GLP principles to ATMPs is under development.	EC/EMA[2]
4	**Focus on benefit-risk assessment by the CAT** ▪ Ensure transparency and communication of the benefit-risk assessment by the CAT	Approaches for conducting and documenting **benefit-risk assessment** are well established in EMA assessment templates and guidelines and equally applicable to all product classes. There is an opportunity to explore the need for introducing adaptations specific to ATMPs, to ensure a consistent, structured approach is used, and to monitor implementation.	EMA[2]
5	**Highlight the potential of the risk-based approach for ATMP developers when preparing the dossier for submission:** ▪ Develop a questions-and-answers (Q&A) document on risk-based approach for minimally manipulated ATMPs ▪ Raise awareness amongst developers, stakeholders and the European Medicines Network	**The risk-based approach** is a tool to provide flexibility in the data requirements for the MAA dossier to take account of the specific features of the product in question and their potential impact on the benefit/risk profile.	EMA[2]
6	**Orphan similarity of ATMPs** • Upon completion of the revision of the framework of the similarity concept (orphan legislation), to provide scientific and regulatory support to the EC in preparation for the future implementation of the revised	**Scientific and regulatory support** is based on experience/lessons-learnt from orphan similarity cases. The EC's proposal includes the description of the principal molecular	EC to lead, EMA[2] to support

CAT work plan 2017 – new topics

- Reflection paper on environmental assessment for gene therapy products / GMO containing ATMPs
- ATMPs and Platform technologies
  - E.g. Gene editing and Haplo cell-banks
- Scientific guideline
  - GL on genetically modified cells (revision); GL on Comparability of ATMPs (new)
- Use of Real-world evidence for the authorisation of ATMPs
- Reflections of benefit-risk assessment of ATMPs (= topic added from ATMP workshop 27/5)
- Scientific workshop/training of academia/SME (= topic added from ATMP workshop 27/5)

 slide provided by Paula Salmikangas

Special issues for ATMPs

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ATMPs are complex pharmaceuticals

- gene therapy: transgene, type of vector, genetically modified cells
- cell therapy: autologous, allogeneic, complex process, combination products
- development requires expertise from several areas e.g. cell and molecular biology, biotechnology, surgery, risk management, medical devices, ethics…

and on REGULATORY REQUIREMENTS

- ATMPs are in the frontline of fast evolving science → a product maybe already ”old”, when reaching the markets
- Manipulation of cells and use of recombinant nucleic acids may bear unknown risks, which may not be solvable through standardisation or quality control
- The product and its´ safety and efficacy profile need to be carefully prospectively planned and the key data should be based on findings that are robust and reliable

slide provided by Paula Salmikangas

ONLINE VOTING
WINNER
Rank #4

Director's CHOICE

Alcázar of Seville, Spain
Margarida Menezes Ferreira
Infarmed, Portugal

20th anniversary photo competition
EU countries - United in diversity

1995 2015
EMA