EMA / EBE Fifth Annual Regulatory Conference
London, December 16th, 2016

Session 4

Listening to the stakeholders of innovative medicinal products. >The Patient perspective

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Vice Chair of IPOPI

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INTERNATIONAL
PATIENT ORGANISATION
FOR PRIMARY IMMUNODEFICIENCIES

IPOPI:

- Has 59 National Member Organisations
- Represents more than 50,000 patients worldwide

THE GLOBAL ORGANISATION WORKING TO **IMPROVE**
THE QUALITY OF LIFE FOR PEOPLE WITH PRIMARY IMMUNODEFICIENCIES

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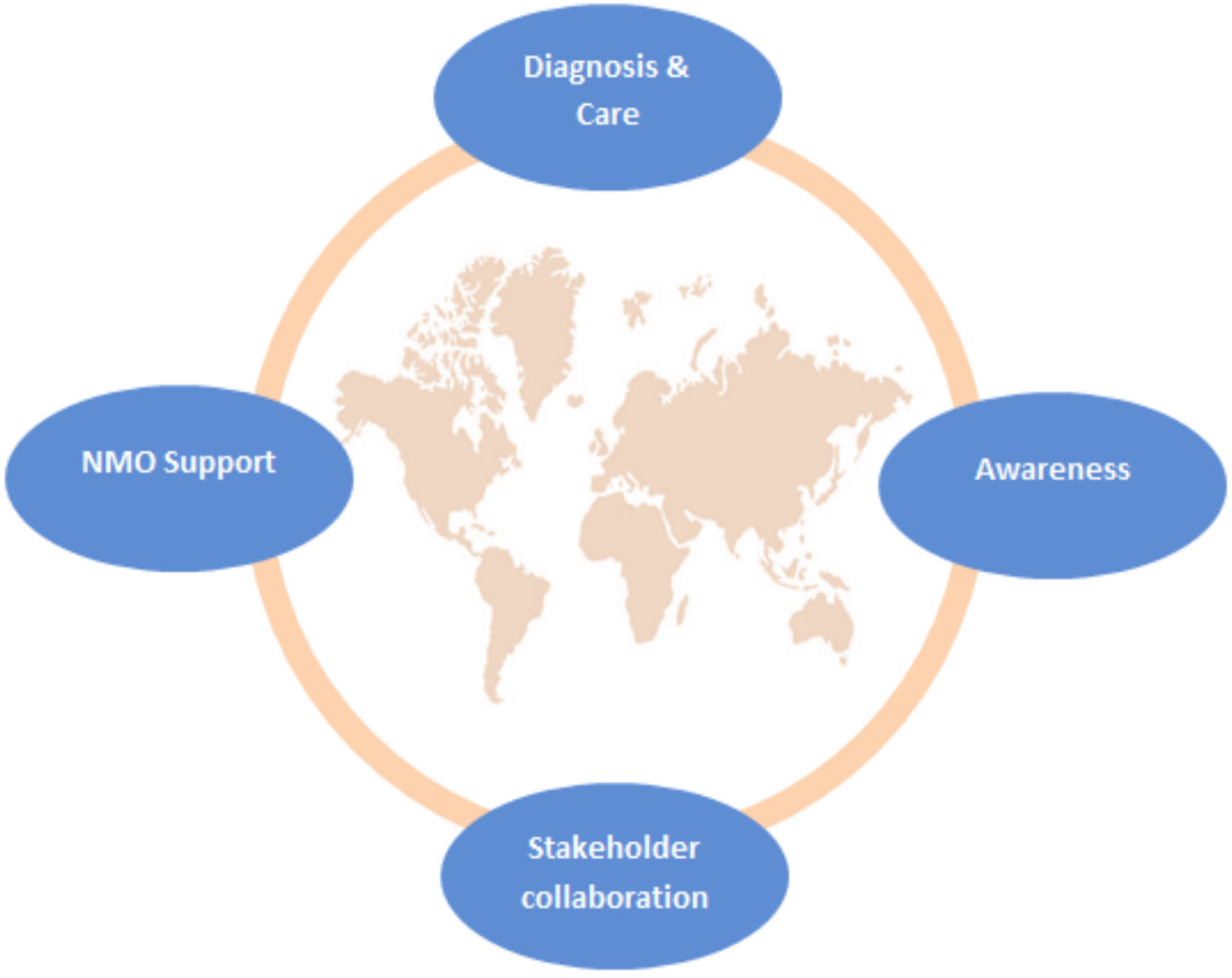
IPOPI strategic objectives



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PID and ATMPs

- **PIDs** are a large group of more than **300 genetic disorders** caused when some components of the immune system (mainly cells and proteins) do not work properly.
  Patients with PID are prone to infections and a high risk of cancer.

- PIDs are a very active and promissing field for ATMPs, with **gene therapy**:
  Clinical trials are advanced : severe combined immunodeficienciency (SCID-X1), Wiskott-Aldrich Syndrome (WAS), adenosine deaminase (ADA-deficient SCID),
  Chronic granulomatous disease (CGD) has started.

Quick survey on ATMPs among IPOPI National Member Organisations

15 EU
Austria
Belgium
Cyprus
Finland
France
Greece
Hungary
Ireland
Italy
Romania
Slovenia
Spain
Sweden
The Netherlands
UK

- With regard to your experience in your country, from a patient perspective:
  - how could/should **access to ATMPs trials** be improved?
  - how could/should **access to ATMPs** be improved?
- When patient organisations should be involved in the development process of ATMPs ?

7 Non EU
Argentina
Australia
Hong Kong
India
Russia
Serbia
USA

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First finding

- No or few knowledge/experience of some Patient Org. on ATMPs
- No full information

  We know about Gene therapy, but other trials must exist we don't know about
- Physicians may be informed on ATMPs, but not all have experienced this

  Access to clinical trials is always suggested by the treating doctor and, therefore, it depends on luck.
- No expert, no access: lack of experts, of centres of expertise

  We don't have ATMPs in our country. For having clinical trials, first of all we need medical expertise centers.
- The field is not so regulated

  With week health system my country is an open field for unfair clinical trials

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Our vision for the patient

Not	But
a Trial subject, nor an End customer	a Partner, a true Stakeholder

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Conditions for success

- Experts, center of **expertise**

  Clinical trials for ATMP should enter our country as any other developing country directly through recognized PID specialists.

- Physician **cooperation**
  - throughout the country

    Healthcare professionals, e.g. in regional immunology centres, must also work with the highly specialised centres to make sure eligible patients are aware of these clinical trials.
  - International cooperation
- **Confidence**

  In order to accept to be part of a trial, we patients need to feel that our doctor is experienced but also is supported by experts from academic centres abroad.

  The circumstances in every clinical trial should be strongly and clearly advertised so they could provide a feeling of safety and protection to the patients.
- **Cross border regulation**
  - Patient rights to access to clear and full information
- **Involvement of relevant patient organisations**

  to ensure patient-centered approach

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How to improve access to ATMPs trials

1- Increase interaction between stakeholders

A greater interaction between all the involved stakeholders in the clinical trials, including patients through patient organisations, from an early stage in the process.

Information

To relevant patient organisations so information can be passed on to patients if appropriate

- What, what for
- When
- Eligibility
- Benefits versus risks

> In lay language

> On/off line (see ex.), fact sheets, …

Consultation

Patient organisations should be consulted on:

- quality-of-life aspects of treatment, highlighting all aspects of the use, efficiency, side-effects ,… of ATMP
- the distribution methods and reimbursement issues.

> Patient Org., patients and caregivers are data resources

Inclusion

Include Patient Org. in the steering committee of the national Reference Center where decisions on ATMPs trials inclusion and management are made, in ethical committee.

> Patient Org., patients and caregivers are stakeholder

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Patient Org. Publications

CGDSociety

Supporting families affected by chronic granulomatous disorder

Become a member

#CGDSOCIETY

Information and Support · Treatments · Research · Get involved · Donate

Search for...

New gene therapy trial for X-CGD

CGD can be cured by bone marrow transplantation. However, this is sometimes associated with significant risk, in part because of toxicity associated with the treatment required to suppress the patient's own bone marrow and allow the donor marrow to establish and grow. This is particularly true if the patient is very unwell at the time of transplant. There may also be toxicity because donor cells can recognise the host as foreign, and can therefore attack and destroy many body tissues. This is called graft versus host disease. To reduce this problem, and to make sure that the new marrow is not itself rejected, the bone marrow from the patient and from the donor are matched in a similar way to that of blood group matching for transfusion using HLA tissue typing. For patients with CGD, most experts would not recommend a bone marrow transplant unless the match was very good, either from a brother or sister, or from another unrelated donor. However, for a significant number of patients, there is no ideal matching donor.

For these reasons, GENETHON, a not for profit French biotechnology laboratory, is testing strategies based on the use of harmless viruses, called lentiviruses, to correct the problem in phagocytic cells, and to provide a lifelong source of corrected cells by introducing the new gene into bone marrow. This is known as gene therapy. These viruses have been specially engineered in the laboratory in such a way that they are harmless, and unable to grow and infect other people. They are therefore simple carriers of the new gene into cells. Once in the cell the new gene is 'spliced' into the existing chromosomes, which carry all our genes. If this new gene can be placed in a special cell called a stem cell, which is normally present in the bone marrow and is like a 'parent' cell, then it will be passed onto all other cells in the blood, or 'daughter cells', including most importantly, the phagocytic cells.

Here we answ

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PID UK

Supporting families affected by primary immunodef

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Home

About us

What are PIDs?

The basics

Types of PID

Inheritance

Symptoms and diagnosis

Treatment »

Management

Patient stories

Research

General FAQs about PIDs

Dictionary of terms

Specific PID conditions

Resources for patients, carers and professionals

Useful contacts and links

Living with PIDs

Advocacy

Get involved

Gene therapy

Great advances made in the last ten y treat and cure primary immunodeficie

What is gene therapy?

Gene therapy is a 'mini gene transpla patient with a PID, replace the defecti fully functioning genes and then give t The cells can then go on to produce th

Having gene therapy is similar to havi need chemotherapy beforehand to ge as possible. This is called 'conditionin immunodeficiency, gene therapy can In most other forms of PID, chemothe bone marrow transplant is needed.

A big advantage of gene therapy is th is not a problem like it can be with bor from another person. Also, because it

La thérapie génique : une idée extraordinaire devenue réalité

Les patients atteints de DIP n'ont pas tous un donneur géno-identique et des complications immunologiques sévères ou infectieuses peuvent entraver les résultats d'une greffe partiellement compatible. La modification génétique des cellules souches malades s'est progressivement imposée... Cette idée extraordinaire est devenue une réalité, suite au premier essai réalisé en France en 1999.

Armand, 14 ans, le jour de la rentrée en 3e

Atteint d'un DICS, sans donneur compatible, Armand est traité par thérapie génique le 4 mai 2001. Avec succès. Mais pour lui, c'est le passé ! Il a une vie tout à fait normale, hormis une restriction concernant la piscine (otite)

Une stratégie bénéfique en l'absence de donneur compatible

Les DIP sont les premières pathologies guéries par thérapie génique. Aujourd'hui, un patient atteint de DIP peut être éligible à la thérapie génique chaque fois qu'il n'y a pas de donneur compatible et qu'il existe un protocole de thérapie génique approuvé. Les résultats cliniques montrent aujourd'hui un bénéfice clinique stable et à long terme pour trois déficits immunitaires : le DICS-X1, le défaut en ADA et le syndrome Wiskott-Aldrich. Pour autant, depuis 1999, nous poursuivons nos efforts de recherche pour toujours améliorer cette procédure.

La thérapie génique donne des résultats comparables – et peut-être meilleurs – que la greffe haplo-identique

Récemment, nous avons fait une comparaison des résultats cliniques et immunologiques obtenus par la thérapie génique, auprès de 14 patients atteints de DICS-X1, avec ceux d'une greffe haplo-identique pour la même maladie, dans la même période et dans le même centre. Les résultats montrent un net avantage

Points sur les essais en cours

DICS, changement de vecteur

Nous avons décidé de changer de vecteur viral, car les lentivirus présentent des avantages sur les rétrovirus. Cela signifie que nous devons reprendre l'essai depuis le début, à savoir, depuis la phase préclinique.

Syndrome de Wiskott-Aldrich (SWA) : Milan et Paris

En 2013, une équipe italienne a montré dans un essai conduit sur 3 patients atteints du SWA les bénéfices de la thérapie génique sur les lymphocytes T, les plaquettes, les lymphocytes B, ainsi que sur les signes cliniques.

Un essai clinique similaire, avec le même vecteur, est en cours à Paris, – les résultats devraient être publiés prochainement. Tout laisse à penser qu'ils sont très encourageants et similaires à ceux rapportés par l'équipe italienne.

Thérapie génique : des DIP à d'autres pathologies

Nous appliquons l'expérience acquise à partir d'une maladie génétique simple à des modèles pathologiques bien plus complexes comme le SWA, ainsi qu'à des maladies touchant l'hémoglobine (

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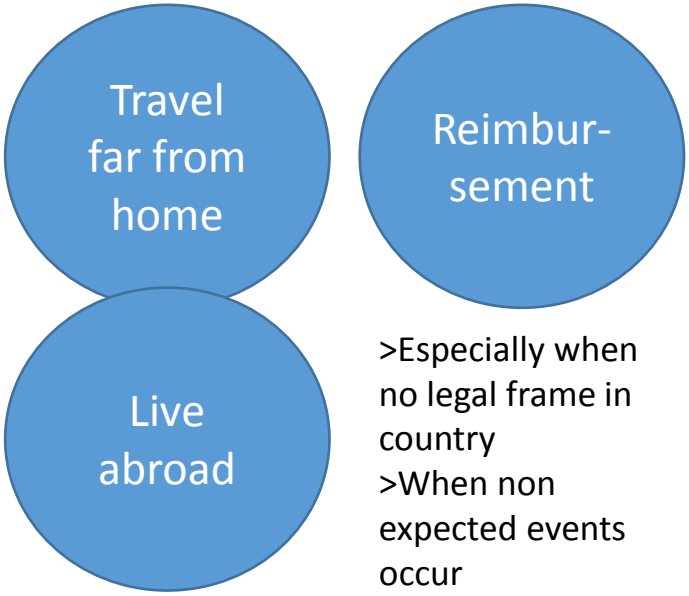
Improve access to ATMPs trials

2- Lower burden of trial

A greater interaction between all the involved stakeholders in the clinical trials, including patients through patient organisations, from an early stage in the process.



>Especially when no legal frame in country
>When non expected events occur

Cases

- *A young patient diagnosed with ADA –SCID with no matched BMT donor. The physician considers gene therapy, but ADA-SCID gene therapy is not authorised in the country and patient need to go abroad. It is not covered by the Social Security, except for special authorisations by the Ministry of Health – a process with which the patient group is not familiar.*
  EU country
- Our experience shows that besides many ethical issues we have to deal with more practical things. Two patients were enrolled for gene therapy trials for WAS in Europe. Both developed acute lymphoblastic leukemia but such complications were not going to be covered. Non EU country
- *We do not have clinical trials based in the country. The few patients taking part in a clinical trial are on the basis of programmes run in the US.* Non EU country

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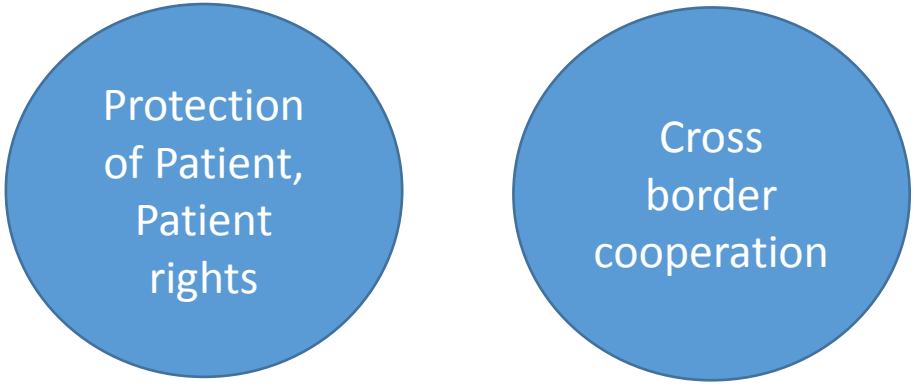
Improve access to ATMPs trials

3- Align regulation



It might be much easier in Europe without boarders to establish multicountries and centres working groups to make sure that patients from one country can have access to ATMP in another.

> A Patient Engagement Framework, including alignment between EMA and FDA

This is a very important question. First, we need to make sure that the regulator understands patient preferences and desires, including patient thoughts on the level of risk they are willing to accept in exchange for certain benefits. Specifically, it should develop a model for incorporating the patient voice and viewpoints within its evaluation ATMPs.

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Access to ATMPs

Availability	**When a patient needs it, wants it, is medically eligible**	*ATMPs should be possible when no other treatment is available*
Accessibility	**Therapy to patient rather than patient to therapy**	*The cost associated with travel and accommodation are to be covered by the sponsor but this does not take into account the problems of up rooting your family*
Affordability	**Price and reimbursement**	*With a price of 600 000 Euro of Strimvelis, not being approved in my country, it can be available for patients with a charity support only.* *Cost is an important factor. It will affect decisions made by policy makers*
Research	**Efficience, safety and convenience**	*Bring ATMPs to patients through innovative pathways. For example, (simplistically) cell collection at treatment centre nearer to patient, transport cells to centre where cells would be treated with gene therapy vector and gene corrected cells returned to treatment centre for infusion into the patient*

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The role of Patient organisations (1)

- Patient organisations could be involved in:
  - **Highlighting patient unmet needs** and so help steer research needs
  - **Support funding grant applications** to support the early development of ATMPs
  - **Supporting calls for funding** for better infrastructure for manufacture facilities for ATMP products
  - Playing a role in **linking patients, researchers and physicians**
  - **Educating people** about these technologies, research processes, clinical trials.
    Encouraging community to ask about clinical trials
  - Helping reach out to patient community **for research samples**
  - Reaching out to community and help **identifying patients who might benefit** from the ATMP

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The role of Patient organisations (2)

- Patient organisations could be involved in:
  - Calling for **streamlined and transparent processes for approval** to ensure timely delivery for patient benefit
  - **Peer reviewing of Marketing Authorisation** for ATMPs
  - **Involvement in ethical review committees**, Committee of Advanced Therapies, Health Technology Assessments etc
  - Providing **patient experts and patient testimony**
  - Advocate to ensure **transparency of decision making** regarding approval ATMPs and pricing
  - Advocate to ensure **transparency of ATMP outcomes** and giving feedback to the community
  - ATMPs have to compete on clinical efficacy with current and future conventional therapies so **helping provide evidence as to patient benefit**, societal benefit and economic cost benefit is vital
  - **Pharmacovigilance activities** and messaging around any adverse events.

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Thank you for your attention!