EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Stakeholders' perspective on the value of orphan designation

Academic perspective

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What is CIBERER?

- **CIBERER:** One of the 11 public consortiums from Carlos III Health Institute (ISCIII). Acts as a National reference, coordinates and fosters research in RDs.

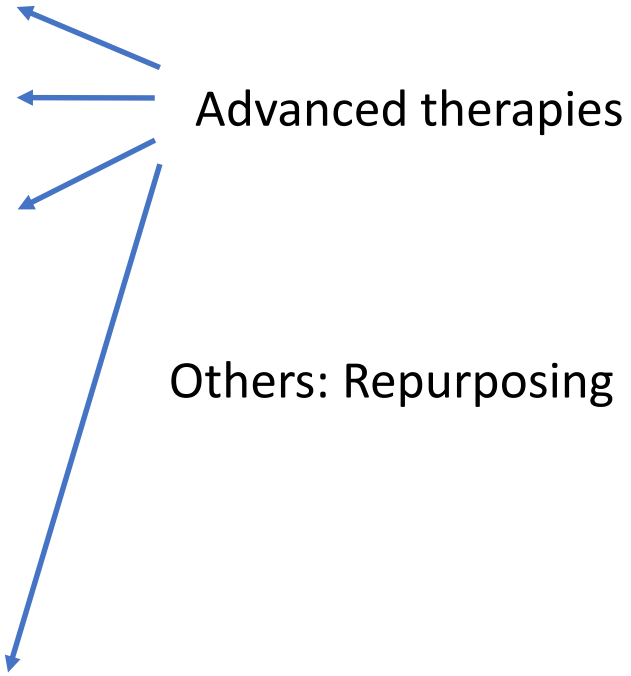
- **Cooperative network structure:** 78 research groups at the main research institutions (research centers, universities and hospitals). More than 700 people devoted to the investigation of different RDs.

- **Aim**: Generation of new scientific knowledge to understand the **biological bases**, improve the **diagnosis** and develop **new therapies** for RRDD.

CIBERER´S experience with ODD

Sponsor of 10 ODD by the EMA (4 of them by the FDA as well).

CIBERER PI	Substance	Indication/RD	Agency	Reference
CIEMAT-IIS FJD	Lentiviral vector carrying the Fanconi anaemia-A (*FANCA*) gene	Fanconi anaemia type A	EMA FDA	EU/3/10/822 FDA 16-5193
CIEMAT-IIS FJD	Lentiviral vector containing the human liver and erythroid pyruvate kinase (*PKLR*) gene	Pyruvate kinase deficiency	EMA FDA	EU/3/14/1330 FDA 16-5168
IDIBELL & CIPF	Temsirolimus	Adrenoleukodystrophy	EMA	EU/3/16/1669
CIEMAT-IIS FJD	Haematopoietic stem cells modified with a lentiviral vector containing the *CD18* gene	Leukocyte adhesion deficiency type I	EMA FDA	EU/3/16/1753 FDA 16-5453
HSJD & UPO	Ubiquinol	Primary coenzyme Q_{10} deficiency syndrome	EMA	EU/3/16/1765
IBV & IIS FJD	Metformin	Progressive myoclonic epilepsy type 2 (Lafora disease)	EMA FDA	EU/3/16/1803 FDA 17-6161
UAB & HSCSP	Gefitinib	Fanconi anaemia	EMA	EU/3/18/2075
UAB & HSCSP	Afatinib	Fanconi anaemia	EMA	EU/3/18/2110
IDIBELL	Dimethyl fumarate	Adrenoleukodystrophy	EMA	EU/3/19/2236
CIEMAT, UC3M & IIS FJD	Autologous skin equivalent graft composed of keratinocytes and fibroblasts genetically corrected by CRISPR/Cas9-mediated excision of mutation-carrying *COL7A1* exon 80	Epidermolysis bullosa	EMA	EU/3/20/2253



Benefits of getting an ODD

- **Affordable to academic groups**: Can be supported by experimental non-clinical *in vitro* and *in vivo* data

- **Added value** to academic research projects:
  - Increases **visibility** to stakeholders
  - Access to specific **funding**
  - Attracts attention of **industries**
  - Enhances relationships with **patients' associations**
  - Protocol Advice, PRIME, etc

Difficulties from the Academic Perspective

❑ Prevalence determinations

- Provide access to information already available (previous ODDs for the same disease).
- Simplify prevalence evaluation for RD clearly below 5/10,000.

❑ OD Application for a recently discovered RD

- Provisional applications for RDs with undetermined prevalence.

Difficulties from the Academic Perspective

- **Limited calls specific for ODD**
  - ✓Specific National and European calls for ODs

- **Modest knowledge in academic groups of regulatory issues related to drug development for RRDD.**
  - ✓Specific training initiatives for academic scientists and clinicians

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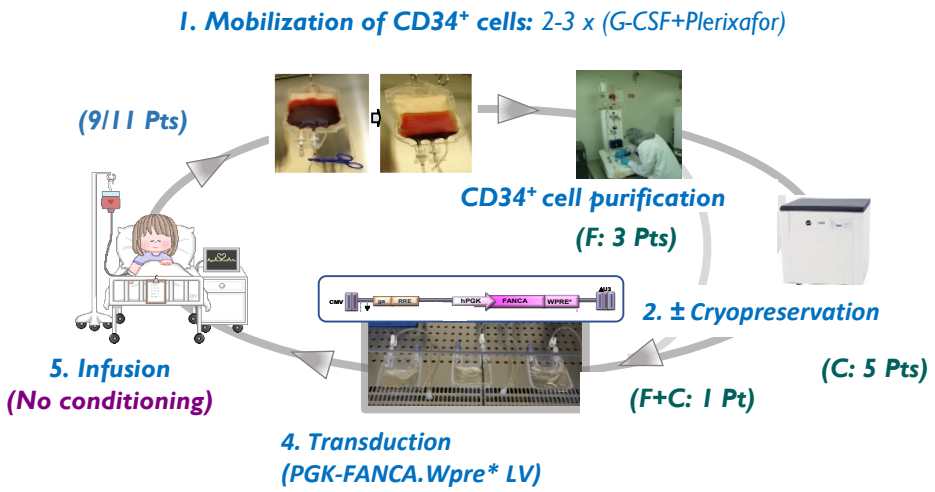
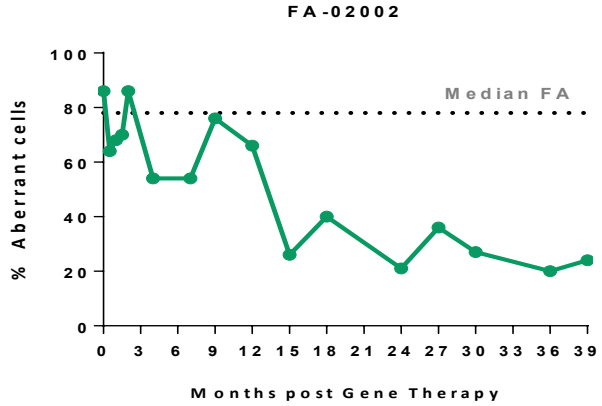
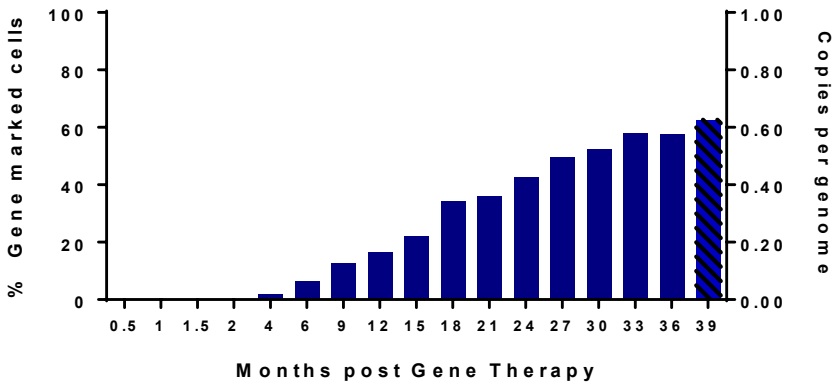
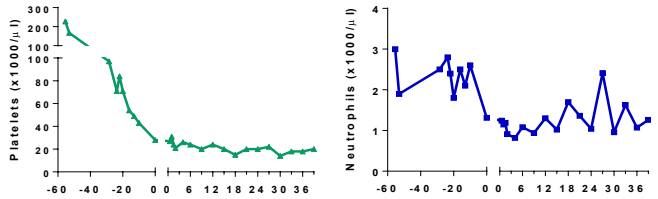
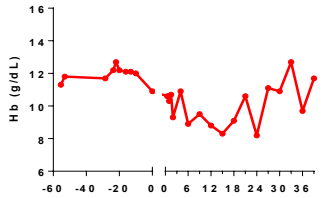
Case study:
Gene therapy for Fanconi anaemia











Case study:
Gene therapy for Fanconi anaemia

2010

- ✓ EMA ODD

2012

- ✓ ODD Call: Spanish Ministry of Health

2013

- ✓ FP7 ODD Call: Eurofancolen I

2015

- ✓ FDA ODD
- ✓ AEMPS Approval: Phase I/II Clinical trial

2016

- ✓ 1st patient treated
- ✓ Licensing therapeutic vector to rocket pharma

2018

- ✓ EMA PA
- ✓ FDA: IND approval
- ✓ AEMPS: Phase II trial
- ✓ RMAT & Fast track designation

2019

- ✓ Last patient Phase I/II
- ✓ 1st patient treated global trial Phase II (Standford U.)
- ✓ EMA: PRIME

Suggestions for Improvement

- Promote **early interaction of researchers with regulators,** ODD, SA, PRIME, etc.

- **Regulatory requirements should be closer to researchers,** by training scientists and technology transfer officers in regulatory matters.

- **Regulatory issues should be considered within research project plans**, i.e. including a specific milestones related to ODD applications.

Conclusions

- The ODD application itself represents a **great opportunity** for the added value of academic groups.
- **Early interaction with EU regulators** is important for academia to understand the regulatory requirements needed to generate robust evidence to assess the efficacy and safety of new drugs for RRDD.
- **Improved collaboration between industry and academic researchers** is necessary for the efficient translation from seminal discoveries to product development.
- Many of the key insights behind **transformative drugs have emerged in publicly funded academic teams,** being further developed through public-private partnerships.

Conclusions

The future of patients suffering from rare diseases will depend on improved **knowledge** of the disease, better **diagnosis** and development of new **therapeutic options**.

Efficient **interactions between academic teams and the industry** are essential to reach these goals.

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Thank you for your attention

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