

ORPHANDEV,
A Clinical Trials Network
Dedicated to Orphan Drugs and therapeutics development for rare diseases

Authors: Yolande Adjibi*, Olivier Blin, Joëlle Micallef-Roll

SUMMARY

Orphandev is a French network dedicated to clinical development of orphan medicinal products. Because leading clinical trials in rare diseases' field is submitted to numerous difficulties, Orphandev gathers skills and strengths in order to make orphan drugs available to the patients as fast as possible.

INTRODUCTION

Rare Diseases issues have grown in interest over the past ten years. This is highly due to general awareness of their existence. Public Authorities have enforced many policies that have the results of boosting research on this filed.

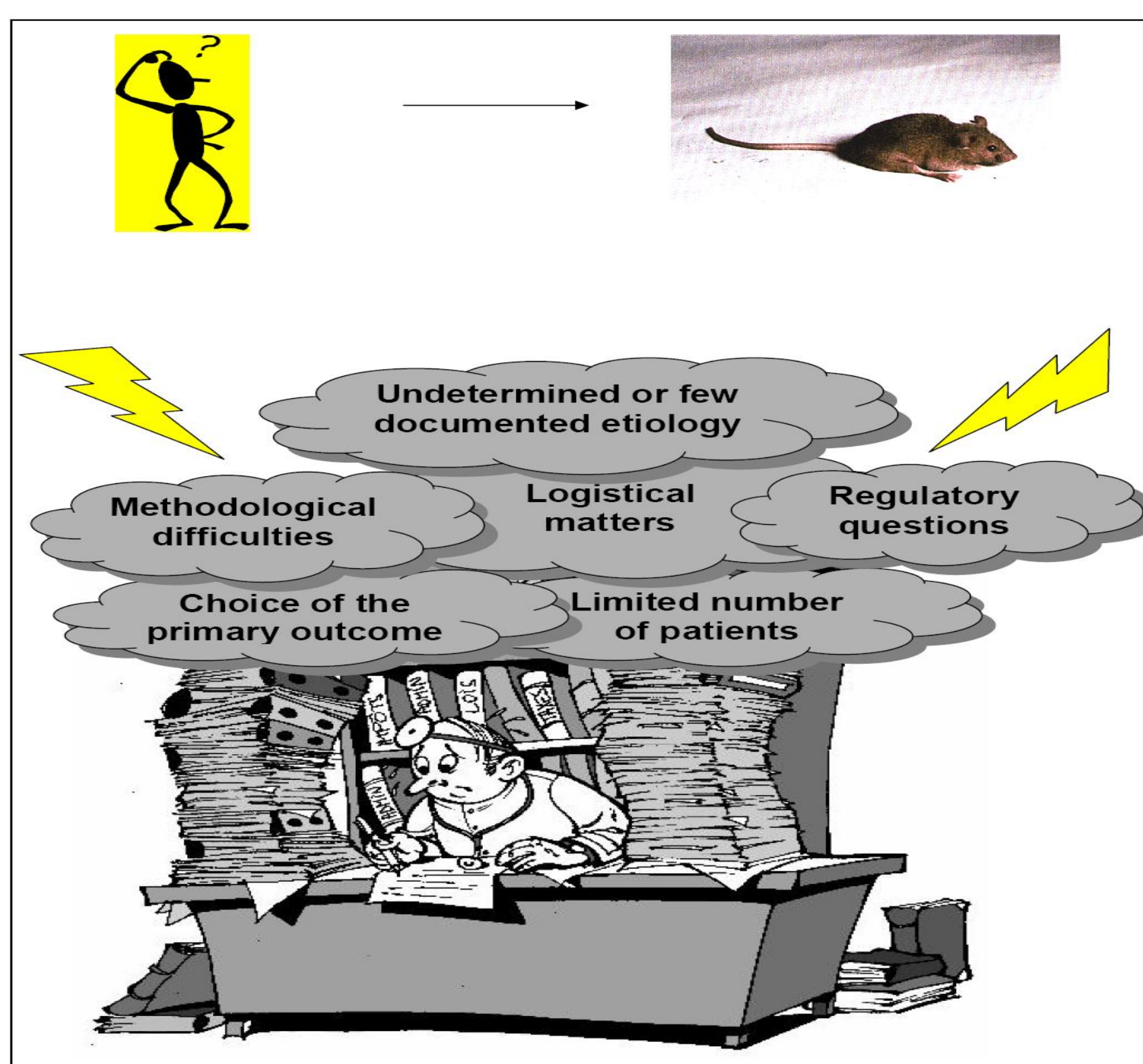
Nevertheless, in spite of the great dynamic cast in Europe, development and availability of orphan therapeutics still be problematic regarding rare diseases' specificities. More than ten years after the European Orphan Drugs Regulatory adoption, difficulties to produce treatments for rare diseases still remain [1]. Indeed in Europe in 10 years of Orphan Drugs Policies, only 59 treatments have been received approvals [2]

This may be due to the difficulties of leading clinical trials in rare diseases' field [3] [4] [5]

In this context it is important to gather skills and strengths to make patients benefit from fundamental research's results and accelerate clinical trials.

WHY DOES DRUGS' DEVELOPMENT FOR RARE DISEASES REQUIRE NETWORKS AND STRUCTURES?

Fig 1



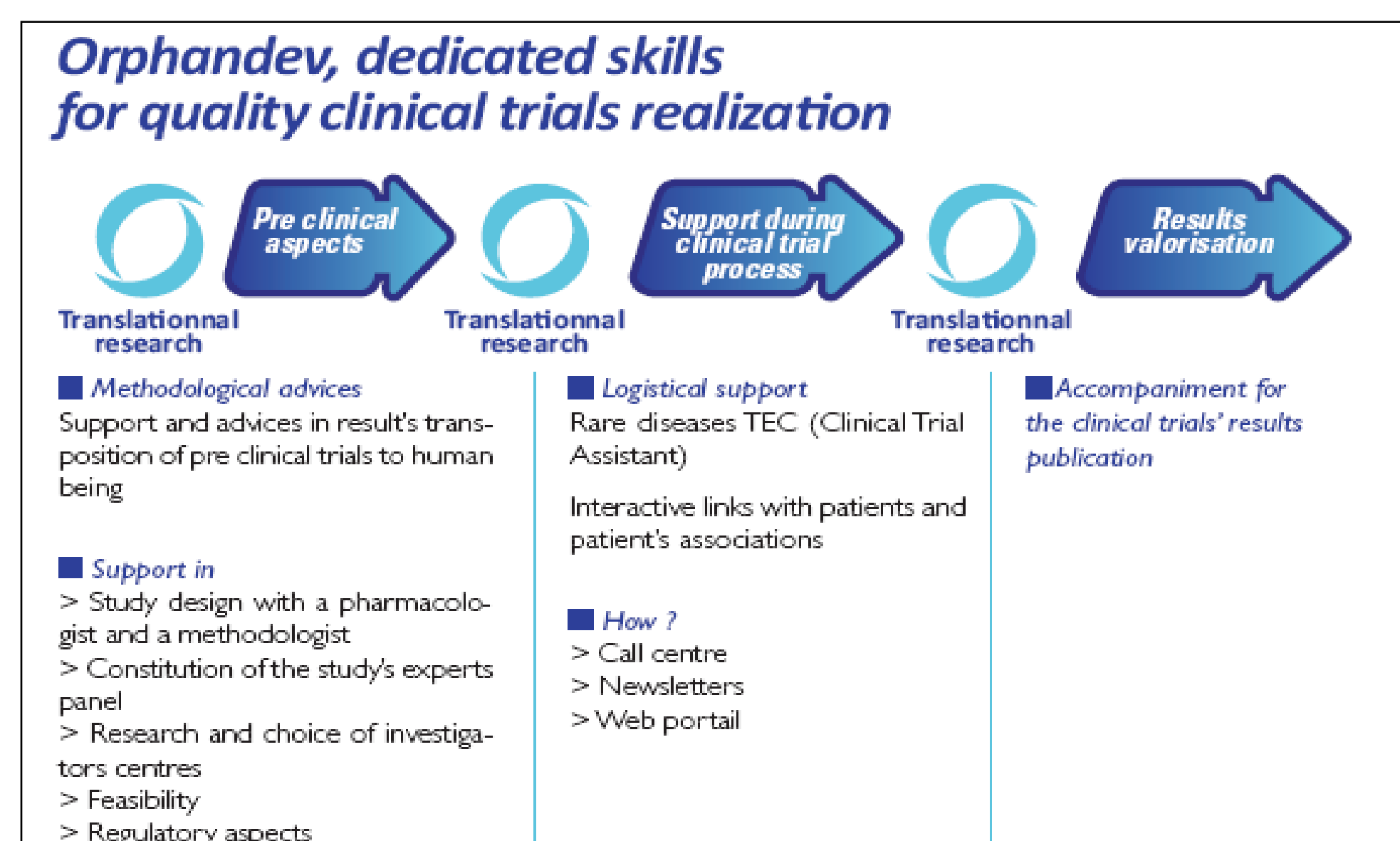
When clinicians or industries want to develop drugs for rare diseases they are confronted to the complexity of clinical trials. The usual difficulties in clinical trial's process add up at each other in a rare disease's context.

This complexity expresses itself in:

- Undetermined or few documented etiology
- Methodological difficulties
- Choice of the primary outcome
- Limited number of patients
- More logistical matters
- Regulatory questions

Facing all these difficulties, promoters of therapeutics for Rare Diseases become discouraged and often give up.

Fig 2



Orphandev is a French Clinical Trials Network based on a strong collaboration principle with all actors involved (academics, industries and patients) dedicated to orphan drugs development. It was created by academics to help academics but also others actors involved in rare diseases' research. It has started from the statement that rare diseases specificities don't allow us to use the same tools in clinical trials process as the available ones for common diseases.

After having experienced this difficulties in orphan drugs' clinical trials (Charcot Marie Tooth – 2004[6], Rett - 2006 and Progeria - 2008) (fig 3) and overcome them with the gained experience and the successful results, we have developed an organisational concept in order to capitalize the lessons learned and optimize the trials process.

FEW EXEMPLES OF OUR EXPERIENCE IN RARE DISEASES CLINICAL TRIALS*

Fig 3

CLINICAL TRIAL	PRINCIPAL INVESTIGATOR	REFERENCE CENTRE	STATUS
2004- CHARCOT MARIE TOOTH IA - ORPHA60779	Dr MICALLEF, Pr POUGET	Reference Centre for neuromuscular diseases and amyotrophic lateral sclerosis	Published
2006- RETT SYNDROME -NCT00990691	Pr MANCINI	Reference Centre for pediatric neurological diseases	Ongoing
2008- PROGERIA -NCT00731016	Pr LEVY	Medical Genetic and Functional Genomic Department	Ongoing

**CT with public funding
 Logistical support in industrial CT for RD:
 Duchenne Muscular Dystrophy, ALS,
 Huntington Chorea*

REFERENCES

1. Joppi R et al, Orphan drug development is progressing too slowly, British Journal of Clinical Pharmacology, 2006
2. Aymé S, Ten years after European Regulation on Orphan Drugs, La Presse Médicale, 2010
3. Heemstra H et al, Orphan drug development across Europe: bottlenecks and opportunities, 2008
4. Buckley B et al, Clinical trials of orphan medicines, Lancet 2008
5. Micallef, Skip vitro models and animal rights: The characteristics of rare diseases are they a hindrance? Establishing proof of concept in the treatment of rare diseases is there a problem?, La Presse Médicale, 2010
6. Micallef et al, Effect of ascorbic acid in patients with Charcot-Marie-Tooth disease type 1A: a multicentre, randomised, double blind, placebo-controlled trial, Lancet Neurology 2009