# PAEDIATRIC CLINICAL TRIALS: INDUSTRY AND NON-INDUSTRY BRINGING DIFFERENT STRENGTHS TOGETHER

Clinical trials are an essential part of advancing knowledge and improving healthcare worldwide. Advances in paediatric research across the globe to improve the lives of babies, children and young people have dramatically reduced rates in morbidity and mortality and increased the quality of life, for example, reducing sudden infant death, increasing the life expectancy for children with thalassemia, cystic fibrosis etc.

However, despite these advances, current data suggests that approximately 50% of children's medicines used across Europe are either unlicensed or off-label, a percentage which rises significantly in neonates (Conroy S. et al. 2000; Teigen A. et al. 2017; Pineiro Pérez R. et al. 2021). This means that many medicines have not yet been tested for efficacy and safety in clinical trials for children or may not be available in a pharmaceutical form suitable for children. This data suggests the ongoing need for clinical trials within the paediatric population that can be conducted as both industry or non-industry trials. But what are the differences between these types of clinical trial?

## Key differences

The main differences between paediatric clinical trials sponsored by academia (non-industry) and those sponsored by industry are centred around:

*Funding* – in non-industry trials the running costs (regulatory, investigators, clinical operations, e-CRF, monitoring, statistics, etc) are covered through grants (governmental, national, EU, charities) whereas in industry trials these costs are paid directly by the company itself.

*Investigators* – within academia, the principal investigators within the institutions are responsible for the running of their clinical trials and finding partners in other sites. Within industry, the investigators can be either directly employed by the company itself or the company can enlist a contract research organisation (CROs) to run the clinical trial including finding investigators and sites.

*Motivation* – both types of trial have the ultimate goal of striving to improve healthcare, by providing evidence of the efficacy and safety of a new product in children. The focal points of both do differ though: industry trials tend to focus on trials which will provide evidence to support use in children and licensing by a regulatory authority. Non-industry trials tend to focus on the unmet medical needs.

*Type of trial* – industry often is researching the efficacy of a new drug or product through clinical trials to support a licence whereas non-industry trials often seek to compare one intervention to another.

*Intellectual Property* – when clinical trials are sponsored by industry they own the rights to the product, clinical data and publication rights. In non-industry trials these rights are owned by the principal investigator(s) and/or university.

According to a global analysis (Atal I. et al., 2015) from 2006 to 2013, the median number of all clinical trials per million inhabitants in high-income countries was 10 times that in low-income countries. Industry sponsors were involved in three times more trials per million inhabitants than non-industry sponsors in high-income countries and in ten times fewer trials

in low-income countries. Only 3% of academic compared to 30% of industry trials were international.

Independent of funding mechanism, the optimal environment for clinical trials involves collaboration between both academia and industry, which is one of the driving forces behind the c4c project. When the financial and organisational strengths of industry are shared with academics, this enables better design, organisation and performance of studies for the benefit of scientific knowledge and healthcare. Industry can benefit from academics in the design of studies, the definition of endpoints, and the selection of centres to perform the research. Sharing the industry database with academics can lead to further exploration of additional questions and raise new hypotheses (Laterre P.F. and François B. 2015).

**Paediatric clinical trials within c4c**

As part of the development of the c4c network, several Proof of Viability studies (clinical trials) are currently either underway or imminently foreseen. 3 non-industry studies are currently running and 4 industry studies are due to open by the end of 2021. A brief overview of the non-industry studies is outlined below:

*TREOCAPA*

The TREOCAPA trial examines the prophylactic use of paracetamol to close a persistent ductus arteriosus (PDA). The ductus arteriosus is a blood vessel that allows the blood to skip the circulation into the lungs when a baby is in the womb. This blood vessel usually closes in babies shortly after birth but very often does not in extremely preterm born babies (23-28 weeks gestational age). A PDA can cause permanent lung damage as well as feeding and growth problems. This study is a Phase II/III randomised, double-blinded trial carried out in 65 neonatal intensive care units of 17 European countries. To date, 19 sites have been opened and 22 patients recruited. For more information please see: https://www.efcni.org/activities/treocapa/

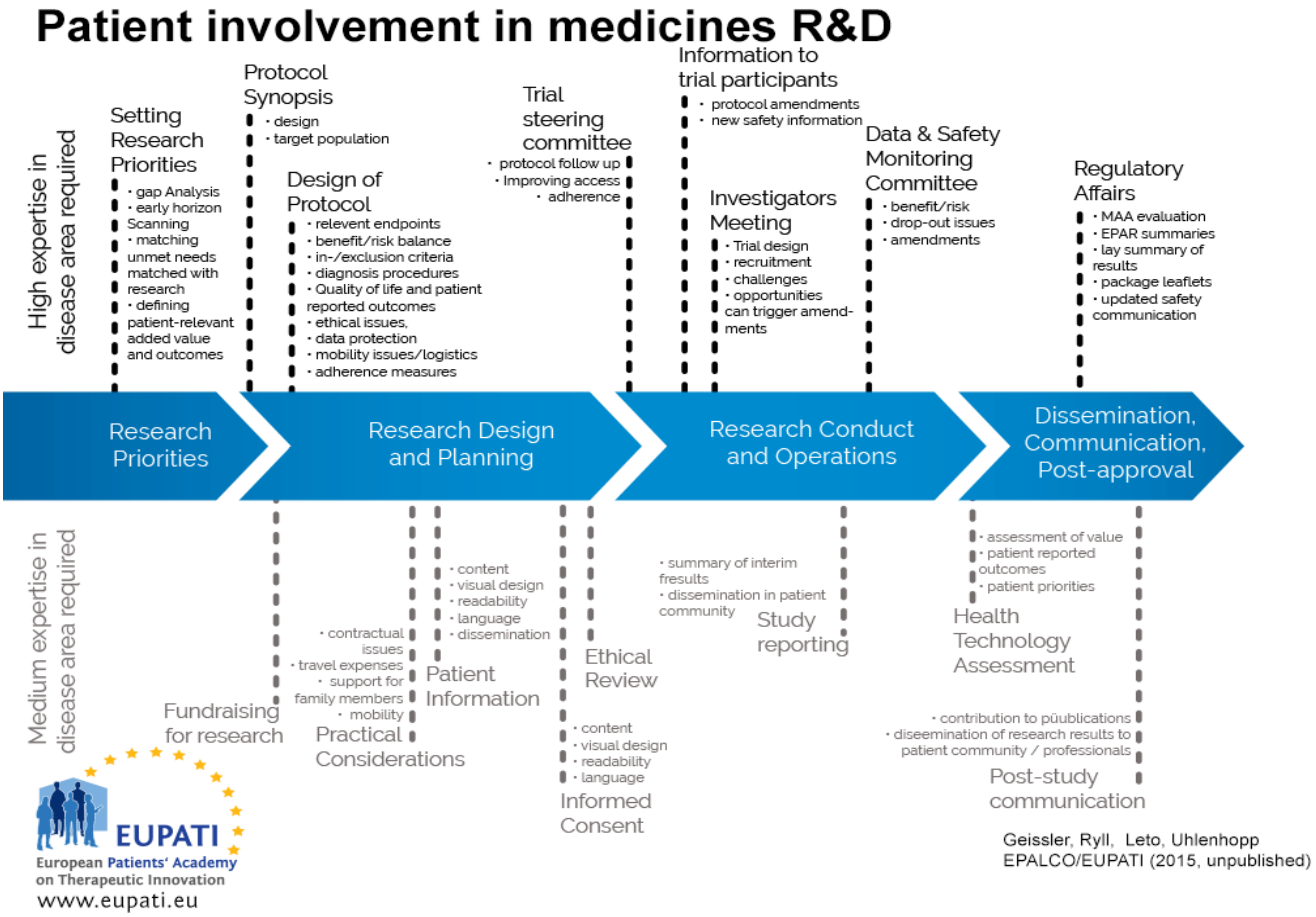
*cASPerCF*

The cASPerCF trial aims to assess the dose of an antifungal drug called posaconazole in children and young people with Cystic Fibrosis who have Aspergillus infection. Aspergillus is a fungus commonly found in our environment. The tiny Aspergillus spores which are transported by air, can enter the lungs during breathing. Normally, this will not cause any problem, but in people with underlying lung disease, it can lead to infection. Children aged between 8 to 17 years old with Cystic Fibrosis across Europe will be recruited into the study. The first site for recruitment has just been opened. For updates and more information please see: https://twitter.com/caspercfstudy?lang=en

*KD-CAAP*

KD-CAAP is a multi-centre, randomised trial of corticosteroids plus standard of care treatment versus standard of care treatment alone to prevent heart complications in Kawasaki disease. Kawasaki disease is a disease where arteries, particularly the coronary arteries in the heart, become inflamed, sometimes causing irreversible heart damage, heart attacks or even death. This study will work out whether corticosteroids plus standard treatment are better than standard treatment alone to treat children and adolescents across Europe aged between 30 days and 15 years who have Kawasaki disease. The first patient has already been recruited into the study. For updates and more information please see: https://twitter.com/kdcaap?lang=en

**The role of PPI (patient public involvement) within clinical trials**




The voice of the patient in clinical research and development is increasingly being taken into account, from the setting of research priorities right through to dissemination of results. This marks a shift in what has historically and culturally been seen, until relatively recently, as research "on" rather than "with" patients. PPI is an inherent part of the c4c project and its clinical trial network and benchmarking activities. The involvement of patients in all c4c clinical trials is assured and currently ongoing within the non-industry studies.

Within the TREOCAPA clinical trial, the European Foundation for the Care of Newborn Infants (EFCNI) is the designated PPI partner. The foundation has been involved since the drafting of the study protocol and has established a dedicated Parent Advisory Board (PAB). Both EFCNI and the PAB provide input into various aspects and materials developed within the framework of the trial. For example, the informed consent forms, patient information summaries, training materials for medical professionals approaching parents, input into follow-up, a video for the general public etc. A dedicated web page to the trial has been set up on EFCNI's website: https://www.efcni.org/activities/treocapa/. EFCNI regularly provides updates and promotes the study on their social media channels.

PPI in the cASPerCF study has been led by a patient representative, a full study team member able to listen and advise on all elements of the trial. Throughout the study, the views of children and young people with Cystic Fibrosis and their families have been sought by forming a focus group. This focus group has had input on the design of the trial and the subsequent materials developed such as the patient information sheet. The study has also created a twitter account, @cASPerCFstudy, for patients, the public, health professionals and researchers to keep up to date on our progress.

Societi, the UK Foundation for Kawasaki Disease is the PPI partner in the KD-CAAP clinical trial. The foundation has been involved with the KD-CAAP trial from initial concept, when Societi's founder brought clinical experts together to focus on developing a clinical trial. In preparation for the first participants joining, materials and resources were produced to help patients and their families understand the trial better and get the information they need. Resources include information leaflets, dedicated web pages at https://www.societi.org.uk/kd-caap/, a Family Resource Portal and newly released My Societi Young People's Portal and a newly established Twitter account dedicated to trial news @KdCaap. There are a range of clinical information resources in addition, including training resources, being made available to trial centres.

Societi have also been involved in producing trial resources including newsletters, a new trial logo and patient consent and assent forms – as well as raising awareness of the trial on Societi Foundation social media channels.