Topic proposal: Platform Trials – other aspects

ACT EU Multi-stakeholder Platform
Advisory Group – 4 July 2024

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Rational

1. The methodology guidance workshop (23/11/2023) was a scene setting regarding Platform Trials
2. The EMA is developing a concept paper (draft 2) (https://www.ema.europa.eu/en/documents/scientific-guideline/concept-paper-platform-trials_en.pdf)
3. There are other aspects requiring some guidance

Rational: methodology guidance workshop (23/11/2023)

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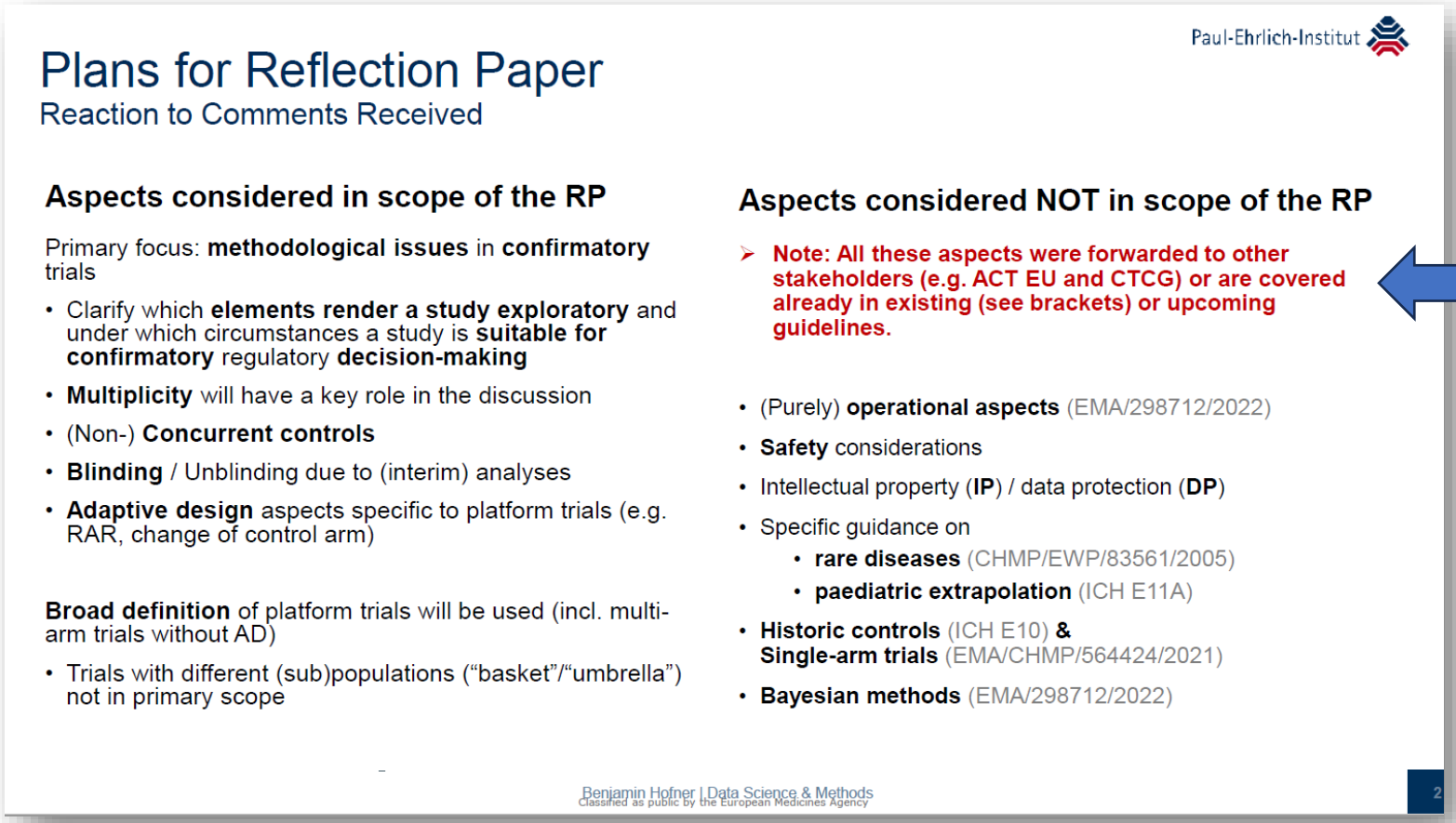

Paul-Ehrlich-Institut

Plans for Reflection Paper

Reaction to Comments Received

Aspects considered in scope of the RP

Primary focus: **methodological issues** in **confirmatory** trials

- Clarify which **elements render a study exploratory** and under which circumstances a study is **suitable for confirmatory** regulatory **decision-making**
- **Multiplicity** will have a key role in the discussion
- (Non-) **Concurrent controls**
- **Blinding** / Unblinding due to (interim) analyses
- **Adaptive design** aspects specific to platform trials (e.g. RAR, change of control arm)

Broad definition of platform trials will be used (incl. multi-arm trials without AD)

- Trials with different (sub)populations ("basket"/"umbrella") not in primary scope

Aspects considered NOT in scope of the RP

- **Note: All these aspects were forwarded to other stakeholders (e.g. ACT EU and CTCG) or are covered already in existing (see brackets) or upcoming guidelines.**

- (Purely) **operational aspects** (EMA/298712/2022)
- **Safety** considerations
- Intellectual property (**IP**) / data protection (**DP**)
- Specific guidance on
  - **rare diseases** (CHMP/EWP/83561/2005)
  - **paediatric extrapolation** (ICH E11A)
- **Historic controls** (ICH E10) **&**
  Single-arm trials (EMA/CHMP/564424/2021)
- **Bayesian methods** (EMA/298712/2022)

Benjamin Hofner | Data Science & Methods

Classified as public by the European Medicines Agency

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Is it the right time to address aspects not in the scope of the concept paper?

- Possible case study: ALS
  - 49 products designated as orphan in the EU, 119 in the US
  - Patients conducted their horizon scanning: 13 products of interest to them
  - There is a platform intended for clinical trials in US (Healey)[1] and in Europe (Tricals)[2]
- Could it serve as a basis to discuss concrete challenges and possible options when designing a Platform Trial?

→ Operational aspects

→ Organisational aspects

→ Governance aspects

→ Ethical aspects

→ IP / data protection

→ Etc.

1: https://www.massgeneral.org/neurology/als/research/platform-trial
2: https://www.tricals.org/en/

Amyotrophic lateral sclerosis Horizon scan

One of the most active rare diseases in terms of orphan drug designations

But one of the most disappointing in terms of successful R&D

Median life expectancy after diagnosis: 24 months

Current interest

- Stakeholders' meetings with ALS Foundation, MoH, ZIN, patients: dashboard of most promising medicines (6 at present)
- Platform trials (USA HEALEY 9 products, EU TRICALS 10 products phase 1 to 3, 16 countries)

Sources of information

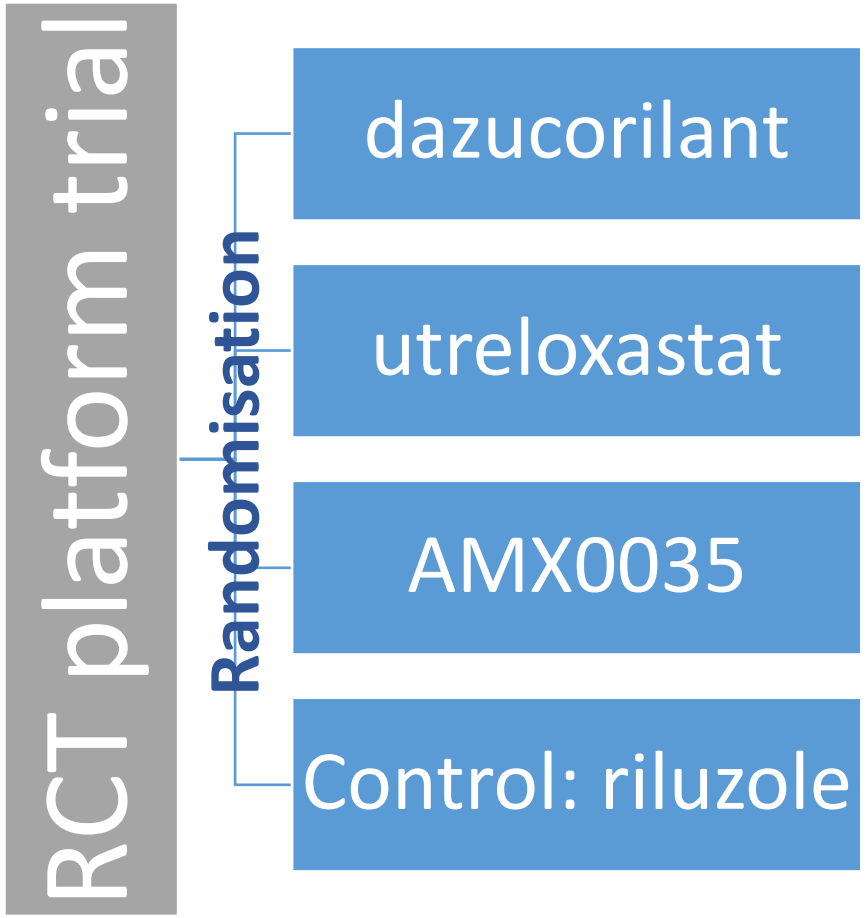
- EUDRACT registry : review of 404 CTs for ALS, 100+ products
- Meetings with Utrecht Uni.
- Pubmed
- Subscription to 10 medical journals of interest for ALS
- Contacts with developers for a platform trial in Europe

Some questions patients have on platform trials

1. How to initiate them ?
   - Discussions between different developers, governance, IP
2. When an arm becomes futile, can patients be randomised to other active arms? When?
3. Possibility to switch-over based on interim results?
4. If one of the trial products is authorised, how to adapt the control arm?
5. Patients not in trial: possibilities for a platform compassionate use programme?

ALS: smarter trial, smarter compassionate use programme?

- R&D



- And for patients not included in CTs

Enough product for all ? If not, lottery?
Cost ? Can company charge for CUP?

Risk to be randomised to control: 25%. Even more unacceptable for patients?
Cannot be easily blinded: 3 placebo needed in each arm, or each product same dose same appearance