CDDF 10TH ALPINE CONFERENCE
CURRENT AND FUTURE CHALLENGES OF INNOVATIVE ONCOLOGY DRUG DEVELOPMENT
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Innsbruck, Austria

CDDF Multistakeholder Workshop

Innovation in Oncology Clinical Trial Design

Frankfurt, Germany
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Disclaimer

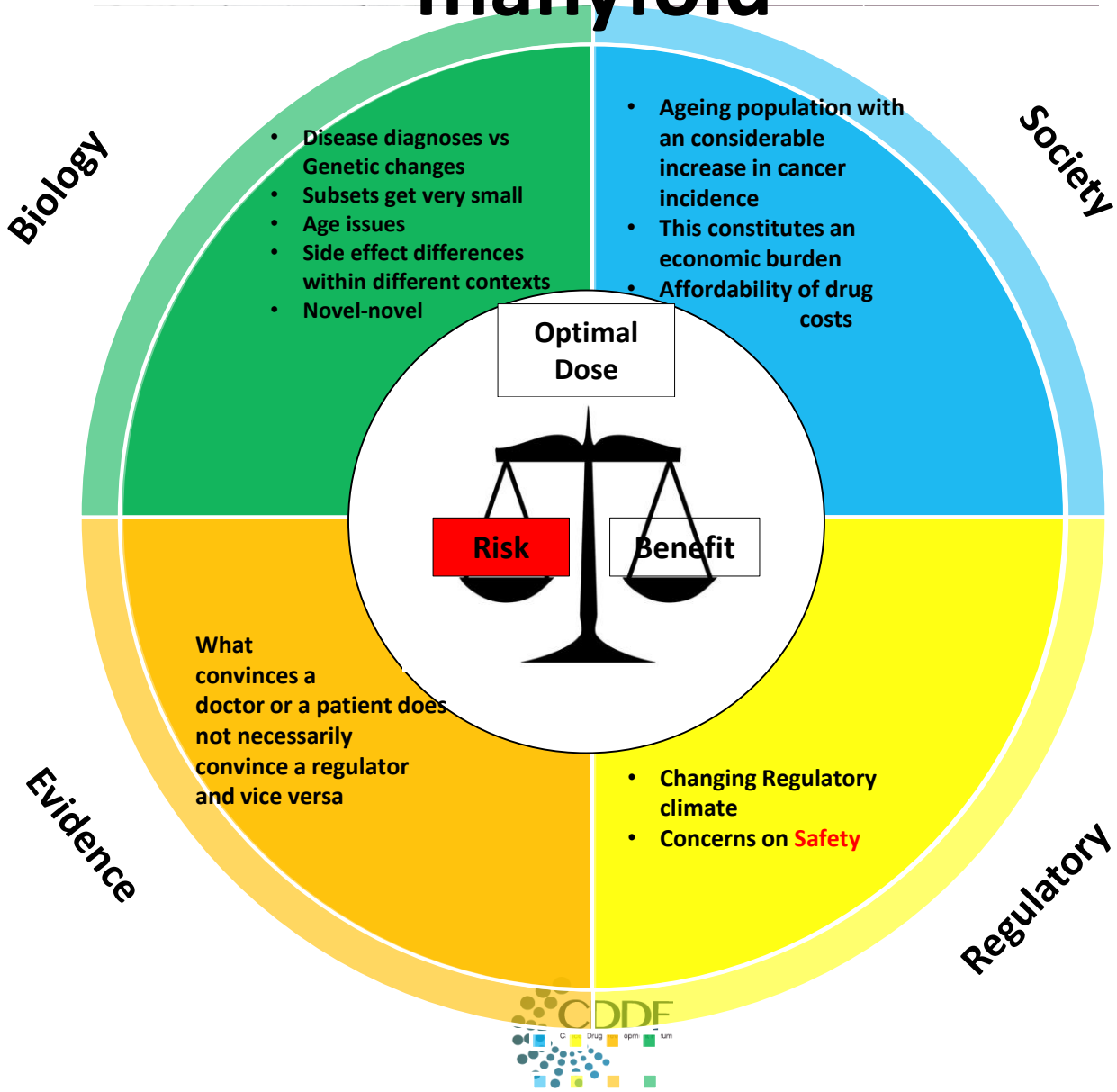
- Honoraria from:
  - Sanofi
  - Sotio
  - Novartis
  - Xbiotech
  - Octimet Oncology

Objectives :

- To better understand the position and concerns of the other stakeholders to ensure better study designs can be developed for more efficient drug development

- to have a multi-stakeholder discussion representing oncologists/scientists, government officials (EMA, policymakers and HTA), pharmaceutical industry representatives and patient advocate groups interested in the topic.

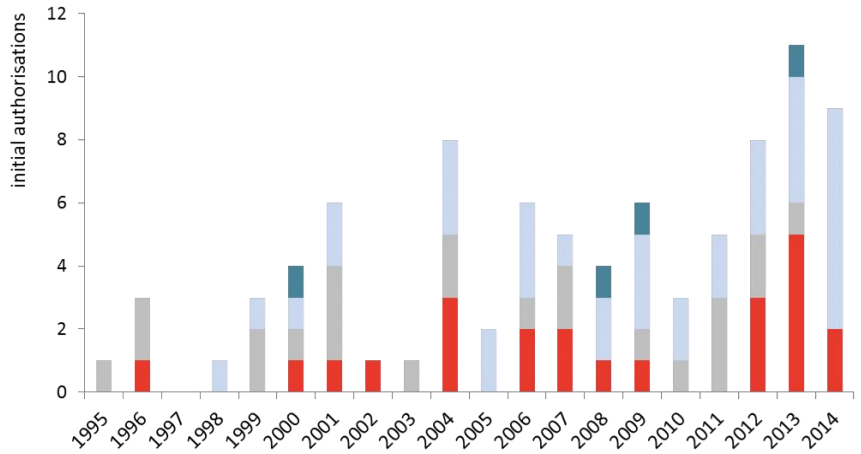
Our challenges are diverse and manyfold

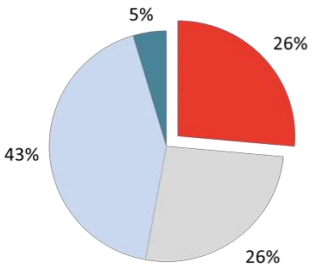


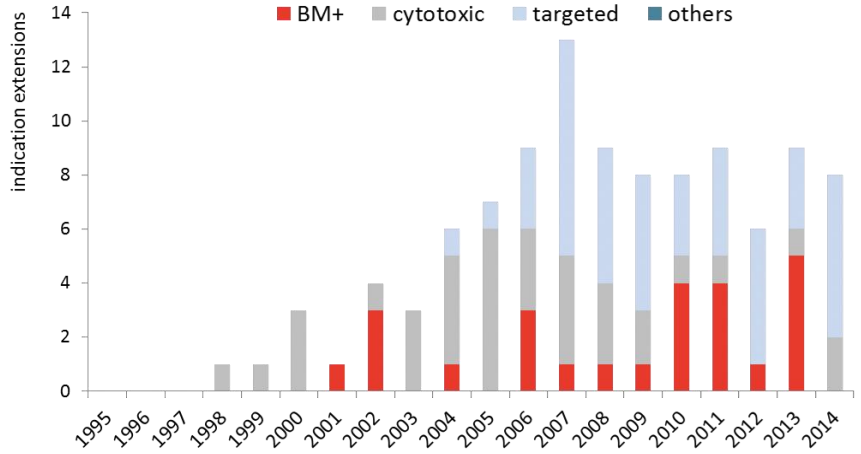
So selection becomes important (via Biomarkers)

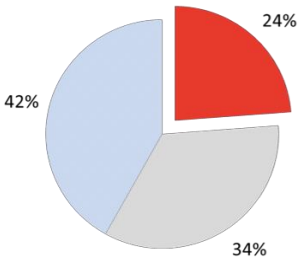
- For Pharma: Reducing Risk
  - Population selection (predictive/selection BM)
  - Pharmacodynamics BM: Assess effect on disease activity early (surrogate?)
  - Strategic choice
  - Biomarker (BM) should be in place in time.
- For investigators:
  - Supporting Trial Methodology
- For healthcare and regulators:
  - Optimize healthcare (Better care; fewer costs)

EU approvals 1995-2014: BM+ vs not







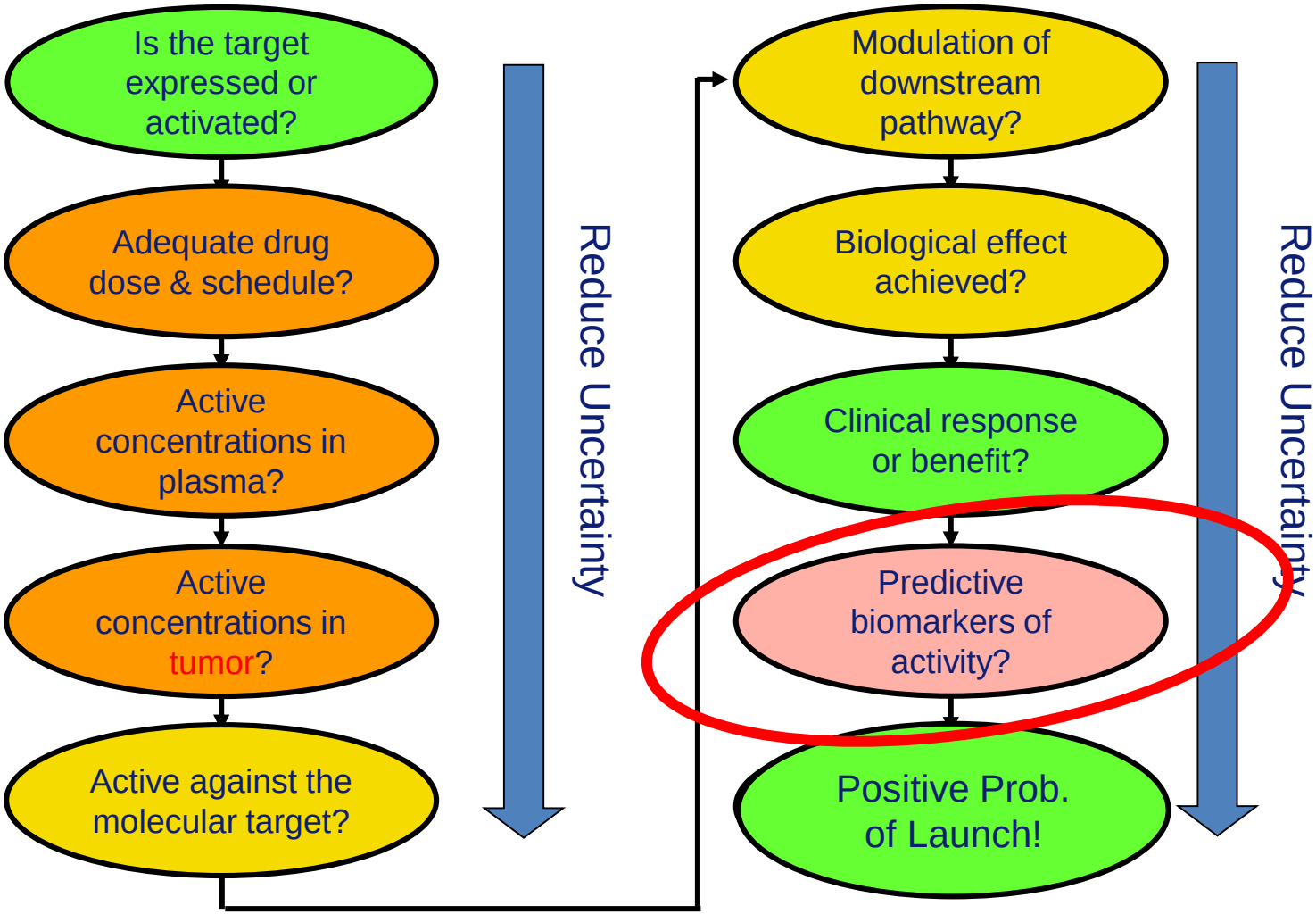


N = 86

High rate (>40%)
'targeted' but no BM

Adopted from Giulliani R, EMA, Rome

The Pharmacological Audit Trail: Concept from 2003 still valid, with a minor change



(Workman et al, Mol Cancer Therap 2003)

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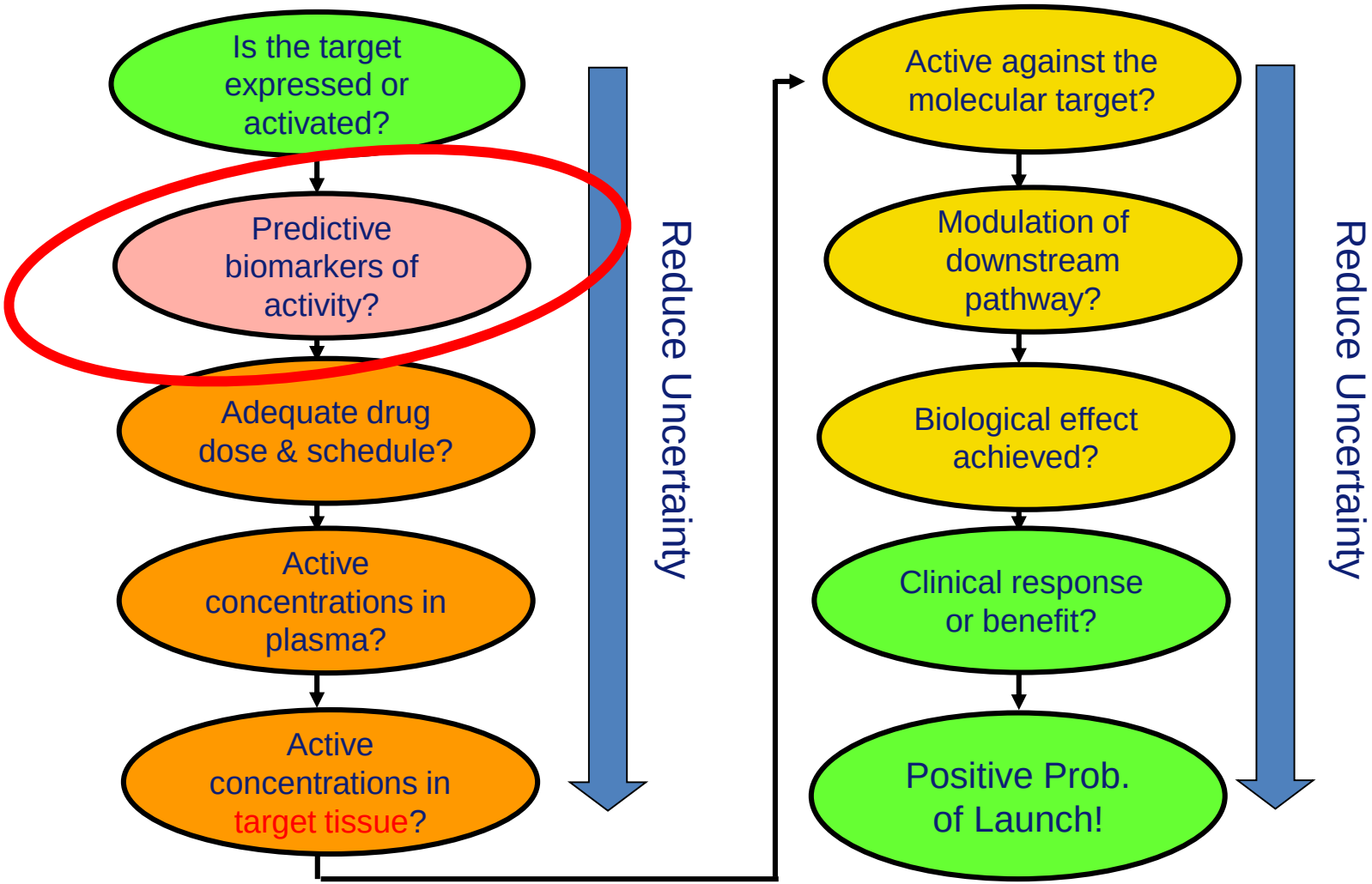
The Pharmacological Audit Trail: Concept from 2003 still valid, with a minor change



(Workman et al, Mol Cancer Therap 2003)

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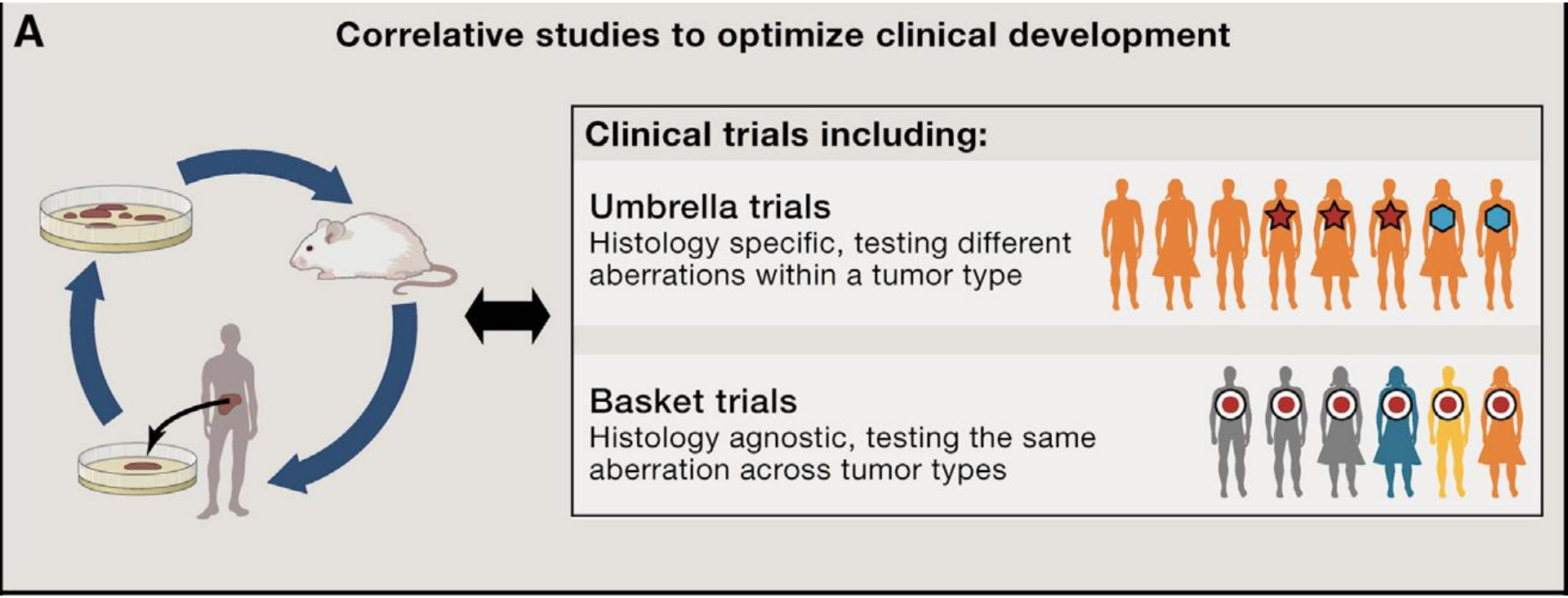
Shifting to Apollo-shaped Drug Development

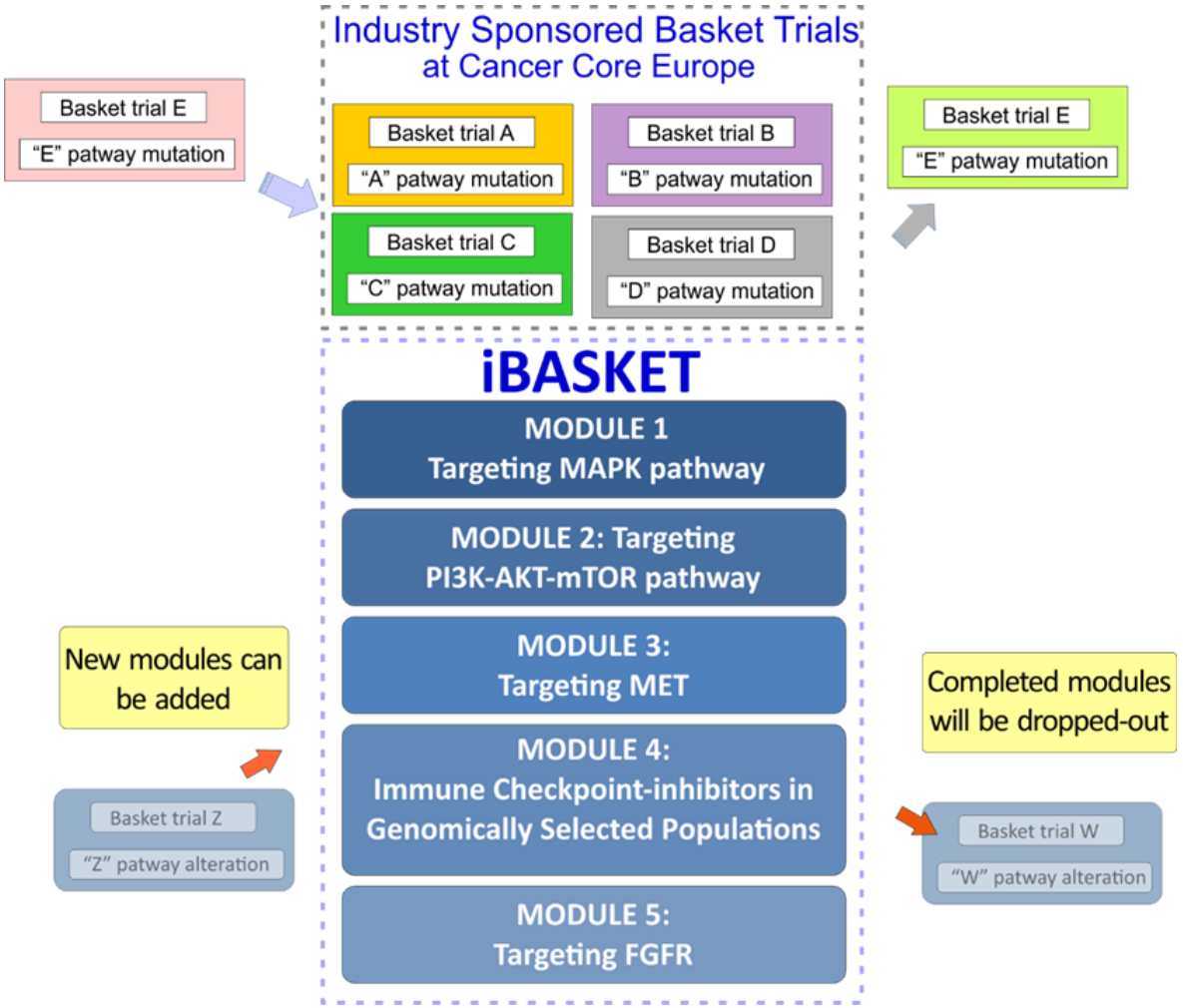
- Designs
  - Phase I Trials with Expansion cohorts
  - Basket Trials
  - Umbrella Trials
  - Parallel Group Design
  - Combo Trial Design
- Statistics
  - In Early Go/No-Go decision making
  - Adaptive Trial Designs
  - Use of Historical Controls
  - Subgroup analysis

Cescon and Siu, Cell 2017, 168:575-578

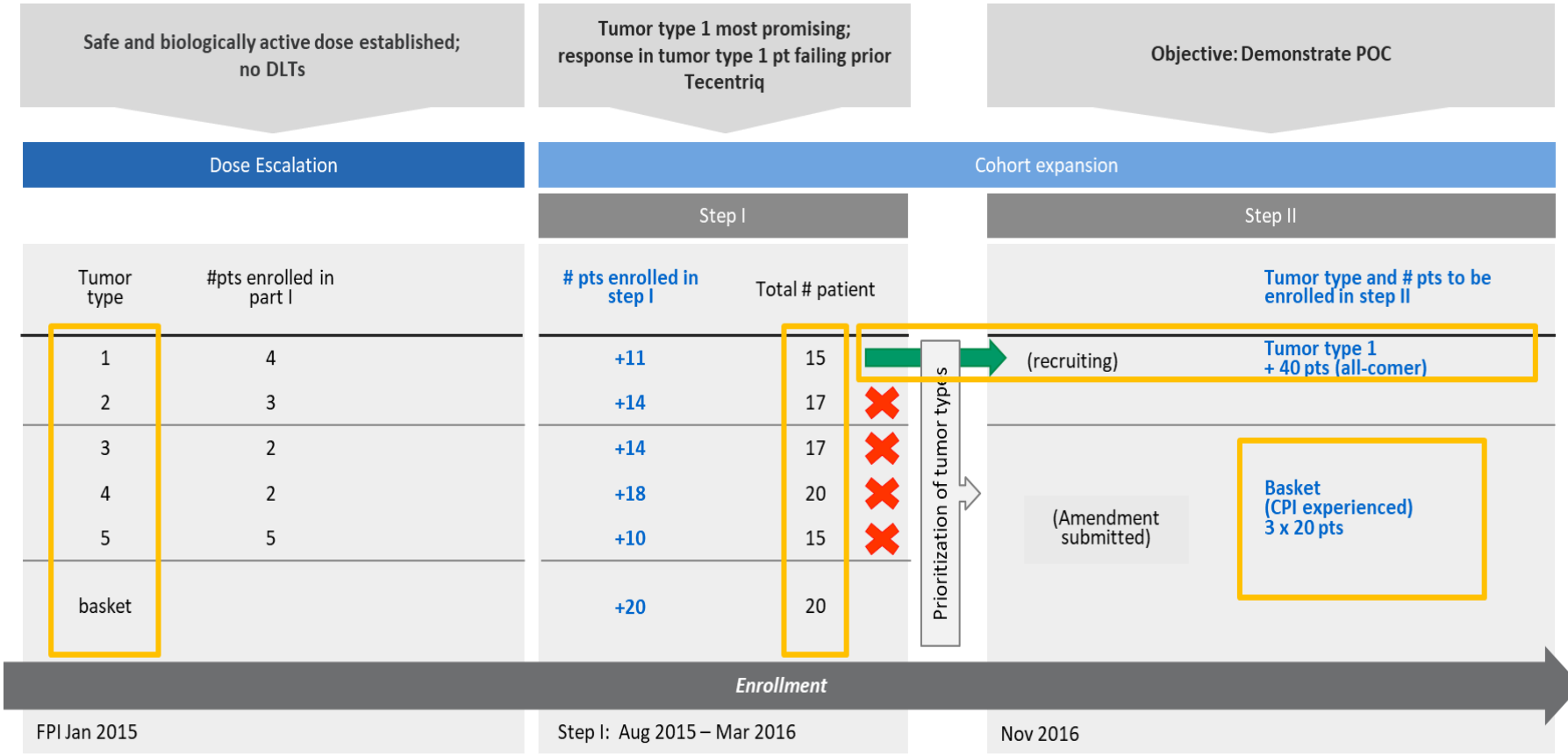


Robust and efficient exchange of knowledge between correlative science studies and clinical trials, including basket and umbrella trials.

Basket of Basket Designs



Multistage Early Clinical Trial Design



General Conclusions (1)

- Molecular profiling results in lower patient numbers in clinical trial arms necessitating innovative trial designs including single arm trials
- High attrition rate of molecular profiled cancer patients in clinical trials is a serious concern
- Historical controls are important to better understand the outcome of single arm trials
- Statistics helpful in the design of tailored clinical trials based on limited information of early clinical studies
- Statistics helpful in go/no go decision making to increase probability of success of a drug in clinical trial
- Proper subgroup analysis contributes to identification of target populations of cancer patients
- Regulatory authorities have developed mechanisms to conditionally approve drugs on limited information, but are restrictive in their approval due to lack of due diligence of conducting post approval trials and favour randomised clinical studies

General Conclusions (2)

- Estimands is a newly developed framework for planning, conducting and interpretation of clinical trials and takes into account intercurrent events to come to a better efficacy estimate
- IVDs and companion diagnostics are becoming more and more important in personalised medicine and patient selection and stratification in clinical trials
- Self-certified CE Marking is required for all IVDs sold in Europe under the current IVD directive, but under the new IVD Regulation (in force 2022) marketing authorisation of companion diagnostics will require two Medicines Authority reviews, one before and one after the clinical studies
- Daily medical practice shows that a molecularly tailored approach only works for a subgroup of patients
- Liquid biopsies should be „mandatory“ for biomarker profiled patients, not only for selection and stratification but also to follow the result of the therapy

THANK YOU FOR YOUR ATTENTION