Perspectives for Effective Cancer Drug Development

The EORTC SPECTA program (Screening Patients for Efficient Clinical Trial Access)

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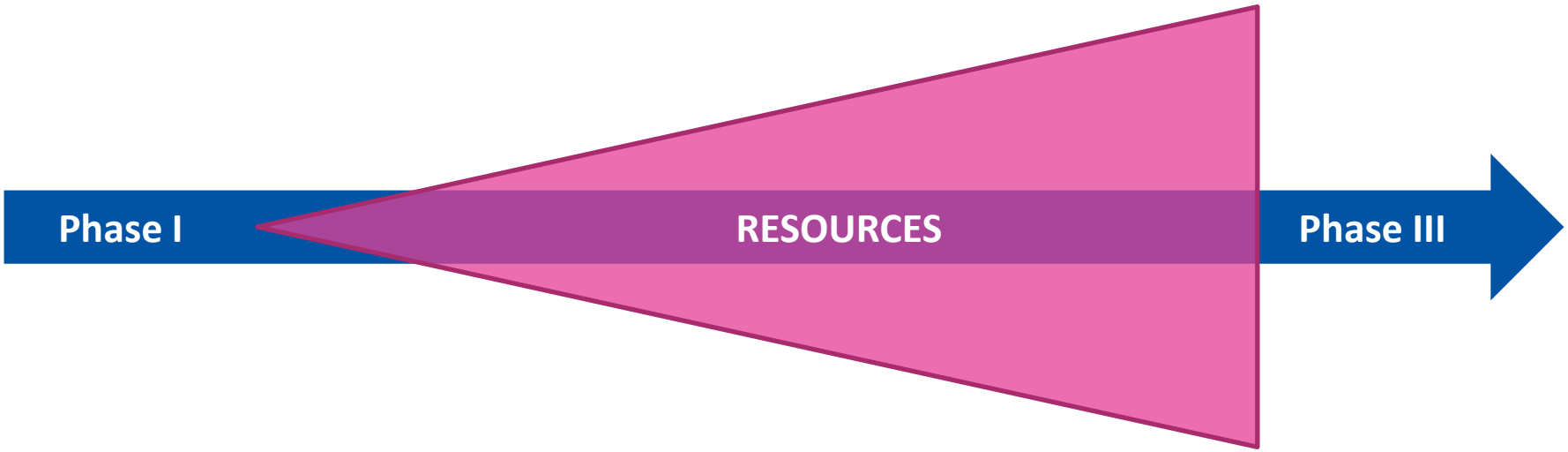
1. Rationale for SPECTA

Changing clinical research pathway (I)

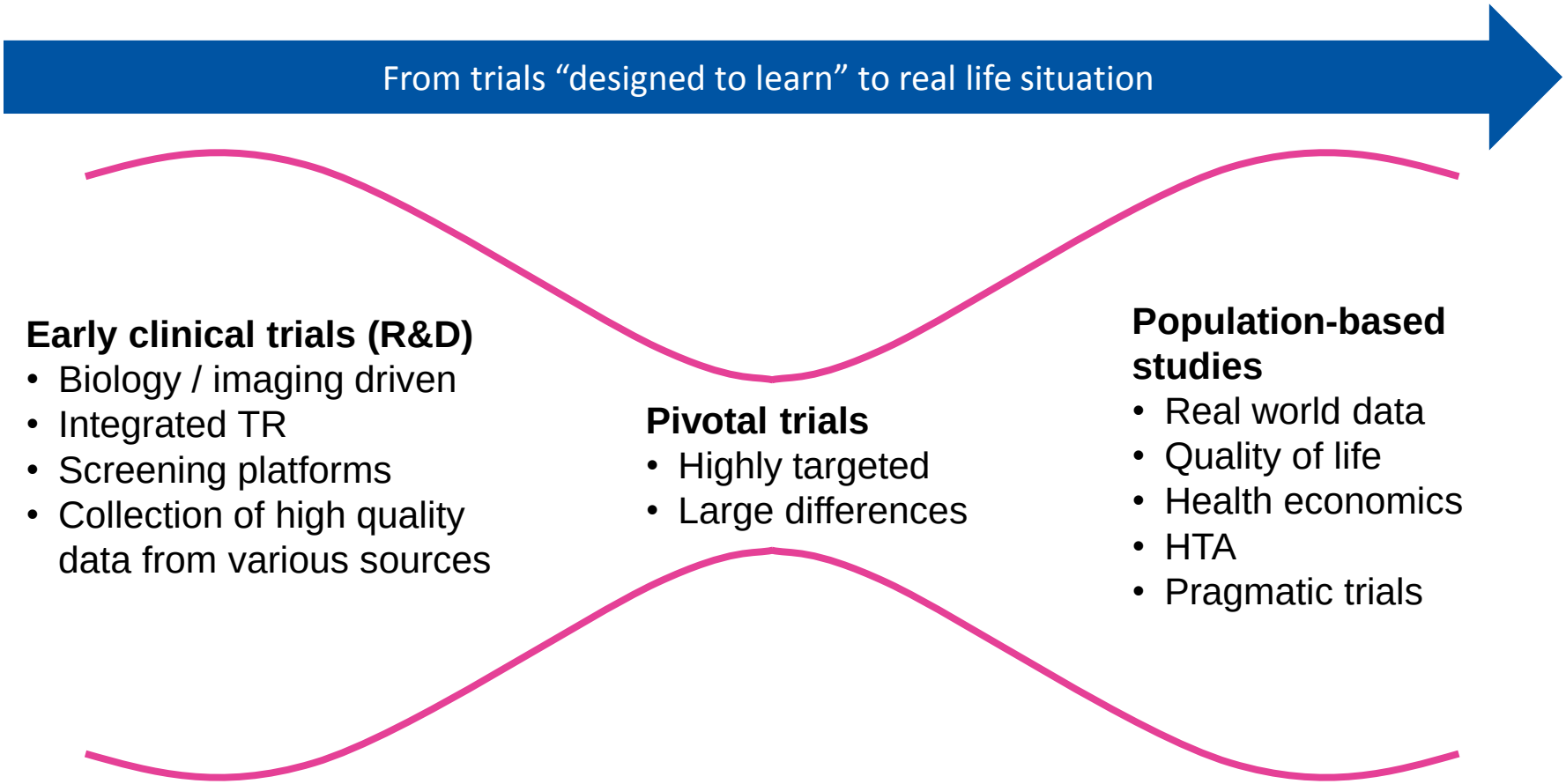
The classical model does not fit disease heterogeneity



The regulatory pathway is evolving towards

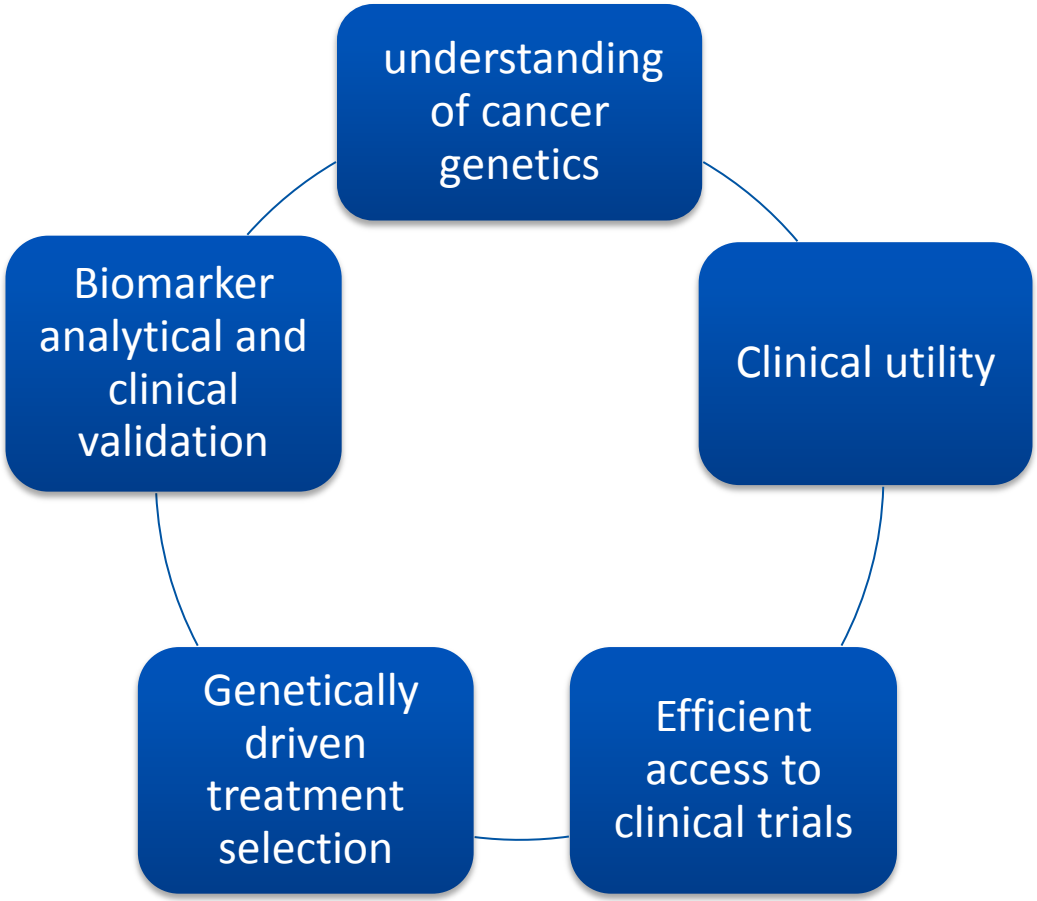
- Either document for sub groups at the end of all comers approach
- Or apply subgroup selection at start of development

The changing clinical research pathway (II)



Burock et al. Eur.J.Cancer (2013), http://dx.doi.org/10.1016/j.ejca,2013.05.016

Towards personalized drug development



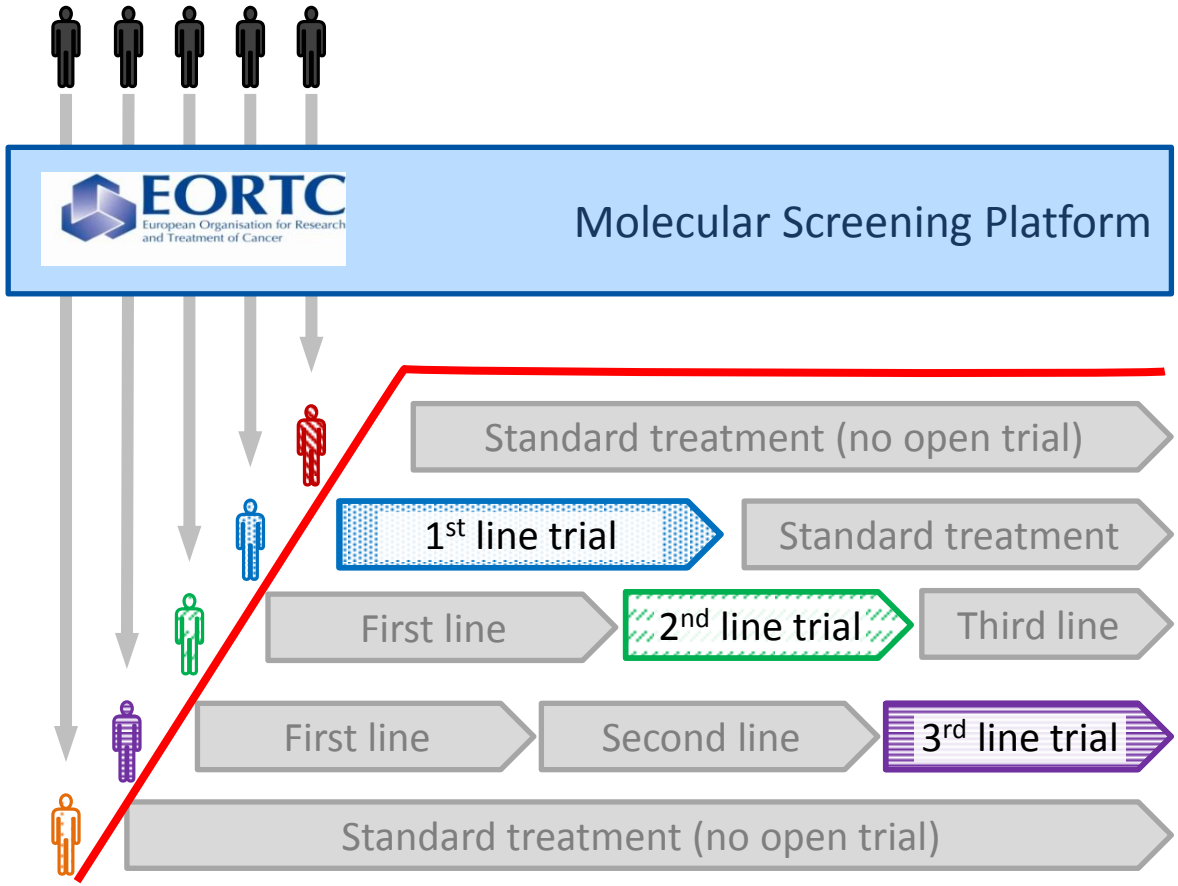
Ambition: bring to Europe an international collaborative think tank infrastructure to build innovative forms and methods of clinical research

Challenges

- Not always clear which alteration to target
  - histology agnostic trials are debatable
  - pathways and cross talks have proven to be highly variable across histologies
  - Sequencing and/or combination of NMEs need biological rationale, access to knowledge
- Numerous emerging NMEs at a pace never seen before
- Gap biomarkers and NMEs
- New technologies need bench-marking
- Payers will close the gap efficacy effectiveness
- Patients will require access if there is a match target/drug even in off label settings
- Access to personalised treatments will require agile and flexible procedures.

2. What is SPECTA?

The SPECTA collaborative platform



Academic capture of biological sub groups coupled with technological expertise

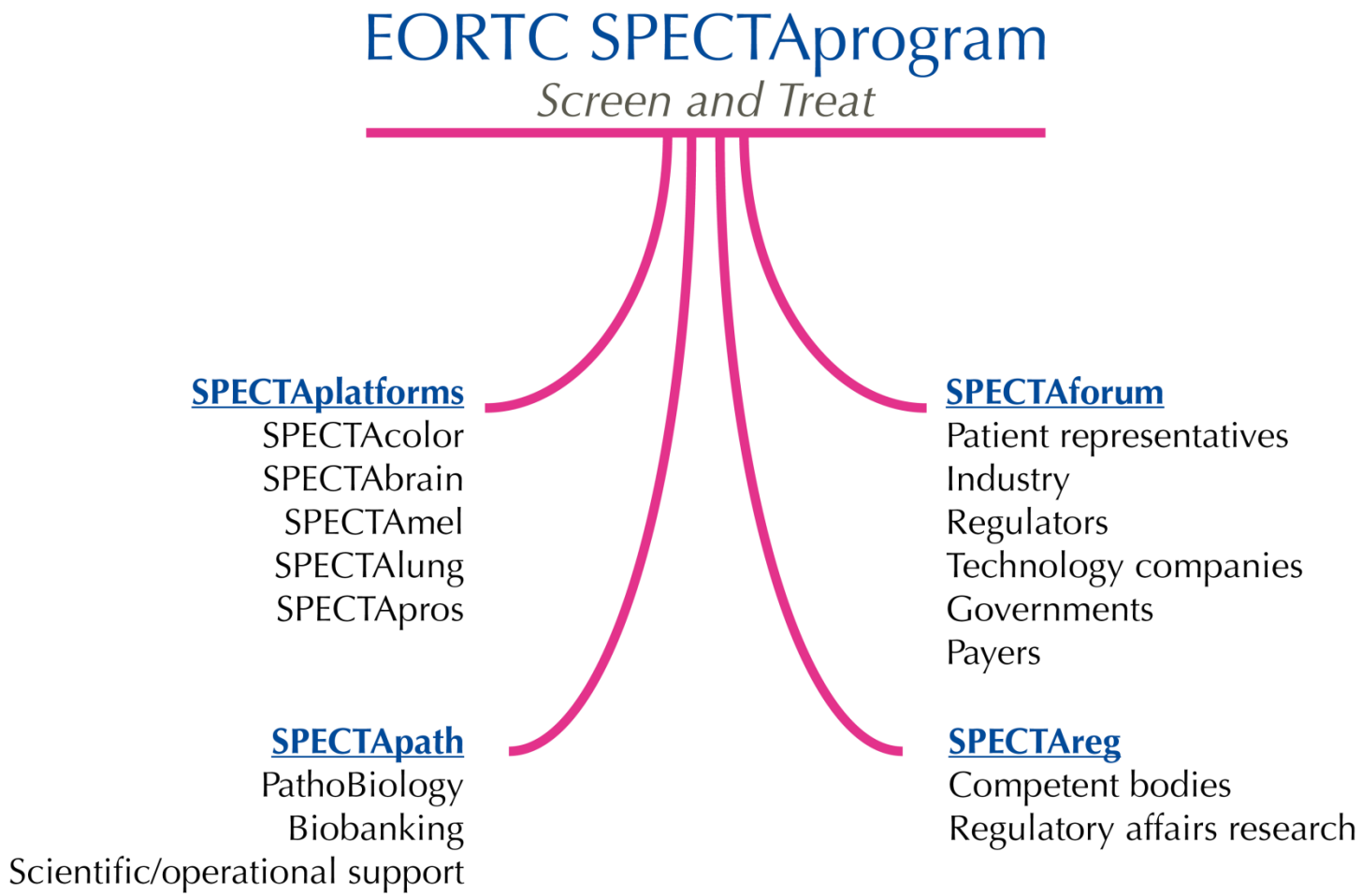
Industry Cooperation for drug development

EVOLVING TO NEW MODELS OF PARTNERSHIP

SPECTA is a value proposition taking into account the interests and needs of all staekholders

- ✓ Breaks the silo approach of drug development
- ✓ Provides clinically annotated biological material across tumor types
- ✓ Streamlines duplicative and costly screening programs
- ✓ Rapid identification of patients with specific genotypes
- ✓ Possibility to call back patients
- ✓ Integrated Drug/Biomarker/Drug Development solutions
- ✓ Cross validation and benchmarking of technologies alongside strict Quality Assurance/Quality Control criteria
- ✓ Chain of custody for biological material documented through e-infrastructure
- ✓ Central biobank audit compliant with regulatory standards
- ✓ Provides systematic NGS for all patients

SPECTA program: a forum for dialog and collaboration



3. How does SPECTA function?

SPECTA Platforms

The status on the SPECTA platforms

SPECTAplatforms:	
• **Colorectal cancer**	Accruing
• **Melanoma**	Protocol being finalized First investigator meeting done
• **Brain tumors**	Protocol being finalized
• **Lung cancer**	EORTC ETOP partnership Protocol being finalized
• **Prostate cancer**	Concept launched

SPECTAcolor actual status by numbers (as of June 12)

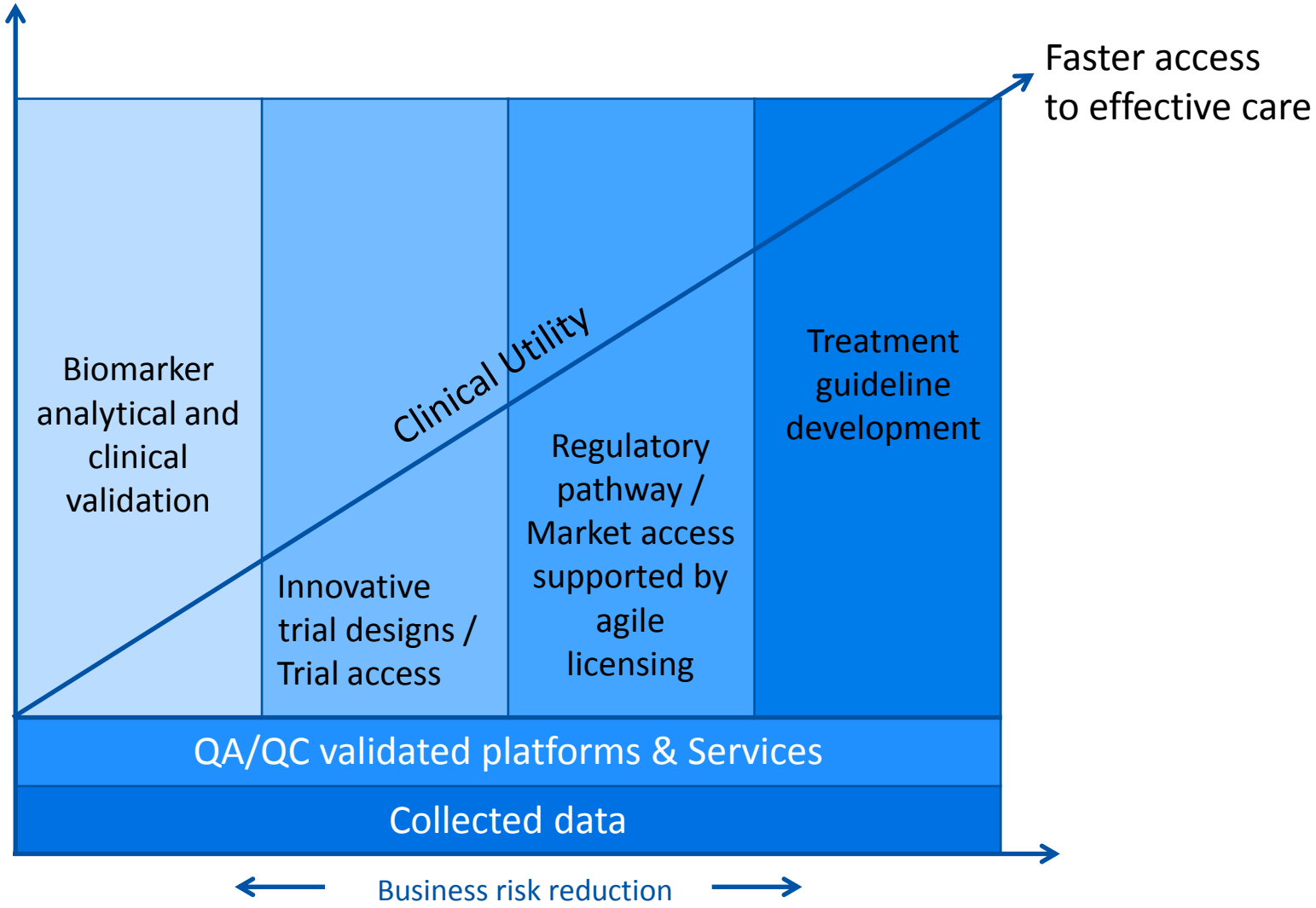
- ✓ 10 countries
- ✓ 30 sites
- ✓ 22 sites have signed the consortium agreement
- ✓ 23 sites with full EC and regulatory approvals
- ✓ 18 sites authorized to enroll patients
- ✓ 12 sites are actively enrolling
- ✓ 223 patients enrolled
- ✓ 3 intergroup set up

4. Ambitions and goals of SPECTA
New partnerships

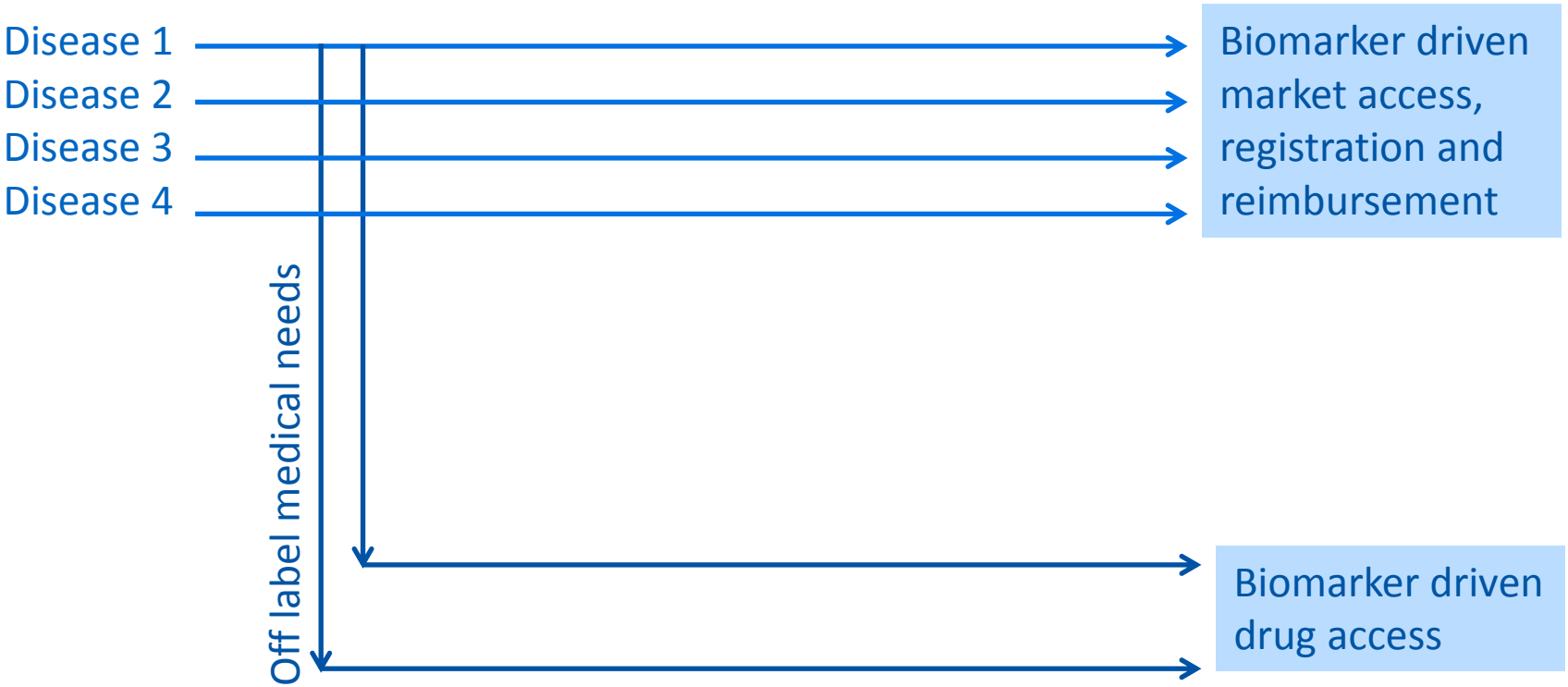
Agile approach to drug development

- Increase the efficiency for clinical trial access
  - Matched opportunities
    - Tumor-drug
    - Drug-biomarker
    - Biomarker-technology
    - Drug developers - Academic researchers
  - Increasing access for patients to trials
  - Scale economy / cost sharing models / PPPs
- Optimise the validation of emerging technologies for the service of drug development based on high QA/QC
- Regulatory acceptability of targets
- Develop a European vision for drug development and health care delivery (data & services)

Towards data driven healthcare delivery



A vision for access to personalized medicine for all patients: A European “independent Pharma”

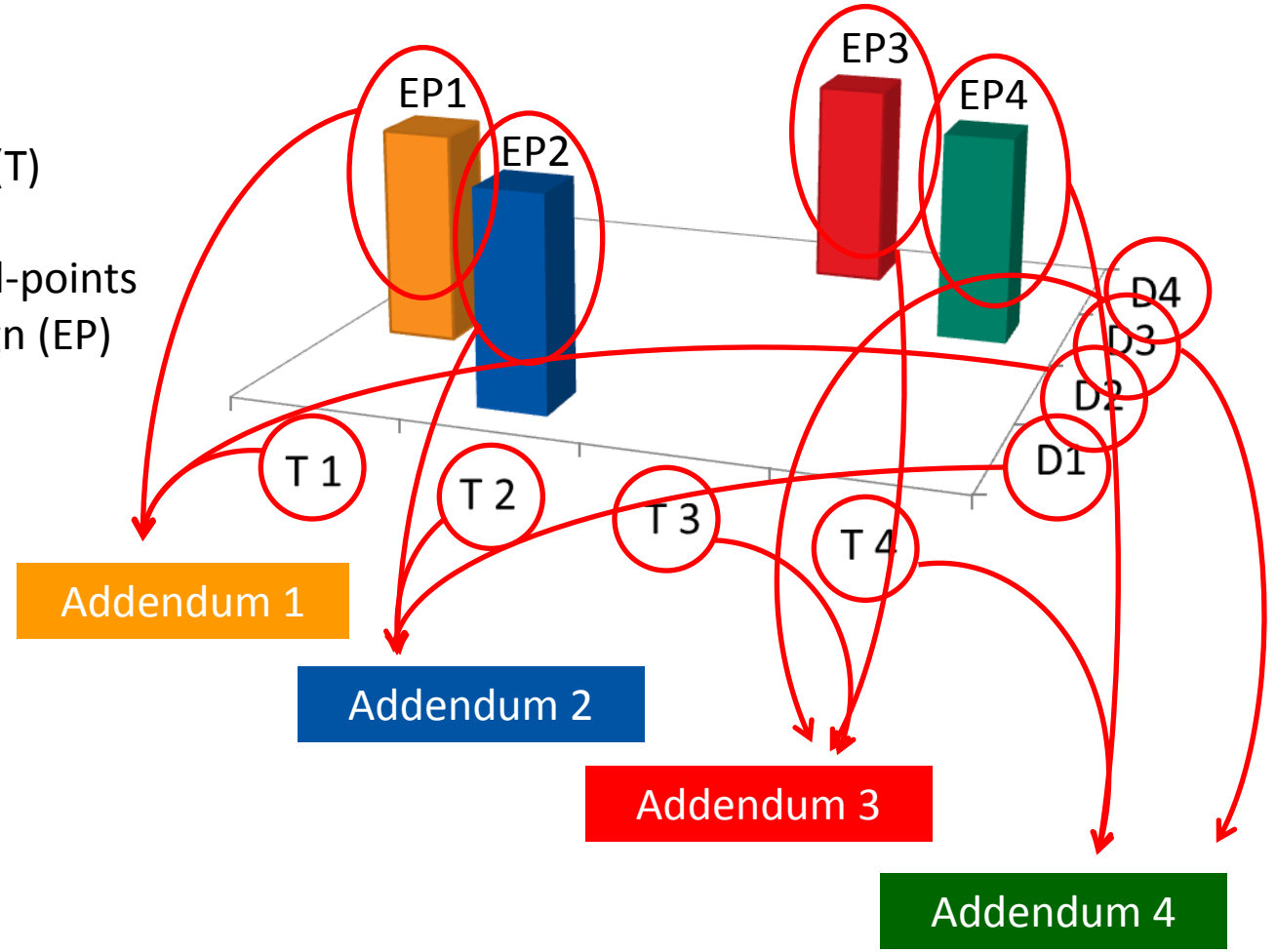


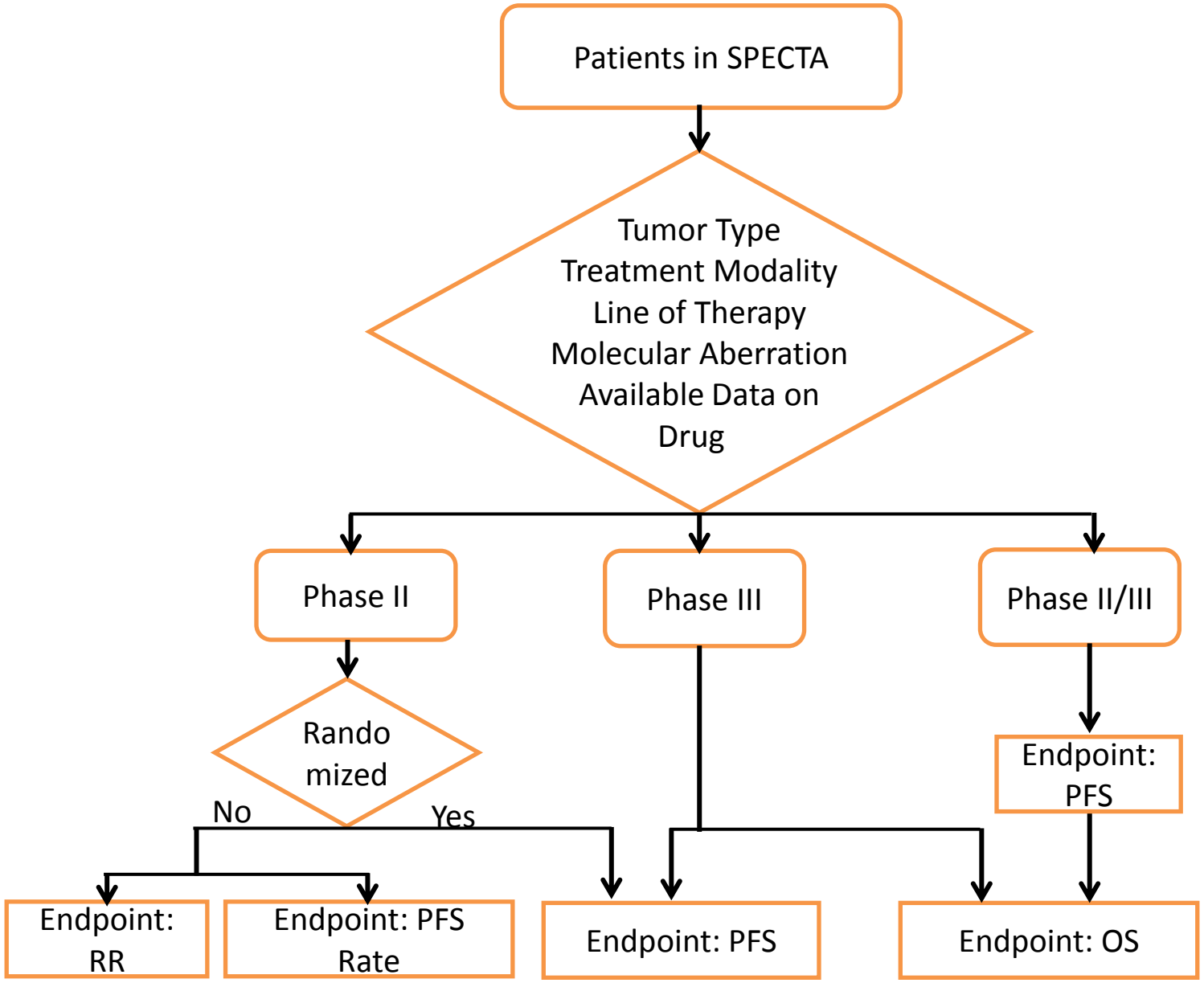
5. Agile access to downstream projects

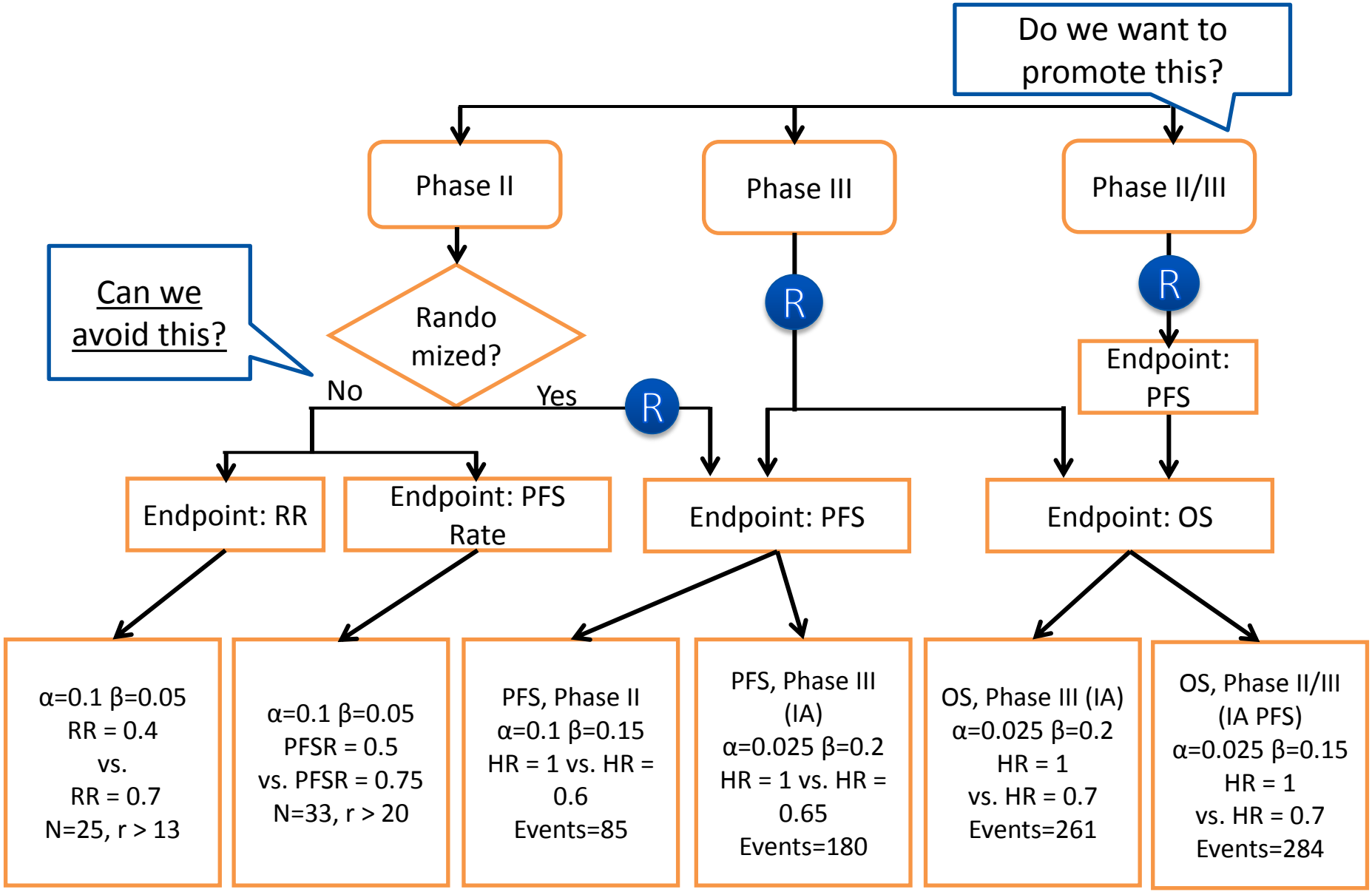
Regulatory flexibility in process

Master protocol

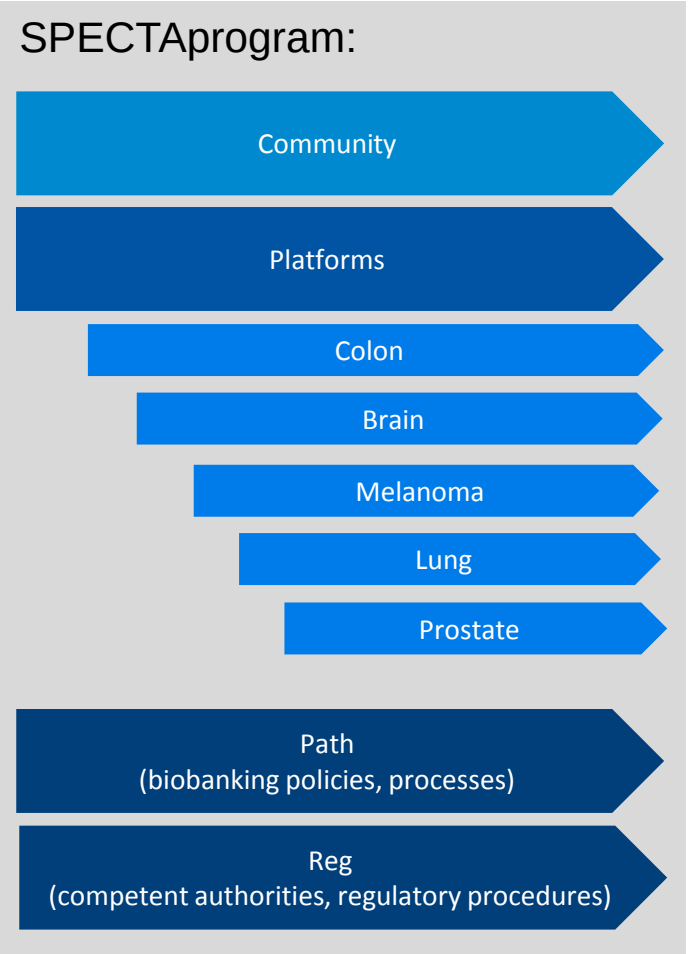
- Tumor eligibility (T)
- Tested drugs (D)
- Pre-specified end-points and related design (EP)




Patients in SPECTA
Tumor Type
Treatment Modality
Line of Therapy
Molecular Aberration
Available Data on
Drug
Phase II
Phase III
Phase II/III
Rando
mized
No
Yes
Endpoint:
PFS
Endpoint:
RR
Endpoint: PFS
Rate
Endpoint: PFS
Endpoint: OS


Do we want to promote this?
Phase II
Phase III
Phase II/III
Can we avoid this?
Rando mized?
No
Yes
R
R
R
Endpoint: PFS
Endpoint: RR
Endpoint: PFS Rate
Endpoint: PFS
Endpoint: OS
α=0.1 β=0.05 RR = 0.4 vs. RR = 0.7 N=25, r > 13
α=0.1 β=0.05 PFSR = 0.5 vs. PFSR = 0.75 N=33, r > 20
PFS, Phase II α=0.1 β=0.15 HR = 1 vs. HR = 0.6 Events=85
PFS, Phase III (IA) α=0.025 β=0.2 HR = 1 vs. HR = 0.65 Events=180
OS, Phase III (IA) α=0.025 β=0.2 HR = 1 vs. HR = 0.7 Events=261
OS, Phase II/III (IA PFS) α=0.025 β=0.15 HR = 1 vs. HR = 0.7 Events=284

The EORTC SPECTAprogram value proposition



SPECTAforum, a place to meet…

- Efficient patient selection and access
- Quality assurance and safety
- Partnership & mutualisation of efforts
- Access to new technologies
- Biomarker qualification and validation
- Cost efficiency / cost sharing
- Business risk reduction
- Addresses the efficacy & effectiveness gap
- Access to knowledge

A major academic commitment…

- EORTC Board
  - R. Stupp
  - S. Tejpar
  - F. Cardoso
  - F. Meunier…
- The EORTC groups
  - Colo-rectal: A. Roth, G. Folprecht
  - Melanoma: L. Eggermont, C. Robert
  - Brain: M Weller, M. van den Bent
  - Lung: B. Besse
  - Prostate: B. Tombal, M Spahn
  - PBG: R. Salgado, D. Aust
- ETOP (SPECTAlung)
  - R. Stahel
  - S. Peters
- EORTC HQ
  - V. Golfinopoulos
  - CRP: C. Messina, R.Karra, S Marreaud, J. Menis
  - TR: E. Varin, E. Szepessy
  - Legal: A. Negrouk
  - And all the operational staff…
- EMA: M. Papaluca, F. Pignatti
- ESP: H. van Krieken, F. Bosman
- Patient advocates