Perspectives for Effective Cancer Drug Development

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

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Contents

• Rationale for SPECTA
• What is SPECTA?
• How does SPECTA function?
• Ambitions and goals of SPECTA
• Agile access to downstream clinical trials
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 subgroups at the end of all comers approach
- Or apply subgroup selection at start of development
The changing clinical research pathway (II)

Early clinical trials (R&D)
- Biology / imaging driven
- Integrated TR
- Screening platforms
- Collection of high quality data from various sources

Pivotal trials
- Highly targeted
- Large differences

Population-based studies
- Real world data
- Quality of life
- Health economics
- HTA
- Pragmatic trials

From trials “designed to learn” to real life situation

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

Molecular Screening Platform

1st line trial

2nd line trial

3rd line trial

Standard treatment (no open trial)

Standard treatment

First line

Second line

Third line

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 stakeholders

✓ 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

EORTC SPECTAprogram

Screen and Treat

SPECTAplatforms
- SPECTAcolor
- SPECTAbrain
- SPECTAmel
- SPECTAlung
- SPECTApros

SPECTAforum
- Patient representatives
- Industry
- Regulators
- Technology companies
- Governments
- Payers

SPECTApath
- PathoBiology
- Biobanking
- Scientific/operational support

SPECTAreg
- Competent bodies
- Regulatory affairs research

The future of cancer therapy
3. How does SPECTA function?
The status on the SPECTA platforms

<table>
<thead>
<tr>
<th>SPECTA platforms:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Colorectal cancer</td>
<td>Accruing</td>
</tr>
<tr>
<td>• Melanoma</td>
<td>Protocol being finalized</td>
</tr>
<tr>
<td></td>
<td>First investigator meeting done</td>
</tr>
<tr>
<td>• Brain tumors</td>
<td>Protocol being finalized</td>
</tr>
<tr>
<td>• Lung cancer</td>
<td>EORTC ETOP partnership</td>
</tr>
<tr>
<td></td>
<td>Protocol being finalized</td>
</tr>
<tr>
<td>• Prostate cancer</td>
<td>Concept launched</td>
</tr>
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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

- QA/QC validated platforms & Services
- Collected data

Biomarker analytical and clinical validation

Clinical Utility

- Innovative trial designs / Trial access
- Regulatory pathway / Market access supported by agile licensing

Treatment guideline development

Faster access to effective care

Business risk reduction

The future of cancer therapy
A vision for access to personalized medicine for all patients: A European “independent Pharma”

Disease 1
Disease 2
Disease 3
Disease 4

Off label medical needs

Biomarker driven market access, registration and reimbursement

Biomarker driven drug access

The future of cancer therapy
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)

Addendum 1
Addendum 2
Addendum 3
Addendum 4
Patients in SPECTA

Tumor Type
Treatment Modality
Line of Therapy
Molecular Aberration
Available Data on Drug

Phase II
Rando mized
No
Endpoint: RR
Yes
Endpoint: PFS Rate

Phase III
Endpoint: PFS

Phase II/III
Endpoint: PFS
Endpoint: OS
\[ \alpha = 0.1 \quad \beta = 0.05 \quad \text{RR} = 0.4 \quad \text{vs.} \quad \text{RR} = 0.7 \quad \text{N}=25, \ r > 13 \]
\[ \alpha = 0.1 \quad \beta = 0.05 \quad \text{PFSR} = 0.5 \quad \text{vs.} \quad \text{PFSR} = 0.75 \quad \text{N}=33, \ r > 20 \]
\[ \text{PFS, Phase II} \]
\[ \alpha = 0.1 \quad \beta = 0.15 \quad \text{HR} = 1 \quad \text{vs.} \quad \text{HR} = 0.6 \quad \text{Events}=85 \]
\[ \text{PFS, Phase III (IA)} \]
\[ \alpha = 0.025 \quad \beta = 0.2 \quad \text{HR} = 1 \quad \text{vs.} \quad \text{HR} = 0.65 \quad \text{Events}=180 \]
\[ \text{OS, Phase III (IA)} \]
\[ \alpha = 0.025 \quad \beta = 0.2 \quad \text{HR} = 1 \quad \text{vs.} \quad \text{HR} = 0.7 \quad \text{Events}=261 \]
\[ \text{OS, Phase II/III (IA PFS)} \]
\[ \alpha = 0.025 \quad \beta = 0.15 \quad \text{HR} = 1 \quad \text{vs.} \quad \text{HR} = 0.7 \quad \text{Events}=284 \]
The EORTC SPECTAprogram value proposition

SPECTAprogram:

- Community
- Platforms
  - Colon
  - Brain
  - Melanoma
  - Lung
  - Prostate
- Path (biobanking policies, processes)
- Reg (competent authorities, regulatory procedures)

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