



Innovative Medicines Initiative

Blood-based biomarker assays for personalised tumour therapy: value of latest circulating biomarkers

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efpia*

Need for public-private collaboration



- Current activities in academia, SMEs and pharmaceutical industry generally focus on **single technologies** for isolation and characterization of CTCs. Comparative studies are lacking and standard protocols are needed for utilizing CTCs as biomarkers.
- The comprehensive evaluation of several different technologies head to head and including them in clinical studies is a **major effort and not feasible for a single pharmaceutical or a few academic institutions**. A public-private partnership in this field would therefore join forces on the development of companion diagnostics using CTCs or circulating nucleic acids:
 - **Pharmaceutical companies**, having the knowledge about the development of new drugs and the need for companion diagnostics,
 - **Diagnostic companies**, having well established tissue based technologies and expertise in companion diagnostic development and their regulatory approval
 - **Biotech companies** with their knowledge about new technologies,
 - **Academia** providing the knowledge on the molecular disease mechanisms and access to clinical samples.
 - **Regulatory authorities** responsible for biomarker qualification and device approval



Objectives of the full project



- The aim of the project is the establishment, technical and clinical validation of methods for blood-based biomarkers enabling prediction (i.e. **patient stratification/ predictive biomarkers**), monitoring of treatment response (i.e. **surrogate biomarkers** and prognosis i.e. **prognostic biomarkers**).
- Ultimate goal is the development of according blood-based **companion diagnostics** (CDx). Such products have significant value for patients, physicians, and payers by avoiding exposure of patients to drugs which are unlikely to be beneficial.
- Validated biomarker assays are extremely important for the pharmaceutical industry as they will help to reduce the very high attrition rate in clinical development, the key cost driver in drug development, by selection of well characterized patients with suitable preconditions for response.



Objectives of the full project



- Currently the most promising approaches within the field are the analyses of
 - i) CTCs
 - ii) ctDNAs and
 - iii) miRNAs (e.g. isolated from exosomes)

Only CTCs offer the chance for isolation and subsequent functional testing, whereas ctDNA and miRNA may be more likely to be detected and therefore suitable especially in early disease stages of cancer.

- **Pre-evaluation phase.** In a first step the most promising concrete technologies (not early ideas!) should be selected based on available data either published or provided by partners. Criteria for evaluation of key parameters needs to be defined (e.g. what defines a circulating tumor cell?). Establishment of SOPs for pre-analytical sample handling (e.g. for phospho-protein analysis)!
- **Technical evaluation phase.** The selected technologies should be applied using the standards defined, preferentially head to head. Using in vitro and animal studies the technologies should be then compared e.g. with regard to sensitivity, reproducibility, predictivity etc.
- **Clinical validation phase.** The technologies selected will be used to analyze in retrospective samples from well-defined patients and in prospective clinical studies.



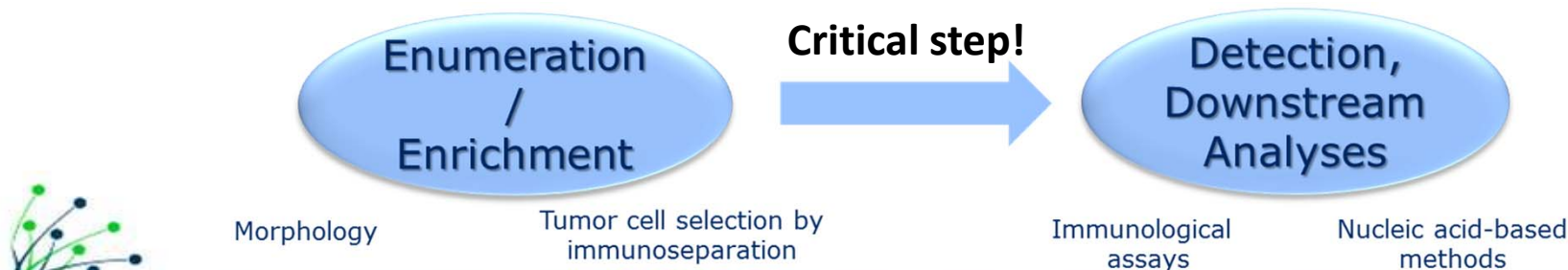
Pre-competitive nature



All information and data generated in the project will be shared according to IMI guidelines, enabling the participants to be at the forefront of CDx development in the CTC/ctDNA field

- EFPIA members agree that CTCs and ctDNAs may have a great impact on prognosis and prediction of treatment success, however, the current FDA approved enumeration approach of CTCs is not sufficient to achieve these goals
- Application of CTCs/ctDNA as blood-based biomarkers would greatly benefit from the establishment of **commonly agreed standards** for the isolation, identification and analysis of material from clinical samples

⇒ Great interest on the EFPIA side to share experiences in the field to facilitate and speed-up the development of CTC/ctDNA based CDx

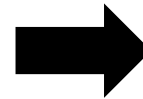


Expected impact on the R&D process



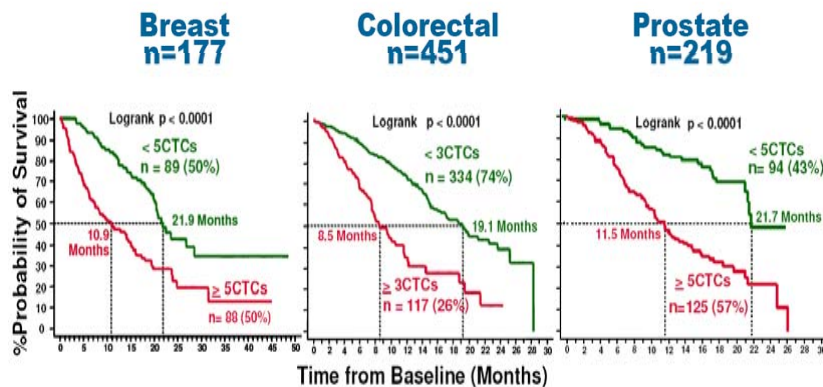
Today

- Counting of CTCs only indicates patient survival (CellSearch™, Veridex)
- CTCs are Merely a Prognostic Indicator Currently



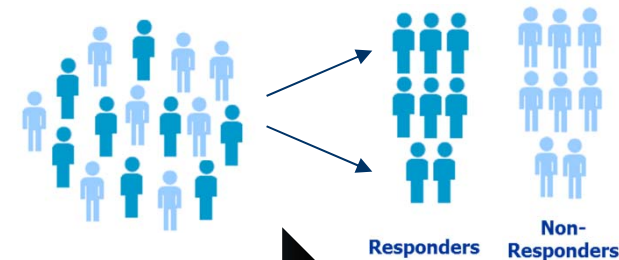
Future

- Into a Source of Predictive Biomarkers
- CTCs can be used to characterize genomic and proteomic content
- Specific markers guide effective personalized treatment



Source: McCormack, Veridex: "Contemporary Issues in Circulating Tumor Cell Testing – ADAPT 2010"

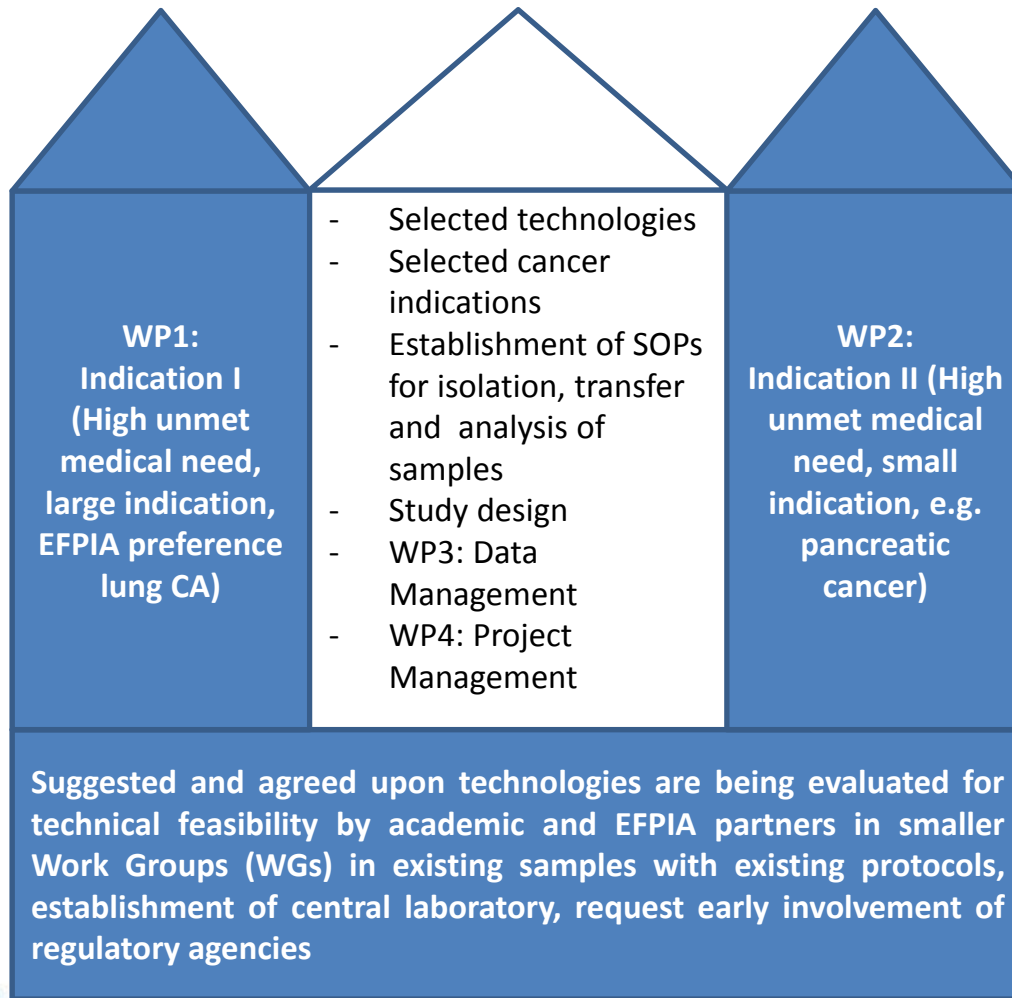
48% of recently approved oncology therapies have predictive biomarkers associated with them



Modified from: Circulating Tumor Cells [CTCs] and Cancer Stem Cells [CSCs] 2013 Market Report; Research Trends and Clinical Utility. <http://www.SelectBiosciences.com/marketreports/>; Jan 2013



Suggested architecture of the project



Clinical evaluation phase
Years 3-5

Technical evaluation phase
in clinical setting
Years 1-4

Pre-evaluation phase
Year 1



Expected contributions of the applicants



- Applicant Consortium should address all research objectives outlined above
 - clinicians with expertise in the field and having access to clinical samples
 - academic research groups with a track record in the molecular analysis of CTCs or ctDNA
 - SMEs with established close-to-the-market technologies for CTC isolation and analysis
 - Additional required expertise includes bioinformatics, *in vivo* and *in vitro* models for CTCs.
- The EFPIA Participants would highly welcome the involvement of regulatory authorities (EMA, FDA) early on in the project either as official partners or as member of the Advisory Board.



Expected (in kind) contributions of EFPIA members



- EFPIA participants: Bayer HealthCare (lead), Boehringer-Ingelheim, Eli Lilly, Menarini, Orion, Servier, Abbvie (under internal evaluation), Ipsen (under internal evaluation). The interest of further EFPIA members in the call is currently being inquired
- The indicative EFPIA in-kind contribution is EUR 7 360 000.
- The indicative IMI JU contribution is up to EUR 6 620 000.
- Each participating company will fund their own participation and provide R&D resources such as staff, laboratory facilities, materials and clinical research:
 - FTEs will perform hands-on scientific work in the laboratories of the EFPIA partners and are involved in project management.
 - Clinical samples collected by EFPIA partners will be provided to the consortium, if useful for its purposes.
 - There is significant experience among EFPIA members with different technologies used for CTC isolation, molecular analysis. These protocols and expertise will be made available to the consortium.



What's in it for you?



- Academic Researchers:
 - High-profile visibility of research to different stakeholders
 - Attractive funding option
 - Networking opportunity with key researchers and pharmaceutical industry
- SMEs:
 - Access to potential customers and samples for testing approaches
 - Funding option for further development of SME's technology
 - Input for further technology development by users and regulatory authorities
- Patients' Organizations:
 - Access to information on latest developments in a field that may have great impact on the choice and availability of future therapies
 - Networking opportunity with Diagnostics R&D at all stages to give feedback on needs and wishes of patients
- Regulatory Authorities:
 - Early-on influence on development of potential CDx



Key deliverables of the full project



- Establish criteria for evaluation of different CTC isolation technologies;
- Setting up a sample collection and developing storage protocols (SOPs) for selected CTC isolation technologies allowing shipment and bio banking for collection and analysis at different research sites;
- Comparison of methods for the molecular analysis of CTCs with respect to correlation with primary tumor material, clinical outcome, treatment response and ctDNA status of patients;
- Evaluation of different ctDNA analysis methodologies in terms of compatibility with sample collection and storage as well as reproducibility in clinical samples;
- Development of database and data analysis infrastructure for correlative studies of CTCs and ctDNA in clinical samples;
- Development of technologies for blood-based companion diagnostics ideally up to proof of clinical utility supporting regulatory approval.



Questions?



- Contact the **IMI Executive Office**

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