IMI CANCER-ID: Validation of novel blood-based biomarker technologies in clinical settings

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INTRODUCTION

• The Innovative Medicines Initiative (IMI) was launched in 2008 as a public-private partnership between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA).
• IMI aims to facilitate the collaboration of healthcare stakeholders, such as academic and clinical researchers, pharmaceutical industry and small- and medium-sized enterprises (SMEs) in Europe, in order to address key issues in drug development and patient access to innovative medicines.
• Major obstacles for cancer diagnosis and treatment are tumor heterogeneity and the dynamic changes at the molecular level during disease progression; this makes longitudinal monitoring of malignant disease highly desirable, in order to choose the best treatment options and to monitor treatment efficacy.
• As access to tumor tissue is often the limiting factor and historic samples are not predictive for the current state of the disease, new blood-based biomarkers are explored as liquid biopsies to support personalized treatment of cancer patients.

OBJECTIVES

I – The science
• CANCER-ID (www.CANCER-ID.eu) was established in 2014.
• The consortium aims to validate technologies for blood-based biomarkers such as circulating tumor cells (CTCs), circulating tumor DNA (ctDNA) and microRNAs (miRNAs) for patient stratification, prediction of treatment response and early detection of developing resistance (Figure 1).
• The focus is on technologies that have the potential to go beyond the current standards (e.g. CellSearch®) and that have the maturity to enter the market within the next 5–7 years.
• To prove multi-center applicability and the clinical utility of the consortium’s technologies and protocols, the validated assays will be deployed in controlled clinical studies (TRACERx, NCT01888601; NVALT17, NTR4410; SPECTAlung, NCT02214134; and patients receiving standard of care [SoC] treatment) in non-small cell lung cancer (NSCLC) and Her2-negative metastatic breast cancer (Her2NMC).
• These indications were chosen based on the limited access to tumor biopsies, low number of CTCs and the relatively well characterized molecular subtypes in NSCLC.
• For comparison, Her2NMC is ideally suited, as higher numbers of CTC can be expected, and resistance is a frequently observed phenomenon (developing under therapy or in treatment-naïve patients).
• A key issue to be addressed in CANCER-ID is the definition of CTCs that includes tumor cells that do not express epithelial cell adhesion molecule (EpCAM), resulting in more precise methods for CTC enumeration and isolation.

II – The consortium
• CANCER-ID is a unique network of experts in the fields of tumor biology, biomarker development, clinical sciences and bioinformatics with a total budget of €14.5 million.
• The consortium joins the forces of 17 academic groups (with 12 clinical sites), 6 EFPIA companies (lead Bayer, co-lead Menarini), 6 SMEs, 2 non-profit organizations, and 2 non-SME/non-EFPIA 33 partners:
  - 6 EFPIA companies (lead Bayer, co-lead Menarini, 11 academic/clinical sites)
  - 6 SMEs
  - 2 non-profit organizations
  - 2 non-SME/non-EFPIA

• In order to fully exploit the synergies created by CANCER-ID, the consortium invites regulatory agencies and patient advocacy groups to take an active role in the project (Figure 2).

Figure 1. Potential of CTCs in personalized medicine

Figure 2. CANCER-ID partners

III – The project frame
• The program is divided into 3 phases: pre-evaluation, technical assay validation and clinical validation.

Figure 3. Experimental strategy and key objectives

Figure 4. Current status of the project

KEY DELIVERABLES OF THE FULL PROJECT

• Establish criteria for evaluation of different CTC isolation technologies
• Sample collection and development of storage protocols for selected CTC isolation technologies, allowing shipment and biobanking 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/mRNA analysis methodologies, in terms of compatibility with sample collection and storage procedures as well as reproducibility in clinical samples
• Development of database and data analysis infrastructure for correlative studies of CTCs, ctDNAs and miRNAs in clinical samples

Acknowledgments
Under the authors’ conceptual direction, editorial assistance was provided by the Prime Medical Group (Knutsford, UK), and was supported by Bayer Procter presented at the American Association for Cancer Research Annual Meeting, 19–23 April 2015, Philadelphia, PA.
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American Association for Cancer Research Annual Meeting
18–22 April 2015, Philadelphia, PA