Prostate cancer PROLIPSY study – what we already know and what is yet to come

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Prostate cancer (PCa) is a major cause of cancer-related mortality and morbidity in men of the western world. Standard PSA screening has a high rate of false-positive findings (up to 60%) and therefore more specific methods for early detection of PCa are urgently needed. Previously, partners of our consortium have played a key role in implementing the concept of "liquid biopsies" (i.e., analysis of tumour cells or tumour cell-derived nucleic acids and exosomes in blood) into research on PCa (TRANSCAN project CTC-SCAN, ended in 2016) and other solid tumours (EU/IMI project CANCER-ID).

The primary aim of this research was to improve blood-based detection of PCa patients by testing of circulating tumour cells (CTCs), tumour-derived exosomes and circulating cell-free DNA (cfDNA) as liquid biopsies. Analysing peripheral blood samples from men with elevated PSA concentrations that undergo prostate biopsy, we stratified patients in cancer and non-cancer cohorts based on the outcome of the histological evaluation of the tissue biopsy. Cancer patients underwent surgical resection or radiotherapy. In the first year (discovery period), we assessed which liquid biopsy marker or combination of markers (i) provided the best discrimination between the two cohorts and (ii) identifies in particular high-risk PCa patients with aggressive tumour as defined by a Gleason score ("gold standard") of 8 or higher. Biobanks from former studies on PCa (e.g., CTC-SCAN) were used in particular for plasma studies (cfDNA, exosomes). Candidates were further explored in the subsequent training and validation study (years 2 and 3) in order to obtain the blood test with the highest sensitivity and specificity for detection of early PCa and/or high-risk PCa. Blood from men with elevated PSA levels (gold standard for PCa screening) were analysed prospectively before tissue biopsy was taken to avoid biopsy-induced interference of blood results.

Comparing the results of liquid biopsy with tissue biopsy histology (gold standard for PCa diagnosis) we identified single and blood-based marker combination with the highest sensitivity and specificity for detection of total PCa and/or high-risk PCa. The unique combination of expertise assembled in this consortium guarantee a complementary investigation of the relevance of liquid biopsy for early detection of PCa at the European level.