Prediction of PARP inhibitor response and resistance utilizing a CTC phenotypic classifier in patients with metastatic castration-resistant prostate cancer (mCRPC): Results from the NIC 9012 trial

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Methods for CTC Detection, Phenotypic, Genomic Characterization

1) Epic CTC identification, enumeration and analysis
2) Segmentation & image analysis
3) Single Cell Sequencing
4) Phenotype to Genotype

Phenotypic & Genomic Profiles of CTCs

Phenotype -> Genotype Association
HRD+ Phenotypic CTC scores have increased Genomic Instability
434 CTCs from 35 patients were measured for HRD Phenotypic classifier trained on a large independent cohort (Scher et al.3)

Association of Single CTC Genomics to Tissue Sequencing

Components of the CTC Classifier

CTC Biomarker Classifier Definition

Patient Baseline Incidence of CTC Classifier in Metabohism

Patient Demographics & CTC Classifier Development

Biomarker +
PARPi (190 in 122 patients) [-15% +20%]

Phenotypic HRD score

CBRACATM Mutant by Tissue
CBRACATM Wildtype by Tissue
Unknown Tissue Status

Component of the CTC Classifier

Blood samples for CTC analysis

Association of Single CTC Genomics to Tissue Sequencing

210 CTCs from 27 patients were sequenced and generated a LST score (y axis), with high scores associating with genomic scars. Each dot represents a single CTC, with significant subclonal heterogeneity observed in multiple patients. Each patient was analyzed for BRCACATM alterations from blood samples (MICOncsex).

Conclusions

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