Background

The presence of genomic instability (GI) has been associated with DNA Damage Response (DDR) genetic profiles. miCRC pts with DDR are responsive to poly ADP ribose polymerase inhibitors (PARPi).

Similar Tx benefit for tumors with DDR(+) profiles has been observed with alkylating agents such as platinum.

Previously we developed an imaging-based phenotypic classifier to predict GI (pGI) from individual genetic profile. mCRPC pts with DDR are responsive to poly ADP ribose polymerase inhibitors (PARPi) vs. taxane alone. 2) pGI(+) CTCs were more likely to be eliminated on Txdue to platinum

High %pGI(+) CTCs Might Be Associated with Improved OS when Platinum added to Taxanes

Patient Selection and Demographics

CTC Monitoring Cohort (Paired samples: pre-Tx and on-Tx)

Outcome Association Cohort (pre-Tx samples only)

Methods for CTC Detection and Characterization

• CTC Monitoring Cohort utilized all available samples with both a baseline (pre-Tx) and Tx draw for pts receiving taxanes or platinum agents

• Outcome Association Cohort utilized all samples prior to any taxane administration, or combination of taxanes and platinum agents. Choice of Tx was at the discretion of the attending physician without CTC results. Pts receiving combination of platinum and taxanes generally had lower PSA

Conclusions

• Those are retrospective analyses of prospectively banked samples

• Pt groups were not randomly assigned, pts receiving platinum agents generally had more aggressive disease

• The relationship between CTC burden, %pGI(+), CTCs, and Tx class with OS was explored with a Cox PH model

• The results suggest that in a properly balanced cohort, pts with high %pGI(+) might have better OS if platinum agents are added to taxanes

• Corroborating this result is the observation that some pts with high %pGI(+) CTCs remained alive for an extended period of time compared to the rest of the cohort (far right)

• Digital Pathology can predict presence of genomic instability of individual CTCs without sequencing pt tumor samples.

• %pGI(+) CTCs have a Tx interaction (HR=0.148, p=0.022) with improved outcome with taxane + platinum over taxane alone, suggesting that a properly balanced cohort might show improved OS for platinum use in pts with high %pGI(+) CTCs.

• Pts receiving platinum chemotherapy alone or in combination, but not taxanes alone, are likely to have a drop of %pGI(+) CTCs after Tx initiation, suggesting that the %pGI(+) phenotype is preferentially sensitive to platinum containing therapeutic regiments.

• Clinical validation of the utility of %pGI(+) CTCs to predict sensitivity to platinum and PARPi agents, and the association with improved pt outcomes, are underway.