Circulating tumor DNA (ctDNA) genomic and epigenomic profiling (Guardant Infinity™) for diagnosis of DNA damage repair (DDR) loss-of-function (LoF) detection and response monitoring in the TRESPR and ATTACC trials

Eva Rossen1, Joseph D. Schernholtz2, Ian M. Silverman3, Anela Valkovska4, Svetlana Seltserman4, Parham Nagel1, Danielle Choupinet1, Julia Yang1, Ined Kini1, Kathar Feil5, Yi Xu1, Enzo Lagana5, Shih Zhang6, Minggang Cao7, Maria Koehler7, Benedetto A. Carninci5, Stephanie Leuenberger7, Michael Csech9, Benjamin Herbst8, Jorge S. Reis-Filho8, Viktornis Rimkus9, Timothy A. Yap8

1Medical Oncology, Alteonio Shilling Center for Cancer Care, New York, NY, USA; 2Memorial Sloan-Kettering Cancer Center, New York, NY, USA; 3Memorial Sloan-Kettering Cancer Center, New York, NY, USA; 4Memorial Sloan-Kettering Cancer Center, New York, NY, USA; 5Memorial Sloan-Kettering Cancer Center, New York, NY, USA; 6Memorial Sloan-Kettering Cancer Center, New York, NY, USA; 7Memorial Sloan-Kettering Cancer Center, New York, NY, USA; 8Memorial Sloan-Kettering Cancer Center, New York, NY, USA; 9Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Study design

Sample collection: Venous blood was collected in Cellfree DNA BCT tubes (Streck Life Sciences). A 4.0 ml Blood Sample was collected within 72 hours of the scheduled start of the chemotherapy. The Cellfree DNA BCT tubes were centrifuged and aliquots of 500 μl were stored at −80°C. Cellfree DNA extracted from the Cellfree DNA BCT tubes was used to measure Cellfree DNA MR, %.

Methods

Additional coverage and optimized bioinformatics allow detection of complex LoF alterations typically not captured by existing ctDNA assays. Additional panel coverage in DDR genes allowed detection of LoF SNVs and Indels. The sensitivity for LoF SNVs and Indels detection in DDR genes was 63% (5/8) of unconfirmed somatic alterations were due to low TF.

Results

Reversions are a validated resistance mechanism for PARPi and likely important for understanding response to therapy. Can second-generation ctDNA assays (Guardant Infinity) better diagnose complex DDR LoF alterations compared to existing assays? Variants derived from CH are widespread in ctDNA and should be interpreted with caution.

Conclusions

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