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Tumor cell-free DNA copy number instability compared to CA19-9 as an early predictor of response to systemic therapy in pancreatic ductal adenocarcinoma (PDAC).

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Abstract Disclosures

Background:
Humoral tumor markers are used clinically for real-time assessment of therapeutic efficacy. In pancreatic ductal adenocarcinoma (PDAC) the predominant marker is CA19-9, which is not expressed by 10 to 30% of patients depending on race. We compared plasma cell-free DNA (cfDNA) copy number based assay with changes in serum CA19-9 levels and radiological responses to predict responses to systemic therapy.

Methods:
In a laboratory blinded, prospective multicenter pilot study, 40 non-resectable PDAC patients, treated with (m)FOLFIRINOX, CAPIRI, or gemcitabine +/- nab-paclitaxel) are currently enrolled. CA19-9 was determined in the local center's laboratory. Tumor cfDNA was measured with a copy-number instability (CNI) scoring assay, determined by next generation sequencing in a centralized laboratory. The CNI score assesses the amount of cfDNA with somatic macro-alterations originating from malignant neoplasms. The difference of the values before commencing therapy (baseline) and prior to cycle 2 (either rising or falling) was calculated as a predictor of standardized radiological evaluation of chemotherapeutic efficacy.

Results:

37 patients (3 drop-outs) had data for baseline and cycle 2, of which CA19-9 was elevated and evaluable in 29 patients. The direction from baseline to cycle 2 of CA19-9 and CNI scores were in agreement in 18/29 patients. 9 of 11 cases with discordant CNI score and CA19-9 had treatment response data, and CNI correlated with 7/9 (78%); in contrast 7/9 had rising CA19-9, when response was stable disease or better (22% concordance). In the 27 patients with available imaging, CNI predicted better (n = 18) than CA19-9 (n = 10) (p = 0.03 Fisher's exact).

Conclusions:

This comparative study on cfDNA versus CA19-9 suggest that cfDNA CNI quantitation is a potentially more reliable blood based marker for early real-time assessment of efficacy in systemic PDAC therapy than CA19-9, compared to standard of care imaging. The better prediction after the first cycle might be due to the very short *in vivo* half-life of cfDNA (< 1hr) compared to about one week for CA19-9. These results justify a larger prospective validation trial.