Title

ASO Author Reflections: Circulating Tumor DNA in Peritoneal Carcinomatosis.

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Author Commentary on “Preoperative Circulating Tumor DNA in Patients with Peritoneal Carcinomatosis Is an Independent Predictor of Progression-Free Survival”

Past

Patients with peritoneal metastases present unique challenges in diagnosis, treatment, predicting future disease behavior. Imaging of peritoneal metastases typically underestimates the disease burden.[1] Surgical treatment, often with complete cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC), can have high morbidity and is most effective in a carefully selected group of patients. Prognosis varies greatly not only by histology, but also by many additional unknown factors. The detection of molecular alterations in tumor tissue via next generation sequencing (NGS) has led to a revolution in the understanding of tumor biology, use of targeted therapies, and assessing response to therapy. Cell-free circulating tumor DNA (ctDNA) shed from tumor is measurable in plasma using modern NGS techniques and has potential to aid in assessments of disease burden and risk of recurrence, in addition to identifying actionable alterations.[2] We sought to assess the detection and utility of ctDNA in patients with peritoneal metastases undergoing surgical resection.

Present

We found that ctDNA is detectable in patients with peritoneal metastases prior to surgical resection, including in 27% of patients with low-grade mucinous appendiceal tumors.[3] The most common detectable alterations were in *TP53* and *KRAS*. A subset of our cohort also underwent tissue-based molecular profiling, and these results were 97% concordant with the ctDNA alterations. Finally, we found that high levels of ctDNA (regardless of the alteration detected) correlated with worse progression-free survival than those with low levels, controlling for grade of disease and extent of surgical resection. These findings collectively suggest that ctDNA may be a useful tool for disease prognostication in patients with peritoneal metastases.

Future

Our results are preliminary and need to be validated in a larger group of patients. In addition, we are currently further exploring use of ctDNA in this population. Namely, we are analyzing whether changes in postoperative ctDNA from preoperative results can further predict oncologic outcomes. We are also attempting to determine whether longitudinal assessments could be used for surveillance after surgery. Hopefully, this test will prove useful in assessing, surveying, and predicting outcomes in this challenging population.

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2. Diehl F, Schmidt K, Choti MA, et al. Circulating mutant DNA to assess tumor dynamics. *Nature medicine.* Sep 2008;14(9):985-990.

3. Baumgartner JM, Raymond VM, Lanman RB, et al. Preoperative Circulating Tumor DNA in Patients with Peritoneal Carcinomatosis is an Independent Predictor of Progression-Free Survival. *Annals of surgical oncology.* Aug 2018;25(8):2400-2408.