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UTILITY OF TUMOR-INFORMED MOLECULAR RESIDUAL DISEASE ASSAYS IN PATIENTS WITH COMPLETE RESPONSE TO IMMUNE CHECKPOINT BLOCKADE

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Background Recent data suggests that responses in patients with mismatch repair deficient (dMMR) tumors tend to be durable and potentially curative. Typically immunotherapy is employed and approved only in metastatic settings. However, it is not uncommon now to consider usage in patients with dMMR tumors secondary to the hypermutated nature of these malignancies alongside the concerns that these do not respond to therapy either through a clinical trial or off-label compassionate access programs. As noted, in patients who have these dramatic and durable responses, the question of foregoing surgery and/or radiation comes up. There is no great test to help predict or guide who are these complete responders. Assessment of molecular residual disease or minimal residual disease through tumor-informed assays is one potential test that can be employed in this setting. We here show the feasibility of such an approach in patients with dMMR tumors who got immunotherapy in the advanced but not metastatic setting.

Methods We identified patients who were enrolled in the serial tumor informed molecular residual disease BESPOKE expanded access ctDNA testing program (Signatera 16-plex bespoke mPCR NGS assay) who got immunotherapy in the neoadjuvant setting and were also enrolled in our biobanking program.

Results We were able to serially do ctDNA analysis in 2 patients (1 with advanced but not metastatic esophageal adenocarcinoma and another patient with advanced but not metastatic nearly obstructing rectal adenocarcinoma with extensive nodal metastases in both situations) who got immunotherapy off-label per physician discretion and tumor board discussion. Of note both these patients also had germline Lynch syndrome. Both of them had robust, dramatic and ongoing responses to immune checkpoint blockade. Of note, while they both had some radiographic question of residual disease, repeated endoscopic ultrasounds and random biopsies have yielded no tumor and all just scarred tissue. Circulating tumor DNA in these instances quickly declined to become undetectable and has remained not detectable to date (figure 1). Surgery and radiation is deferred and close follow up alongside serial endoscopic/radiographic assessment in addition to novel usage of ctDNA MRD assays is being employed.

Conclusions Data regarding neoadjuvant usage of immunotherapy is scarce pertaining to mismatch repair deficient tumors. There is a case series of 3 patients with rectal cancer that was just reported this year. Here we not only report a case of an advanced rectal cancer, but also a case of an advanced esophageal cancer who have achieved dramatic responses with no evidence of disease on repeated sampling. It is rare for surgery or radiation to be deferred in these situations. However, with added utility of ctDNA MRD assays, it gives us one more tool in our toolbox in terms of applying it to patients suitable for these ‘watch & wait’ approaches.

Ethics Approval The study has been approved by University of Iowa’s Institutional Review Board IRB#201202743.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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LINE OF THERAPY ADJUSTMENT IN A PATIENT WITH ADVANCED TRIPLE-NEGATIVE BREAST CANCER (TNBC) BY USING PERSONALIZED CTDNA TEST FOR TREATMENT RESPONSE MONITORING

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Background Triple negative breast cancer (TNBC) is an aggressive form of breast cancer that is most difficult to treat due to the absence of hormone/growth factor receptors.1 2 Metastatic TNBC (mTNBC) is particularly challenging, given the limited efficacy and duration of response to chemotherapy.3 The repertoire of therapeutic options for mTNBC patients continues to increase with chemotherapeutic and immuno oncology based treatments and now includes sacituzumab govitecan, a novel antibody-chemotherapy conjugate.4

Methods Here we present a case study of a 40-year-old female who on biopsy of her left breast mass was diagnosed with TNBC. The patient underwent neoadjuvant chemotherapy with weekly administration of paclitaxel and carboplatin followed by dose-dense doxorubicin with cyclophosphamide. Following one-month, the patient underwent bilateral mastectomy, showing pathological staging ypT2 pN0. The patient underwent periodic radiological imaging along with the assessment of circulating tumor DNA in blood using a personalized and tumor-informed multiplex PCR, next-generation sequencing assay (Signatera bespoke, mPCR NGS assay) to identify the minimal residual disease (MRD) and treatment response.

Results After surgery, MRD assessment revealed ctDNA positive status (0.41 MTM/mL) prompting PET/CT scan that revealed liver metastasis. Continued ctDNA monitoring