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Case Discussion: How Do I Manage Patients With TNBC?

Announcer:
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Dr. Bardia:
Hello, my name is Aditya Bardia. I'm an attending physician at Mass General Cancer Center. Associate Professor, Harvard Medical School. I'll review how I manage patient with metastatic triple negative breast cancer. I'll review first line therapy and second line and plus therapy. So let's start with the patient story. A 44-year-old female who noticed increase in shortness of breath, which prompted restaging scans that revealed presence of pulmonary and liver lesions. CT guided biopsy revealed breast adenocarcinoma that was essentially triple negative, ER, PR, HER2 negative. So how would you treat this patient in the first line setting? And the germline BRCA testing was negative. Carboplatin, eribulin, paclitaxel, capecitabine, or it depends need additional information. The last option essentially is correct. We need additional information and the key information that's needed is if the tumor is PD-L1 positive or PD-L1 negative.

So in this patient PD-L1 testing was done and the tumor was PD-L1 positive. And this is important because the Keynote 355 trial which looked at combination of chemotherapy plus pembrolizumab was chemotherapy versus placebo, demonstrated an improvement in progression-free survival in patients who received pembrolizumab. The median progression-free survival being 9.7 months was as 5.6 months with chemo plus placebo without immunotherapy. And there was also an improvement in overall survival. And these results led to the FDA approval of pembrolizumab In combination with chemotherapy, either ataxin or platinum for patients with PD-L1 positive metastatic triple-negative breast cancer.

It should be noted, another drug atezolizumab was initially approved by the FDA but in August, 2021, after discussion with the FDA, the indication of atezolizumab was withdrawn by the manufacturer. So at this time the only immunotherapy agent that's FDA-approved for a patient with PD-L1 positive metastatic, TNBC, is pembrolizumab.

How about if this patient has known germline BRCA mutation then what should be the treatment of choice? In a patient with germline BRCA mutation PARP inhibitors should be considered, either Olaparib or Talazoparib. And that's based on pivotal randomized phase three trials which led to the approval of both Olaparib and Talazoparib for patients with HER2 negative metastatic breast cancer who also have germline BRCA mutation in general. These agents are used in the second line in place setting. All those. Some also use it in the first line. particularly if a patient is interested in oral options and the tumor is PD-L1 negative.

Okay, so we reviewed two therapies in the first line setting, immunotherapy as well as PARP inhibitors, PARP inhibitors again can be used in the second line setting as well. So let's come back to the case. 35 year old female who had pulmonary metastases was found to have PD-L1 positive tumor received carboplatinum plus pembrolizumab then had disease progression then received capecitabine. Now the question is what therapy should one consider next? And that's where Sacituzumab Govitecan can comes in. It's a novel Trop-2 directed antibody drug conjugate that was evaluated in the ascent trial and demonstrated more than doubling of both progression-free survival and overall survival. Overall survival improved from 6.7 months with standard chemotherapy to 12.1 months with Sacituzumab Govitecan. And this led to the FDA approval of Sacituzumab Govitecan for patients with pretreated metastatic TNBC. Pretreated

defined as at least one prior therapy for metastatic breast cancer. So in terms of the treatment algorithm this slide summarizes my treatment algorithm. Patient with metastatic TNBC, check for PD-L1. If the tumor is PD-L1 positive, consider the use of pembrolizumab with chemotherapy the type of chemotherapy dictated by how long it's been since the adjuvant treatment. If a tumor is PD-L1 negative, Also look for BRCA. If patient has germline BRCA one could consider PARP inhibitor in the first line or even later line setting. And if it's negative, then use of chemotherapy. In the second line setting I tend to prefer Sacituzumab Govitecan, consistent with the FDA label. And then after that in the third line beyond setting other chemotherapy agents or novel therapies.

So in conclusion in the first line, chemotherapy plus pembrolizumab is the preferred therapy for patients with metastatic TNBC that's PD-L1 positive. In the second, third, and plus setting one could use PARP inhibitors for patients with germline BRCA mutation, Sacituzumab Govitecan in the second line beyond setting for patients with metastatic TNBC and other chemotherapy agents Like capecitabine, erubilin for third line and beyond metastatic TNBC. Thank you so much for your attention.

Announcer:
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