CME Exam 3: Real-time Targeted Genome Profile Analysis of Pancreatic Ductal Adenocarcinomas Identifies Genetic Alterations that Might be Targeted With Existing Drugs or Used as Biomarkers

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Question 1:

The tumor biopsy for your 60-year-old woman with locally advanced pancreatic ductal adenocarcinoma (PDAC) was evaluated for mismatch repair deficiency. Per the pathology report, immunohistochemical stains for MLH1 and PMS2 demonstrated loss of nuclear expression within the neoplastic cells, while MSH2 and MSH6 showed preserved nuclear expression. These findings are consistent with microsatellite instability (MSI). The patient would like you to explain the ramifications of the immunohistochemical testing on her tumor. Which of the following is the best response at this point?

a. Tell your patient that these findings have no consequence on treatment and do not require further testing.

b. Discuss with patient that findings of MSI in her PDAC has important ramifications on medical treatment, such as immunotherapy, and that germline testing could impact her personal and family predisposition of not only developing PDAC, but other neoplasms as well—making additional evaluation and testing required.

c. Inform your patient that the presence of MSI in her PDAC impacts her family’s predisposition in developing PDAC, but is otherwise irrelevant to her medical treatment.

d. Inform the patient that she is a candidate for immunotherapy and does not require further germline testing.

Question 2:

A 48-year-old man with metastatic PDAC is seen in your outpatient clinic. Targeted genomic profiling was performed on his PDAC and identified an ALK fusion gene and an absence of other genomic alterations in the receptor tyrosine kinase (RTK)/Ras/mitogen-activated protein kinase (MAPK) pathway, such as KRAS. Your patient would like you to explain the ramifications of an ALK fusion gene within his PDAC. What is the best response at this point?

a. The presence of an ALK fusion gene is inconsequential and has no bearing on further management.

b. Inform the patient that he may be a candidate for a platinum-based regimen or PARP inhibitor.

c. The presence of the ALK fusion gene is hereditary and he should undergo further germline testing.

d. The ALK fusion gene is potentially targetable with known kinase inhibitors, such as alectinib, but further evaluation is required to determine if he is a candidate for this form of medical therapy.

Question 3:

A 48-year-old woman with metastatic PDAC states she has a long family history of breast and ovarian cancers. She reports that her sister and mother were previously diagnosed with breast cancer and her grandmother had ovarian cancer. In addition, your patient has 2 daughters and a son, who are alive and well. Considering the possible treatment and hereditary consequences, which of the following is the most appropriate next step?

a. Tell your patient that her family history is interesting, but is otherwise not pertinent to her management and is unlikely to impact her children or other family members.

b. Discuss with your patient that she may have Lynch syndrome and that her tumor should be evaluated for MSI.

c. The patient should be informed that she and her family members may have hereditary breast and ovarian cancer that has been linked to genes within the BRCA-FANC DNA repair pathway and advise her to see a genetic counselor as she may require germline testing. If a genomic alteration in the BRCA-FANC pathway is identified, then she may also be a candidate for receiving a platinum-based regimen or a PARP inhibitor.

d. Notify the patient that her family members likely have hereditary breast and ovarian cancer, but your patient does not because she has PDAC and therefore no further testing is required.
A 41-year-old male patient you are seeing in outpatient clinic has a 3.2-cm pancreatic cyst in the head of his pancreas. An endoscopic ultrasound-fine needle aspiration (EUS-FNA) was performed and other than a pancreatic cyst >3.0 cm, no worrisome features or high-risk stigmata as per the Fukuoka consensus guidelines (2017) were identified. The corresponding pancreatic cyst fluid was submitted for cytopathologic evaluation and molecular testing. There was insufficient fluid for carcinoembryonic antigen testing. Cytology was nondiagnostic and molecular testing identified mutations in KRAS, GNAS, and SMAD4. What is the significance of these genomic alterations in the patient’s pancreatic cyst fluid?

a. The genomic alterations are indicative of a serous cystadenoma and the patient does not require further follow-up or management.

b. The presence of a GNAS mutation in his pancreatic cyst fluid has a strong correlation with an intraductal papillary mucinous neoplasm (IPMN). Furthermore, the detection of a mutation in SMAD4 may indicate the presence of either high-grade dysplasia or an undetectable adenocarcinoma arising in the patient’s IPMN. These findings warrant further evaluation, such as repeat EUS-FNA, and potentially surgical intervention.

c. Inform the patient that he has a mucinous cystic neoplasm and it should be followed yearly by radiographic imaging.

d. The genomic profile within his pancreatic cyst fluid would indicate he has an IPMN and can be followed yearly by radiographic imaging.