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NCCN Guidelines Panel: Cutaneous Melanoma

Specific changes:

1) On page ME-1, add a third arrow in the flow chart from "Biopsy" to "Melanoma not confirmed" with a new footnote reading:

   "If melanoma not confirmed, review risk factors, including consideration of multigene panel testing for hereditary risk, and counsel patient on strategies for melanoma prevention and screening. See Risk Factors for Melanoma Development (ME-A) and Common Follow-up Recommendations for All Patients (ME-11)."

2) On page ME-A (RISK FACTORS FOR DEVELOPMENT OF SINGLE OR MULTIPLE PRIMARY MELANOMAS), under "Genetic predisposition":

   Add *TERT*, *MITF* and *PTEN* to the list of genes predisposing to melanoma in the first sub-bullet.

   Add renal and breast cancer to the list of relevant family history malignancies and add citation 3 for the second sub-bullet.

3) On page ME-11 (COMMON FOLLOW-UP RECOMMENDATIONS FOR ALL PATIENTS), under the last bullet (pertaining to multigene testing):

   Add the following sentence to the first sub-bullet – "Multigene panel testing that includes *CDKN2A* is also recommended for all patients if they have a first-degree relative diagnosed with pancreatic cancer (see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic)."

   Add PTEN to the list of genes in the second sub-bullet.

Rationale:

Regarding #1 – The proposed additional outcome and footnote will clarify that patients in whom melanoma is not diagnosed after biopsy of a suspicious lesion may still be at increased risk due to clinical and/or genetic factors, and may therefore benefit from genetic testing and information regarding strategies for melanoma prevention and screening.

Regarding #2 – *TERT* and *MITF* are already included in the list of genes related to hereditary melanoma risk on page ME-11. *PTEN* has also been established as a hereditary melanoma risk gene. Renal cancer is associated with germline mutations in *TERT, MITF* and *PTEN*. Breast cancer is associated with mutations in *BRCA2* and *PTEN*. Breast and renal cancer are already included as relevant cancers on page ME-11.

Regarding #3 – The cited NCCN panel, as well as other professional groups, recommends multigene panel testing, including *CDKN2A*, for first-degree relatives of pancreatic cancer patients who were themselves not tested. If *PTEN* is added to the list of genes on page ME-A, it should also be added to the list on page ME-11.

Cited Literature:

Bubien V, et al. High cumulative risks of cancer in patients with *PTEN* hamartoma tumour syndrome. J Med Genet. 2013 50:255-63. PMID: 23335809.

Daly M et al. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast, Ovarian and Pancreatic. V 1.2020. Dec 4. Available at http://www.nccn.org.

Goggins M, et al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. Gut. 2020 69:7-17. PMID: 31672839.

Tan MH, et al. Lifetime cancer risks in individuals with germline *PTEN* mutations. Clin Cancer Res. 2012 18:400-7. PMID: 22252256.