

Put It on the Board

AMP reports on use of guidelines for sequence variants in cancer

January 2023—The Association for Molecular Pathology last month released a report on somatic variant classification using 2017 standards and guidelines for interpreting and reporting such variants, which were a consensus recommendation of the AMP, CAP, and American Society of Clinical Oncology.

The new report is based on variant interpretation challenges and a guideline implementation survey conducted by an AMP working group (Li MM, et al. *J Mol Diagn*. Published online Dec. 9, 2022. doi:10.1016/j.jmoldx.2022.11.002). The group's aim was to identify classification inconsistencies and evaluate barriers to implementing the 2017 standards and guidelines (Li MM, et al. *J Mol Diagn*. 2017;19[1]:4-23).

In the guidelines, the AMP, CAP, and ASCO proposed a tiered system to categorize somatic sequence variants. In tier one are variants with strong clinical significance; tier two, variants with potential clinical significance; tier three, variants of unknown clinical significance; and tier four, variants deemed benign or likely benign (most commonly representing rare germline variants with no known cancer association).

There were 134 participants in the variant interpretation challenge, and 86 percent correctly differentiated clinically significant variants from variants of uncertain significance and benign/likely benign variants. More than 70 percent agreed in judging the potential for germline variants. Seventy-one percent of respondents to the implementation survey (157/220) implemented the guidelines for variant classification and more than 90 percent of them used the recommended tier-based reporting system.

FDA clears Roche's CSF assays for Alzheimer's

Roche's Elecsys beta-Amyloid (1-42) CSF II (Abeta42) and Elecsys Phospho-Tau (181P) CSF (pTau181) assays have received Food and Drug Administration 510(k) clearance. The Elecsys AD CSF Abeta42 and pTau181 assays (used as a pTau181/Abeta42 ratio) measure beta-amyloid and tau proteins in adults 55 and older evaluated for the disease. Both assays are traceable to reference materials.

The ratio of these biomarkers (pTau181/Abeta42) is consistent with a negative beta-amyloid PET scan if the result is less than or equal to the cutoff (negative), and with a positive beta-amyloid PET scan if the result is above the ratio cutoff (positive).

Abeta42 and pTau181 assays are intended to be used in addition to other clinical diagnostic evaluations to determine whether a person has Alzheimer's. A positive pTau181/Abeta42 ratio result in CSF does not establish a diagnosis of Alzheimer's disease.

FDA approves CDx to Krazati in NSCLC

The Food and Drug Administration approved Qiagen's Therascreen KRAS RGQ PCR kit as a companion diagnostic test to Mirati Therapeutics' drug Krazati (adagrasib) for non-small cell lung cancer.

Qiagen and Mirati announced their cooperation in May 2021. The tissue-based KRAS companion diagnostic assay, which Qiagen developed to identify patients with NSCLC who have a KRAS G12C mutation, is instrumental in determining who may benefit from treatment with Krazati. The drug is indicated for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic NSCLC, as determined by an FDA-approved test, who have received at least one prior systemic therapy.

De novo classification granted to HLA typing test for use as CDx

The Food and Drug Administration granted de novo classification to Thermo Fisher's SeCore CDx HLA Sequencing System for use as a companion diagnostic with Kimmtrak (tebentafusp-tebn), Immunocore's T-cell receptor

therapy for HLA-A*02:01-positive adults with metastatic or unresectable uveal melanoma. The marketing authorization makes the SeCore CDx HLA Sequencing System the only commercially available HLA typing companion diagnostic.

Kimmtrak, the only FDA-approved T-cell receptor therapy for metastatic or unresectable uveal melanoma, is indicated for adults who are HLA-A*02:01 positive. The SeCore CDx HLA Sequencing System was used to identify HLA-A*02:01-positive patients for enrollment in Kimmtrak clinical trials.