Put It on the Board

For *HER2*-mutant NSCLC, FDA grants accelerated approval to Enhertu, approves companion diagnostics

September 2022—The Food and Drug Administration on Aug. 11 granted accelerated approval to Enhertu for adult patients with unresectable or metastatic non-small cell lung cancer whose tumors have activating *HER2* (*ERBB2*) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy. Enhertu (AstraZeneca and Daiichi Sankyo) is the first drug approved for *HER2*-mutant NSCLC.

The FDA also approved Thermo Fisher Scientific's Oncomine Dx Target Test and Guardant Health's Guardant360 CDx liquid biopsy test as companion diagnostics to identify patients whose tumors have *HER2* (*ERBB2*) activating mutations in NSCLC and may benefit from treatment with Enhertu (trastuzumab deruxtecan). If no mutation is detected in a plasma specimen, the FDA said in its release, the tumor tissue should be tested.

Efficacy for accelerated approval was based on DESTINY-Lung02, a multicenter, multi-cohort, randomized, blinded, dose-optimization trial. The confirmed objective response rate was 58 percent (95 percent CI: 43, 71), and the median duration of response was 8.7 months (95 percent CI: 7.1, not estimable).

FDA approves Enhertu for patients with HER2-low metastatic breast cancer

AstraZeneca and Daiichi Sankyo's Enhertu (trastuzumab deruxtecan) has been approved in the U.S. for the treatment of adult patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within six months of completing adjuvant chemotherapy.

Enhertu is a specifically engineered HER2-directed antibody drug conjugate. The FDA's approval was based on results from the DESTINY-Breast04 phase three trial. In the trial, Enhertu reduced the risk of disease progression or death by 50 percent versus the physician's choice of chemotherapy in patients with HER2-low metastatic breast cancer with hormone-receptor-positive disease or HR-negative disease (median progression-free survival 9.9 versus 5.1 months; hazard ratio 0.50; 95 percent CI: 0.40–0.63). A median overall survival of 23.4 months was seen in patients treated with Enhertu versus 16.8 months in those treated with chemotherapy.

The expanded approval for Enhertu in the U.S., following its previous approval in second-line HER2-positive metastatic breast cancer, enables its use across a spectrum of HER2-expressing breast cancer, including patients with HER2-low disease.

The DESTINY-Breast04 phase three trial results were presented at this year's American Society of Clinical Oncology annual meeting and published in July (Modi S, et al. *N Engl J Med*. 2022;387[1]:9–20).

AMP publishes *TPMT* and *NUDT15* report

The Association for Molecular Pathology on Aug. 25 published consensus recommendations to aid in the design and validation of clinical *TPMT* and *NUDT15* genotyping assays.

The recommendations are a consensus of the AMP, CAP, Clinical Pharmacogenetics Implementation Consortium, Dutch Pharmacogenetics Working Group of the Royal Dutch Pharmacists Association, European Society for Pharmacogenomics and Personalized Therapy, and Pharmacogenomics Knowledgebase.

The full article is available at https://bit.ly/TPMT-NUDT15.

Rapid AST system receives breakthrough device designation

The Food and Drug Administration has granted its breakthrough device designation for the Specific Reveal Rapid Antimicrobial Susceptibility Test (AST) System. The system was developed by Specific Diagnostics, which was acquired by BioMérieux in May. It provides phenotypic antibiotic susceptibility test results in an average of 5.5 hours from availability of a positive blood culture.

“Specific Reveal is perfectly aligned with BioMérieux’s priority to provide innovative diagnostics to support antimicrobial stewardship,” Pierre Boulud, chief operating officer, clinical operations, BioMérieux, said in an Aug. 22 news release.

FDA approves CDx to identify dMMR solid tumor patients for anti-PD-1 immunotherapy

Roche announced Food and Drug Administration approval of a label expansion for the Ventana MMR RxDx Panel. It is the first immunohistochemistry companion diagnostic to aid in identifying patients whose solid tumors are deficient in DNA mismatch repair (dMMR) and who may be eligible for Keytruda (pembrolizumab).

The panel is also the first companion diagnostic to aid in identifying endometrial cancer patients whose tumors are proficient in DNA mismatch repair (pMMR) and who may be eligible for a combination of Keytruda and tyrosine kinase inhibitor Lenvima (lenvatinib).

The label expansion follows the April 2021 FDA approval of the Ventana MMR RxDx Panel as the first IHC predictive test to identify endometrial carcinoma patients eligible for treatment with the anti-PD-1 immunotherapy Jemperli (dostarlimab-gxly). That approval was expanded for the following indications: dMMR solid tumor patients for treatment with Jemperli (August 2021), dMMR solid tumor patients for treatment with Keytruda (March 2022), and pMMR solid tumor patients for treatment with a combination of Keytruda and Lenvima (June 2022).