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NCCN Guidelines Panel: Breast Cancer

On behalf of Immunomedics, I respectfully request the NCCN (Breast Cancer Guidelines Panel) to review the enclosed data for inclusion of Trodelvy™ (sacituzumab govitecan-hziy), now approved by the FDA for the treatment of adult patients with metastatic triple-negative breast cancer (mTNBC) who have received at least two prior therapies for metastatic disease on April 22, 2020.

This request is an update to the version sent on April 21, 2020, which was made prior to FDA approval.

Specific Change within the Guidelines and Compendium
To recommend the preferred use of sacituzumab govitecan-hziy for patients with mTNBC who previously received at least two prior therapies for metastatic disease.

FDA Clearance
Sacituzumab govitecan-hziy was approved by the FDA for this indication on April 22, 2020.

Rationale
Sacituzumab govitecan-hziy is a new treatment option that will fulfill an unmet need for patients with mTNBC who develop resistance or intolerance to prior therapies for metastatic disease. In support of the proposed change, sacituzumab govitecan-hziy received breakthrough designation by the FDA. The FDA approval was based on results from the IMMU-132-01 study. In addition, on April 6, 2020, the Data Safety Monitoring Committee (DSMC) unanimously recommended the Phase 3 ASCENT study (IMMU-132-05) be halted due to compelling efficacy.

Clinical Summary
Sacituzumab govitecan-hziy was evaluated in an open-label, uncontrolled, single-arm Phase 1/2 study (IMMU-132-01; NCT01631552) in 108 patients with metastatic TNBC who had received at least two prior treatments for metastatic disease. Patients received sacituzumab govitecan-hziy intravenously at a dose of 10 mg/kg on Days 1 and 8 of continuous 21-day treatment cycles. Patients were treated with sacituzumab govitecan-hziy until disease progression or intolerance to the therapy. Study endpoints include response evaluation by investigators according to RECIST 1.1, duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety.

At the data cutoff of December 1, 2017, treatment with sacituzumab govitecan-hziy resulted in an objective response rate (ORR) of 33.3% (95% CI, 24.6–43.1), with 3% of patients achieving a complete response (CR) and 33% achieving a partial response (PR). The median DOR was 7.7 months (95% CI, 4.9–10.8) by local assessment. Median PFS by local assessment was 5.5 months (95% CI, 4.1–6.3), median OS was 13.0 months (95% CI, 11.2–13.7), and the clinical benefit rate (CBR) was 45.4% (95% CI, 35.8–55.2). Independent central review results are similar with ORR of 34.3% (95% CI, 25.4–44.0) and median DOR of 9.1 months (95% CI, 4.6–11.3). Among patients

who had received previous programmed death 1-based therapy or programmed death ligand 1-based therapy, the response rate was 44% (8 of 18).

The most common AEs irrespective of relationship to sacituzumab govitecan-hziy included nausea (67%), neutropenia (64%), and diarrhea (62%). The most frequent grade 3 AEs were neutropenia (26%), anemia (11%), and hypophosphatemia (9%). The most frequent grade 4 AEs were neutropenia (16%), followed by decreased WBC count (3%) and febrile neutropenia (2%). Severe drug-related neuropathy or cardiac AEs were not observed. No treatment-related deaths occurred and 3 (3%) patients discontinued treatment due to AEs.

Sacituzumab govitecan-hziy is also being studied in ASCENT (IMMU-132-05; NCT02574455). ASCENT is a global, open-label, 1:1 randomized Phase 3 confirmatory trial that is investigating the efficacy and tolerability of sacituzumab govitecan-hziy versus treatment of physicians' choice (eribulin, vinorelbine, capecitabine, or gemcitabine) in patients who had received at least two prior treatments for metastatic disease. The primary endpoint is PFS. Secondary endpoints include a comparison between treatment arms of OS, ORR, time to onset of response, DOR, quality of life, and safety measures. On April 6, 2020, the DSMC lead by Dr. Julie Gralow, MD of Fred Hutchinson Cancer Center, Seattle, unanimously recommended ASCENT be halted due to compelling efficacy of sacituzumab govitecan-hziy. Results of this study are not yet available and will be presented at a congress in the second half of 2020.
The articles listed below are submitted in support of this proposed change. Thank you for your review and consideration.

Supporting Documentation

1. Immunomedics. Trodelvy™ (sacituzumab govitecan-hziy) Prescribing Information. April, 2020.
2. Bardia A, Mayer IA, Vahdat LT, et al. Sacituzumab govitecan-hziy in refractory metastatic triple negative breast cancer. *N Engl J Med*. 2019;380:741-751.
3. Bardia A, Mayer IA, Diamond JR, et al. Efficacy and safety of anti-Trop-2 antibody drug conjugate sacituzumab govitecan (IMMU-132) in heavily pretreated patients with metastatic triple-negative breast cancer. *J Clin Oncology*. 2017;35(19):2141-2148.
4. Bardia A, Vahdat LT, Diamond JR, et al. Sacituzumab govitecan (IMMU-132), an anti-Trop-2-SN-38 antibody-drug conjugate, as ≥3rd-line therapeutic option for patients with relapsed/refractory metastatic triple-negative breast cancer (metastatic TNBC): efficacy results. *Paper presented at: San Antonio Breast Cancer Symposium*. December 5-9, 2017; San Antonio, TX.
5. Kalinsky K, Iskoff SJ, Tolaney SM, et al. Safety and efficacy of sacituzumab govitecan-hziy (anti-trop-2-SN-38 antibody-drug conjugate) as ≥3rd-line therapeutic option for treatment-refractory HER2-negative metastatic breast cancer. Paper presented at: San Antonio Breast Cancer Symposium 2018.
6. Immunomedics announces ASCENT study to be stopped for compelling efficacy [press release]. April 6, 2020.
7. ASCENT - Study of sacituzumab govitecan in refractory/relapsed triple-negative breast cancer. https://clinicaltrials.gov/ct2/show/NCT02574455. Accessed April 21, 2020.

Sincerely,

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