Published OnlineFirst November 9, 2020; DOI: 10.1158/1078-0432.CCR-20-3119

FDA Approval Summary: Accelerated Approval of Sacituzumab Govitecan-hziy for Third-line Treatment of Metastatic Triple-negative Breast Cancer

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ABSTRACT

On April 22, 2020, the FDA granted accelerated approval to sacituzumab govitecan-hziy (TRODELVY; Immunomedics, Inc.) for the treatment of patients with metastatic triple-negative breast cancer (mTNBC) who have received at least two prior therapies for metastatic disease. Approval was based on data from the IMMU-132-01 trial, a single-arm, multicohort, multicenter, phase I/II trial of sacituzumab govitecan. The assessment of efficacy was based on 108 patients with mTNBC who had previously received at least two prior lines of therapy in the metastatic setting and who received sacituzumab govitecan 10 mg/kg i.v. The assessment of safety was based on 408 patients with advanced solid tumors who had received sacituzumab govitecan at doses up to 10 mg/kg i.v. The primary efficacy endpoint was investigator-assessed objective response rate (ORR) and duration of response (DoR) was a key secondary endpoint. The ORR was 33.3% [36/108; 95% confidence interval (CI), 24.6–43.1], and median DoR among responders was 7.7 months (95% CI, 4.9–10.8). The most common adverse reactions occurring in ≥25% of patients were nausea, neutropenia, diarrhea, fatigue, anemia, vomiting, alopecia, constipation, rash, decreased appetite, and abdominal pain. This article summarizes the FDA review process and data supporting the approval of sacituzumab govitecan.

Introduction

Breast cancer is the most common cancer in women in the United States, with 276,000 new cases and 42,000 deaths estimated in 2020 (1). Breast cancer is rare in men, with less than 1% of cases reported in the United States. Approximately 10%–20% of all breast cancer diagnoses are triple-negative breast cancer (TNBC). This subtype is more aggressive, and is characterized by the absence of tumor expression of estrogen receptor (ER), progesterone receptor (PR), and HER2, which renders patients with TNBC unable to benefit from hormonal therapy and anti-HER2–targeted therapies (2–4). Most patients with metastatic TNBC (mTNBC) have visceral organ involvement, commonly with metastases to the brain and lungs. The estimated 5-year overall survival (OS) in patients with mTNBC is 11% (4).

Chemotherapy has been the main treatment option for patients with mTNBC, and several chemotherapy regimens may be used, however, most patients experience relapse rapidly following a response to chemotherapy. Monotherapy ixabepilone and eribulin are FDA-approved therapies for patients with metastatic breast cancer who have received at least two prior therapies in the metastatic setting (5, 6). The PARP inhibitors, olaparib and talazoparib, are more recently FDA approved, in 2018, for patients with HER2-negative breast cancer (including those with mTNBC) who harbor a germline BRCA1 or BRCA2 mutation and who have been previously treated with chemotherapy. Finally, the regimen of atezolizumab in combination with paclitaxel protein bound was approved in 2019 under the accelerated approval pathway for patients with mTNBC whose tumors express PD-L1 (PD-L1–stained tumor-infiltrating immune cells of any intensity covering ≥1% of the tumor area).

The authors provide the summary of FDA's review of the Biologics License Application (BLA) for sacituzumab govitecan-hziy (TRODELVY), which was approved for the third-line treatment of adult patients with mTNBC. Sacituzumab govitecan received FDA's breakthrough therapy designation in February 2016 for the treatment of patients with mTNBC who have received at least two prior therapies for metastatic disease. The BLA was originally submitted to the FDA in May 2018, and was granted a priority review designation. The IMMU-132-01 trial (NCT01631552) provided the primary safety and efficacy data for sacituzumab govitecan monotherapy to support the BLA. During the FDA review of the original BLA's chemistry, manufacturing, and controls (CMC) data, FDA determined that some of the data submitted to support the product quality assessment were inadequate. Specifically, the methodologies and processes used for the hRS7 antibody intermediate, IMMU-132 drug substance and drug product manufacturing, release testing, and stability testing did not provide assurance of a consistent, safe, pure, and potent product. These deficiencies served as the basis for the complete response (CR) action in January 2019. Immunomedics subsequently resubmitted the BLA in December 2019; FDA concluded that the CMC deficiencies had been satisfactorily addressed and granted accelerated approval of sacituzumab govitecan-hziy on April 22, 2020 (7, 8).

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Clin Cancer Res 2021;27:1–5

doi: 10.1158/1078-0432.CCR-20-3119

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Nonclinical Pharmacology and Toxicology

Sacituzumab govitecan is a first-in-class antibody–drug conjugate (ADC) that consists of a humanized IgG1K and anti-Trop 2 mAb (hRS7) that is covalently linked via a hydrolysable linker (CL2A) to the cytotoxic agent, SN-38, the active metabolite of irinotecan. Sacituzumab govitecan binds Trop-2 (trophoblast cell surface antigen-2) expressed on cancer cells and delivers SN-38 to the tumor upon the cleavage of CL2A linker. SN-38 interacts with topoisomerase I and prevents religation of topoisomerase I–induced single-strand breaks, ultimately resulting in apoptosis and cell death. Trop-2 antigen is expressed in a variety of epithelial cancers, and has been associated with more aggressive tumors (9). In breast cancer, Trop-2 has been found to be more commonly expressed in ER-negative, HER2-positive tumors, but less commonly expressed in patients with ER-positive, HER2-negative disease, suggesting that Trop-2 overexpression may be associated with less favorable phenotypes (9).

Treatment with sacituzumab govitecan induced proapoptotic signaling and double-strand DNA breaks in Trop-2–expressing cancer cell lines and decreased tumor growth in mouse xenograft models of TNBC (10, 11). In the acute and 13-week toxicity studies, the primary toxicologic findings in monkeys were consistent with adverse events of gastrointestinal and hematologic toxicities observed in clinical trials, and were expected on the basis of the mechanism of action of sacituzumab govitecan. Administration of sacituzumab govitecan also resulted in adverse effects on female reproductive organs in monkeys, indicating the potential for impairment of female fertility. SN-38 is genotoxic and targets rapidly dividing cells and as such, teratogenicity or embryo-fetal lethality is expected with sacituzumab govitecan. Females of reproductive potential and male patients with female partners of reproductive potential should use effective contraception during and following treatment with sacituzumab govitecan.

Clinical Pharmacology

The proposed dosing regimen of sacituzumab govitecan is 10 mg/kg administered as an intravenous infusion on days 1 and 8 of each 21-day treatment cycle. In the IMMU-132-01 trial, escalating dose levels of sacituzumab govitecan (8, 10, 12, and 18 mg/kg i.v.) were investigated. Dose-limiting toxicity was observed at 18 mg/kg, and 12 mg/kg was declared as the MTD. Because of dose delays and dose reductions at the 12 mg/kg dose, lower doses (8 and 10 mg/kg) were chosen for further investigation. The dose expansion portion of the IMMU-132-01 trial investigated sacituzumab govitecan in patients with various solid tumors who received the 8 ($n = 81$) and 10 mg/kg ($n = 97$) doses. While the safety profiles of the two investigated dose levels appeared comparable, the observed response rate was numerically higher at the 10 mg/kg dose compared with the 8 mg/kg dose, and, thus, the 10 mg/kg dose was selected for further clinical development (12). No dose adjustments were required for patients with renal impairment or mild hepatic impairment. However, an adequate starting dose in patients with moderate hepatic impairment is unknown. The FDA requested a safety and pharmacokinetics study in patients with moderate hepatic impairment to determine the adequate starting dose, as a postmarketing requirement (PMR).

Uridine diphosphate-glucuronosyltransferase 1A1 (UGT1A1) is involved in the metabolism of SN-38 to SN-glucuronide, and concomitant administration of drugs that alter UGT1A1 activity should be avoided to minimize the potential for increased frequency and severity of adverse reactions (13). In addition, patients homozygous for the UGT1A1*28 allele are at an increased risk for adverse reactions, especially neutropenia; the appropriate dose in these patients is not known. Given the concern regarding the UGT1A1 genotype and increased risk of toxicities, a PMR was agreed upon, which will further characterize the impact of UGT1A1 variants and toxicity. In addition, labeling included information cautioning use in patients homozygous for the UGT1A1*28 allele. The observed unconjugated SN-38 concentrations with the approved dose of sacituzumab govitecan were present at substantially higher concentrations compared with the SN-38 concentrations observed with the highest approved dose of irinotecan, and the potential for QT interval prolongation cannot be ruled out at such a high exposure of SN-38. Another study to evaluate the risk of QT prolongation with sacituzumab govitecan therapy will be conducted as a PMR.

Clinical Trial Design

IMMU-132-01 (NCT01631552) is a single-arm, open-label, dose escalation and dose expansion, multicenter (U.S. only) phase I/II trial of sacituzumab govitecan in patients with advanced solid tumors (14). The dose escalation portion of the trial employed a 3+3 design to evaluate escalating doses of sacituzumab govitecan. The dose expansion portion of the trial enrolled patients into four single-arm cohorts, one of which enrolled patients with mTNBC. The primary endpoint of the dose expansion portion of the trial was confirmed objective response rate (ORR) according to the RECIST version 1.1 guidelines, as assessed by the investigator. Duration of response (DoR) was a secondary endpoint. Sacituzumab govitecan was administered at doses of 8 and 10 mg/kg until evidence of disease progression or unacceptable toxicities.

Originally submitted to the FDA in May 2018, the efficacy analysis set for this approval consisted of the 108 patients with mTNBC enrolled in the dose escalation and dose expansion portion of IMMU-132-01 trial who had received at least two prior lines of therapy in the metastatic setting, and who have received sacituzumab govitecan at 10 mg/kg dose via intravenous infusion on days 1 and 8 of continuous 21-day cycles, at the time of the initial data cutoff of 30 June 2017. The safety analysis set included the 408 patients with various solid tumors in the IMMU-132-01 trial who had received at least one dose of sacituzumab govitecan, including the subgroup of 108 patients with mTNBC who comprised the efficacy set.

Results

Patient characteristics

The baseline demographics of the mTNBC patient population ($N = 108$) were as follows: median age, 55 years (range, 31–80); 99% female; 76% White; 29% and 71% with an Eastern Cooperative Oncology Group performance status of 0 and 1, respectively; 76% with visceral disease; and 2% with brain metastases. At baseline, 60% of patients had received two prior chemotherapies and 40% had received three or more prior chemotherapies in the metastatic setting; all patients had measurable disease.

Efficacy

The efficacy results for the mTNBC patient cohort of IMMU-132-01 trial are summarized in **Table 1**. Sacituzumab govitecan at the 10 mg/kg i.v. dose demonstrated an ORR of 33.3% [95% confidence interval (CI), 24.6%–43.1%] consisting of three CRs (2.8%) and 33 partial responses

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Table 1. Confirmed ORR and DoR by investigator per RECIST v1.1 for the mTNBC cohort of IMMU-132-01 trial.

	mTNBC population *N* = 108
ORR (%)	36 (33.3%)
95% CI	(24.6–43.1)
CR, *n* (%)	3 (2.8)
PR, *n* (%)	33 (30.6)
DOR (months), range of response	7.7 (4.9–10.8)
DOR ≥ 6 months, *n* (%)	20 (55.6)
DOR ≥ 12 months, *n* (%)	6 (16.7)

Abbreviation: PR, partial response.

(PR, 30.6%), according to RECIST v1.1, at the initial data cutoff of 30 June 2017. The median DoR was 7.7 months (95% CI, 4.9–10.8) on the basis of an updated data cutoff of 1 December 2017. Fifty-six percent of responders had a DoR ≥ 6 months and 17% had a DoR ≥ 12 months. Blinded, independent review of a subgroup of patients ($n = 55$) who had CR, PR, or at least 20% shrinkage by investigator assessment was consistent with the investigator assessment.

Safety

The safety profile of sacituzumab govitecan was assessed in the overall study population in IMMU-132-01 trial who received sacituzumab govitecan at doses up to 10 mg/kg ($N = 408$), and in the subset of patients who comprised the efficacy mTNBC population ($N = 108$). In the mTNBC population, the median exposure to sacituzumab govitecan was 5.1 months, and no deaths within 30 days of ending study treatment were associated with study therapy. Dose interruptions and dose reductions due to adverse reactions were reported in 45% and 33% of patients, respectively. The most common adverse reactions leading to dose interruptions and dose reductions were neutropenia/febrile neutropenia. Treatment discontinuation due to adverse reactions was reported in 2% of patients. Adverse reactions leading to discontinuation were anaphylaxis, anorexia/fatigue, and headache.

Serious adverse reactions (SAR) were reported in 31% of the patients. The most common SARs (i.e., occurring in >1% of patients) were febrile neutropenia (6%), vomiting (5%), nausea (3%), dyspnea (3%), diarrhea (4%), anemia (2%), and pleural effusion, neutropenia, pneumonia, and dehydration (each 2%). Grade 3–4 adverse reactions were observed in 72% of patients. The most common grade 3–4 adverse reactions (i.e., occurring in ≥5% of patients) by preferred term were neutropenia (43%), anemia (12%), diarrhea and hypophosphatemia (9% each), fatigue and febrile neutropenia (8%, each), vomiting (6%), and dehydration (5%). Among the 84% (343/408) of patients who received sacituzumab govitecan (up to 10 mg/kg dose), and had retrospective UGT1A1 genotype results available, the incidence of grade 4 neutropenia was 26% (10/39) in patients homozygous for the UGT1A1*28 allele, 13% (20/155) in patients heterozygous for the UGT1A1*28 allele, and 11% (16/149) in patients homozygous for the wild-type allele. Patients with known reduced UGT1A1 activity should be monitored for severe neutropenia.

The most common all-grade adverse reactions (≥25% in incidence: nausea, neutropenia, diarrhea, fatigue, anemia, vomiting, alopecia, constipation, rash, decreased appetite, and abdominal pain) were manageable with monitoring, dose modifications, and supportive measures.

Regulatory Insights

The FDA's accelerated approval of sacituzumab govitecan on April 22, 2020 was the first approval for sacituzumab govitecan worldwide. It is also the first ADC approved by the FDA specifically for mTNBC. Patients living with mTNBC have limited treatment options and urgently need new safe and effective therapies, particularly for patients who are heavily pretreated, as was the case in patients enrolled in the IMMU-132-01 trial. This approval addresses this unmet medical need. Some of the limitations of the trial include the enrollment of a limited number (2%) of patients who had brain metastases at baseline, and despite the disproportionate representation of African American women among cases of mTNBC, only 7% of the patients in the trial were Black. While the demographics of the mTNBC patient population in the IMMU-132-01 trial were generally consistent with the U.S. population that would be eligible to receive sacituzumab govitecan treatment, Blacks were underrepresented in the IMMU-132-01 trial relative to their representation among cases of the disease (15–17). This finding has also been observed in other recent trials supporting the approval of drugs intended for the treatment of patients with breast cancer, with the proportion of Black or African American patients enrolled ranging between 2.2% and 8.9% of the study population (18–20). Given that approximately 20% of the Black or African American population, compared with 10% of the White population, are homozygous for the UGT1A1*28 allele, additional information obtained with the PMR will be particularly important to understand use in this population. In addition, further measures to improve enrollment of this demographic subgroup in clinical trials are needed.

ORR is a commonly used regulatory endpoint in oncology as it is directly attributable to the drug activity. Tumor measurements are relevant for clinical decision-making and can be supported by DoR. ORR with supportive DoR, which allow for smaller sample sizes and study in single-arm trials, is most frequently used for accelerated approval. Accelerated approval requires a drug to be better than available therapies with an endpoint earlier then survival that is reasonably likely to predict clinical benefit. The two FDA-approved agents for third and later lines of therapy in the metastatic breast cancer space are eribulin and ixabepilone. The ORR of sacituzumab govitecan was clearly improved above that of ixabepilone (12.4%; 95% CI, 6.9–19.9; median DoR, 6 months) and eribulin (11%; 95% CI, 8.6–14.3; median DoR, 4.2 months). The FDA risk–benefit analysis is shown in **Table 2** (8). Sacituzumab govitecan's improvement in ORR and DoR over available therapy, coupled with the acceptable safety profile, supported the use of the accelerated approval pathway for sacituzumab govitecan; at the time of approval, the ongoing confirmatory trial was underway to confirm clinical benefit. ASCENT (NCT02574455) is a randomized, open-label, phase III trial of sacituzumab govitecan versus treatment of physician's choice (TPC) in patients with mTNBC after ≥2 prior chemotherapies for advanced disease or >1 therapy for patients who progressed within 12 months of adjuvant therapy. This study was designed under an FDA special protocol assessment indicating concurrence by FDA with the adequacy and acceptability of specific critical elements of overall protocol design (e.g., entry criteria, dose selection, endpoints, and planned analyses) for a study intended to support a future marketing application (21). Patients were randomized 1:1 to receive either sacituzumab govitecan or TPC. The primary endpoint was progression-free survival (PFS) as assessed by blinded, independent review. Secondary endpoints include OS, ORR, DOR, safety, and quality of life. On 6 April 2020, it was

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Table 2. FDA risk–benefit assessment.

Dimension	Evidence and uncertainties	Conclusions and reasons
Analysis of condition	• Breast cancer is the most common cancer in women with more than 260,000 new cases and 40,000 deaths annually. Approximately 10%–15% of patients with breast cancer have TNBCs. • mTNBC has a poor prognosis with an estimated median OS of approximately 13 months.	mTNBC is a serious and life-threatening condition with an estimated median OS of approximately 13 months.
Current treatment options	• The goals of treating mTNBC are palliative in nature with the aim of prolonging survival and reducing cancer-related symptoms. Available therapies for the treatment of patients with mTNBC who have had two prior lines of therapy include ixabepilone and eribulin; for patients with a BRCA1 or BRCA2 mutation, olaparib and talazoparib are available.	There is an unmet medical need to improve the outcomes of patients with mTNBC who have received two or more prior therapies, and patients may benefit from an agent with a more favorable response rate and DoR as compared with available therapy.
Benefit	• The efficacy of sacituzumab was evaluated in IMMU-132-01 trial. • In the 108 patients who comprised the efficacy population, the confirmed ORR was 33% (95% CI, 24.6–43.1) with an estimated median DoR of 7.7 months (95% CI, 4.9–10.8) per local investigator assessment.	Study IMMU-132-01 demonstrated an improvement over available therapy based on response rate, an endpoint reasonably likely to predict clinical benefit.
Risk and risk management	• In the efficacy population, 33% of patients experienced SAEs compared with 41% of patients in the pooled safety population. • The serious risks of sacituzumab include diarrhea, neutropenia, nausea, vomiting, and infusion-related reactions. Patients who are homozygous for the UGT1A1*28 allele are at increased risk for neutropenia. • One death in the overall safety population was due to neutropenic typhlitis.	The safety profile of sacituzumab is acceptable when assessed in the context of the life-threatening nature of mTNBC that has progressed following two or more therapies. Significant and SARs, including neutropenia and diarrhea can be adequately managed with close monitoring, dose modifications, and supportive measures, and this risk should be conveyed in labeling. Patients with known reduced UGT1A1 activity should be monitored for severe neutropenia.

Note: From FDA. FDA drug approval and databases, available from: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/761115Orig1s000MultidisciplineR.pdf (8).

reported that ASCENT was a positive study with subsequent results reported as demonstrating an improvement in PFS, OS, and ORR with sacituzumab govitecan (22).

Conclusions

mTNBC is an aggressive phenotype of breast cancer; patients who have received two prior therapies for metastatic disease have an advanced condition that is life-threatening and have an unmet medical need. Results from the IMMU-132-01 trial demonstrated a favorable benefit–risk profile for sacituzumab govitecan with an improved ORR and DoR over available therapies. The most common adverse reactions associated with sacituzumab govitecan therapy were nausea, neutropenia, diarrhea, fatigue, anemia, vomiting, alopecia, constipation, rash, decreased appetite, and abdominal pain. These adverse reactions are acceptable with monitoring, dose modifications, and supportive measures. Overall, sacituzumab govitecan exhibited a favorable benefit–risk profile and met criteria for accelerated approval, resulting in a new targeted therapy for the treatment of an aggressive malignancy that affects younger patients and for whom available treatment options are very limited.

Authors' Disclosures

No disclosures were reported.

Disclaimer

The Editor handling the peer review and decision-making process for this article has no relevant employment associations to disclose.

Received August 25, 2020; revised October 8, 2020; accepted November 5, 2020; published first November 9, 2020.

References

1. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer stat facts: female breast cancer. Available from: https://seer.cancer.gov/statfacts/html/breast.html.
2. Dent R, Trudeau M, Pritchard KI, Hanna WM, Kahn HK, Sawka CA, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. Clin Cancer Res 2007;13:4429–34.
3. Foulkes WD, Smith IE, Reis-Filho JS. Triple-negative breast cancer. N Engl J Med 2010;363:1938–48.
4. American Cancer Society. Breast cancer facts and figures 2019–2020. Available from: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2019-2020.pdf.
5. U.S. Food and Drug Administration. Ixabepilone prescribing information. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/022065s006lbl.pdf.
6. U.S. Food and Drug Administration. Eribulin prescribing information. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/201532s016lbl.pdf.
7. Accelerated approval of biological products for serious or life-threatening illnesses, 21 C.F.R. Sect. 601. Subpart E. Available from: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=601&showFR=1&subpartNode=21:7.0.1.1.2.5.
8. U.S. Food and Drug Administration. FDA drug approval and databases. Multidiscipline review. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/761115Orig1s000MultidisciplineR.pdf.

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9. Shvartsur A, Bonavida B. Trop2 and its overexpression in cancers: regulation and clinical/therapeutic implications. Genes Cancer 2015;6:84–105.
10. Goldenberg DM, Cardillo TM, Govindan SV, Rossi EA, Sharkey RM. Trop-2 is a novel target for solid cancer therapy with sacituzumab govitecan (IMMU-132), an antibody-drug conjugate (ADC). Oncotarget 2015;6:22496–512.
11. Cardillo TM, Govindan SV, Sharky RM, Trisal P, Arrojo R, Liu D, et al. Sacituzumab govitecan (IMMU-132), an anti-Trop-2/SN-38 antibody—drug conjugate: characterization and efficacy in pancreatic, gastric, and other cancers. Bioconjug Chem 2015;26:919–31.
12. Ocean AJ, Starodub AN, Bardia A, Vahdat LT, Isakoff SJ, Guarino M, et al. Sacituzumab govitecan (IMMU-132), an anti-Trop-2-SN-38 antibody-drug conjugate for the treatment of diverse epithelial cancers: safety and pharmacokinetics. Cancer 2017;123:3843–54.
13. Campbell JM, Stephenson MD, Bateman E, Peters MD, Keefe DM, Bowen JM. Irinotecan-induced toxicity pharmacogenetics: an umbrella review of systematic reviews and meta-analyses. Pharmacogenomics J 2017;17:21–8.
14. Bardia A, Mayer IA, Vahdat LT, Tolaney SM, Isakoff SJ, Diamond JR, et al. Sacituzumab govitecan-hziy in refractory metastatic triple-negative breast cancer. N Engl J Med 2019;380:741–51.
15. Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. JAMA 2006;295:2492–502.
16. Lund MJ, Trivers KF, Porter PL, Coates RJ, Leyland-Jones B, Brawley OW, et al. Race and triple negative threats to breast cancer survival: a population-based study in Atlanta, GA. Breast Cancer Res Treat 2019;113:357–70.
17. Regnante JM, Richie NA, Fashoyin-Aje LA, Vichnin M, Ford M, Roy UB, et al. US cancer centers of excellence strategies for increased inclusion of racial and ethnic minorities in clinical trials. Clin Oncol Pract 2019;15:289–99.
18. Schmid P, Adams S, Rugo HS, Schneeweiss A, Barrios CH, Iwata H, et al. Atezolizumab and nab-paclitaxel in advanced triple negative breast cancer. N Engl J Med 2018;379:2108–21.
19. Murthy RK, Loi S, Okines A, Paplomata E, Hamilton E, Hurvitz SA, et al. Tucatinib, trastuzumab, and capecitabine for HER2-positive metastatic breast cancer. N Engl J Med 2020;382:597–609.
20. Modi S, Saura C, Yamashita T, Park YH, Kim S-B, Tamura K, et al. Trastuzumab deruxtecan in previously treated HER2-positive breast cancer. N Engl J Med 2020;382:610–21.
21. U.S. Food and Drug Administration. Special protocol assessment guidance for industry. Available from: https://www.fda.gov/media/97618/download.
22. Bardia A, Tolaney SM, Loirat D, Punie K, Oliveira M, Rugo HS, et al. ASCENT: a randomized phase 3 study of sacituzumab govitecan (SG) vs treatment of physician's choice (TPC) in patients (pts) with previously treated metastatic triple-negative breast cancer (mTNBC). Ann Oncol 2020;31:S1142–S1215.

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