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A SPECIAL MEETING REVIEW EDITION

Highlights in Metastatic Breast Cancer From the 2024 San Antonio Breast Cancer Symposium

A Review of Selected Presentations From SABCS 2024 • December 10-13, 2024 • San Antonio, Texas

Special Reporting on:

- Primary Results of the Randomized Phase 4 Trial Comparing First-Line Endocrine Therapy + Palbociclib vs Standard Mono-chemotherapy in Women With High-Risk HER2–/HR+ Metastatic Breast Cancer and Indication for Chemotherapy: PADMA Study
- Efficacy and Safety of Trastuzumab Deruxtecan vs Physician's Choice of Chemotherapy by Pace of Disease Progression on Prior Endocrine-Based Therapy: Additional Analysis From DESTINY-Breast06
- PRESERVE 2: A Randomized, Phase 3, Double-Blind Trial of Trilaciclib or Placebo in Patients Receiving First-Line Gemcitabine/Carboplatin for Locally Advanced or Metastatic Triple-Negative Breast Cancer
- Quality-Adjusted Time Without Symptoms of Disease Progression or Toxicity of Treatment (Q-TWiST) Analysis of Sacituzumab Govitecan vs Chemotherapy in Previously Treated Patients with HR+/HER2– Metastatic Breast Cancer
- AFT-38 PATINA: A Randomized, Open-Label, Phase 3 Trial to Evaluate the Efficacy and Safety of Palbociclib + Anti-HER2 Therapy + Endocrine Therapy vs Anti-HER2 Therapy + Endocrine Therapy After Induction Treatment for HR+/HER2+ Metastatic Breast Cancer
- Imlunestrant, an Oral Selective Estrogen Receptor Degrader, as Monotherapy and Combined With Abemaciclib, for Patients with ER+, HER2– Advanced Breast Cancer, Pretreated With Endocrine Therapy: Results of the Phase 3 EMBER-3 Trial

PLUS Meeting Abstract Summaries

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TRODELVY®
sacituzumab govitecan-hziy
180 mg for injection

What is available for your patients with pretreated HR+/HER2- mBC?[1]

TRODELVY® is the only Trop-2–directed ADC to significantly improve overall survival for these patients[1]

Management strategies are available for select side effects in the Prescribing Information[1]

Survival Elevated

TRODELVY provided a statistically significant and clinically meaningful mPFS benefit[1]

5.5 months with TRODELVY (95% CI: 4.2–7.0) (n=272) versus **4.0 months with single-agent chemotherapy** (95% CI: 3.1–4.4) (n=271); HR=0.66 (95% CI: 0.53–0.83); *P*=0.0003[1,2]

Help give your patients more time: 3.2 more months of OS with TRODELVY[1,2]

14.4 months with TRODELVY (95% CI: 13.0–15.7) (n=272) versus **11.2 months with single-agent chemotherapy** (95% CI: 10.1–12.7) (n=271); HR=0.79 (95% CI: 0.65–0.96); *P*=0.02[1]

TROPiCS-02: Phase 3, randomized, active-controlled, open-label study (N=543) in patients with HR+/HER2- mBC who were previously treated with ≥1 endocrine therapy, a CDK4/6i, and a taxane in any setting, and who received 2 to 4 lines of chemotherapy in the metastatic setting. The study assessed PFS by BICR per RECIST 1.1 criteria (primary endpoint) and OS (secondary endpoint). Patients were randomized (1:1) to receive TRODELVY 10 mg/kg as an IV infusion on Days 1 and 8 of a 21-day cycle (n=272) or investigator's choice of single-agent chemotherapy (n=271), which included eribulin, vinorelbine, gemcitabine, or capecitabine. Patients were treated until disease progression or unacceptable toxicity.[1,3,4]

ADC=antibody-drug conjugate; BICR=blinded independent central review; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; CI=confidence interval; HER2-=human epidermal growth factor receptor 2–negative; HR=hazard ratio; HR+=hormone receptor–positive; IV=intravenous; mBC=metastatic breast cancer; mPFS=median progression-free survival; OS=overall survival; PFS=progression-free survival; RECIST=Response Evaluation Criteria in Solid Tumors.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: NEUTROPENIA AND DIARRHEA

- **Severe or life-threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm³ or neutropenic fever. Monitor blood cell counts periodically during treatment. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patients with febrile neutropenia without delay.**
- **Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold TRODELVY until resolved to ≤Grade 1 and reduce subsequent doses.**

CONTRAINDICATIONS

- Severe hypersensitivity reaction to TRODELVY.

WARNINGS AND PRECAUTIONS

Neutropenia: Severe, life-threatening, or fatal neutropenia can occur and may require dose modification. Neutropenia occurred in 64% of patients treated with TRODELVY. Grade 3-4 neutropenia occurred in 49% of patients. Febrile neutropenia occurred in 6%. Neutropenic colitis occurred in 1.4%. Withhold TRODELVY for absolute neutrophil count below 1500/mm³ on Day 1 of any cycle or neutrophil count below 1000/mm³ on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Administer G-CSF as clinically indicated or indicated in Table 1 of USPI.

Please see additional Important Safety Information on the next page.

INDICATION

TRODELVY® (sacituzumab govitecan-hziy) is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.

IMPORTANT SAFETY INFORMATION *(cont'd)*

WARNINGS AND PRECAUTIONS *(cont'd)*

Diarrhea: Diarrhea occurred in 64% of all patients treated with TRODELVY. Grade 3-4 diarrhea occurred in 11% of patients. One patient had intestinal perforation following diarrhea. Diarrhea that led to dehydration and subsequent acute kidney injury occurred in 0.7% of all patients. Withhold TRODELVY for Grade 3-4 diarrhea and resume when resolved to ≤Grade 1. At onset, evaluate for infectious causes and if negative, promptly initiate loperamide, 4 mg initially followed by 2 mg with every episode of diarrhea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures (e.g., fluid and electrolyte substitution) may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment can receive appropriate premedication (e.g., atropine) for subsequent treatments.

Hypersensitivity and Infusion-Related Reactions: Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 35% of patients. Grade 3-4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.2%. The incidence of anaphylactic reactions was 0.2%. Pre-infusion medication is recommended. Have medications and emergency equipment to treat such reactions available for immediate use. Observe patients closely for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Permanently discontinue TRODELVY for Grade 4 infusion-related reactions.

Nausea and Vomiting: Nausea occurred in 64% of all patients treated with TRODELVY and Grade 3-4 nausea occurred in 3% of these patients. Vomiting occurred in 35% of patients and Grade 3-4 vomiting occurred in 2% of these patients. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK_1 receptor antagonist as well as other drugs as indicated) for prevention of chemotherapy-induced nausea and vomiting (CINV). Withhold TRODELVY doses for Grade 3 nausea or Grade 3-4 vomiting and resume with additional supportive measures when resolved to Grade ≤1. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting.

Increased Risk of Adverse Reactions in Patients with Reduced UGT1A1 Activity: Patients homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk for neutropenia, febrile neutropenia, and anemia and may be at increased risk for other adverse reactions with TRODELVY. The incidence of Grade 3-4 neutropenia was 58% in patients homozygous for the UGT1A1*28, 49% in patients heterozygous for the UGT1A1*28 allele, and 43% in patients homozygous for the wild-type allele. The incidence of Grade 3-4 anemia was 21% in patients homozygous for the UGT1A1*28 allele, 10% in patients heterozygous for the UGT1A1*28 allele, and 9% in patients homozygous for the wild-type allele. Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue TRODELVY based on clinical assessment of the onset, duration and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced UGT1A1 function.

Embryo-Fetal Toxicity: Based on its mechanism of action, TRODELVY can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. TRODELVY contains a genotoxic component, SN-38, and targets rapidly dividing cells. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose.

ADVERSE REACTIONS

In the pooled safety population, the most common (≥25%) adverse reactions including laboratory abnormalities were decreased leukocyte count (84%), decreased neutrophil count (75%), decreased hemoglobin (69%), diarrhea (64%), nausea (64%), decreased lymphocyte count (63%), fatigue (51%), alopecia (45%), constipation (37%), increased glucose (37%), decreased albumin (35%), vomiting (35%), decreased appetite (30%), decreased creatinine clearance (28%), increased alkaline phosphatase (28%), decreased magnesium (27%), decreased potassium (26%), and decreased sodium (26%).

In the TROPiCS-02 study, the most common adverse reactions (incidence ≥25%) were diarrhea, fatigue, nausea, alopecia, and constipation. The most frequent serious adverse reactions (SAR) (>1%) were diarrhea (5%), febrile neutropenia (4%), neutropenia (3%), abdominal pain, colitis, neutropenic colitis, pneumonia, and vomiting (each 2%). SAR were reported in 28% of patients, and 6% discontinued therapy due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence ≥25%) in the TROPiCS-02 study were reduced neutrophils and leukocytes.

DRUG INTERACTIONS

UGT1A1 Inhibitors: Concomitant administration of TRODELVY with inhibitors of UGT1A1 may increase the incidence of adverse reactions due to potential increase in systemic exposure to SN-38. Avoid administering UGT1A1 inhibitors with TRODELVY.

UGT1A1 Inducers: Exposure to SN-38 may be reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY.

Please see Brief Summary of full Prescribing Information, including BOXED WARNING, on the next page.

References: 1. TRODELVY. Prescribing information. Gilead Sciences, Inc.; February 2023. **2.** Rugo HS, Bardia A, Marmé F, et al. Overall survival with sacituzumab govitecan in hormone receptor-positive and human epidermal growth factor receptor 2-negative metastatic breast cancer (TROPiCS-02): a randomised, open-label, multicentre, phase 3 trial. *Lancet.* 2023;402:1423-1433. **3.** Rugo HS, Bardia A, Marmé F, et al. Sacituzumab govitecan in hormone receptor–positive/human epidermal growth factor receptor 2–negative metastatic breast cancer. *J Clin Oncol.* 2022;40(29):3365-3376. **4.** Immunomedics, Inc. Phase 3 study of sacituzumab govitecan (IMMU-132) versus treatment of physician's choice (TPC) in subjects with hormonal receptor-positive (HR+) human epidermal growth factor receptor 2 (HER2) negative metastatic breast cancer (MBC) who have failed at least two prior chemotherapy regimens. Published December 21, 2018. Accessed January 18, 2024. https://ascopubs.org/doi/suppl/10.1200/JCO.22.01002/suppl_file/protocol_JCO.22.01002.pdf

TRODELVY® (sacituzumab govitecan-hziy) for injection, for intravenous use
Brief Summary of full Prescribing Information. See full Prescribing Information. Rx Only.

WARNING: NEUTROPENIA AND DIARRHEA

- **Severe or life-threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Monitor blood cell counts periodically during treatment. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patients with febrile neutropenia without delay.**
- **Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold TRODELVY until resolved to ≤ Grade 1 and reduce subsequent doses.**

[See Warnings and Precautions and Dosage and Administration]

INDICATIONS AND USAGE

*Also see **Clinical Studies***

TRODELVY (sacituzumab govitecan-hziy) is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with:

- Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.
- Unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.
- Locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and either programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

DOSAGE AND ADMINISTRATION

*Also see **Warnings and Precautions***

Do NOT substitute TRODELVY for or use with other drugs containing irinotecan or its active metabolite SN-38.

The recommended dosage of TRODELVY is 10 mg/kg administered as an intravenous infusion once weekly on Days 1 and 8 of 21-day treatment cycles. Continue treatment until disease progression or unacceptable toxicity. Do not administer TRODELVY at doses greater than 10 mg/kg. Administer TRODELVY as an intravenous infusion only. Do not administer as an intravenous push or bolus.

- First infusion: Administer infusion over 3 hours. Observe patients during the infusion and for at least 30 minutes following the initial dose, for signs or symptoms of infusion-related reactions
- Subsequent infusions: Administer infusion over 1 to 2 hours if prior infusions were tolerated. Observe patients during the infusion and for at least 30 minutes after infusion.
- Premedication: Prior to each dose of TRODELVY, premedication for prevention of infusion reactions and prevention of chemotherapy-induced nausea and vomiting (CINV) is recommended. Premedicate with antipyretics, H1 and H2 blockers prior to infusion, and corticosteroids may be used for patients who had prior infusion reactions. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK$_1$ receptor antagonist, as well as other drugs as indicated).

Dose Modifications for Infusion-related Reactions: Slow or interrupt the infusion rate of TRODELVY if the patient develops an infusion-related reaction. Permanently discontinue TRODELVY for life-threatening infusion-related reactions.

Dose Modifications for Adverse Reactions: Withhold or discontinue TRODELVY to manage adverse reactions as described below. Do not re-escalate the TRODELVY dose after a dose reduction for adverse reactions has been made.

Severe Neutropenia, defined as Grade 4 neutropenia ≥7 days, OR Grade 3-4 febrile neutropenia, OR at time of scheduled treatment, Grade 3-4 neutropenia which delays dosing by 2 or 3 weeks for recovery to ≤ Grade 1:

- At first occurrence, 25% dose reduction and administer granulocyte-colony stimulating factor (G-CSF). At second occurrence, 50% dose reduction and administer G-CSF. At third occurrence, discontinue TRODELVY and administer G-CSF.
- At time of scheduled treatment, if Grade 3-4 neutropenia occurs which delays dosing beyond 3 weeks for recovery to ≤ Grade 1, discontinue TRODELVY and administer G-CSF at first occurrence.

Severe Non-Neutropenic Toxicity, defined as Grade 4 non-hematologic toxicity of any duration, OR any Grade 3-4 nausea, vomiting or diarrhea due to treatment that is not controlled with antiemetics and anti-diarrheal agents, OR other Grade 3-4 non-hematologic toxicity persisting >48 hours despite optimal medical management, OR at time of scheduled treatment, Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, which delays dose by 2 or 3 weeks for recovery to ≤Grade 1:

- At first occurrence, 25% dose reduction. At second occurrence, 50% dose reduction. At third occurrence, discontinue TRODELVY.
- In the event of Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, which does not recover to ≤Grade 1 within 3 weeks, discontinue TRODELVY at first occurrence.

CONTRAINDICATIONS

*Also see **Warnings and Precautions***

TRODELVY is contraindicated in patients who have experienced a severe hypersensitivity reaction to TRODELVY.

WARNINGS AND PRECAUTIONS

*Also see **BOXED WARNING, Dosage and Administration, Contraindications, Clinical Pharmacology, Nonclinical Toxicology,** and **Use in Specific Populations***

Neutropenia: Severe, life-threatening, or fatal neutropenia can occur in patients treated with TRODELVY. Neutropenia occurred in 64% of patients treated with TRODELVY. Grade 3-4 neutropenia occurred in 49% of patients. Febrile neutropenia occurred in 6% of patients. The median time to first onset of neutropenia (including febrile neutropenia) was 16 days and has occurred earlier in some patient populations. Neutropenic colitis occurred in 1.4% of patients. Withhold TRODELVY for ANC below 1500/mm^3 on Day 1 of any cycle or neutrophil count below 1000/mm^3 on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Dose modifications may be required due to neutropenia. Administer G-CSF as clinically indicated or indicated in Table 1 of full Prescribing Information.

Diarrhea: TRODELVY can cause severe diarrhea. Diarrhea occurred in 64% of all patients treated with TRODELVY. Grade 3-4 diarrhea occurred in 11% of all patients treated with TRODELVY. One patient had intestinal perforation following diarrhea. Diarrhea that led to dehydration and subsequent acute kidney injury occurred in 0.7% of all patients. Withhold TRODELVY for Grade 3-4 diarrhea at the time of scheduled treatment administration and resume when resolved to ≤ Grade 1. At the onset of diarrhea, evaluate for infectious causes and if negative, promptly initiate loperamide, 4 mg initially followed by 2 mg with every episode of diarrhea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures (e.g., fluid and electrolyte substitution) may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment with TRODELVY (e.g., abdominal cramping, diarrhea, salivation, etc.) can receive appropriate premedication (e.g., atropine) for subsequent treatments.

Hypersensitivity and Infusion-Related Reactions: Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY treatment. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 35% of patients treated with TRODELVY. Grade 3-4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.2%. The incidence of anaphylactic reactions was 0.2%. Premedication for infusion reactions in patients receiving TRODELVY is recommended. Have medications and emergency equipment to treat infusion-related reactions, including anaphylaxis, available for immediate use when administering TRODELVY. Closely monitor patients for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Permanently discontinue TRODELVY for Grade 4 infusion-related reactions.

Nausea and Vomiting: TRODELVY is emetogenic. Nausea occurred in 64% of all patients treated with TRODELVY. Grade 3-4 nausea occurred in 3% of patients. Vomiting occurred in 35% of patients. Grade 3-4 vomiting occurred in 2% of these patients. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK$_1$ receptor antagonist as well as other drugs as indicated) for prevention of CINV. Withhold TRODELVY doses for Grade 3 nausea or Grade 3-4 vomiting and resume with additional supportive measures when resolved to ≤Grade 1. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting.

Increased Risk of Adverse Reactions in Patients with Reduced UGT1A1 Activity: Patients homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk for neutropenia, febrile neutropenia, and anemia and may be at increased risk for other adverse reactions with TRODELVY. The incidence of neutropenia and anemia was analyzed in 948 patients who received TRODELVY and had UGT1A1 genotype results. The incidence of Grade 3-4 neutropenia was 58% in patients homozygous for the UGT1A1*28 allele (n=112), 49% in patients heterozygous for the UGT1A1*28 allele (n=420), and 43% in patients homozygous for the wild-type allele (n=416). The incidence of Grade 3-4 anemia was 21% in patients homozygous for the UGT1A1*28 allele, 10% in patients heterozygous for the UGT1A1*28 allele, and 9% in patients homozygous for the wild-type allele. The median time to first neutropenia including febrile neutropenia was 9 days in patients homozygous for the UGT1A1*28 allele, 15 days in patients heterozygous for the UGT1A1*28 allele, and 20 days in patients homozygous for the wild-type allele. The median time to first anemia was 21 days in patients homozygous for the UGT1A1*28 allele, 25 days in patients heterozygous for the UGT1A1*28 allele, and 28 days in patients homozygous for the wild-type allele. Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue TRODELVY based on onset, duration, and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced UGT1A1 enzyme activity.

Embryo-Fetal Toxicity: Based on its mechanism of action, TRODELVY can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. TRODELVY contains a genotoxic component, SN-38, and targets rapidly dividing cells. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose.

ADVERSE REACTIONS

*Also see **BOXED WARNING, Warnings and Precautions,** and **Clinical Studies***

The pooled safety population described in the Warnings and Precautions section reflect exposure to TRODELVY in 1063 patients from four studies, IMMU-132-01, ASCENT, TROPiCS-02, and TROPHY which included 366 patients with mTNBC, 322 patients with HR+/HER2- breast cancer, and 180 patients with mUC. Among the 1063 patients treated with TRODELVY, the median duration of treatment was 4.1 months (range: 0 to 63 months). The most common (≥ 25%) adverse reactions including laboratory abnormalities were decreased leukocyte count (84%), decreased neutrophil count (75%), decreased hemoglobin (69%), diarrhea (64%), nausea (64%), decreased lymphocyte count (63%), fatigue (51%), alopecia (45%), constipation (37%), increased glucose (37%), decreased albumin (35%), vomiting (35%), decreased appetite (30%), decreased creatinine clearance (28%), increased alkaline phosphatase (28%), decreased magnesium (27%), decreased potassium (26%), and decreased sodium (26%).

Locally Advanced or Metastatic Triple-Negative Breast Cancer

The safety of TRODELVY was evaluated in a randomized, active-controlled, open-label study (ASCENT) in patients with mTNBC who had previously received a taxane and at least two prior chemotherapies. Patients were randomized (1:1) to receive either TRODELVY (n=258) or single agent chemotherapy (n=224) and were treated until disease progression or unacceptable toxicity. For patients treated with TRODELVY, the median duration of treatment was 4.4 months (range: 0 to 23 months). Serious adverse reactions occurred in 27% of patients, and those in > 1% included neutropenia (7%), diarrhea (4%), and pneumonia (3%). Fatal adverse reactions occurred in 1.2% of patients, including respiratory failure (0.8%) and pneumonia (0.4%). TRODELVY was permanently discontinued for adverse reactions in 5% of patients. These adverse reactions (≥1%) were pneumonia (1%) and fatigue (1%). The most frequent (≥5%) adverse reactions leading to a treatment interruption in 63% of patients were neutropenia (47%), diarrhea (5%), respiratory infection (5%), and leukopenia (5%). The most frequent (>4%) adverse reactions leading to a dose reduction in 22% of patients were neutropenia (11%) and diarrhea (5%). G-CSF was used in 44% of patients who received TRODELVY. The most common (≥25%) adverse reactions including lab abnormalities were decreased hemoglobin (94%), decreased lymphocyte count (88%), decreased leukocyte count (86%), decreased neutrophil count (78%), fatigue (65%), diarrhea (59%), nausea (57%), increased glucose (49%), alopecia (47%), constipation (37%), decreased calcium (36%), vomiting (33%), decreased magnesium (33%), decreased potassium (33%), increased albumin (32%), abdominal pain (30%), decreased appetite (28%), increased aspartate aminotransferase (27%), increased alanine aminotransferase (26%), increased alkaline phosphatase (26%), and decreased phosphate (26%).

Locally Advanced or Metastatic HR-Positive, HER2-Negative Breast Cancer

The safety of TRODELVY was evaluated in a randomized, active-controlled, open-label study (TROPiCS-02) in patients with unresectable locally advanced or metastatic HR+/HER2- breast cancer whose disease has progressed after the following in any setting: a CDK 4/6 inhibitor, endocrine therapy, and a taxane; patients received at least two prior chemotherapies in the metastatic setting (one of which could be in the neoadjuvant or adjuvant setting if progression occurred within 12 months). Patients were randomized (1:1) to receive either TRODELVY (n=268) or single agent chemotherapy (n=249) and were treated until disease progression or unacceptable toxicity. For patients treated with TRODELVY, the median duration of treatment was 4.1 months (range: 0 to 63 months). Serious adverse reactions occurred in 28% of patients, and those in >1% of patients included diarrhea (5%), febrile neutropenia (4%), neutropenia (3%), abdominal pain, colitis, neutropenic colitis, pneumonia, and vomiting (each 2%). Fatal adverse reactions occurred in 2% of patients, including arrhythmia, COVID-19, nervous system disorder, pulmonary embolism, and septic shock (each 0.4%). TRODELVY was permanently discontinued for adverse reactions in 6% of patients. The most frequent (≥0.5%) of these adverse reactions were asthenia, general physical health deterioration, and neutropenia (each 0.7%). The most frequent (≥5%) adverse reaction leading to treatment interruption in 66% of patients was neutropenia (50%). The most frequent (>5%) adverse reactions leading to dose reduction in 33% of patients were neutropenia (16%) and diarrhea (8%). G-CSF was used in 54% of patients who received TRODELVY. The most common (≥25%) adverse reactions including lab abnormalities were decreased leukocyte count (88%), decreased neutrophil count (83%), decreased hemoglobin (73%), and decreased lymphocyte count (65%); diarrhea (62%), fatigue (60%), nausea (59%), alopecia (48%), increased glucose (37%), constipation (34%), and decreased albumin (32%). Other clinically significant adverse reactions in TROPiCS-02 (≤ 10%) include: hypotension (5%), pain (5%), rhinorrhea (5%), hypocalcemia (3%), nasal congestion (3%), skin hyperpigmentation (3%), colitis or neutropenic colitis (2%), hyponatremia (2%), pneumonia (2%), proteinuria (1%), enteritis (0.4%).

Locally Advanced or Metastatic Urothelial Cancer

The safety of TRODELVY was evaluated in a single-arm, open-label study (TROPHY) in patients (n=113) with mUC who had received previous platinum-based and anti-PD-1/PD-L1 therapy. Serious adverse reactions occurred in 44% of patients, and those in >1% included infection (18%), neutropenia (12%, including febrile neutropenia in 10%), acute kidney injury (6%), urinary tract infection (6%), sepsis or bacteremia (5%), diarrhea (4%), anemia, venous thromboembolism, and small intestinal obstruction (3% each), pneumonia, abdominal pain, pyrexia, and thrombocytopenia (2% each). Fatal adverse reactions occurred in 3.6% of patients, including sepsis, respiratory failure, epistaxis, and completed suicide. TRODELVY was permanently discontinued for adverse reactions in 10% of patients. The most frequent of these adverse reactions was neutropenia (4%, including febrile neutropenia in 2%). The most common adverse reactions leading to dose interruption in 52% of patients were neutropenia (27%, including febrile neutropenia in 2%), infection (12%), and acute kidney injury (8%). The most common (>4%) adverse reactions leading to a dose reduction in 42% of patients were neutropenia (13%, including febrile neutropenia in 3%), diarrhea (11%), fatigue (8%), and infection (4%). G-CSF was used in 47% of patients who received TRODELVY. The most common (≥25%) adverse reactions including lab abnormalities were decreased leukocyte count (78%), diarrhea (72%), decreased hemoglobin (71%), decreased lymphocyte count (71%), fatigue (68%), decreased neutrophil count (67%), nausea (66%), increased glucose (59%), decreased albumin (51%), any infection (50%), alopecia (49%), decreased calcium (46%), decreased sodium (43%), decreased appetite (41%), decreased phosphate (41%), increased alkaline phosphatase (36%), constipation (34%), vomiting (34%), increased activated partial thromboplastin time (33%), increased creatinine (32%), rash (32%), decreased magnesium (31%), abdominal pain (31%), increased alanine aminotransferase (28%), increased lactate dehydrogenase (28%), decreased potassium (27%), increased aspartate aminotransferase (26%), and decreased platelet count (25%). Other clinically significant adverse reactions (≤15%) include: peripheral neuropathy (12%), sepsis or bacteremia (9%), and pneumonia (4%).

DRUG INTERACTIONS

*Also see **Warnings and Precautions** and **Clinical Pharmacology***

UGT1A1 Inhibitors: Concomitant administration of TRODELVY with inhibitors of UGT1A1 may increase the incidence of adverse reactions due to potential increase in systemic exposure to SN-38. Avoid administering UGT1A1 inhibitors with TRODELVY.

UGT1A1 Inducers: Exposure to SN-38 may be reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY

USE IN SPECIFIC POPULATIONS

*Also see **Warnings and Precautions, Clinical Pharmacology,** and **Nonclinical Toxicology***

Pregnancy: TRODELVY can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. There are no available data in pregnant women to inform the drug-associated risk. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

Lactation: There is no information regarding the presence of sacituzumab govitecan-hziy or SN-38 in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment and for 1 month after the last dose of TRODELVY.

Females and Males of Reproductive Potential: Verify the pregnancy status of females of reproductive potential prior to initiation. TRODELVY can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose.

Males: Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose.

Infertility: Based on findings in animals, TRODELVY may impair fertility in females of reproductive potential.

Pediatric Use: Safety and effectiveness of TRODELVY have not been established in pediatric patients.

Geriatric Use:

Of the 366 patients with TNBC who were treated with TRODELVY, 19% of patients were 65 years and 3% were 75 years and older. No overall differences in safety and effectiveness were observed between patients ≥ 65 years of age and younger patients.

Of the 322 patients with HR+/HER2- breast cancer who were treated with TRODELVY, 26% of patients were ≥ 65 years and 6% were ≥ 75 years. No overall differences in effectiveness were observed between patients ≥ 65 years of age and younger patients. There was a higher discontinuation rate due to adverse reactions in patients aged 65 years or older (14%) compared with younger patients (3%).

Of the 180 patients with UC who were treated with TRODELVY, 59% of patients were ≥ 65 years and 27% were ≥ 75 years. No overall differences in effectiveness were observed between patients ≥ 65 years of age and younger patients. There was a higher discontinuation rate due to adverse reactions in patients aged 65 years or older (14%) compared with younger patients (8%).

Hepatic Impairment: No adjustment to the starting dose is required when administering TRODELVY to patients with mild hepatic impairment. The safety of TRODELVY in patients with moderate or severe hepatic impairment has not been established, and no recommendations can be made for the starting dose in these patients.

761115-GS-007 Feb 2023

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Primary Results of the Randomized Phase 4 Trial Comparing First-Line Endocrine Therapy + Palbociclib vs Standard Mono-chemotherapy in Women With High-Risk HER2–/HR+ Metastatic Breast Cancer and Indication for Chemotherapy: PADMA Study

For several years, the guideline-recommended initial regimen for patients with hormone receptor–positive (HR+), human epidermal growth factor receptor 2 (HER2)–negative (HER2–) metastatic breast cancer (mBC) has been CDK4/6 inhibitors plus endocrine therapy (ET).[1,2] However, despite the establishment of this regimen, many patients continued to receive chemotherapy as first-line treatment because of a lack of prospective data comparing ET with standard chemotherapy.

The randomized, open-label, multicenter, phase 4 PADMA trial was therefore designed to evaluate the efficacy and safety of a CDK4/6 inhibitor plus ET vs standard single-agent chemotherapy with or without maintenance ET in patients with high-risk mBC with an indication for chemotherapy. Primary results of the PADMA trial were presented at SABCS 2024 by Sibylle Loibl, MD, PhD (Table 1).[3]

The trial enrolled patients with HR+/HER2– breast cancer with an indication for single-agent chemotherapy with no prior treatment for metastatic or relapsed disease; no asymptomatic bone-only, oligometastatic disease; no uncontrolled or untreated central nervous system metastases; and a life expectancy exceeding 6 months. A total of 130 patients were stratified based on endocrine sensitivity and presence of symptoms, then randomly assigned to ET plus palbociclib (n=61) or chemotherapy treatment of the physician's choice (TPC) with or without ET maintenance therapy (n=59). Options for ET given with palbociclib included an aromatase inhibitor (AI) or fulvestrant with or without a gonadotropin-releasing hormone agonist (GnRHa). Options for ET given as maintenance therapy included tamoxifen, an AI, or fulvestrant with or without GnRHa.

The median age of enrolled patients was 62 years (range, 31-85); 88.3% were postmenopausal, 41.7% had liver metastases, and 31.7% had endocrine resistance at baseline. Prior neoadjuvant chemotherapy had been administered to 45.0% of patients, and 66.4% of patients tested (n=71) had HER2-low disease. Pathogenic variants, tested in 81 patients, included *PIK3CA* (22.5%), *BRCA1/2* (5.8%), and *ESR1* (1.7%). Types of TPC included capecitabine (69.0%), paclitaxel (29.3%), and vinorelbine (1.7%). Post-chemotherapy maintenance with ET was administered to 22.4%. Types of ET administered in the palbociclib plus ET group included an AI (77.4%) and fulvestrant (22.6%). Types of ET administered in the TPC group included an AI (15.5%), tamoxifen (5.2%), and fulvestrant (1.7%). The median duration of treatment was 51.0 weeks for palbociclib and 19.5 weeks with chemotherapy.

After a median follow-up of 36.8 months, the trial met its primary endpoint, demonstrating an improvement in median time-to-treatment failure with palbociclib plus ET over chemotherapy (17.2 vs 6.1 months; hazard

Table 1. Primary and Secondary Endpoint Analyses Comparing First-Line ET+ Palbociclib vs Standard Mono-chemotherapy in Randomized Phase 4 PADMA Study

Endpoint	Treatment group	
	Palbociclib + ET	Chemotherapy
TTF		
Events, n (%)	45 (73.8)	55 (93.2)
Median, mo	**17.2**	**6.1**
HR (95% CI)	**0.46** (0.31-0.69); *P*<.001 (log-rank)	
PFS		
Events, n (%)	40 (65.6)	50 (84.7)
Median, mo	**18.7**	**7.8**
HR (95% CI)	**0.45** (0.29-0.70); *P*<.001 (log-rank)	
OS		
Events, n (%)	25 (41.0)	24 (40.7)
Median, mo	**46.1**	**36.8**
HR (95% CI)	Proportional hazard cannot be assumed	

ET, endocrine therapy; HR, hazard ratio; mo, months; OS, overall survival; PFS, progression-free survival; TTF, time-to-treatment failure.

Adapted from Loibl et al. Presented at: 2024 San Antonio Breast Cancer Symposium; December 10-13, 2024; San Antonio, Texas, USA. Abstract LB1-03.

ABSTRACT SUMMARY Real World Data With Standard and Reduced Dose Sacituzumab Govitecan in mTNBC and ER+/HER2– mBC

A retrospective single-institution cohort study reported treatment patterns and outcomes with SG administered at a standard dose vs a reduced dose in patients with mBC (Abstract P3-12-14). The cohort included 47 patients (71% with mTNBC and 29% with HR+/HER2– mBC). SG was administered at an initial standard dose of 10 mg/kg in 24 patients (50%) and at a reduced dose (median, 8 mg/kg) in 23 patients (50%). In the overall cohort, there were no significant differences with standard-dose vs reduced-dose SG in median treatment duration (98 vs 107 days; *P*=.71), median PFS from the start of SG (3 vs 3 months; *P*=.9), or median OS (10 vs 8 months; *P*=.6). Use of myeloid growth factor was significantly higher with standard-dose vs reduced-dose SG (62.5% vs 0%; *P*<.001).

ratio [HR], 0.46; 95% CI, 0.31-0.69; *P*<.001). Median progression-free survival (PFS) was also significantly longer with palbociclib plus ET vs chemotherapy (18.7 vs 7.8 months; HR, 0.45; 95% CI, 0.29-0.70; *P*<.001). Median overall survival (OS) was 46.1 months and 36.8 months, respectively.

Investigators noted no new safety signals. Rates of hematologic toxicity were significantly higher in the palbociclib plus ET group than in the chemotherapy-based group (96.8% vs 58.6%; *P*<.001), whereas rates of nonhematologic treatment-related adverse events (AEs) were similar between groups at 82.3% and 93.1%, respectively. Rates of treatment-related serious AEs were 11.3% with palbociclib plus ET and 10.3% with chemotherapy. One treatment-related death occurred due to septic shock in the palbociclib plus ET group.

The investigators concluded that the findings support current international guidelines recommending the use of ET plus a CDK4/6 inhibitor as standard first-line treatment in patients with HR+/HER2– mBC.

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The RIGHT Choice study had shown that in patients with HR+ mBC, a CDK4/6 inhibitor plus ET is better than chemotherapy in the first-line setting. The PADMA study provides further evidence that patients who are candidates for CDK4/6 inhibitors in the first-line setting should receive a CDK4/6 inhibitor plus ET over chemotherapy, including patients with visceral disease or high visceral burden.

—Aditya Bardia, MD, MPH

Efficacy and Safety of Trastuzumab Deruxtecan vs Physician's Choice of Chemotherapy by Pace of Disease Progression on Prior Endocrine-Based Therapy: Additional Analysis From DESTINY-Breast06

Aditya Bardia, MD, MPH, presented additional analyses from the DESTINY-Breast06 trial, a randomized, multicenter, open-label, phase 3 trial evaluating trastuzumab deruxtecan (T-DXd) vs TPC in patients with HR+, HER2-low or HER2-ultralow advanced or metastatic breast cancer previously treated with ET (Table 2).[1]

DESTINY-Breast06 trial enrolled patients who had received at least 2 prior lines of ET in the metastatic setting or had received 1 line of ET for mBC and either had disease progression within 6 months of starting first-line ET plus a CDK4/6 inhibitor or had a recurrence within 2 years of starting adjuvant ET.[2]

A total of 866 patients were randomly assigned to T-DXd 5.4 mg/kg

Table 2. Efficacy of Trastuzumab Deruxtecan vs Physician's Choice of Chemotherapy by Pace of Disease Progression on Prior Endocrine-Based Therapy and Measures of Disease Burden: Additional Analysis From Phase 3 DESTINY-Breast06 Trial

Patient group	Endpoint	Treatment group	
		Trastuzumab deruxtecan	Physician's choice of chemotherapy
<6-mo first-line TTP	n	65	59
	Median PFS, mo	**14.0**	**6.5**
	HR (95% CI)[a]	**0.38** (0.25-0.59)	
	Median PFS2, mo	**18.9**	**15.2**
	HR (95% CI)[a]	**0.73** (0.46-1.14)	
6–12-mo first-line TTP	n	60	52
	Median PFS, mo	**13.2**	**6.9**
	HR (95% CI)[a]	**0.69** (0.43-1.12)	
	Median PFS2, mo	**17.1**	**13.7**
	HR (95% CI)[a]	**0.59** (0.37-0.94)	
>12-mo first-line TTP	n	168	166
	Median PFS, mo	**12.9**	**8.2**
	HR (95% CI)[a]	**0.67** (0.51-0.88)	
	Median PFS2, mo	**20.0**	**14.3**
	HR (95% CI)[a]	**0.57** (0.43-0.75)	
Overall ITT population	n	436	430
	Median PFS2, mo	**20.3**	**14.7**
	HR (95% CI)[a]	**0.62** (0.52-0.74) *P*<.0001	
Primary endocrine resistance[b]	n	128	140
	Median PFS, mo	**12.4**	**6.6**
	HR (95% CI)[a]	**0.57** (0.42-0.77)	
Secondary endocrine resistance[c]	n	308	288
	Median PFS, mo	**13.2**	**9.5**
	HR (95% CI)[a]	**0.68** (0.55-0.84)	
<3 local/ metastatic sites at baseline	n	198	180
	Median PFS, mo	**15.3**	**8.4**
	HR (95% CI)	**0.55** (0.42-0.72)	
≥3 local/ metastatic sites at baseline	n	238	250
	Median PFS, mo	**11.4**	**7.2**
	HR (95% CI)	**0.71** (0.57-0.89)	

[a]HR and its CI were estimated from an unstratified Cox proportional hazards model.
[b]Primary endocrine resistance was defined as relapse within the first 2 years of adjuvant ET, or progressive disease less than 6 months of first-line ET for mBC.
[c]Secondary (acquired) endocrine resistance was defined as relapse after the first 2 years on adjuvant ET, or relapse within 12 months of completing adjuvant ET, or progressive disease >6 months after initiating ET for mBC.
ET, endocrine therapy; HR, hazard ratio; ITT, intent-to-treat; mBC, metastatic breast cancer; mo, months; PFS, progression-free survival; PFS2, time from randomization to second progression or death; TTP, time to progression.

Adapted from Bardia et al. Presented at: 2024 San Antonio Breast Cancer Symposium; December 10-13, 2024; San Antonio, Texas, USA. Abstract LB1-04.

ABSTRACT SUMMARY Health-Related Quality of Life With Sacituzumab Govitecan vs Treatment of Physician's Choice in Previously Treated HR+/HER2– Metastatic Breast Cancer: A Meta-analysis of TROPiCS-02 and EVER-132-002 Trials

Hope S. Rugo and colleagues presented a meta-analysis of HRQOL outcomes with SG and chemotherapy in the TROPiCS-2 and EVER-132-002 trials and assessed the impact of prior CDK4/6 inhibitors (Abstract P2-07-19). In the overall population, SG was associated with a significant increase in median time to first clinically meaningful deterioration compared with chemotherapy for 6 of the 15 EORTC QLQ-C30 domains—Global Health Status/QOL, physical functioning, emotional functioning, fatigue, pain, and dyspnea. These improvements were maintained in patients previously treated with a CDK4/6 inhibitor and in the subset of patients considered fast progressors who had a prior CDK4/6 inhibitor treatment duration of 12 months or less. Additionally in the fast progressors, time to worsening of financial difficulties was significantly better but nausea/vomiting and diarrhea significantly worse with SG vs chemotherapy. Investigators noted that nausea/vomiting and diarrhea—known part of the safety profile of SG—are manageable using established guidelines. In a sensitivity analysis in which death was considered an event, HRQOL findings were mostly consistent across the overall population and in patients previously treated with a CDK4/6 inhibitor. Notably, the benefit with SG in the pain domain was no longer significant, and in financial difficulties gained statistical significance. Outcomes were consistent in the fast progressor subgroup, although benefit with SG in insomnia gained statistical significance. Analyses of median time to deterioration using the EQ-5D-5L VAS also showed benefits with SG over TPC in the overall population, CDK4/6 inhibitor–pretreated patients, and fast progressors.

every 3 weeks (n=436) or TPC (n=430) consisting of capecitabine (59.8%), nab-paclitaxel (24.4%), or paclitaxel (15.8%). Patients had disease that was either HER2-low (1+ or 2+ on immunohistochemical [IHC] analysis and negative results on in situ hybridization; n=713) or HER2-ultralow (IHC 0 with membrane staining; n=153). The median age of enrolled patients was 58 years. Approximately 42% had an Eastern Cooperative Oncology Group performance status of 1 or greater. Liver metastases were present at baseline in approximately 67% of patients, 85% of patients had visceral disease, and 31% of patients had de novo mBC. Primary endocrine resistance was present in 31% of patients.

As previously reported, the trial met its primary endpoint, demonstrating a significant improvement in PFS by blinded independent central review with T-DXd vs TPC in patients with HER2-low disease (median PFS, 13.2 vs 8.1 months; HR, 0.62; $P<.001$).[2] T-DXd was also associated with an improvement in PFS over TPC in an intention-to-treat analysis in patients with HER2-low or HER2-ultralow disease (median PFS, 13.2 vs 8.1 months; HR, 0.64; $P<.0001$).

At SABCS 2024, investigators reported additional secondary outcomes from DESTINY-Breast06, including efficacy and safety outcomes in different patient subsets. T-DXd was associated with improvements in PFS over TPC regardless of the time to progression on first-line ET plus CDK4/6 inhibitor, whether the patient had progression within 6 months (HR, 0.38; 95% CI, 0.25-0.59), in 6 to 12 months (HR, 0.69; 95% CI, 0.43-1.12), or after 12 months (HR, 0.67; 95% CI, 0.51-0.88). T-DXd was also associated with improvements in PFS in patients with primary endocrine resistance (median PFS, 12.4 vs 6.6 months; HR, 0.57; 95% CI, 0.42-0.77) and in patients with secondary endocrine resistance (median PFS, 13.2 vs 9.5 months; HR, 0.68; 95% CI, 0.55-0.84). Objective response rates (ORR) and duration of response were also improved with T-DXd over

The DESTINY-Breast06 study looked at additional analyses of patients who had rapid disease progression on a first-line CDK4/6 inhibitor plus ET (with rapid progression defined as patients who had disease progression within 6 months). In that subgroup, trastuzumab deruxtecan showed benefit vs chemotherapy when given as the next line of therapy. This highlights that in patients who have rapid disease progression on a first-line CDK4/6 inhibitor, trastuzumab deruxtecan might be an option to consider in the second-line setting.

—Aditya Bardia, MD, MPH

TPC regardless of time to progression on first-line therapy or type of endocrine resistance.

To assess the efficacy of subsequent therapies after progression on T-DXd or TPC, investigators evaluated PFS2, defined as the time from randomization to second progression or death. T-DXd was associated with a significant improvement in PFS2 over TPC (median PFS2, 20.3 vs 14.7 months; HR, 0.62; 95% CI, 0.52-0.74; *P*<.0001), with the benefit observed regardless of time to progression on first-line therapy.

The PFS benefit with T-DXd over TPC was also observed regardless of disease burden, although the efficacy advantage was more evident in patients with lower disease burden. In patients with fewer than 3 metastatic sites at baseline, median PFS with T-DXd and TPC was 15.3 months and 8.4 months, respectively (HR, 0.55; 95% CI, 0.42-0.72). In patients with 3 or more metastatic sites at baseline, median PFS was 11.4 months and 7.2 months, respectively (HR, 0.71; 95% CI, 0.57-0.89). Safety outcomes with T-DXd and TPC in the time-to-progression and disease burden subgroups were consistent with the overall population.

Investigators concluded that T-DXd is an effective option for patients with HR+, HER2-low or HER2-ultralow mBC previously treated with at least 1 endocrine-based therapy.

References

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PRESERVE 2: A Randomized, Phase 3, Double-Blind Trial of Trilaciclib or Placebo in Patients Receiving First-Line Gemcitabine/Carboplatin for Locally Advanced or Metastatic Triple-Negative Breast Cancer

Trilaciclib is an intravenously administered, selective, reversible CDK4/6 inhibitor that is approved by the US Food and Drug Administration (FDA) to reduce the frequency of chemotherapy-induced bone marrow suppression in adults receiving chemotherapy for extensive-stage small cell lung cancer.[1] In a randomized, phase 3 trial in patients with previously treated metastatic triple-negative breast cancer (mTNBC), trilaciclib administered prior to gemcitabine and carboplatin (GCb) was associated with a significant OS improvement over GCb alone (median OS, 19.8 vs 12.6 months; HR, 0.37; *P*<.0001). The OS benefit occurred regardless of programmed death-ligand 1 (PD-L1) status but was greater in patients with PD-L1–positive TNBC.[2]

At SABCS 2024, Shom Goel, MD, PhD, presented results from the multinational, double-blind, placebo-controlled, phase 3 PRESERVE 2 trial, which further evaluated the efficacy and safety of trilaciclib prior to GCb in patients with previously untreated mTNBC (Table 3).[3] The trial was open to patients who were ineligible for, or unable to receive, programmed cell death protein 1 (PD-1)/PD-L1 inhibitors. A total of 187 patients were randomly assigned to receive intravenous trilaciclib 240 mg/m^2 (n=96) or placebo (n=91) prior to GCb on days 1 and 8 every 21 days.

The study did not meet its primary endpoint, reporting no significant difference in OS with trilaciclib vs placebo (median OS, 17.4 vs 17.8 months; HR, 0.91; *P*=.884). Among patients with PD-L1–positive disease (n=37 in each group), median OS with trilaciclib and placebo was 23.1 months and 21.8 months, respectively (HR, 1.0;

Table 3. Overall Survival With Trilaciclib or Placebo in Patients Receiving First-Line Gemcitabine/Carboplatin for Locally Advanced or Metastatic Triple-Negative Breast Cancer: Analysis of Phase 3 PRESERVE 2 Trial

Patient group	Trilaciclib prior to gemcitabine/carboplatin	Placebo prior to gemcitabine/carboplatin
Overall population		
Median (95% CI) OS, mo	**17.4** (12.4-21.3)	**17.8** (13.3-22.5)
HR (95% CI)	**0.91** (0.62-1.3); *P*=.884	
PD-L1–positive disease		
Median (95% CI) OS, mo	**23.1** (9.1-not estimable)	**21.8** (14.9-26.0)
HR (95% CI)	**1.0** (0.51-1.96); *P*=.923	
PD-L1–negative disease		
Median (95% CI) OS, mo	**15.7** (11.9-20.9)	**14.9** (9.9-22.4)
HR (95% CI)	**0.92** (0.57-1.49); *P*=.913	

HR, hazard ratio; mo, months; OS, overall survival; PD-L1, programed death-ligand 1.
Adapted from Goel et al. Presented at: 2024 San Antonio Breast Cancer Symposium; December 10-13, 2024; San Antonio, Texas, USA. Abstract PS2-05.

ABSTRACT SUMMARY Pyrotinib or Placebo in Combination With Trastuzumab and Docetaxel for Untreated HER2+ mBC: Prespecified Final Analysis of PFS of the Phase 3 PHILA Trial

The randomized, placebo-controlled, phase 3 PHILA trial, conducted in China, demonstrated a significant improvement in PFS with the addition of pyrotinib to trastuzumab and docetaxel (HT) in 590 patients with untreated HER2+ mBC (Ma. *BMJ*. 2023.). At SABCS 2024, an update was presented from the PHILA trial after additional follow-up (Abstract GS1-03). After a median follow-up of approximately 34 to 36 months, pyrotinib plus HT continued to show an improvement in investigator-assessed PFS over placebo plus HT (median, 22.1 vs 10.5 months; HR, 0.44; 1-sided *P*<.0001) and a significant improvement in OS (HR, 0.64; 1-sided *P*=.0038). The 4-year OS rate was 74.5% and 64.3%, respectively. The most frequent grade 3 or higher treatment-related AEs reported with pyrotinib plus HT and placebo plus HT, respectively, were decreased neutrophil count (63.0% vs 64.8%) and decreased white blood cell count (53.2% vs 50.9%). Treatment-related serious AEs developed in 27.3% and 7.5% of patients, respectively.

P=.923) and in patients with PD-L1–negative disease (n=59 [trilaciclib] and n=54 [placebo]), median OS was 15.7 months and 14.9 months, respectively (HR, 0.92; *P*=.913).

Overall, the median PFS with trilaciclib and placebo was 6.3 months and 6.4 months, respectively (HR, 1.17; *P*=.434). Confirmed ORR among evaluable patients was 29.5% with trilaciclib (n=95) and 38.2% with placebo (n=89). The median duration of confirmed response was 7.6 months and 8.3 months, respectively.

The rate of grade 4 neutropenia was significantly lower with trilaciclib vs placebo (8.3% vs 28.6%; *P*=.018), as was the percentage of patients requiring granulocyte colony-stimulating factor (G-CSF) (58.3% vs 61.5%; *P*=.031). Results for other myeloprotection endpoints were not significantly different between groups. Any-grade and grade 3 or 4 AEs occurred at a similar frequency between groups. AEs led to discontinuation of any study drug in 22.6% of patients in the trilaciclib group and 25.8% of patients in the placebo group.

Investigators concluded that administering trilaciclib prior to GCb was not associated with a significant improvement in OS in patients with mTNBC but it was associated with a significant reduction in the frequency of grade 4 neutropenia and reduced the need for G-CSF administration.

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The PRESERVE 2 study showed that the addition of trilaciclib was not associated with improved outcomes in patients receiving first-line gemcitabine/carboplatin for locally advanced or metastatic triple-negative breast cancer. These results are different from what was seen in the randomized phase 2 trials and highlight the need for well-powered phase 3 clinical trials for clinical decision making. —Aditya Bardia, MD, MPH

Quality-Adjusted Time Without Symptoms of Disease Progression or Toxicity of Treatment (Q-TWiST) Analysis of Sacituzumab Govitecan vs Chemotherapy in Previously Treated Patients with HR+/HER2– Metastatic Breast Cancer

The randomized, open-label, phase 3 TROPiCS-02 trial demonstrated a significant OS improvement with SG over chemotherapy TPC in patients with HR+/HER2– mBC previously treated with endocrine-based therapy and at least 2 additional systemic therapies.[1] After a median follow-up of 12.5 months, median OS was 14.4 months with SG vs 11.2 months with TPC (HR, 0.79; *P*=.020). SG was also associated with significant improvements over TPC in time to deterioration of global health status and quality of life (median, 4.3

Table 4. Mean Duration of Health States and Q-TWiST (TEAE ≥ 3, Base Case) Associated With Sacituzumab Govitecan vs Chemotherapy in Previously Treated Patients With HR+/HER2– mBC

Duration (95% CI), mo	Sacituzumab govitecan (n=272)	Treatment of physician's choice (n=271)	Difference	*P* value
OS	17.0 (15.8-18.4)	14.8 (13.4-16.2)	**2.3** (0.5-4.3)	.0168
PFS	8.3 (7.0-9.7)	6.0 (4.6-7.7)	**2.3** (0.1-4.2)	.0289
TOX[a]	1.0 (0.8-1.4)	0.8 (0.7-1.0)	**0.2** (–0.1-0.6)	.2590
REL[b]	8.8 (7.5-10.1)	8.7 (7.1-10.4)	**<0.1** (–2.0-2.3)	.9937
TWiST[c]	7.3 (6.1-8.6)	5.2 (3.8-6.8)	**2.1** (0.1-3.9)	.0417
Q-TWiST	9.7 (8.9-10.5)	8.1 (7.3-9.0)	**1.6** (0.5-2.7)	.0067

[a]SG, n=183; TPC, n=130. [b]SG, n=239; TPC, n=241. [c]SG, n=272; TPC, n=271.
HER2–, human epidermal growth factor receptor 2–negative; HR+, hormone receptor–positive; mBC, metastatic breast cancer; mo, months; OS, overall survival; PFS, progression-free survival; Q-TWiST, Quality-adjusted Time Without Symptoms of disease progression or Toxicity of treatment; REL, relapse; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event; TOX, toxicity; TPC, treatment of physician's choice; TWiST, Time Without Symptoms of disease progression or Toxicity of treatment.

Adapted from Rugo et al. Presented at: 2024 San Antonio Breast Cancer Symposium; December 10-13, 2024; San Antonio, Texas, USA. Abstract P2-01-05.

vs 3.0 months; HR, 0.75; *P*=.0059) and fatigue (median, 2.2 vs 1.4 months; HR, 0.73; *P*=.0021).

At SABCS 2024, Hope S. Rugo, MD, presented results of a Quality-adjusted Time Without Symptoms of disease progression or Toxicity of treatment (Q-TWiST) analysis from TROPiCS-02 to further assess the benefits and risks of SG vs chemotherapy while accounting for patient quality of life (QOL) (Table 4).[2] Q-TWiST allows a comparison of treatments that weighs benefit vs risk in the context of patient preferences by incorporating survival differences and toxicity differences and adjusting for QOL utilities.

The analysis found a significant improvement in mean TWiST with SG vs chemotherapy (7.3 vs 5.2 months; *P*=.0417) and in mean Q-TWiST, which accounts for both survival and toxicity adjusted for QOL (9.7 vs 8.1 months; *P*=.0067). The related gain in Q-TWiST with SG of 10.8% exceeded the threshold for clinical importance of greater than 10%.

The analysis also confirmed the previously reported improvements with SG vs TPC in OS (mean, 17.0 vs 14.8 months; *P*=.0168) and PFS (mean, 8.3 vs 6.0 months; *P*=.0289). Initially there was a nonsignificant increase in time spent with grade 3 or higher treatment-emergent AEs (TEAEs) with SG vs TPC; however, this difference stabilized over time.

In sensitivity analyses, the relative gain in Q-TWiST with SG over TPC was primarily driven by differences in the amount of time patients spent experiencing TEAEs. In an analysis of Q-TWiST by follow-up time, the benefits of SG over TPC initially increased before stabilizing out to month 38. The relative Q-TWiST gain with SG over TPC exceeded the clinically important difference threshold at 17 months and remained there until month 38.

Investigators concluded that the long-term survival benefit observed with SG over TPC was attained without reducing QOL and without unmanageable toxicities, and continued to grow over time.

ABSTRACT SUMMARY Effects of Trastuzumab Deruxtecan on HRQOL and Neurological Function in Patients With HER2+ Advanced/Metastatic Breast Cancer With or Without Brain Metastases: DESTINY-Breast12 Results

The phase 3b/4 DESTINY-Breast12 trial demonstrated overall and intracranial clinical activity of trastuzumab deruxtecan in patients with HER2+ mBC, including in patients with brain metastases [Harbeck. *Nat Med*. 2024;30:3717.]. At SABCS 2024, Nadia Harbeck and colleagues reported HRQOL and neurologic function outcomes from DESTINY-Breast12 in patients with and without brain metastases (Abstract PS14-10). At 12 months, more than 50% of patients remained free from deterioration of cognitive, emotional, physical, and social functioning, and of pain scores, regardless of the presence of stable or active baseline brain metastases. Among patients with baseline brain metastases, 86.6% had neurologic stability at baseline that was maintained throughout treatment in 55.1%. The severity of most brain tumor–specific symptoms remained below 3 on a 10-point scale at all timepoints assessed in more than 10 patients. Among patients without brain metastases at baseline, 91.9% had neurologic stability at baseline that was maintained in 72.9%.

Q-TWiST is a robust methodology for assessment of health-related quality of life. This study highlights that sacituzumab govitecan is superior to standard chemotherapy in terms of this quality of life measure, cementing its role in a late-line HR+/HER2– mBC setting. —Aditya Bardia, MD, MPH

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AFT-38 PATINA: A Randomized, Open-Label, Phase 3 Trial to Evaluate the Efficacy and Safety of Palbociclib + Anti-HER2 Therapy + Endocrine Therapy vs Anti-HER2 Therapy + Endocrine Therapy After Induction Treatment for HR+/HER2+ Metastatic Breast Cancer

The CDK4/6 inhibitor palbociclib has demonstrated a clinically meaningful improvement in PFS in patients with HR+/HER2– breast cancer.[1] There is also a rationale for blocking CDK4/6 in patients with HER2+ disease.[2] Moreover, blocking both HER2 and CDK4/6 pathways could enhance antiproliferative activity by suppressing Rb phosphorylation and mTORC1 activity.[2]

At SABCS 2024, Otto Metzger, MD, presented results from the randomized, open-label, phase 3 AFT-38 PATINA trial designed to evaluate the efficacy and safety of adding palbociclib to anti-HER2 therapy and ET in patients with previously untreated HR+/HER+ mBC (Table 5).[3] Patients had received 6 to 8 cycles of treatment including trastuzumab with or without pertuzumab and taxane/vinorelbine. All patients had completed induction chemotherapy and had no evidence of disease progression.

A total of 518 patients were randomly assigned to palbociclib 125 mg orally once daily on days 1 to 21 plus trastuzumab with or without pertuzumab and ET (n=261), or trastuzumab with or without pertuzumab and ET (n=257). The median age of enrolled patients was 53.4 years; 91.7% of patients were White. Patients were

Table 5. Primary Endpoint and Subgroup Analyses of Investigator-Assessed PFS Evaluating Palbociclib + Anti-HER2 Therapy + Endocrine Therapy vs Anti-HER2 Therapy + Endocrine Therapy After Induction Treatment for HR+/HER2+ mBC in Phase 3 AFT-38 PATINA Trial

Patient group	Treatment group	
	Palbociclib + anti-HER2 therapy +ET	Anti-HER2 therapy + ET
All patients		
Events/Total	126/261	136/257
Median (95% CI) PFS, mo	**44.3** (32.4-60.9)	**29.1** (23.3-38.6)
HR (95% CI)	**0.74** (0.58-0.94) Nominal 1-sided *P*-value: .0074	
Prior anti-HER2 therapy		
Events/Total	186/372	
HR (95% CI)	**0.76** (0.57-1.01)	
No prior anti-HER2 therapy		
Events/Total	76/146	
HR (95% CI)	**0.68** (0.543-1.07)	
Best response to induction (complete response or partial response)		
Events/Total	182/355	
HR (95% CI)	**0.76** (0.57-1.02)	
Best response to induction (stable disease)		
Events/Total	80/163	
HR (95% CI)	**0.72** (0.47-1.12)	

ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; HR+, hormone receptor–positive; mBC, metastatic breast cancer; mo, months; PFS, progression-free survival. Adapted from Metzger et al. Presented at: 2024 San Antonio Breast Cancer Symposium; December 10-13, 2024; San Antonio, Texas, USA. Abstract GS2-12.

stratified by pertuzumab use, which was allowed in up to 20% of the population, prior anti-HER2 therapy in the (neo)adjuvant setting, response to induction therapy, and type of ET.

The trial met its primary endpoint, demonstrating a significant improvement in investigator-assessed PFS with palbociclib plus anti-HER2 therapy and ET over anti-HER2 therapy and ET (median PFS, 44.3 vs 29.1 months; HR, 0.74; nominal 1-sided *P*=.0074). The confirmed ORR was also significantly higher with palbociclib plus anti-HER2 therapy and ET over anti-HER2 therapy and ET (29.9% vs 22.2%; *P*=.046), as was the clinical benefit rate (CBR) (89.3% vs 81.3%; *P*=.01). Median OS was not reached in the palbociclib-containing treatment group vs 77 months in the control group; 5-year OS was 74.3% and 69.8%, respectively (HR, 0.86; 95% CI, 0.6-1.24).

The most frequent grade 3 or 4 AEs were neutropenia (67.8% vs 4.4%), decreased white blood cell count (11.9% vs 0%), and diarrhea (11.1% vs 1.6%). The incidence of grade 4 or higher AEs was similar in the palbociclib-containing treatment group and the control group (12.3% vs 8.9%; *P*=.21). The rate of treatment discontinuations due to AEs in the palbociclib-containing treatment group was 7.5%. No treatment-related deaths were reported in either study group.

The investigators concluded that the addition of palbociclib to anti-HER2 therapy and ET was associated with a significant improvement in PFS in patients with previously untreated HR+/HER2+ mBC, with a manageable safety profile.

ABSTRACT SUMMARY NRG-BR004: A Randomized, Double-Blind, Phase 3 Trial of Taxane/Trastuzumab/Pertuzumab With Atezolizumab or Placebo in First-Line HER2+ mBC

Vicente Valero and colleagues presented results of the randomized, phase 3 BR004 trial, which evaluated the addition of atezolizumab to THP in the first-line treatment of patients with HER2+ mBC (Abstract RF3-04). The trial planned to enroll 600 patients to be randomly assigned to atezolizumab or placebo, each with a taxane plus trastuzumab and pertuzumab. In May 2022, after 190 patients had enrolled, the trial closed to enrollment due to poor accrual and an imbalance in grade 5 AEs. At that time, grade 5 events had occurred in 6 patients in the atezolizumab group and no patients in the placebo group, leading to unblinding and discontinuation of atezolizumab/placebo. Total grade 2, 3, and 4 AEs were similar between groups. The 2-year PFS rates with atezolizumab plus THP and placebo plus THP were 54.0% and 45.6%, respectively; 3-year OS rates were 86.4% and 81.7%, respectively.

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The AFT-38 PATINA study demonstrated the role of palbociclib plus ET in the maintenance setting for patients with HR+/HER2– mBC and highlights the role of CDK4/6 inhibition in HER2+ breast cancer also.
—Aditya Bardia, MD, MPH

Imlunestrant, an Oral Selective Estrogen Receptor Degrader, as Monotherapy and Combined With Abemaciclib, for Patients with ER+, HER2– Advanced Breast Cancer, Pretreated With Endocrine Therapy: Results of the Phase 3 EMBER-3 Trial

Currently, fulvestrant is the only selective estrogen receptor degrader (SERD) that is approved as monotherapy and in combination.[1] However, there are limitations with fulvestrant, including limited efficacy in patients with *ESR1* mutations and the requirement for intramuscular administration. Elacestrant is an orally administered SERD with dose-dependent estrogen receptor (ER) agonist and antagonist activity that is FDA approved as a single agent for patients with ER+/HER2–, *ESR1*-mutated advanced or metastatic breast cancer with progression after at least 1 line of ET.[2] The next-generation oral SERD imlunestrant is an ER

Table 6. Primary Endpoint and Subgroup Analyses of Investigator-Assessed PFS Evaluating Imlunestrant as Monotherapy and Combined With Abemaciclib for Patients With ER+, HER2– Advanced Breast Cancer Pretreated With Endocrine Therapy in Phase 3 EMBER-3 Trial

Patient group	Treatment group	
	Imlunestrant	SOC ET
All patients		
Events/Total	237/331	253/330
Median (95% CI) PFS, mo	**5.6** (5.3-7.3)	**5.5** (4.6-5.6)
HR (95% CI)	**0.87** (0.72-1.04); *P*=.12	
Patients with *ESR1*m		
Events/Total	109/138	102/118
Median (95% CI) PFS, mo	**5.5** (3.9-7.4)	**3.8** (3.7-5.5)
HR (95% CI)	**0.62** (0.46-0.82)[a]; *P*<.001	
Patient group	**Treatment group**	
	Imlunestrant + Abemaciclib	**Imlunestrant**
All patients		
Events/Total	114/213	149/213[b]
Median (95% CI) PFS, mo	**9.4** (7.5-11.9)	**5.5** (3.8-5.6)
HR (95% CI)	**0.57** (0.44-0.73), *P*<.001	
Patients with *ESR1*m		
Events/Total	36/67	71/92
Median (95% CI) PFS, mo	**11.1** (7.4-13.7)	**5.5** (3.8-7.2)
HR (95% CI)	**0.53** (0.35-0.80)	
Patients with prior CDK4/6i treatment		
Events/Total	79/139	109/140
Median (95% CI) PFS, mo	**9.1** (7.2-11.2)	**3.7** (2.1-5.5)
HR (95% CI)	**0.51** (0.38-0.68)	
Patients with PI3K pathway mutation[c]		
Events/Total	55/88	70/84
Median (95% CI) PFS, mo	**7.6** (5.6-11.0)	**3.8** (3.1-5.5)
HR (95% CI)	**0.61** (0.42-0.87)	

[a]Due to evidence of non-proportional hazards, a sensitivity analysis of PFS using RMST was conducted. Estimated RSMT at 19.4 months was 7.9 months (95% CI, 6.8-9.1) in the imlunestrant group vs 5.4 months (95% CI, 4.6-6.2) in the SOC ET group (difference, 2.6 months [1.2-3.9]).

[b]Efficacy analyses confined to the imlunestrant population concurrently randomized to imlunestrant plus abemaciclib treatment group.

[c]Includes single nucleotide variants and insertions/deletions of *PIK3CA*, *AKT1*, or *PTEN* analyzed by Guardant 360 ctDNA assay.

CDK4/6i, CDK4/6 inhibitor; ER+, estrogen receptor–positive; *ESR1*m, *ESR1* mutation; HER2–, human epidermal growth factor receptor 2–negative; HR, hazard ratio; mo, months; PFS, progression-free survival; RMST, restricted mean survival time; SOC ET, standard-of-care endocrine therapy.

Adapted from Jhaveri et al. Presented at: 2024 San Antonio Breast Cancer Symposium; December 10-13, 2024; San Antonio, Texas, USA. Abstract GS1-01.

antagonist that penetrates the central nervous system and delivers continuous ER inhibition.[3] The phase 1 EMBER trial demonstrated the activity of imlunestrant plus abemaciclib in patients with ER+/HER2– advanced breast cancer.

At SABCS 2024, and concurrently published in the *New England Journal of Medicine,* Komal L. Jhaveri, MD, and colleagues reported results from the randomized, phase 3 EMBER-3 trial, comparing imlunestrant alone or with abemaciclib against standard-of-care (SOC) ET in patients with ER+/HER2– advanced breast cancer with recurrence while receiving or within 12 months of completing an AI with or without a CDK4/6 inhibitor, or with progression on a first-line AI with or without a CDK4/6 inhibitor, for advanced breast cancer (Table 6).[4,5] No other therapies for advanced breast cancer were permitted. Patients were stratified by prior CDK4/6 inhibitor therapy, visceral metastases, and region, and randomly assigned 1:1:1 to imlunestrant 400 mg once daily (n=331), SOC ET with fulvestrant or exemestane (n=330), or imlunestrant 400 mg once daily plus abemaciclib (n=213). Baseline characteristics were generally well balanced, including in the approximately 32% to 42% of patients with *ESR1* mutations.

The primary endpoint was investigator-assessed PFS in different comparisons and patient populations, including imlunestrant vs SOC ET in patients with *ESR1* mutations, imlunestrant vs SOC ET in all patients, and imlunestrant plus abemaciclib vs imlunestrant alone in all patients.

In patients with *ESR1* mutations, imlunestrant was associated with a significant PFS benefit over SOC ET (median PFS, 5.5 vs 3.8 months; HR, 0.62; *P*<.001) that was consistent across subgroups. In the overall population, there was no significant difference in PFS with imlunestrant vs SOC ET (median PFS, 5.6 vs 5.5 months; HR, 0.87; *P*=.12). However, the combina-

tion of imlunestrant plus abemaciclib was associated with a significant improvement in PFS over imlunestrant alone (median PFS, 9.4 vs 5.5 months; HR, 0.57; *P*<.001), and this benefit was consistent across clinical subgroups and *ESR1* mutation status. OS analyses were immature and are ongoing.

Safety analyses showed a generally favorable toxicity profile with imlunestrant alone or with abemaciclib. The rate of grade 3 or higher TEAEs was 17% with imlunestrant, 21% with SOC ET, and 49% with imlunestrant plus abemaciclib. No oral SERD-specific events such as ocular or cardiac toxicities were noted. The rate of discontinuation due to AEs was 4%, 1%, and 6%, respectively. Investigators concluded that imlunestrant was associated with a significant PFS improvement over SOC ET in patients with *ESR1*-mutated ER+/HER2– advanced breast cancer, and that imlunestrant plus abemaciclib provides a significant PFS improvement over imlunestrant regardless of *ESR1* mutation status.

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ABSTRACT SUMMARY Elacestrant vs SOC in ER+, HER2– Advanced or Metastatic Breast Cancer With *ESR1*-Mutated Tumors: *ESR1* Allelic Frequencies and Clinical Activity From the Phase 3 EMERALD Trial

Aditya Bardia presented an analysis of the clinical benefit of single-agent elacestrant based on *ESR1* variant allele frequency (VAF) in the phase 3 EMERALD trial (Abstract P1-01-25). The EMERALD trial previously reported a significant improvement in PFS with elacestrant vs SOC ET in patients with ER+/HER2– mBC with *ESR1*-mutated tumors following progression on prior ET plus CDK4/6 inhibitor (HR, 0.55; *P*=.0005) [Bidard. *J Clin Oncol*. 2022;40:3246.]. The current analysis found that the PFS improvement with elacestrant vs SOC ET occurred regardless of the *ESR1* VAF (high vs low) or the type of *ESR1* mutation variant. The PFS benefit with elacestrant vs SOC ET was also observed in patients with coexisting *ESR1* and *PIK3CA* mutations (median PFS, 5.45 vs 1.94 months; HR, 0.423; 95% CI, 0.176-0.941), despite the *ESR1* mutation VAF being lower than the *PIK3CA* mutation VAF in 89% of these patients.

ABSTRACT SUMMARY SARELIFE Study: Safety and Efficacy of Sacituzumab Govitecan in Pretreated mTNBC—A Multicentric, Real-Life Study

The observational SARELIFE study assessed the efficacy and safety of SG in a real-world population of 128 Italian patients with mTNBC (Abstract P3-12-07). The median patient age was 58 years (range, 30-86). Patients had received a median of 2 prior lines of treatment (range, 0-9). In the safety analysis (n=122), the most frequent AEs were neutropenia (51.2%), fatigue (47.6%), nausea (43.9%), diarrhea (34.1%), anemia (28%), and febrile neutropenia (6.1%). One case of grade 3 pneumonitis was reported. There were no grade 5 AEs. After a median follow-up of 12.7 months, the median PFS and OS were 5.9 months and 14.6 months, respectively. Best responses in the 116 evaluable patients were complete response (0.9%), partial response (31%), stable disease (38.8%), and progressive disease (29.3%). The median time to onset of first AE was 21 days. Four patients (3.3%) discontinued SG due to toxicity.

The EMBER-3 study highlights the role of a novel oral SERD, imlunestrant. The results, similar to what was seen previously with other studies including EMERALD, demonstrated that imlunestrant monotherapy was superior to standard ET in patients with *ESR1*-mutated advanced breast cancer. This study also highlights the role of combination therapy with abemaciclib in this setting and we eagerly await regulatory decision.

—Aditya Bardia, MD, MPH