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A SPECIAL MEETING REVIEW EDITION

Highlights in Metastatic Urothelial Cancer From the European Society for Medical Oncology Congress 2023

A Review of Selected Presentations From the ESMO Congress 2023 • October 20-24, 2023 • Madrid, Spain

Special Reporting on:

- The Double Antibody Drug Conjugate (DAD) Phase I Trial: Sacituzumab Govitecan (SG) Plus Enfortumab Vedotin (EV) as ≥ Second-Line Therapy for Metastatic Urothelial Carcinoma (mUC)
- Efficacy of Paclitaxel With Tremelimumab +/- Durvalumab in Metastatic Urothelial Carcinoma After Progression on Platinum Chemotherapy and Anti-PD-(L)1
- EV-302/KEYNOTE-A39: Open-Label, Randomized Phase III Study of Enfortumab Vedotin in Combination With Pembrolizumab (EV+P) vs Chemotherapy (Chemo) in Previously Untreated Locally Advanced Metastatic Urothelial Carcinoma (la/mUC)
- Nivolumab Plus Gemcitabine-Cisplatin Versus Gemcitabine-Cisplatin Alone for Previously Untreated Unresectable or Metastatic Urothelial Carcinoma: Results From the Phase III CheckMate 901 Trial
- Phase III THOR Study: Results of Erdafitinib vs Pembrolizumab in Pretreated Patients With Advanced or Metastatic Urothelial Cancer With Select Fibroblast Growth Factor Receptor Alterations (FGFRalt)
- Erdafitinib (erda) vs Chemotherapy (chemo) in Patients (pts) With Advanced or Metastatic Urothelial Cancer (mUC) With Select FGFR Alterations (FGFRalt): Subgroups From the Phase III THOR Study
- Real-World Efficacy and Treatment Patterns of Enfortumab Vedotin and Avelumab

PLUS Meeting Abstract Summaries

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ON THE WEB:
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The first and only Trop-2–directed ADC for mUC[1]

Elevate the Possibilities With TRODELVY®

mUC

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

IMPORTANT SAFETY INFORMATION

BOXED 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.**

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/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. Administer G-CSF as clinically indicated or indicated in Table 1 of USPI.

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.

Nearly 30% of patients responded, with ~5% experiencing complete response[1]

TRODELVY®
sacituzumab govitecan-hziy
180 mg for injection

TRODELVY was evaluated in TROPHY, a Phase 2, single-arm, open-label, multicenter study (N=112) in patients with locally advanced or mUC who received prior treatment with a platinum-containing chemotherapy and either PD-1 or PD-L1 inhibitor

ORR*

27.7%

(95% CI: 19.6–36.9)
Complete Response (CR): 5.4%
Partial Response (PR): 22.3%
N=112

Median DOR*

7.2 months (range 1.4+, 13.7)

(95% CI: 4.7–8.6)
Number of responders: 31
+: denotes ongoing

See more data from the TROPHY study at **TRODELVYHCP.com**

*By IRA based on RECIST 1.1.

ADC=antibody-drug conjugate; CI=confidence interval; DOR=Duration of Response; IRA=independent review assessment; ORR=Objective Response Rate; RECIST=Response Evaluation Criteria in Solid Tumors.

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 TROPHY study, the most common adverse reactions (incidence ≥25%) were diarrhea, fatigue, nausea, any infection, alopecia, decreased appetite, constipation, vomiting, rash, and abdominal pain. The most frequent serious adverse reactions (SAR) (≥5%) were infection (18%), neutropenia (12%, including febrile neutropenia in 10%), acute kidney injury (6%), urinary tract infection (6%), and sepsis or bacteremia (5%). SAR were reported in 44% of patients, and 10% discontinued due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence ≥25%) in the TROPHY study were reduced neutrophils, leukocytes, and lymphocytes.

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.

Reference: 1. TRODELVY [package insert]. Foster City, CA: Gilead Sciences, Inc.; February 2023.

GILEAD | Oncology

Scan the QR code to watch a TROPHY study investigator discuss the data

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.

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GILEAD

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sacituzumab govitecan-hziy
180 mg for injection

The Double Antibody Drug Conjugate (DAD) Phase I Trial: Sacituzumab Govitecan (SG) Plus Enfortumab Vedotin (EV) as ≥ Second-Line Therapy for Metastatic Urothelial Carcinoma (mUC)

Metastatic urothelial cancer (mUC) continues to present treatment challenges.[1] However, the addition of immune checkpoint inhibitors (ICIs) and antibody-drug conjugates (ADCs) has improved the outlook for patients with mUC. ADCs that have received approval in the United States for the treatment of mUC include sacituzumab govitecan (SG) and enfortumab vedotin (EV).[2,3] In SG, an antibody that binds to Trop-2 is conjugated by a hydrolyzable linker to SN-38, the active metabolite of irinotecan.[4] In EV, an antibody against nectin-4 is conjugated by a hydrolyzable linker to monomethyl auristatin E, a microtubule-disrupting agent.[5] These 2 ADCs have different antibody-binding targets, different mechanisms of action, and different toxicity profiles, and they are typically used sequentially in the treatment of mUC.

The phase 1 Double Antibody Drug Conjugate (DAD) trial evaluated the safety and maximum tolerated dose (MTD) of SG plus EV in patients with treatment-resistant mUC.[6] The investigator-initiated trial enrolled patients who had mUC that had progressed on platinum plus immunotherapy or who were ineligible to receive cisplatin. The patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 and had received at least 1 prior line of therapy. The trial design was based on a Bayesian Optimal Interval strategy. SG and EV were administered on days 1 and 8 of each 21-day cycle. Dose levels of SG ranged from 6 to 10 mg/kg, and dose levels of EV ranged from 1.0 to 1.25 mg/kg. Patients were required to receive both drugs on day 1 of each cycle to be able to continue on the study therapy. The primary endpoint was to assess the feasibility of the double ADC combination on the basis of the MTD determined during cycle 1 of the trial.

The DAD trial enrolled 23 patients with a median age of 70 years (range, 41-88). Of these, 78% were male and 83% were white. The primary site of cancer was the bladder in 70% of the patients, upper tract in 26%, and urethra in 4%. Pure urothelial cell histology was noted in 70% of the patients. The number of prior lines of therapy was 3 to 5 in 48% of the patients, 2 in another 48%, and 1 in 4%. The most common metastatic sites included the lymph nodes (74%), bone (26%), and liver (26%). The study enrolled 9 patients at dose level 1 (SG at 8 mg/kg plus EV at 1.0 mg/kg), 8 patients at dose level 2 (SG at 8 mg/kg plus EV at 1.25 mg/kg), and 5 patients at dose level 3 (SG at 10 mg/kg plus EV at 1.25 mg/kg). Dose level 3 was determined to be the MTD. Dose-limiting toxicities observed in this cohort included febrile neutropenia, mucositis, and delay in treatment. Across all dose levels, the most common adverse events (AEs) observed with the double ADC therapy were diarrhea, anemia, and neutropenia. One patient died of pneumonitis, possibly as a consequence of EV therapy in the setting of other medical problems. Any degree of shrinkage of target lesions occurred in 20 patients (87%). The objective response rate (ORR) was 70%. After a median follow-up of 14.9 months, 3 patients had a complete response (CR) and 13 had a partial response (PR) (Table 1).

Table 1. Efficacy of SG and EV in Patients With mUC in the DAD Study

	Overall (N=23)	DL1 (N=9)	DL2 (N=8)	DL3 (N=5)
ORR, % (95% CI)	70 (47-87)	78 (40-97)	75 (35-97)	50 (12-88)
Best overall response				
CR	3	1	1	1
PR	13	6	5	2
SD	3	1	1	1
PD	3	1	1	1
NE	1	0	0	1
Total	23	9	8	6

CR, complete response; DL, dose level; EV, enfortumab vedotin; mUC, metastatic urothelial carcinoma; NE, not evaluated; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SG, sacituzumab govitecan.

Adapted from McGregor et al. Abstract 2360O. Presented at: ESMO Congress 2023; October 20-24, 2023; Madrid, Spain.[6]

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Efficacy of Paclitaxel With Tremelimumab +/- Durvalumab in Metastatic Urothelial Carcinoma After Progression on Platinum Chemotherapy and Anti-PD-(L)1

Therapeutic options for patients with mUC after progression on platinum plus immune checkpoint therapy are limited.[1,2] Tremelimumab is an anti-cytotoxic T-lymphocyte–associated protein 4 (CTLA4) antibody with single-agent activity in patients who have mUC.[3] The phase 1/2 ICRA trial evaluated tremelimumab in combination with paclitaxel and/or durvalumab in patients with previously treated mUC.[4] The trial enrolled 20 patients in arm A, 12 in arm B, and 12 in arm C. Patients in arm A received paclitaxel at 70 mg/m^2 plus 750 mg of tremelimumab; patients in arm B received paclitaxel at 70 mg/m^2, 300 mg of tremelimumab, and 1500 mg of durvalumab; and patients in arm C received 750 mg of tremelimumab alone. The primary objective of the trial was the confirmed ORR according to RECIST 1.1 criteria.[5]

Across the 3 arms, most of the patients were male (75%-95%), and the median age ranged from 64 to 71 years (range, 56-78). Liver metastasis was observed in 20% of the patients in arm A, 0% in arm B, and 17% in arm C. Between 25% and 33% of the patients had received 3 or more prior lines of therapy. The 2 grade 3 treatment-related AEs observed during the run-in phase of the study were both blood transfusions for anemia. During the entire study, the most common immune-related AEs of any grade were rash and pruritus, hypothyroidism, and colitis. The most common chemotherapy-related AEs of any grade were nausea/fatigue, anemia, and neuropathy. The rates of grade 3/4

Table 2. Efficacy of Paclitaxel Plus Tremelimumab With or Without Durvalumab in Patients With mUC

	Arm A **n=20[a]** **Paclitaxel 70mg/m2** **Tremelimumab 750mg**	**Arm B** **n=12** **Paclitaxel 70 mg/m2** **Tremelimumab 300 mg** **Durvalumab 1500 mg**	**Arm C** **n=12** **Tremelimumab 750 mg**
ORR, n (%) **88% CI**	**5 (26)** **14-37**	**1 (8)** **0.5-33**	**1 (8)** **0.5-33**
Clinical benefit rate, n (%) 88% CI	6 (32) 18-42	4 (33) 13-60	2 (17) 3-42
Best overall response,[b] n (%) CR PR SD Progression	1 (5) 7 (35) 6 (30) 6 (30)	0 (0) 4 (33) 6 (50) 2 (17)	1 (8) 0 (0) 3 (25) 8 (67)

[a]Of 20 evaluable patients; 1 was unevaluable after unconfirmed PR.
[b]unconfirmed response.
CR, complete response; mUC, metastatic urothelial carcinoma; ORR, objective (confirmed) response rate; PR, partial response; SD, stable disease.
Adapted from Einerhand et al. Abstract LBA103. Presented at: ESMO Congress 2023; October 20-24, 2023; Madrid, Spain.[4]

treatment-related AEs were 55% in arm A, 67% in arm B, and 33% in arm C. The rates of grade 3/4 immune-related AEs were 30% in arm A, 25% in arm B, and 33% in arm C.

The confirmed ORR was 26% in arm A (88% CI, 14%-37%), 8% in arm B (88% CI, 0.5%-33%), and 8% in arm C (88% CI, 0.5%-33%) (Table 2). A reduction in tumor size was observed in 50% of the patients in arm A, 67% of those in arm B, and 17% of those who received tremelimumab monotherapy (arm C). After a median follow-up of 9.5 months, the median overall survival (OS) was 16.0 months (95% CI, 4.4-27.5) in arm A, 13.9 months (95% CI, 9.5-18.3) in arm B, and 6.6 months (95% CI, 0.0-14.8) in arm C (*P*=.68). Median progression-free survival (PFS) was 5.7 months (95% CI, 4.0-7.3) in arm A, 6.5 months (95% CI, 3.7-9.4) in arm B, and 2.8 months (95% CI, 0.0-5.7) in arm C (*P*=.27).

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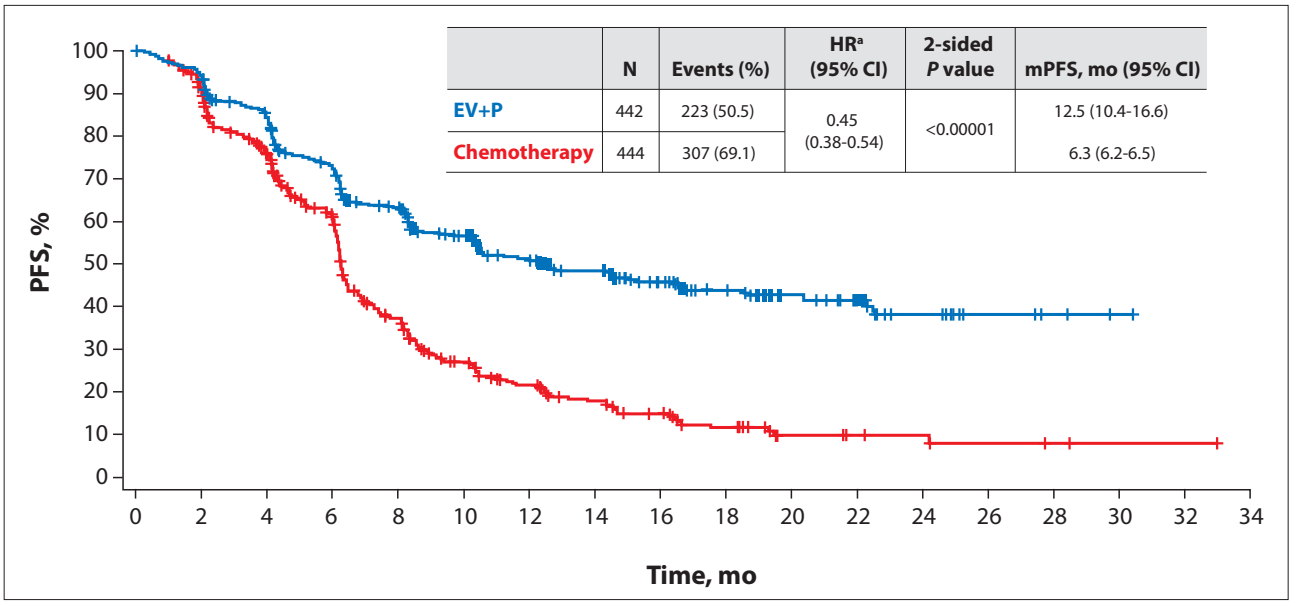
EV-302/KEYNOTE-A39: Open-Label, Randomized Phase III Study of Enfortumab Vedotin in Combination With Pembrolizumab (EV+P) vs Chemotherapy (Chemo) in Previously Untreated Locally Advanced Metastatic Urothelial Carcinoma (la/mUC)

Among patients with mUC at diagnosis, the 5-year survival rate is only 8.3%.[1] Targeted therapies are being investigated as alternatives to platinum compounds for the treatment of patients with locally advanced or metastatic urothelial carcinoma (la/mUC). EV is an ADC that binds to nectin-4 and delivers monomethyl auristatin E, causing apoptosis of the targeted cell.[2] Pembrolizumab is an ICI that binds to programmed death 1 (PD-1).[3] The combination of these 2 antibodies was approved for the treatment of patients with la/mUC who are ineligible for cisplatin therapy.

The international phase 3 EV-302/KEYNOTE-A39 trial evaluated EV plus pembrolizumab (EV+P) as first-line therapy in patients with la/mUC regardless of their cisplatin eligibility and level of programmed death ligand 1 (PD-L1) expression.[4] Stratification factors included cisplatin eligibility, PD-L1 expression level, and liver metastasis. Investigators evenly randomized 886 patients to receive either 35 cycles of EV+P or a maximum of 6 cycles of chemotherapy consisting of cisplatin or carboplatin plus gemcitabine. The 2 primary endpoints were PFS by blinded independent review and OS. Baseline characteristics were well balanced between the 2 arms. Of the total number of patients, 77% were male and 68% were White. The median age was 69 years (range, 22-91). The primary tumor location was the lower tract in 69% to 76% of patients in the 2 arms. More than half

ABSTRACT SUMMARY: Split-Dose Cisplatin Plus Gemcitabine Use and Associated Clinical Outcomes in the First-Line (1L) Treatment of Locally Advanced or Metastatic Urothelial Cancer (la/mUC): Results of a Retrospective Observational Study in Germany (CONVINCE)

The retrospective observational CONVINCE study assessed real-world outcomes in patients with locally advanced or mUC who received split-dose cisplatin plus gemcitabine (Abstract 2388P). The study included patients who received first-line platinum-based chemotherapy from 2019 to 2020 at 27 treating institutions in Germany. Of 124 patients who received first-line platinum-based therapy with gemcitabine, 27 (21.8%) received split-dose cisplatin, 75 (60.5%) received standard cisplatin, and 22 (17.7%) received carboplatin. The median follow-up was 16.5 months. After adjustment for age, sex, ECOG performance status, and comorbidities, no significant differences in real-world median PFS were observed between the split-dose cohort and either standard-dose cohort (*P*>.20). Real-world median OS was numerically lower with the split dose than with the standard dose of cisplatin (14.4 vs 18.8 months; *P*=.06).



	N	Events (%)	HR[a] (95% CI)	2-sided *P* value	mPFS, mo (95% CI)
EV+P	442	223 (50.5)	0.45 (0.38-0.54)	<0.00001	12.5 (10.4-16.6)
Chemotherapy	444	307 (69.1)			6.3 (6.2-6.5)

Figure 1. The PFS per BICR of EV+P vs chemotherapy in patients with previously untreated laUC or mUC from the phase 3 EV-302/KEYNOTE-A39 study.

[a]Calculated with a stratified Cox proportional hazards model; a hazard ratio of less than 1 favors the EV+P arm.

BICR, blinded independent central review; EV, enfortumab vedotin; HR, hazard ratio; laUC, locally advanced urothelial carcinoma; mo, months; mPFS, median progression-free survival; mUC, metastatic urothelial carcinoma; P, pembrolizumab.

Adapted from Powles et al. Abstract LBA6. Presented at: ESMO Congress 2023; October 20-24, 2023; Madrid, Spain.[4]

(54%) of the patients were ineligible for cisplatin, and the majority (72%) had visceral metastasis.

Compared with chemotherapy, treatment with EV+P reduced the risk of disease progression or death by 55% (hazard ratio [HR], 0.45; *P*<.00001). The median PFS was 12.5 months (95% CI, 10.4-16.6) with EV+P vs 6.3 months (95% CI, 6.2-6.5) with chemotherapy (Figure 1). A clear PFS benefit was observed in prespecified subgroups based on age, sex, ECOG performance status, primary tumor site, liver metastasis, PD-L1 expression level, and cisplatin eligibility. After a median follow-up of 17.2 months, the dual-antibody combination also yielded a superior OS in comparison with chemotherapy (31.5 vs 16.1 months; HR, 0.47; *P*<.00001). An OS benefit was observed with EV+P vs chemotherapy in patients who were eligible for cisplatin therapy (HR, 0.53; 95% CI, 0.39-0.72) as well as in those who were not (HR, 0.43; 95% CI, 0.31-0.59). EV+P also yielded a superior OS benefit vs chemotherapy in patients with a high level of PD-L1 expression (HR, 0.49; 95% CI, 0.37-0.66) or a low level of PD-L1 expression (HR, 0.44; 95% CI, 0.31-0.61). In a blinded independent review, the CR rate was 29.1% with the dual-antibody combination vs 12.5% with chemotherapy, and the PR rate was 38.7% with the dual-antibody combination vs 32.0% with chemotherapy. The most

ABSTRACT SUMMARY: Platinum Rechallenge in the Era of Immune Checkpoint Inhibitor in Locally Advanced/Metastatic Urothelial Carcinoma: Multicenter Retrospective Study

A retrospective multicenter study of Korean patients with mUC evaluated outcomes in those who initially received platinum-based chemotherapy, followed by an ICI, followed by rechallenge with another platinum-based therapy (Abstract 2384P). Rechallenge regimens could include gemcitabine plus cisplatin or carboplatin (n=28); methotrexate, vinblastine, and doxorubicin plus cisplatin or carboplatin (MVAC) or dose-dense MVAC (n=35); or other (n=3). After rechallenge with platinum, the ORR was 40.9%, the median PFS was 4.5 months, and the median OS was 8.7 months. Among 24 patients who received gemcitabine plus platinum as first-line and rechallenge therapy, the ORR after rechallenge was 66.7%. The median OS was significantly longer in patients who received ICI therapy between first-line and rechallenge regimens than in those who did not (12.4 vs 6.5 months; *P*=.004).

common treatment-related AEs of grade 3 or higher in the EV+P arm were maculopapular rash (7.7%), anemia (4.8%), diarrhea (3.6%), and peripheral sensory neuropathy (3.6%). In the chemotherapy arm, the most common treatment-related AEs of at least grade 3 were hematologic, including anemia (31.4%), neutropenia (20.0%), and thrombocytopenia (19.4%). In each arm, 4 patients died of a treatment-related AE. These included asthenia, diarrhea, immune-mediated lung disease, and multiple organ dysfunction syndrome in the EV+P arm and febrile neutropenia, myocardial infarction, neutropenic sepsis, and sepsis in the chemotherapy arm. In the EV+P arm, the most common AEs of special interest of at least grade 3 were skin reactions (15.5%), peripheral neuropathy (6.8%), and hyperglycemia (6.1%).

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Nivolumab Plus Gemcitabine-Cisplatin Versus Gemcitabine-Cisplatin Alone for Previously Untreated Unresectable or Metastatic Urothelial Carcinoma: Results From the Phase III CheckMate 901 Trial

The mechanisms of action of targeted therapies are different from those of chemotherapy in the treatment of mUC.[1-3] The international, open-label, phase 3 CheckMate 901 trial investigated nivolumab plus cisplatin/gemcitabine vs chemotherapy alone as first-line therapy in patients with unresectable or mUC.[4] The trial enrolled 608 patients with treatment-naive unresectable or mUC involving the renal pelvis, ureter, urethra, or bladder. All patients were eligible for cisplatin therapy and had an ECOG performance status of 0 or 1. Stratification factors included level of tumor PD-L1 expression and liver metastasis. All patients received

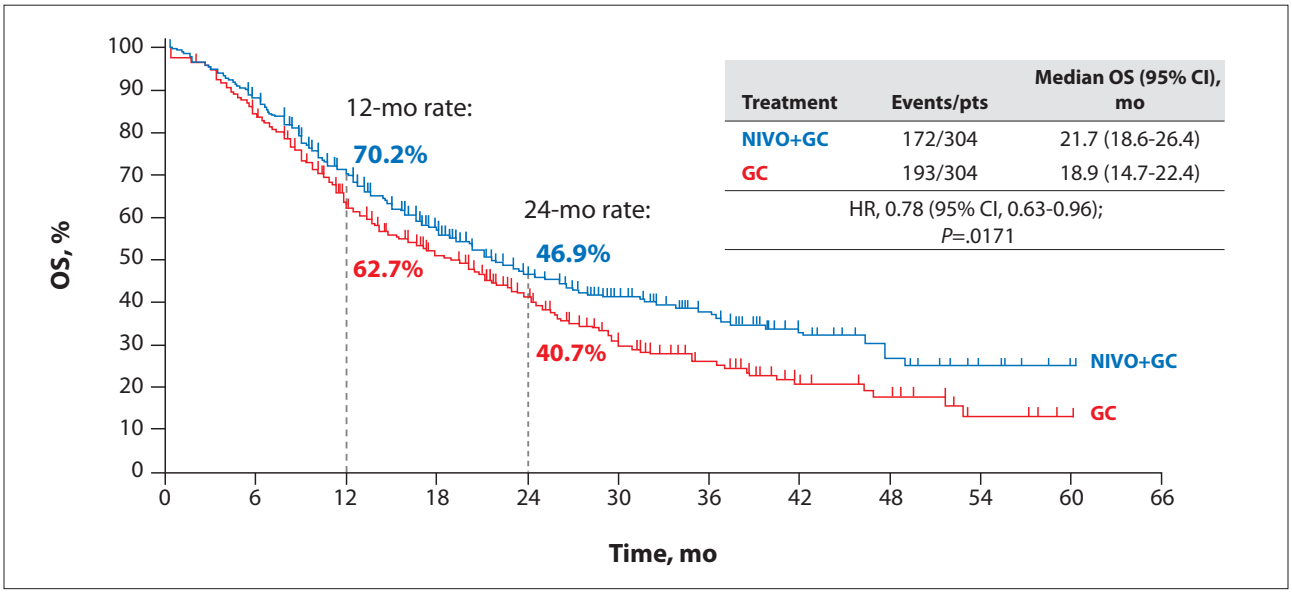

Figure 2. The OS of NIVO plus GC vs GC alone in patients with previously untreated unresectable or mUC from the phase 3 CheckMate 901 trial.

GC, gemcitabine/cisplatin; HR, hazard ratio; mo, months; mUC, metastatic urothelial carcinoma; NIVO, nivolumab; OS, overall survival. Adapted from van der Heijden et al. Abstract LBA7. Presented at: ESMO Congress 2023; October 20-24, 2023; Madrid, Spain.[4]

gemcitabine (1000 mg/m^2) on days 1 and 8 plus cisplatin (70 mg/m^2) on day 1 every 3 weeks for up to 6 cycles. Patients in the experimental arm also received nivolumab (360 mg) on day 1 of each cycle. After 6 cycles of therapy, patients in the nivolumab arm received nivolumab (480 mg) every 4 weeks until disease progression, unacceptable toxicity, or withdrawal, for up to 24 months. The primary endpoints were OS and PFS according to blinded independent review.

Baseline characteristics were well balanced between the 2 arms. Patients had a median age of 65 years (range, 32-86), and the majority were White (69%-74%). Most of the primary tumors were located in the bladder (72%-77%), and 64% of the patients in each arm had liver metastasis. The level of PD-L1 expression was less than 1% in 64% of the patients. The median follow-up was 33.6 months (range, 7.4-62.4). The median duration of study treatment was 7.4 months (range, 0.0-47.9) in the nivolumab combination arm vs 3.7 months (range, 0.0-14.2) in the chemotherapy arm. The proportion of patients who completed 6 cycles of therapy was 74% in the nivolumab combination arm vs 55% in the chemotherapy arm.

The CheckMate 901 trial met its primary endpoint, demonstrating superior OS with nivolumab plus chemotherapy vs chemotherapy alone (21.7 vs 18.9 months; HR, 0.78; 95% CI, 0.63-0.96; *P*=.0171) (Figure 2). A significant benefit with the nivolumab combination vs chemotherapy alone was observed among patients younger than 65 years, male patients, those with an ECOG performance status of 0, patients without liver metastasis, and those who were treatment-naive at baseline. The median PFS was 7.9 months (95% CI, 7.6-9.5) with nivolumab plus chemotherapy vs 7.6 months (95% CI, 6.1-7.8) with chemotherapy alone (HR, 0.72; 95% CI, 0.59-0.88; *P*=.0012). In most of the subgroups examined, median PFS was superior with nivolumab plus chemotherapy vs chemotherapy alone. In the nivolumab combination arm vs the chemotherapy arm, the CR rate was 21.7% vs 11.8% and the PR rate was 35.9% vs 31.3%, respectively. The median duration of response was longer with the addition of nivolumab to chemotherapy than with chemotherapy alone (9.5 vs 7.3 months). The rate of AEs of grade 3 or higher was 62% with the nivolumab combination vs 52% with chemotherapy alone. In the nivolumab combination arm, the most common AEs of grade 3 or higher were anemia (22%), neutropenia (19%), and decreased neutrophil count (14%). In the chemotherapy-only arm, the most common AEs of at least grade 3 were anemia (18%), neutropenia (15%), and decreased neutrophil count (11%).

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Phase III THOR Study: Results of Erdafitinib vs Pembrolizumab in Pretreated Patients With Advanced or Metastatic Urothelial Cancer With Select Fibroblast Growth Factor Receptor Alterations (FGFRalt)

The fibroblast growth factor receptor (FGFR) is altered in approximately one-fifth of patients with advanced UC or mUC of the bladder.[1-4] Erdafitinib is an orally administered selective tyrosine kinase inhibitor (TKI) of FGFR1-4 that is approved to treat advanced or mUC with *FGFR* alteration after progression on platinum-containing therapy.[5] The open-label, international, phase 3 THOR study investigated the safety and efficacy of erdafitinib in previously treated patients with unresectable advanced or mUC.[6-8] In cohort 1, a total of 200 patients were randomized to receive erdafitinib monotherapy vs the physician's choice of chemotherapy.[6,8] Results from cohort 1 showed a superior median OS (12.1 vs 7.8 months; *P*=.0050) and a superior median PFS (5.6 vs 2.7 months; *P*=.0002) with the TKI vs chemotherapy.

Cohort 2 of the THOR trial included 351 patients with unresectable or mUC who were evenly randomized into 2 arms.[7] Enrolled patients had confirmed disease progression on 1 prior regimen, no prior exposure to anti–PD-L1 therapy, and 1 or 2 specified *FGFR3* translocations or mutations. Stratification factors

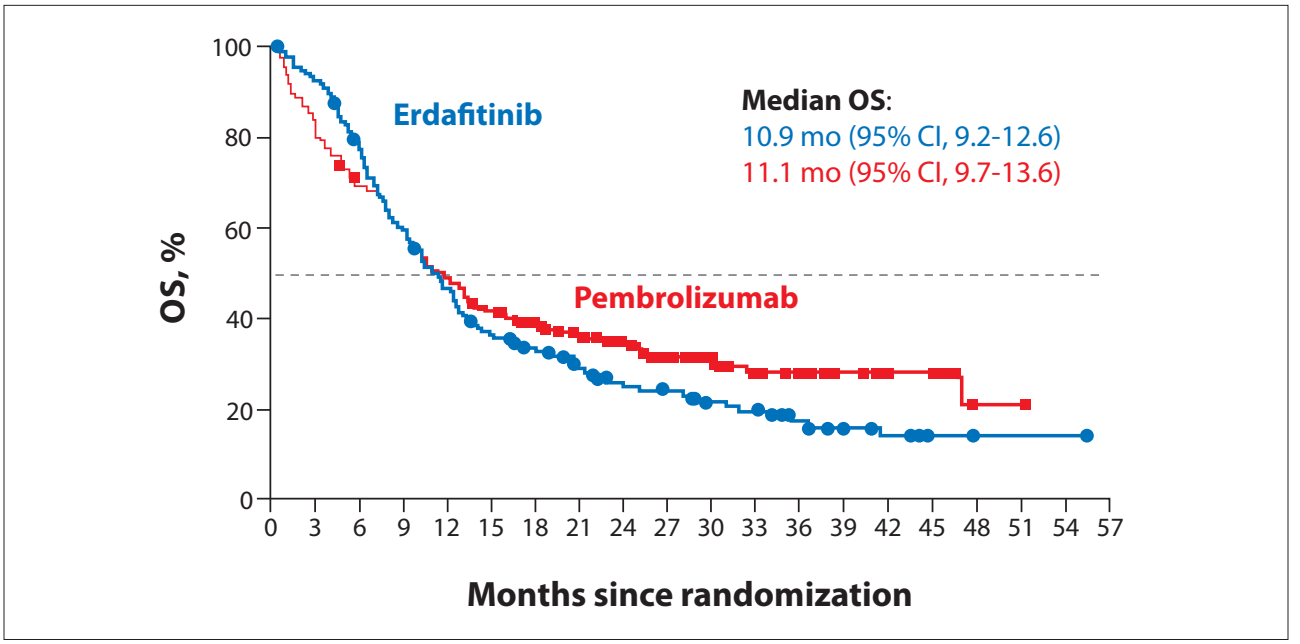

Figure 3. OS with erdafitinib vs pembrolizumab in patients with mUC and select *FGFR* alterations from the phase 3 THOR study.
mo, months; mUC, metastatic urothelial carcinoma; OS, overall survival.
Adapted from Siefker-Radtke et al. Abstract 2359O. Presented at: ESMO Congress 2023; October 20-24, 2023; Madrid, Spain.[7]

included region, performance status, and disease distribution. Patients in arm 1 received erdafitinib (8 mg, daily) with dose escalation up to 9 mg daily on the basis of pharmacodynamic data. Patients in arm 2 received pembrolizumab (200 mg, once every 3 weeks). The primary endpoint was OS. Baseline characteristics were well balanced between the 2 arms. Patients had a median age of 67.5 years (range, 31-87), and the majority were male (75%-81%). More than half of the patients (54%-63%) were White, and the primary tumor was in the upper tract in one-fourth of patients. Visceral metastasis was noted in 67% of patients in the erdafitinib arm and 76% of patients in the pembrolizumab arm. Approximately 90% of the patients had a PD-L1 combined positive score (CPS) of less than 10.

The trial failed to meet its primary endpoint, showing similar median OS with erdafitinib vs pembrolizumab (10.9 vs 11.1 months, respectively; HR, 1.18; 95% CI, 0.9-1.5; *P*=.18) (Figure 3). Median OS was also similar with erdafitinib vs pembrolizumab in subgroups based on age, sex, primary tumor location, FGFR or PD-L1 status, and other factors. The median PFS was 4.4 months with erdafitinib vs 2.7 months with pembrolizumab (HR, 0.88; 95% CI, 0.70-1.10; *P*=.26). In the erdafitinib arm, the ORR was 40%, including a CR rate of 6.3%. In the pembrolizumab arm, the ORR was 21.6%, including a CR rate of 4.5%. The median duration of response was 4.3 months with the TKI vs 14.4 months with the ICI. Safety outcomes were consistent with prior results in this patient setting.

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Erdafitinib (erda) vs Chemotherapy (chemo) in Patients (pts) With Advanced or Metastatic Urothelial Cancer (mUC) With Select FGFR Alterations (FGFRalt): Subgroups From the Phase III THOR Study

ICIs are used in both first- and second-line settings to treat mUC; however, treatment options are limited after progression.[1] In cohort 1 of the phase 3 THOR study, researchers investigated erdafitinib vs the physician's choice of chemotherapy in patients with mUC harboring *FGFR* alteration.[2,3] Enrolled patients had unresectable or mUC, prior anti–PD-L1 therapy, and disease progression after 1 or 2 prior lines of therapy. Included patients had 1 or 2 specified alterations in the *FGFR* gene. Patients in the experimental arm received erdafitinib (8 mg, daily), with the dose increased to 9 mg on the basis of pharmacodynamic results. Patients in the control arm received the physician's choice of chemotherapy. Stratification factors included region, performance status, and disease distribution. The primary endpoint was OS.

An earlier interim analysis of data from cohort 1 showed both a superior median OS (12.1 vs 7.8 months; HR, 0.64; 95% CI, 0.47-0.88; *P*=.005) (Figure 4) and a superior median PFS (5.6 vs 2.7 months; HR, 0.58; 95% CI, 0.44-0.78; *P*=.0002) with erdafitinib vs chemotherapy.[3] To further elucidate the activity of erdafitinib in this patient setting, subgroup analysis was performed.[2] The analysis showed a superior OS benefit with erdafitinib vs chemotherapy in most subgroups based on age, sex, *FGFR* alteration, and primary tumor location. Patients with a PD-L1 CPS of less than 10 experienced a benefit with erdafitinib vs chemotherapy; however, only 7 patients had a PD-L1 CPS of 10 or higher, and the analysis favored chemotherapy in these patients. Erdafitinib generally yielded a superior OS benefit in comparison with chemotherapy in subgroups based on the following: number of lines of prior treatment; prior exposure to platinum, docetaxel, or vinflunine; prior anti–PD-L1 therapy; and the presence of bone, liver, or lung metastasis, but not all of the OS comparisons reached statistical significance.

Observed toxicities were consistent with previously reported safety profiles for erdafitinib and chemotherapy. Approximately 46% of patients in each arm had treatment-related grade 3/4 AEs. Serious treatment-related AEs were more common in the chemotherapy arm (24.1% vs 13.3%), and treatment-related deaths were also more common in the chemotherapy arm (6 vs 1). AEs related to treatment with erdafitinib were generally well managed with dose modifications and supportive care. The most common AEs of any grade in the erdafitinib arm were hyperphosphatemia (78.5%), diarrhea (54.8%), and stomatitis (45.9%). The most common AEs of any grade in

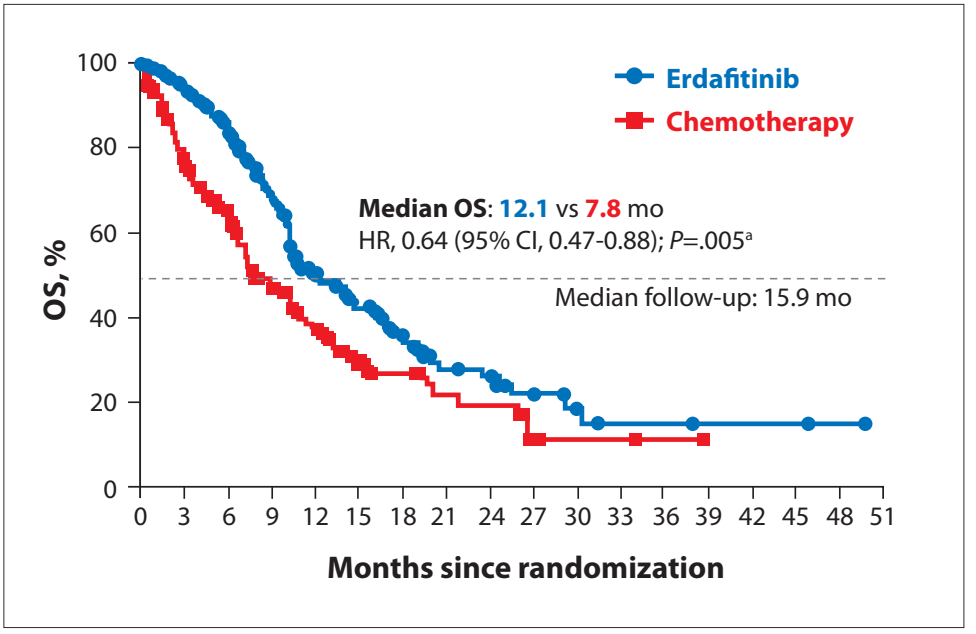

Figure 4. OS with erdafitinib vs chemotherapy in a subgroup of patients with advanced or mUC with select *FGFR* alterations from the phase 3 THOR study.
[a]the significant level for stopping for efficacy was *P*=.019, corresponding to an HR of 0.69.
FGFR, fibroblast growth factor receptor gene; HR, hazard ratio; mUC, metastatic urothelial carcinoma.
Adapted from Loriot et al. Abstract 2362MO. Presented at: ESMO Congress 2023; October 20-24, 2023; Madrid, Spain.[2]

the chemotherapy arm were anemia (27.7%), alopecia (21.4%), and nausea (19.6%).

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Real-World Efficacy and Treatment Patterns of Enfortumab Vedotin and Avelumab

EV is an ADCs indicated for the treatment of mUC in patients who have previously received a PD-1 or PD-L1 inhibitor and platinum-containing chemotherapy, or who are ineligible for cisplatin and have received at least 1 prior line of therapy.[1] Real-world outcomes with EV according to line of therapy and the effect of prior therapy have not been well documented. A retrospective study evaluated these parameters in patients with mUC identified in a United States–based nationwide database. Included patients had advanced, recurrent, or mUC in the upper or lower urinary tract and had received single-agent EV as therapy for their second or later line of therapy.[2] Patients were treated after December 18, 2019, the accelerated approval date from the US Food and Drug Administration (FDA). Patients with no documentation of their first-line therapy were not included. Patients who had had no contact with the treating institution for 90 days from diagnosis were also excluded to ensure that patients who received care at the institution providing the data were selected.

Among 6566 patients with mUC, 431 had received EV from January 2020 to September 2022. EV demonstrated activity even when used as the fifth line of therapy. Among patients who received EV as the second, third, fourth, or fifth line of therapy, the median time to next treatment (TTNT) ranged from 4.1 to 6.2 months; the TTNT among patients with prior platinum exposure ranged from 3.4 to 11.0 months; and the TTNT among patients with prior exposure to a PD-1 or PD-L1 inhibitor ranged from 4.6 to 7.4 months. In this same set of patients, the median OS ranged from 7.2 to 11.0 months; the median OS among patients with prior platinum exposure ranged from 5.4 to 14 months; and the median OS among patients with prior exposure to a PD-1 or PD-L1 inhibitor ranged from 6.3 to 11.0 months (Table 3). The study showed that EV continued to provide efficacy among patients with mUC regardless of prior platinum or ICI therapy and when administered as late as the fifth line of therapy.

Avelumab is approved in the United States as maintenance therapy for patients who have locally advanced or mUC without disease progression following first-line platinum-based chemotherapy.[3] A retrospective study assessed real-world outcomes in

Table 3. Median TTNT and OS of EV in Patients With mUC.

Line, n	TTNT Overall, mo	TTNT Prior Platinum, mo	TTNT Prior PD-1/PD-L1 Inhibitor, mo	OS Overall, mo	OS Prior Platinum, mo	OS Prior PD-1/PD-L1 Inhibitor, mo
2nd, 157	5.3	Y 6.3 N 4.4	Y 4.8 N 5.8	7.8	Y 11 N 6.0	Y 6.3 N 9.8
3rd, 132	4.5	Y 5.5 N 4.5	Y 4.6 N 4.5	11	Y 8.6 N 11	Y 11 N 10
4th, 62	6.2	Y 11 N 6.2	Y 6.8 N 6.2	9.3	Y 14 N 9.0	Y 8.7 N 11
5th, 20	4.1	Y 3.4 N 4.6	Y 7.4 N 4.0	7.2	Y 5.4 N 7.2	Y 8.5 N 6.1

EV, enfortumab vedotin; mUC, metastatic urothelial carcinoma; N, no; NA, not applicable; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; TTNT, time to next therapy; Y, yes.
Adapted from Sayegh et al. Abstract 2380P. Presented at: ESMO Congress 2023; October 20-24, 2023; Madrid, Spain.[2]

ABSTRACT SUMMARY: EBANO Study: Clinical Characteristics, Treatment Patterns, and Survival Results in Patients With Locally Advanced/Metastatic Urothelial Carcinoma (la/mUC) in Northern Spain

A retrospective study conducted across 16 hospitals in Spain evaluated real-world outcomes in 1231 patients with locally advanced or mUC (Abstract 2382P). Patients had a median age of 68 years, 83% were male, and 74% had 1 or more medical comorbidities. Of the 1231 patients, 70% had localized UC at diagnosis, and 292 patients (24%) had never received systemic therapy. Of the remaining 939 patients, 50% were considered fit for cisplatin-based therapy. Second-line therapy was administered to 53% of the patients and third-line therapy to 22%. Chemotherapy was the most common treatment as first-line (92%), second-line (74%), and third-line (74%) therapy, with immunotherapy representing 3%, 25%, and 22% of regimens, respectively. There were 28 patients who participated in clinical trials. The median OS was 12.1 months (95% CI, 11.3-12.9) in the overall group and was 14.5 months among the patients treated with first-line cisplatin plus gemcitabine.

patients with locally advanced or mUC who received avelumab as maintenance therapy.[4] The study included patients with locally advanced or mUC in a US database whose disease was diagnosed between January 2016 and March 2023. Patients who had completed first-line platinum-containing therapy after the date of approval of avelumab for this indication were considered eligible for avelumab as maintenance therapy. Among 3299 patients originally identified in the database, 1939 (59%) had received first-line systemic therapy, and 644 patients had received platinum-based chemotherapy as their first-line regimen. The median real-world OS was 13.6 months. After completing first-line therapy, 574 patients (89%) had no evidence of disease progression. Among these patients, 219 (38%) received first-line maintenance therapy, including 135 patients who received avelumab. Among these 135 patients, the median follow-up from the start of maintenance therapy was 8.9 months; 108 patients (80%) patients were still alive at 6 months, and 85 patients (63%) were alive at 12 months. The real-world median PFS from the start of avelumab maintenance therapy was 6.4 months, and the median time on therapy was 3.85 months.

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Highlights in Metastatic Urothelial Carcinoma From the European Society for Medical Oncology Congress 2023: Commentary

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Several presentations at the European Society for Medical Oncology (ESMO) Congress 2023, which was held in Madrid, Spain, this October, provided important insights into the management of metastatic urothelial carcinoma (mUC). Data were presented on a variety of antibody-drug conjugates (ADCs), including sacituzumab govitecan and enfortumab vedotin, as well as on the relative efficacy of single agents, such as erdafitinib vs pembrolizumab, and more.

Antibody-Drug Conjugates: Sacituzumab Govitecan Plus Enfortumab Vedotin

ADCs have revolutionized the treatment of UC. Sacituzumab govitecan and enfortumab vedotin are both approved for sequential use in the management of treatment-resistant UC.[1,2] We frequently combine different chemotherapies, so why not explore combining ADCs?

In this investigator-initiated trial, patients with treatment-resistant mUC received a combination of sacituzumab govitecan and enfortumab vedotin.[3] The primary endpoint was to assess feasibility and safety by determining the maximum tolerated dose on the basis of dose-limiting toxicities experienced during cycle 1 in a Bayesian Optimal Interval design. We found that the drugs can be safely combined. In fact, it was possible to administer both drugs at their maximum tolerated doses on days 1 and 8 of a 21-day cycle, although this approach was associated with cumulative toxicities in subsequent cycles. Importantly, no synergistic toxicities were observed. The recommended phase 2 dose would involve a lower dose of sacituzumab govitecan, at 8 mg/kg, with a full dose of enfortumab vedotin, administered on days 1 and 8 of a 21-day cycle. This combination resulted in a 70% objective response rate (ORR), with no significant toxicity signals observed, although it was administered with the support of granulocyte-colony stimulating factor (G-CSF). These are exciting data from the first trial to combine 2 ADCs in the treatment of any malignancy. We are hopeful that combining ADCs will have applications in UC as we look to do expansion cohorts of sacituzumab govitecan and enfortumab vedotin in treatment-resistant settings, as well as in combination with pembrolizumab in the treatment-naive setting (DAD-IO phase 1), looking to build upon the success of EV-302.[4,5] Furthermore, the concept may extend to other diseases for which ADCs are approved, allowing us to explore combinations for the treatment of other diseases and enhance outcomes for our patients.

ABSTRACT SUMMARY: Factors Associated With Not Receiving Systemic Treatment (TX) in Patients (Pts) With Metastatic Urothelial Carcinoma (mUC): Results of a Retrospective Observational Study in Germany

A retrospective study examined outcomes in patients with mUC identified in a German health insurance database who did not receive systemic therapy as first-line treatment (Abstract 2386P). The mean follow-up was 13.8 months for 3226 patients. More than half of the patients (58.6%) did not receive systemic therapy within 12 months of diagnosis, and the median OS of these patients was shorter than the median OS of the patients who did receive systemic therapy (3.0 vs 13.7 months for one cohort and 3.6 vs 13.8 months for a second cohort). Untreated patients were significantly older and had significantly more comorbidities in comparison with patients who received systemic therapy (P<.001).

Cisplatin Eligibility

For years, patients with metastatic disease were classified as either cisplatin-eligible or cisplatin-ineligible, and our treatment decisions were based on that classification. The EV-302/KEYNOTE-A39 trial looked to break the mold, including patients with mUC who were cisplatin-eligible or -ineligible and randomizing them to the combination of enfortumab vedotin plus pembrolizumab or to chemotherapy alone.[5] Pembrolizumab was administered for up to 2 years; enfortumab vedotin, an ADC, was administered indefinitely until unacceptable toxicity or progression. This trial is quite remarkable in that the risk of progression or death was reduced by 53% in the patients who received enfortumab vedotin

plus pembrolizumab as opposed to platinum chemotherapy. Even more remarkable was the nearly doubled median overall survival (OS), which increased from 16.1 to an impressive 31.5 months. This result was independent of cisplatin eligibility and independent of programmed death ligand 1 expression. However, it came with a unique toxicity profile, including rash, hypoglycemia, and neuropathy. With a response rate approaching 70% and a complete response (CR) rate approaching 30%, the combination represents a new standard of care in the treatment of UC.

Enfortumab vedotin plus pembrolizumab is already approved in the United States by the US Food and Drug Administration (FDA) for cisplatin-ineligible patients on the basis of early phase 2 data.[6] This trial represents a paradigm shift in our approach. As we consider frontline treatments, we may no longer need to factor in cisplatin eligibility; the combination of enfortumab vedotin plus pembrolizumab offers remarkable results, which is probably why this presentation received a standing ovation at ESMO.

Immunotherapy: Nivolumab

The phase 3 CheckMate 901 was also presented at ESMO.[7] Several trials have looked to combine immunotherapy with platinum therapy in the frontline treatment of UC, with no clinically significant improvement in outcomes. However, in exploratory analyses, a potential benefit was noted in the patients treated with cisplatin. The CheckMate 901 trial constituted one arm of a larger study. Patients with previously untreated unresectable or mUC in this arm received gemcitabine/cisplatin with or without nivolumab and underwent chemotherapy for up to 6 cycles. Then, they proceeded to maintenance nivolumab if they showed a response. Notably, the ORR when we added nivolumab went up significantly from 43.1% to 57.6%, and the CR rate increased to 21.7%. When we looked specifically at CRs, the median CR duration was more than 37 months. No new toxicity signals appeared, even though quite a few patients in the gemcitabine/cisplatin-only group went on to receive maintenance nivolumab. These are exciting data. CheckMate 901 is the first trial to show improved outcomes with nivolumab plus gemcitabine/cisplatin vs gemcitabine/cisplatin alone, although the role of the combination will need to be defined with data from EV-302.[5]

FGFR Alterations: Erdafitinib

Erdafitinib has been FDA-approved on an accelerated basis for some time, on the basis of results of a single-arm phase 2 trial for patients with select fibroblast growth factor receptor (*FGFR)* mutations. The phase 3 THOR trial comparing erdafitinib with chemotherapy demonstrated a clear advantage of erdafitinib across all subgroups.[8] THOR highlights the importance of considering erdafitinib as a treatment option for patients with *FGFR* mutations, with benefit seen across subgroups. At ESMO, we also saw data from another arm, which compared erdafitinib with pembrolizumab.[9] Although the ORR was higher with erdafitinib than with pembrolizumab, the response rate with pembrolizumab approached what is seen in an *FGFR* unselected population. Moreover, these responses were quite durable. The durable responses to pembrolizumab sort of muddied the waters when the overall data were evaluated—and it just goes to show that we have so much to learn about treatments. Finding the right biomarker for immunotherapy is incredibly challenging, and it is very clear that *FGFR* mutations are not associated with less response to immunotherapy. Overall, immunotherapy should continue to play an important role in the management of UC, independently of *FGFR* mutations.

ABSTRACT SUMMARY: Efficacy of a Tailored Approach with Nivolumab (N) and Nivolumab+Ipilimumab (N+I) as Immuno-therapeutic Boost in Metastatic Urothelial Carcinoma (mUC) – Final Results of TITAN-TCC

The single-arm phase 2 TITAN-TCC trial evaluated nivolumab induction followed by nivolumab plus ipilimumab as second-line therapy for patients with mUC (Abstract 2472P). Cohort 1-1L enrolled 42 patients for first-line therapy, cohort 1-2/3L enrolled 44 patients for second- or third-line therapy, and cohort 2-2/3L of the trial enrolled 83 patients for second- or third-line treatment. All patients received nivolumab as induction therapy. Patients without a response to nivolumab monotherapy at week 8 received a "boost" of nivolumab plus high-dose ipilimumab. After induction, ORRs ranged from 20% to 29%. Among patients who received the boost therapy, the ORR was 27% in cohort 1-2/3L, 33% in cohort 2-2/3L, and 48% in cohort 1-1L. The median OS was 16.4 months in cohort 1-1L, 8.3 months in cohort 1-2/3L, and 7.6 months in cohort 2-2/3L.

Real-World Setting

Enfortumab Vedotin

The introduction of maintenance therapy involving immunotherapy and ADCs indicates a significant evolution in the UC treatment landscape. At ESMO, we saw some nice real-world data presented on posters drawn from different databases. In my assessment, when we examine data on enfortumab vedotin in the real-world setting, we observe responses that are comparable with what we have seen overall.[10] We may not have specific response data, but we do have valuable data regarding time to the next therapy and OS. Although this real-word evidence may not quite

match the robustness of phase 3 trial data, it convincingly shows the activity of these drugs and emphasizes the importance of enfortumab vedotin in the management of UC.

Avelumab

At the same time, we saw real-world data on the use of maintenance avelumab. The data showed an early adoption of this approach in first-line maintenance for patients whose disease had not progressed.[11] With the paradigm-shifting data recently presented at ESMO, it is evident that we now need to develop new real-world data, including understanding the adoption of the combination of enfortumab vedotin plus pembrolizumab in clinical practice and assessing its effect on future treatment strategies.

Immune Checkpoint Inhibitors

In the phase 2 ICRA trial, patients with mUC that was refractory to checkpoint blockade showed a response to paclitaxel plus the cytotoxic T-lymphocyte–associated antigen 4 inhibitor tremelimumab.[12] Although a small trial, ICRA is thought-provoking and highlights the potential for novel therapeutic approaches in the ICI-refractory setting.

Future Outlooks

This was a remarkable ESMO meeting for bladder cancer. In the frontline setting, it has been decades since we have seen such progress. Not one trial was able to show an improvement over platinum-based doublet. And here we had 2 presentations, one right after the other, that both showed an improvement over platinum. One involved the addition of nivolumab to cisplatin, and the other compared enfortumab vedotin plus pembrolizumab with cisplatin or carboplatin–I think this is an exciting time. These studies truly signify a paradigm shift in our approach to bladder cancer, and I look forward to the next trial designs, which we hope will advance treatment for metastatic disease still further. Additionally, we aim to draw lessons from this disease in the metastatic setting and apply similar strategies in the perioperative setting to prevent more patients' disease from progressing to that point.

ABSTRACT SUMMARY: Updated Results of PEANUT Trial: Pembrolizumab and Nab-Paclitaxel as Salvage Therapy for Platinum-Treated, Locally Advanced or Metastatic Urothelial Carcinoma (mUC)

The open-label, single-arm, phase 2 PEANUT trial evaluated 21-day cycles of pembrolizumab (200 mg, day 1) plus nab-paclitaxel (125 mg/m^2, days 1 and 8) in 70 patients who had mUC with disease progression after 1 or 2 platinum-containing regimens (Abstract 2370P). Of these patients, 76% had received 1 and 24% had received 2 prior lines of therapy. After a median follow-up of 48.6 months, 11 patients (15.7%) were in CR. The median OS was 11.0 months (95% CI, 7.6-16.8), the median PFS was 5.1 months (95% CI, 4.1-7.37), and the ORR was 50.0%. Among patients who achieved a PR or CR, the median OS was 28.4 months (95% CI, 16.2 months-not evaluable). The OS rate was 27.1% (n=19) at 46 months. Treatment discontinuation due to toxicity occurred in 17.4% of patients.

Disclosures

Dr McGregor has received honoraria from Seagen, Gilead, Pfizer, BMS, Exelixis, and Eisai and has received funding from Seagen, Gilead, Exelixis, Pfizer, and BMS.

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