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Supportive Care in Patients with Pretreated HR+/HER2- mBC

ReachMD Announcer:
Welcome to *Project Oncology* on ReachMD. This medical industry feature, titled "Supportive Care in Patients with Pretreated HR-Positive, HER2-Negative Metastatic Breast Cancer," has been created and paid for by Gilead Oncology.

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Here is your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and here with me today to discuss supportive care for pretreated HR-positive HER2-negative metastatic breast cancer patients receiving TRODELVY®, a TROP-2-directed antibody-drug conjugate, also known as sacituzumab govitecan-hziy, are Drs. Aashini Master and Neil Iyengar. Dr. Master is a breast medical oncologist and Associate Professor at UCLA Health in Los Angeles. She also serves as the Clinical Director of the High Risk Breast Program.

Dr. Master, thanks for joining us today.

Dr. Master:
Thanks for having me.

Dr. Turck:
Also with us is Dr. Neil Iyengar. He is the Co-Director of the Breast Oncology Program and Director of the Cancer Survivorship Service at Winship Cancer Institute at Emory University. Dr. Iyengar, it's great to have you with us as well.

Dr. Iyengar:
It's great to be here.

Dr. Turck:
Now, before we begin, let's take a moment to review the Indication and some Important Safety Information for TRODELVY.

ReachMD Announcer:
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

BOXED WARNING: NEUTROPENIA AND DIARRHEA

- TRODELVY can cause severe, life-threatening, or fatal neutropenia. Withhold TRODELVY for absolute neutrophil count below 1500/mm3 or neutropenic fever. Monitor blood cell counts periodically during treatment. Primary prophylaxis with G-CSF is recommended for all patients at increased risk of febrile neutropenia. Initiate anti-infective treatment in patients with febrile neutropenia without delay.
- TRODELVY can cause severe diarrhea. 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.

To see full Prescribing Information, including BOXED WARNING, please click on the link on the ReachMD landing page or visit TRODELVYHCP.com, and please stay tuned for continued Important Safety Information later in this video.

Dr. Turck:
With that Important Safety Information in mind, let's dive in, starting with you, Dr. Master.

We spoke in the first program about the efficacy and safety profile of TRODELVY, but can you elaborate now on some of those specific side effects and how to manage them?

Dr. Master:
Of course. TRODELVY is the first FDA-approved Trop-2 directed antibody drug conjugate, or ADC, in patients with pretreated HR-positive, HER2-negative metastatic breast cancer,[1,2] which is very exciting. But understanding certain side effects and management strategies are important while they're receiving treatment.

As a brief overview of the first program, some common side effects of TRODELVY were diarrhea, nausea, vomiting, and neutropenia.[1]

Dr. Iyengar, does that align with what you've seen in your clinical practice?

Dr. Iyengar:
Yes. In my experience, gastrointestinal events often happen in patients receiving TRODELVY, but there are medications available that may help prevent or manage them.[1]

Premedication with dexamethasone and a 5-HT3 or NK_1 receptor antagonist can help prevent chemotherapy-induced nausea and vomiting, while antipyretics, H1 and H2 blockers, or corticosteroids can help prevent infusion reactions.[1] And patients who exhibit an excessive cholinergic response to treatment with TRODELVY, such as abdominal cramping, diarrhea, or salivation, can receive appropriate premedication with atropine or similar drugs for subsequent treatments.[1]

Taking these kinds of proactive measures may help them continue treatment as appropriate.

However, the same side effects aren't a given for everybody, so I also want to emphasize that providers should individualize treatment plans to each patient.

Dr. Turck:
Now, Dr. Iyengar, what can you tell us about the risk of neutropenia based on the findings from the TROPiCS-02 trial?

Dr. Iyengar:
As providers, it's important that we prepare our patients with information about the possibility of developing neutropenia while on TRODELVY, because it can be severe, life-threatening, or even fatal as early as the first cycle of treatment.[1]

Now for some background on the TROPiCS-02 study, this was a randomized, active-controlled, open-label trial that included 543 patients with unresectable locally advanced or metastatic HR-positive, HER2-negative breast cancer. 272 patients were given TRODELVY ten milligrams per kilogram as an intravenous infusion on days one and eight of a 21-day treatment cycle, while 271 patients received investigator-selected single-agent chemotherapy, including eribulin, vinorelbine, gemcitabine, or capecitabine. Patients were treated until disease progression or unacceptable toxicity, and investigated the safety of both treatment arms.[1,3,4]

Now going back to your question, neutropenia occurred in 64 percent of patients treated with TRODELVY, with 49 percent experiencing

grade three to four neutropenia. Febrile neutropenia also occurred in six percent of patients, while neutropenic colitis occurred in 1.4 percent.[1]

The median time to first onset of neutropenia – including febrile neutropenia – in patients receiving TRODELVY was 16 days, although it occurred earlier in patients with reduced UGT1A1 activity.[1]

Now if we take a closer look, a prespecified descriptive analysis of the TROPiCS-02 study provided further insight into the timing and duration of treatment-related neutropenia. In this analysis, neutropenia included the preferred terms neutropenia, neutrophil count decreased, and febrile neutropenia.[5]

The findings showed that the median time to onset of the first event of treatment-related neutropenia of any grade was 20 days.[5]

The median time to onset of the first event of grade three or higher treatment-related neutropenia was 16 days.[5]

And the average duration of any grade neutropenia and grade three or higher neutropenia was eight days.[5]

Sharing this timeline with patients can help them be aware of potential neutropenia side effects, and we should encourage them to notify their healthcare team promptly if they experience fevers, chills, or other signs of infection.

Dr. Turck:
Now with that in mind, Dr. Master, what strategies can we use to proactively manage neutropenia?

Dr. Master:
As stated in the TRODELVY USPI, primary prophylaxis with G-CSF is recommended starting in the first cycle of treatment for all patients at increased risk of neutropenia. This includes older patients, patients with previous neutropenia, or patients with poor performance status, organ dysfunction, or multiple health issues.[1]

Providers should monitor absolute neutrophil count, or ANC, during treatment. Neutropenia management strategies may include temporary interruption, dose reduction, or treatment discontinuation of TRODELVY alongside G-CSF administration.

For example, for each occurrence of grade three or four neutropenia – where the ANC is below 1,000 cells per cubic millimeter– or if febrile neutropenia occurs, TRODELVY should be withheld until the ANC recovers to at least 1,500 cells per cubic millimeter on day one of any treatment cycle, or at least 1,000 cells per cubic millimeter on day eight.[1] Providers should administer G-CSF during treatment as clinically indicated, and use it prophylactically in subsequent TRODELVY cycles as clinically indicated or indicated in the USPI.

At each occurrence of febrile neutropenia or prolonged grade three to four neutropenia, TRODELVY's dose should be reduced from the recommended starting dose of 10 milligrams per kilogram once weekly on days one and eight of each 21-day treatment cycle. Doses should be reduced to:

- 7.5 milligrams per kilogram at the first occurrence and
- five milligrams per kilogram at the second occurrence.
- If further dose reductions are required, permanently discontinue TRODELVY.[1]

It's important to note that the TRODELVY dose should not be re-escalated after a dose reduction for adverse reactions has been made.[1]

Now, sacituzumab govitecan-hziy, or TRODELVY, is classified as an intermediate risk of 10 to 20 percent for febrile neutropenia per NCCN Clinical Practice Guidelines in Oncology, or NCCN Guidelines®.[6]

So when it comes to proactive management, it's important to be aware of the risk factors for febrile neutropenia, which, according to the NCCN Guidelines®, include:[6]

- prior chemotherapy or radiation therapy;
- persistent neutropenia;
- recent surgery or open wounds;
- being over 65 years old and receiving full-dose chemotherapy;
- bone marrow involvement by the tumor; and
- liver or kidney dysfunction

For patients with one or more of these risk factors, prophylactic treatment with granulocyte colony-stimulating factor, or G-CSF, can be considered.[6]

However, we should keep in mind that the NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.[6]

But by clearly communicating these potential risk factors and management strategies, we can empower patients to recognize and report symptoms early.

Dr. Turck:
Now, let's turn our focus to diarrhea. Dr. Master, how can we help prepare patients for this adverse event?

Dr. Master:
Similarly to neutropenia, we can take a proactive approach to prepare patients for diarrhea and its management.

Diarrhea occurred in 64 percent of patients treated with TRODELVY and 11 percent reported grade three or four, which is considered severe.[1] One patient had intestinal perforation following diarrhea and 0.7 percent of all patients had diarrhea that led to dehydration and subsequent acute kidney injury.[1]

Data from the prespecified descriptive analysis of the TROPiCS-02 study showed that the median time to onset of the first event of diarrhea related to TRODELVY occurred 15 days after treatment initiation, with symptoms lasting a median of eight days.[5] It's important to highlight that in the TROPiCS-02 study, there were no known TRODELVY-related deaths due to diarrhea.[3]

So we can help patients prepare for the possibility of diarrhea by discussing the expected timeline.

Dr. Turck:
And if a patient does experience diarrhea, Dr. Iyengar, what steps should we take to help manage it?

Dr. Iyengar:
If diarrhea occurs, the first step is to rule out infectious causes. Once an infection is excluded, promptly initiate loperamide at a dose of four milligrams initially followed by two milligrams with every episode of diarrhea for a maximum of 16 milligrams daily – and discontinue loperamide 12 hours after diarrhea resolves. We can also add supportive measures such as administration of fluids and electrolytes if clinically indicated.[1]

And patients who exhibit an excessive cholinergic response to treatment with TRODELVY can receive appropriate premedication, such as atropine, for subsequent treatments.[1]

Although temporary interruption, dose reduction, or treatment discontinuation of TRODELVY may help with severe diarrhea management when appropriate.[1]

For example, TRODELVY should be withheld for patients with grade three or four diarrhea that is not controlled by anti-diarrheal agents, and should only be resumed once symptoms resolve to grade one or less.[1]

Just like with neutropenic adverse reactions, we should also implement dose reductions for severe diarrhea. For each occurrence of grade three to four diarrhea that isn't controlled with anti-diarrheal agents, the TRODELVY dose should be reduced from the recommended starting dose of 10 milligrams per kilogram once weekly on days one and eight of each 21 day treatment cycle. Doses should be reduced to:

- 7.5 milligrams per kilogram at the first occurrence, and
- Five milligrams per kilogram at the second occurrence.
- Treatment should be permanently discontinued if further dose reductions are required and should not be re-escalated after a dose reduction for an adverse event has been made.[1]

Dr. Turck:
Well, as we near the end of today's program, I'd like to focus for a moment on the patient experience, and Dr. Master, I'll start with you. How do you approach conversations about starting TRODELVY with patients?

Dr. Master:
First and foremost, open and empathetic communication is key to helping patients navigate a difficult decision.

When talking to patients about TRODELVY, I make sure to listen and address all their questions, which typically include concerns like, “How long will I need treatment?”, “What are the potential side effects?”, or “How will this affect my daily life?” Patients seek to manage their cancer journey, and they are striving to understand the impact of side effects on their daily lives. Because of this, I like to walk them through the potential management strategies for each one.

Dr. Turck:
And Dr. Iyengar, do you have any closing insights on discussing TRODELVY with patients?

Dr. Iyengar:
Yes, I’d like to emphasize that addressing the potential side effects head-on is essential to helping patients set realistic expectations. But at the same time, we can remind them that certain side effects have managements strategies, including proactive care, that can be found in the USPI.[1]

Dr. Turck:
Well, with that call to action in mind, I want to thank my guests, Dr. Aashini Master and Dr. Neil Iyengar, for discussing supportive care in pretreated HR-positive HER2-negative metastatic breast cancer patients being treated with TRODELVY. Dr. Master, Dr. Iyengar, it was great speaking with you both today.

Dr. Master:
Thank you for having me!

Dr. Iyengar:
It’s been my pleasure.

Dr. Turck:
To learn more about the efficacy and safety of TRODELVY, check out the first program in this two-part series.

Please stay tuned to hear Important Safety Information. For ReachMD, I’m Dr. Charles Turck.

ReachMD Announcer:
WARNINGS AND PRECAUTIONS

Neutropenia: Severe, life-threatening, or fatal neutropenia can occur as early as the first cycle of treatment 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%. Primary prophylaxis with G-CSF is recommended starting in the first cycle of treatment in all patients at increased risk of febrile neutropenia, including older patients, patients with previous neutropenia, poor performance status, organ dysfunction, or multiple comorbidities. Monitor absolute neutrophil count (ANC) during treatment. Withhold TRODELVY for ANC below 1500/mm^3 on Day 1 of any cycle or below 1000/mm^3 on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Treat neutropenia with G-CSF and administer prophylaxis in subsequent cycles as clinically indicated or indicated in Table 2 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: TRODELVY can cause serious hypersensitivity reactions including life-threatening anaphylactic reactions. 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: TRODELVY is emetogenic and can cause severe 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 (locally advanced or metastatic HR-positive, HER2-negative breast cancer), 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 full Prescribing Information, including BOXED WARNING by clicking on the link on the ReachMD landing page or visiting TRODELVYHCP.com.

ReachMD Announcer:

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References:

1. TRODELVY. Prescribing information. Gilead Sciences, Inc.; March 2025.
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(10411):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 April 4, 2025. https://ascopubs.org/doi/suppl/10.1200/JCO.22.01002/suppl_file/protocol_JCO.22.01002.pdf.
5. Data on file. Gilead Sciences, Inc. July 2022.
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