Sacituzumab Govitecan-Hziy (Trodelvy™)

BY JENNIFER HEDGECORTH, PHARMD, BCPS

What is sacituzumab govitecan-hziy?
Sacituzumab govitecan is an antibody-drug conjugate composed of humanized antiproliferative antibody fragment (hR5 IgG1 or sacituzumab) bound to a topoisomerase inhibitor (SN-38) via a cleavable linker. For each sacituzumab antibody molecule, there is an average of 7-8 SN-38 molecules. SN-38 is the active metabolite of irinotecan.

The antibody moiety of sacituzumab govitecan selectively binds to Trop-2 receptors that are expressed on cancer cells. Trop-2 is a transmembrane calcium signal transducer that can stimulate cancer cell growth, is overexpressed in many epithelial cancers, and has been found on breast cancer cells. After binding to Trop-2, sacituzumab govitecan is internalized. Once inside the cell, the topoisomerase inhibitor SN-38 is released and results in DNA damage, apoptosis, and cell death.

What is this approved for?
Sacituzumab govitecan is approved for the treatment of adult patients with metastatic triple-negative breast cancer (TNBC) who have previously received two or more therapies for metastatic disease (N Engl J Med 2019;380:741-751; J Clin Oncol 2017; 35(19):2141-2148).

Sacituzumab govitecan was approved based on the results of the IMMU-132-01 Phase I/II trial. This multicenter, basket-design, open-label, single-group trial initially enrolled patients with various types of advanced solid cancers who had received at least one prior therapy for metastatic disease. The IMMU-132-01 protocol was amended to increase enrollment of patients with metastatic TNBC who had received at least two prior therapies for metastatic disease. The dose evaluated was sacituzumab govitecan 10 mg/kg IV on days 1 and 8 of a 21-day cycle (n=108 for metastatic TNBC). The primary efficacy outcome measured was overall response rate (ORR). The ORR was 33.3 percent (95% CI: 24.6, 43.1), the median time to response was 2 months (1.6 - 13.5), and the median response duration was 7.7 months (95% CI: 4.9, 10.8). Three patients had a complete response to treatment.

How do you administer this drug?
Sacituzumab govitecan is administered at a dose of 10 mg/kg (actual body weight) intravenously on days 1 and 8 of a 21-day treatment cycle. The first infusion is over 3 hours and subsequent infusions can be 1-2 hours if previously well-tolerated. Patients should be observed for 30 minutes following each infusion for signs or symptoms of infusion-related reactions.

Are there any premedications needed for sacituzumab govitecan-hziy?
Premedications are recommended prior to each sacituzumab govitecan dose for the prevention of infusion reactions, as well as prevention of chemotherapy-induced nausea and vomiting (CINV). The package insert recommends antipyretics, H1 antagonists, and H2 antagonists prior to infusions. Corticosteroids may be used for patients who have had prior infusion reactions.

Sacituzumab govitecan is considered to be moderately emetogenic; patients should be premedicated with a two or three drug combination, such as dexamethasone with a 5-HT3 receptor antagonist +/- an NK1 receptor antagonist. Other antiemetic medications may also be considered for use or added based on patients’ reports of CINV.

Sacituzumab govitecan may cause excessive cholinergic response; use of atropine in subsequent infusions is an option if these symptoms present.

What are the common side effects associated with sacituzumab govitecan-hziy (> or =10%)?
The most common adverse effects observed at greater than or equal to 10 percent incidence include nausea (69%), vomiting (49%), diarrhea (63%), constipation (34%), abdominal pain, mucositis, fatigue (57%), edema, pyrexia, neutropenia (64%), anemia, thrombocytopenia, prolonged PTT, decreased appetite, hyperglycemia (24%), hypomagnesemia, hypokalemia, hypophosphatemia, dehydration, alopecia (38%), rash (31%), pruritis, dry skin, headache, dizziness, neuropathy (24%), dysgeusia, UTI, respiratory tract infection, back pain, arthralgia, pain in extremities, cough, dyspnea, and insomnia.

What are the uncommon side effects associated with sacituzumab govitecan-hziy (less than 10%)?
Additional side effects include pneumonia (2%), neutropenic enterocolitis (1-2%), febrile neutropenia (6%), antibody development (2%), pleural effusion (2%), esophagitis, anaphylaxis, asthma, and periorbital edema (incidence not reported for percentages not listed).

Are there any important drug interactions I should be aware of?
Avoid the concomitant use of UGT1A1 inducers or inhibitors with sacituzumab govitecan. UGT1A1 inhibitors may increase the risk of adverse reactions due to increased exposure to SN-38. Inducers may decrease the exposure to SN-38, leading to reduced efficacy.

How do I adjust the dose in the setting of renal or hepatic insufficiency?
There are no recommended dose adjustments for renal or hepatic impairment provided by the manufacturer’s labeling. The package insert states that patients with moderate or severe hepatic impairment were not included in trials and a starting dose cannot be recommended. In patients with bilirubin >1.5 times upper limit of normal (ULN) or AST and ALT >3 times ULN (or AST and ALT >5 times ULN in patients with liver metastases), the exposure to SN-38 may be increased due to decreased UGT1A1 activity and increased risk of side effects.

What should my patients know about sacituzumab govitecan-hziy?
Important counseling points for patients include education on reduced blood cell counts, risk for infection and when to seek medical attention, use of antiemetic agents for nausea and vomiting, severe diarrhea and risk for dehydration/electrolyte imbalance, neuropathy, mucositis, hair loss, and use of effective contraception during treatment due to risk of embryo-fetal toxicity.

What else should I know about sacituzumab govitecan-hziy?
There is a boxed warning for severe neutropenia with sacituzumab govitecan. It is recommended to withhold sacituzumab govitecan for absolute neutrophil count (ANC) below 1,500/mm³ on Day 1 of any

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important to educate your team about which devices and which online platform will be used.”

She said her organization uses Zoom and Doxy.me, and added that FaceTime is the simplest platform. She also noted that the lack of consistency in telehealth platforms can be a barrier not only between patients and providers but even from hospital to hospital.

Like other speakers, Garzon said licensing reimbursements—especially across state lines—are a major issue for telehealth reimbursement. “I do think we have to maintain the momentum here after COVID-19,” she said of expanded coverage and flexibility for telehealth visits due to the pandemic, adding that she hopes for parity in reimbursement for in-person visits and telehealth visits.

Changes to in-person care delivery. COVID-19 safety guidelines have not only required mask mandates and stringent infection control procedures, but also different facility configurations for seeing patients, several speakers noted.

“We had to redesign the way we deliver ambulatory care,” said Riker. The waiting room was abolished, and cancer patients wait in their cars to be called in for appointments. “I’m glad waiting rooms are gone,” he stated, noting they were a huge source of patient dissatisfaction. Isola agreed, saying the waiting room is “a wasted experience for patients.”

Opportunities for remote symptom management. The pandemic has heightened the need to recognize and address patient-reported symptoms early, said Ethan Basch, MD, MSc, Chief of the Division of Oncology and Physician-in-Chief at NC Cancer Hospital. He described a workflow model for using electronic patient self-reported outcomes and symptoms—ePROs—in oncology clinical practice.

In this model, patients send symptom alerts—such as chemotherapy side effects—to a medical practice via a Web-based, mobile, or automated telephone system. Basch noted that, not only does such a patient-driven system drive down emergency room visits, but it also fosters improvements in survival, quality of life, and physical function.

While integrating ePROs into clinical practice has been slow, Basch emphasized that implementing such a system with high patient usability has many benefits for patient management. He did say that nurses can find addressing the alerts an added burden, and the clinic workflow has to make an accommodation for responding to them.

“Clinic measures do not capture how a patient feels or functions or what they want to achieve from a treatment,” said Bruno Lempernese, CEO of Carevive Systems, Inc., which has developed an electronic system of patient-generated symptoms. Nadia Still, DNP, RN, Senior Director of Client Services for Carevive Systems, said that when practitioners commit resources to this system of receiving and evaluating symptoms remotely, it leads to cancer care team satisfaction, as well as patient satisfaction. In addition to helping patients avoid emergency room visits and hospitalizations, she said the system prompts also enhance the evaluation of patient treatment usage, adoption, and compliance.

Other sessions at the meeting covered the following topics:

• Mobile screening vans can be used to improve cancer screening rates by taking screening to the people. Renea Austin-Duffin, MPA, described the “Prevention on the Go” program of the Mary Bird Perkins Cancer Center, which takes cancer screenings and education on-site to workplaces in Louisiana and Mississippi. Employees pre-register for cancer screenings, said Austin-Duffin, and “It has worked extremely well.”

• The pandemic has forced hospitals to get creative with cell phones and Zoom calls for visits with cancer inpatients. Not having visitors was a huge source of dissatisfaction, said Mary Miller, MSN, RN-BC, OCN, Nurse Manager at Franciscan Health Center in Indianapolis. Miller noted that social isolation is devastating for patients, and that visits are important to the healing process. Pelusi agreed. “We forget that the isolation is huge,” she said. “I think there’s more for us to do in terms of support.”

• It is important to collect data on telehealth to document its efficiency and efficacy in care delivery. Some policy makers are still reluctant to embrace telehealth, said Mei Wa Kwong, JD, Executive Director of the Center for Connected Health Policy. So they will need data to convince them. Agreeing was Frank Cicchino, Vice President for Public Policy and Communications at the National Committee for Quality Assurance. “We really need data, and we need to be impartial about the data, he said. “Data wins the day.” One concern is that telehealth could exacerbate health disparities because of a “digital divide” due to differences in patients’ accessibility to the Internet and online access tools.

• Staff members, who are exhausted by the demands of the pandemic, need mentoring and support. Miller said she started a video chat program to communicate with her nurses, which worked very well. “We’ve learned a lot this year, and I hope we don’t go back to our old ways,” said Miller, pointing out the need for constant innovation because of a “digital divide” due to differences in patients’ accessibility to the Internet and online access tools.

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Peggy Eastman is a contributing writer.

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cycle or ANC below 1,000/mm^3 on Day 8 of any cycle. Drug should be withheld for neutropenic fever. Providers may consider using G-CSF for secondary prophylaxis.

Severe diarrhea may occur with sacituzumab govitecan and is reported as a black box warning. Patients can experience early and late-onset diarrhea; use of atropine for excessive cholinergic response or loperamide for late-onset diarrhea can be recommended.

Patients who are homozygous for UGT1A1*28 allele are at an increased risk for neutropenia, diarrhea, and other adverse reactions when receiving sacituzumab govitecan. Genotype analysis can be ordered to determine UGT1A1 activity. The appropriate dose for patients who are homozygous for UGT1A1*28 is unknown, but generally dose reductions and monitoring individual patient tolerance to treatment can be utilized to while on therapy.

What useful links are available regarding sacituzumab govitecan-hziy?


Any ongoing clinical trials related to sacituzumab govitecan-hziy?

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