NEW DRUGS

Aust Prescr 2022;45:144–5
https://doi.org/10.18773/austprescr.2022.042
First published 7 July 2022

Sacituzumab govitecan

Approved indication: breast cancer

Trodelvy (Gilead Sciences)
vials containing 180 mg powder for reconstitution with 0.9% sodium chloride

Breast cancer typically expresses one or more of three key receptors, which are the oestrogen, progesterone and HER2 receptors. Triple-negative breast cancer is a type of breast cancer that does not express any of these receptors, so it is not responsive to hormonal drugs or drugs that target HER2. Patients with previously treated metastatic triple-negative breast cancer have a poor prognosis as standard chemotherapy has a low response rate and progression-free survival is short. In most cases of triple-negative breast cancer, trophoblastic antigen-2 (Trop-2) is highly expressed and is therefore a feasible therapeutic target. Sacituzumab govitecan consists of an antibody against Trop-2 conjugated with SN-38, the active metabolite of the topoisomerase inhibitor irinotecan. Sacituzumab govitecan binds to the cancer cells, and the release of SN-38 within the cells leads to apoptosis.

The recommended dose is 10 mg/kg via slow intravenous infusion once per week on days 1 and 8 of continuous 21-day treatment cycles until disease progression or unacceptable toxicity. There have been no studies of the metabolism of sacituzumab govitecan, but SN-38 is metabolised by uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1). The activity of this enzyme may be reduced by certain genetic variants of the UGT1A1 gene. These variants may put some patients at an increased risk of adverse reactions such as neutropenia and anaemia. Co-treatment with UGT1A1 inhibitors, such as propofol, ketoconazole and EGFR tyrosine kinase inhibitors, may increase the risk of adverse reactions due to an increase in exposure to SN-38. Co-treatment with UGT1A1 inducers, such as carbamazepine, phenytoin, rifampicin, ritonavir and tipranavir, should also be avoided due to a substantial reduction in exposure to SN-38. However, no drug–drug interaction studies have been conducted. The efficacy and safety of sacituzumab govitecan in patients with moderate to severe renal or hepatic impairment are currently unknown.

Sacituzumab govitecan was compared to chemotherapy with eribulin, vinorelbine, capecitabine or gemcitabine in the ASCENT study.[1] This multicentre, open-label phase III trial randomised patients with metastatic triple-negative breast cancer who had previously received a taxane and at least two chemotherapies. All the patients in the trial received treatment until disease progression or unacceptable toxicity occurred. Although the trial included some patients with brain metastases, they were excluded from the primary analysis to minimise the confounding effects of this factor for poor prognosis. After a median follow-up of 17.7 months, a complete or partial clinical response was achieved in 35% (82/235) of the patients receiving sacituzumab govitecan and in 5% (11/233) of the patients receiving chemotherapy. The median duration of response was longer with sacituzumab govitecan than with chemotherapy (6.3 months vs 3.6 months). The median time to response was 1.5 months in both treatment arms. The median duration of progression-free survival was 5.6 months with sacituzumab govitecan and 1.7 months with chemotherapy. The median overall survival was 12.1 months with sacituzumab govitecan and 6.7 months with chemotherapy.[1]

In the ASCENT study, haematological treatment-related events of grade 3 or higher severity included neutropenia (51% with sacituzumab govitecan vs 33% with chemotherapy), leukopenia (10% vs 5%), anaemia (8% vs 5%) and febrile neutropenia (6% vs 2%). Severe gastrointestinal treatment-related events included diarrhoea (10% with sacituzumab govitecan vs <1% with chemotherapy), with lower incidences of nausea, vomiting and abdominal pain that were more frequent with sacituzumab govitecan than with chemotherapy. Fatigue and asthenia of all grades were also frequent with sacituzumab govitecan,[1] and caution is advised when driving or operating machines. Adverse events led to 5% of the patients in each arm of the ASCENT study discontinuing treatment. There were three deaths owing to adverse events in each arm.[1]

Sacituzumab govitecan can cause hypersensitivity reactions, including anaphylaxis. To prevent infusion reactions, antipyretics and H_1 and H_2 antagonists should be given before each dose, and corticosteroids may be given to patients with a history of infusion reactions. In addition, to prevent chemotherapy-induced nausea and vomiting, a two- or three-drug antiemetic combination regimen should be given before each dose. Doses of sacituzumab govitecan are reduced or discontinued to manage adverse reactions. The dose should not be re-escalated after it has been reduced.

Based on animal studies, sacituzumab govitecan may impair fertility in women of reproductive potential. It can cause teratogenicity and embryo-fetal lethality. Women should be advised of the potential risk to a fetus and should use contraception during treatment and for six months after the last dose. Male patients with female partners should use contraception during treatment and for three months after the last dose.

In terms of clinical benefit, the ASCENT trial favoured sacituzumab govitecan over chemotherapy in patients with metastatic triple-negative breast cancer previously treated for unresectable locally advanced or metastatic disease. However, the treatment has several well-defined toxic effects that require early recognition and management. Further studies of sacituzumab govitecan as a component of different combination and neoadjuvant regimens for breast cancer are ongoing.[1]

T manufacturer provided relevant information

REFERENCE

1. Bardia A, Hurvitz SA, Tolaney SM, Loirat D, Punie K, Oliveira M, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. New Engl J Med 2021;384:1529–41. https://doi.org/10.1056/nejmoa2028485

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.