Report TRODELVY® sacituzumab govitecan

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: sacituzumab govitecan **Brand Name:** Trodelvy **Originator/licensee:** Gilead Sciences Ireland UC **Classification:** NCE **ATC code:** L01FX17 **Orphan Status:** **Eu:** No **Us:** No **Mechanism of action:** sacituzumab govitecan-hziy binds to Trop-2-expressing cancer cells and is internalized with the subsequent release of SN-38 via hydrolysis of the linker. SN-38 interacts with topoisomerase I and prevents re-ligation of topoisomerase I-induced single strand breaks. The resulting DNA damage leads to apoptosis and cell death [1]	**Authorized Indication:** **EMA:** Sacituzumab as monotherapy is indicated for the treatment of adult pts with unresectable or mTNBC who have received two or more prior systemic therapies, including at least one of them for advanced disease [2]. **FDA**: Sacituzumab is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult pts with mTNBC who have received at least two prior therapies for metastatic disease [1]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 14/10/2021 **FDA M.A. date:** 22/04/2020 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** Yes --- **ABBREVIATIONS:** **AE:** adverse events **BL:** baseline **BRCAmut:** Breast Cancer gene mutation **CHMP**: Committee for Medicinal Products for Human Use **ESMO**: European Society for Medical Oncology **gBRCAm:** germline BRCA1/2 mutation **HER2:** human epidermal growth factor receptor 2 **HR:** hazard ratio **IRC**: Independent Radiologic Review **ITT:** intention-to-treat populations **IV:** intravenous infusion **MA:** Marketing Authorization **mTNBC**: Metastatic Triple-Negative Breast Cancer **OS:** overall survival **p:** p-value **PD-L1:** Programmed Cell Death Receptor- Ligand 1 **PFS:** progression-free survival **PO**: Positive Opinion **PARPis:** polyadenosine diphosphate-ribose polymerase inhibitors **pts**: patients **RECIST v1.1:** Response Evaluation Criteria in Solid Tumors version 1.1. **SN-38**: 7-ethyl-10-hydroxyl camptothecin **TPC:** single-agent chemotherapy treatment of physician's choice **Trop-2**: trophoblast cell-surface antigen 2 **vs.:** versus **TNBC**: Triple-Negative Breast Cancer	**Summary of clinical EFFICACY:** **ASCENT (NCT02574455)** is a multicenter, open-label, randomized study in 529 pts with unresectable locally advanced mTNBC who had relapsed after at least two prior chemotherapies. All pts either received previous taxane treatment in the adjuvant, neoadjuvant, or advanced stage unless there was a contraindication or intolerance to taxanes during or at the end of the first taxane cycle. 15% of the pts had brain metastases. Pts were randomized to receive IV sacituzumab govitecan 10 mg/kg on Days 1 and 8 of a 21-day cycle (n=267) or TPC (n=262) which included: eribulin, capecitabine, gemcitabine, or vinorelbine. Pts were treated until disease progression or unacceptable toxicity. The primary endpoint was PFS in pts without brain metastases at BL assessed by IRC, according to RECIST v1.1. In pts without brain metastases median PFS was 5.6 months in sacituzumab govitecan arm (n=235) vs. 1.7 months in TPC arm (n=233; HR = 0.41; 95%CI: 0.32 to 0.52; p<0.0001). Additional efficacy measures included PFS for the ITT population (all patients with and without brain metastases) and OS. For this population the median PFS was 4.8 months in those treated with sacituzumab govitecan (n=267) vs. 1.7 months in those receiving TPC (n=262; HR = 0.43; 95%CI: 0.35 to 0.4; p<0.0001). There was an increase of 4.9 months in median OS with sacituzumab govitecan vs. TPC (11.8 months [95% CI, 10.5 to 13.8] vs. 6.9 months [95% CI, 5.9 to 7.7], respectively) [1,3]. **Summary of clinical SAFETY:** ASCENT trial reported that serious AE occurred in 27% of the pts in the sacituzumab govitecan arm vs. 28% of the subjects in the TPC arm and were, respectively: neutropenia (5% vs. 2%), diarrhea (4% vs. 0%), and pneumonia (3% vs. 2%). Almost all pts included into the study had non-serious AE and occurred in 99% of those in the sacituzumab govitecan arm vs. 95% of the subjects in the TPC arm and included, respectively: diarrhoea (65% vs.17%), nausea (62% vs. 30%), neutropenia (42% vs. 25%), anaemia (40% vs. 27%), vomiting (33% vs. 16%), decreased appetite (28% vs. 21%). [3] **Ongoing studies:** ● ***For the same indication:*** Yes ● ***For other indications:*** Yes **Discontinued studies (for the same indication):** No --- **References:** 1.https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761115s005s013lbl.pdf 2.https://www.ema.europa.eu/en/medicines/human/summaries-opinion/trodelvy 3.https://clinicaltrials.gov/ct2/show/results/NCT02574455?view=results 4.https://www.drugs.com/price-guide/trodelvy 5.https://www.aiom.it/wp-content/uploads/2020/10/2020_Numeri_Cancro-operatori_web.pdf 6. Gennari, A et al. "ESMO Clinical Practice Guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer." Annals of oncology : official journal of the European Society for Medical Oncology, S0923-7534(21)04498-7. 19 Oct. 2021, doi:10.1016/j.annonc.2021.09.019 7.https://clinicaltrials.gov/ct2/results?cond=&term=&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&intr=Sacituzumab+govitecan&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= 8.https://clinicaltrials.gov/ct2/results?cond=Triple+Negative+Breast+Cancer&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&type=Intr&rslt=&phase=2&Search=Apply	**Cost of therapy:** In USA, sacituzumab govitecan (180 mg IV powder for injection) costs $2,238.51. [4] **Epidemiology:** In Italy, among women, breast cancer is the most common cancer, with 54,976 new diagnoses estimated for 2020. Around 15% of breast cancers are classified as TNBC. More than one-third of pts with TNBC will present distant metastases, either recurrent or as de novo metastatic disease [5,6] --- **POSSIBLE PLACE IN THERAPY** In pts with TNBC in progression after anthracyclines and taxanes, sacituzumab govitecan might be considered as the preferred treatment option; particularly if pts have also received carboplatin and capecitabine in the adjuvant setting and if no theragnostic markers are available such as gBRCAm. After progression on sacituzumab, all chemotherapy recommendations for HER2-negative disease also apply for TNBC such as eribulin, capecitabine and vinorelbine. [6] **OTHER INDICATIONS IN DEVELOPMENT:** non-small cell lung cancer, urothelial cancer, endometrial carcinoma, prostate cancer, glioblastoma, ovarian cancer [7] **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** - **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** camrelizumab, olaparib+pembro, serplulimab, etoposide+anlotinib, anlotinib+tislelizumab+anthracycline/nab-paclitaxel, zoledronate, ipatasertib, toripalimab+nab-paclitaxel, trilaciclib, epetraborole, capivasertib, eryaspase+chemotherapy, alpelisib + nab-paclitaxel [8] *Service reorganization No *Possible off label use: Yes

Issued on:

Issued on: