Sacituzumab govitecan: a new antibody-drug conjugates in the cancer treatment landscape

Yuchen Cai[1, †], Yidan Ma[2, †], Shulei Ren[3, †], Shenyue Zhao[4, †, *]

[1]College of Traditional Chinese Medicine, China pharmaceutical university, Nanjing, China

2020192301@stu.cpu.edu.cn

[2]College of Life Sciences and Technology, China pharmaceutical university, Nanjing, China

2020171998@stu.cpu.edu.cn

[3]Bachelor of Biomedicine, The University of Melbourne, Melbourne, Australia

shuleir@student.unimelb.edu.au

[4]Bachelor of Biomedicine, The University of Melbourne, Melbourne, Victoria, Australia

shenyuez@student.unimelb.edu.au

*Corresponding author: shenyuez@student.unimelb.edu.au

[†]These authors contributed equally.

Keywords: Sacituzumab Govitivan (Trodelvy), Trophoblast cell antigen 2 (Trop-2), Antibody-drug conjugates (ADC), Mechanism, Clinical trials, Toxicity.

Abstract: Cancer is the leading cause of death around whole world, has a high incidence rate and a high fatality rate, accounting for millions of deaths in recent years. Metastatic tumour spreads to other organs and tissues of the body and remains an incurable disease. There is an urgent need for developing one drug that can kill tumour cells with the most precise and selective targeting method. Sacituzumab govitecan (Trodelvy) is an antibody-drug conjugate (ADC) that target human trophoblast cell antigen 2 (Trop-2), which overexpresses in various type of tumour cells, such as triple-negative breast cancer (TNBC). Once Sacituzumab Govitecan's antibody part identifies Trop-2 molecule on the cell surface, Sacituzumab Govitecan will attach the cancer cell and directly deliver anti-cancer component into cells killing the cancer cell. In both basket-designed phase I/II study and third phase clinical trial, Sacituzumab Govitecan showed promising monotherapy activity among multiple cancer cohorts, together with a satisfactory relief rate and few side effects. For example, Triple-negative breast cancer patient that has been through at least two previous treatments in a metastatic setting can receive Sacituzumab Govitecan treatment. That leads the US Food and Drug Administration to accelerate approving Sacituzumab Govitecan to treat metastatic disease cancer patients. This review gives information about the component and mechanisms of Sacituzumab Govitecan and the clinical trials and their data analysis.

1. Introduction

Sacituzumab govitecan is the first drug affirmed by FDA for the treatment of TNBC, and also the first antibody conjugate drug which target Trop-2. It was firstly approved by FDA for the treatment to the adult patients who have metastatic triple-negative breast cancer(mTNBC) and have already received at least two prior therapies with metastatic cancer in USA on 22 April 2020[1].

Antigen-targeting human trophoblast cell antigen 2 (Trop-2) is a glycoprotein produced by the TACSTD2 gene. Not only does Trop-2 have a highly conserved HIKE-like phosphoinositide-binding motif, which is frequently present in signal transducers, but it also plays a crucial part in the metastasis of tumour cells from the initial to the prostate stage. The occurrence of cancer metastasis depends on the loss of contact between cells, the ability to migrate through the extracellular matrix (ECM) and invading surrounding tissues.

The integrin family proteins mediate the interaction between cells and ECM. Integrin beta1, together with fibronectin, plays a crucial role in cell adhesion and cell migration. However, Trop-2 binds and colocalizes with β1 integrin at the cell frontier, preventing β1 integrin from recruiting to focal adhesion (FA) sites. This repositioning of β1 integrins and the reconstruction of FAs accomplished by trop2-driven transfer and local adhesion kinase (FAK) hyperphosphorylation (Resulting in cells separating and migrating from the surrounding ECM).

We first introduce Sacituzumab govitecan's molecular structure and explain its pharmacological mechanism. After that, we reviewed clinical trials and emphasized clinical effects to help doctors make better decisions in drug selection and clinical applications.

2. The overview of Sacituzumab govitecan

2.1 The structure of Sacituzumab govitecan

Sacituzumab govitecan is an ADC of a Trop-2 targeted antibody and a topoisomerase inhibitor conjugate, contains the following components: a Trop-2 targeted antibody, a topoisomerase inhibitor conjugate, and linkers [2]. As shown in figure 1.

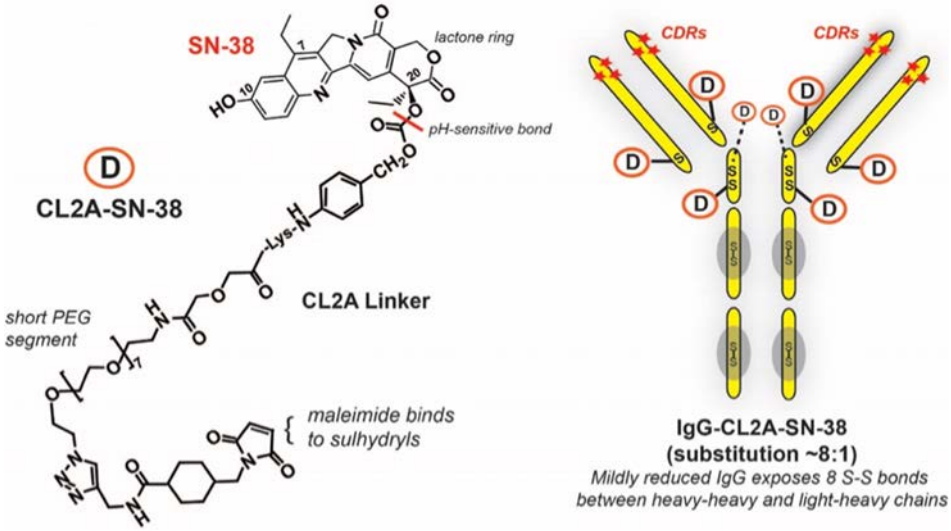

Figure 1. The component of sacituzumab govitecan [2].

The recombinant monoclonal antibody is created by mammalian cells, hRS7 IgG1κ (Sacituzumab), which ties to Trop-2 which is over expressed in numerous tumor cells. The antibody is slightly decreased to expose 8 sulfhydryl-binding site which are binded with linker. The hydrolysable linker (CL2A) connects the anti-cancer drug to the antibody, which has short polyethylene glycol groups to improve solution and a maleimide group to connect with the sulfhdryl groups generated on IgG. And there is a pH sensitive bond which can release SN-18 in a low pH environment [3].

The drug, 7-ethyl-10-hydroxycamptothecin (SN-38), is a topoisomerase inhibitor that is irinotecan's active component. The tenth position of SN-38 can protect from glucuronidation when SN-38 is combined with the IgG. Therefore, when SN-38 is bound to the antibody, it can remain its most potent form until released into the nucleus. SN-38 function inhibits the Topo I enzyme, an essential enzyme for cellular processes such as replication and transcription of DNA. Topo I is an enzyme that corrects DNA serial numbers by cutting off the phosphate diester bond in one or both strands of DNA and then rewrapping and sealing it [4].

2.2 Mechanism of Sacituzumab govitecan for killing the cancer cell

Sacituzumab govitecan is composed of a humanized monoclonal LG, which target Trop-2 and allows the intracellular of SN-38 (figure 2) [5]. The mechanism of drug action divides into the following three parts: attach, internalization and destroy. Firstly, Sacituzumab Govitecan finds and attaches the cancer cells by identifying the Trop-2 target. Once attached, the Sacituzumab govitecan

can directly deliver the anti-cancer drug to the cell. After that, the Sacituzumab govitecan-Trop-2 complex will be reduced by lysosome and release the SN-38 to the cancer cell's environment. Then SN-38 will nick Topoisomerase I and inhibit its function, which causes the double-strand DNA breaks. Eventually, it will cause cancer cell death.

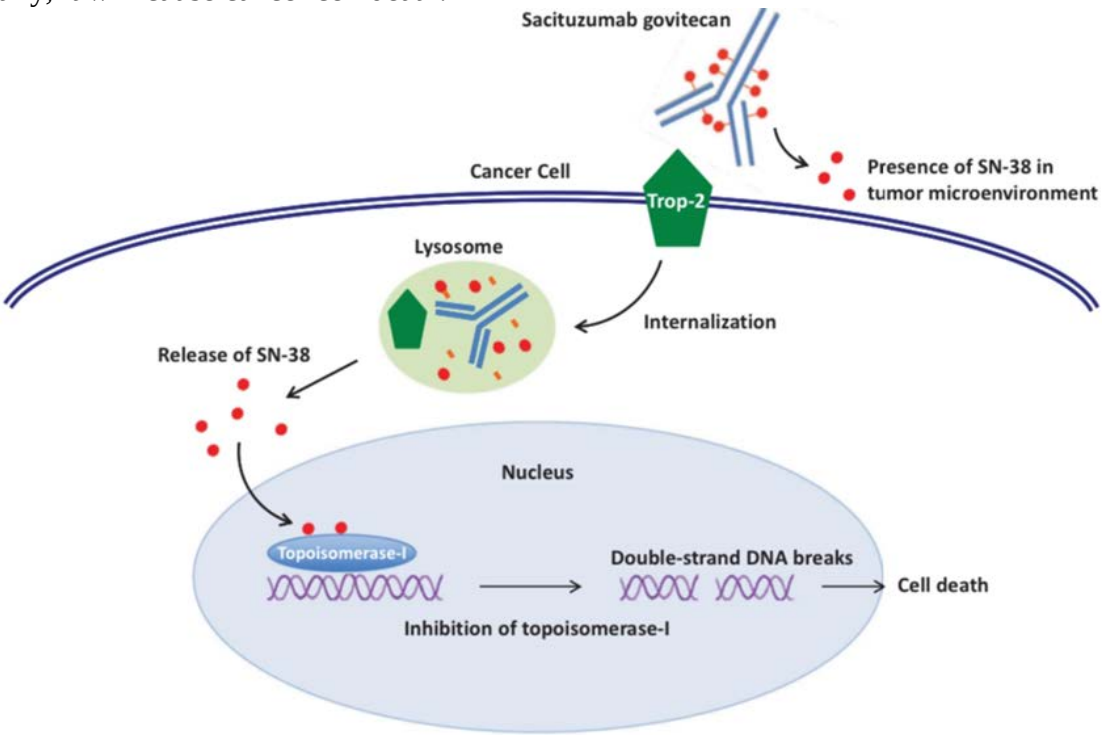

Figure 2. The mechanism of Sacituzumab govitecan killing cancer cells [5].

3. Clinical trials of Sacituzumab Govitecan for the treatment of cancer

3.1 Clinical trial of Sacituzumab govitecan in metastatic triple-negative breast cancer (mTNBC)

The phase 1/2 clinical trial (IMMU-132–01) of sacituzumab govitecan was conducted in humans to evaluate the efficacy and safety. In the series of experiments, the researchers demonstrated that Sacituzumab govitecan represented a remarkable clinical effect in select cancer types, including metastatic triple-negative breast cancer, metastatic platinum-resistant urothelium carcinoma, and non-small-cell lung cancer. Besides, we review and analyze some data of phase 1/2 clinical trials in different tumour types, such as median progression-free survival and response rate. Finally, we get more familiar with the clinical trials of this drug. In total, phase1 was targeted to determine tolerated dose (MTD) in maximum of Sacituzumab govitecan and its potential toxicity [6]. Based on the promising phase I results reported by Starodub et al., the phase II portion of this clinical trial expanded to patients who have different cancer types, including mTNBC [7].

IMMU-132-01 was a phase I/II, basket design and single-group trial. In the survey, some patients with mTNBC that have accepted first-line treatment have a poor prognosis with limited treatment options. However, the Sacituzumab govitecan (SG) is a novel antibody-drug conjugate (ADC) that has shown a significant advantage in mTNBC [8]. In an experiment, all patients are 108, and these patients have developed metastatic triple-negative breast cancer. As a result, these researchers observed that a favourable response rate is 33%. During this process, the median progression-free survival was 5.5 months. The trial also reported that the median overall survival of these patients taking sacituzumab govitecan was 13.0 months [9]. Plus, the author also carried out this trial on a total of 108 patients who had developed mTNBC. Noticeably, these patients had received the sacituzumab govitecan as a final or upper option. In the end, the median duration in sacituzumab govitecan treatment was 5.1 months. It was worth noticing that this result was nearly twice that of previous tumour treatments (2.5 months), emphasizing the clinical effect of Sacituzumab govitecan in mTNBC patients, which is hard to cure

by routine chemotherapy [10]. The data also shows that Sacituzumab govitecan has a significant advantage over traditional single-agent cytotoxicity chemotherapy in treating metastatic triple-negative breast cancer. In a word, the clinical data show that Sacituzumab govitecan thus presents an effective therapeutic selection for patients who develop the refractory mTNBC.

Based on the experimental data from phase 1-2 trials, scientists conducted a phase 3 trial- ASCENT trial, a global, open-label, randomized trial aiming to compare the efficacy and safety and efficacy of Sacituzumab govitecan with chemotherapy of physician's choice in patients with refractory triple-negative cancer. 529 patients in total with triple-negative breast cancer (TNBC)were randomized to receive Sacituzumab govitecan or chemotherapies in the ratio of 1:1 [11].

Up to the baseline, a total of 468 patients were observed with no proof of brain metastases, and they were considered as the primary evidence to analyse the efficacy. The investigator assigned 235 patients randomized to receive Sacituzumab govitecan and 233 patients receiving with single-agent chemotherapy. Median age was 54 years old, and all the patients used taxenes before. The median progression-free survival rate of the patients with chemotherapies (hazard ratio for death or cancer progression, 0.41; 95% CI, 0.32 to 0.52; P<0.001) was found to be 1.7 months (95% CI, 1.5 to 2.6). Moreover, the result of Progression-free survival from the central review was also consistent with the result collected by the investigator. There was also a massive difference between the median overall survival time of the patients under Sacituzumab govitecan treatments and patients undertaking chemotherapies. The median overall survival of patients with Sacituzumab govitecan was 12.1 months (95% CI, 10.7 to 14.0), while the median overall survival time of patients with chemotherapies was only 6.7 months (95% CI, 5.8 to 7.7).

Furthermore, by analyzing the data from each subgroup, the progression-free survival as well as overall survival of patients with Sacituzumab govitecan were better than patients who received chemotherapies. Besides, the percentage of objective response was 35%, while only 5% for the patients with chemotherapies and all the subgroups showed clinical benefit for the patients with Sacituzumab govitecan [12]. From the comparison between Sacituzumab govitecan and previous chemotherapies, we can see that Sacituzumab govitecan is a novel first-in-class antibody-drug conjugate. It also shows enormous potential for treating triple-negative breast cancer from progression-free and overall survival.

However, there were still 61 patients who were observed with brain metastases. They represented a poor prognosis inspite of a high unmet clinical need. Sixty-one patients were randomized to Sacituzumab govitecan(n=32) and treatment of physician choice (TPC) (n=29). As for the result, the median progression-free survival was 2.8 months (1.5-3.9,95% CI,) for the SG group compared with 1.6 months (1.3-2.9, 95% CI,) for the TPC group. The median overall survival was 6.8 months (4.7-14.1, 95% CI,), while the median overall survival for TPC was 7.5 months (4.7-11.1, 95% CI,). Besides, the objective response rate with Sacituzumab govitecan was 3%, while for the patients choosing physician's treatment, the objective response rate (ORR) appeared to be 0%. Like the patients with no evidence of brain metastases, Sacituzumab govitecan was better than treatments of physician's choice for overall survival, progression-free survival and objective response rate [13]. It also indicates that for the poor cohort population, Sacituzumab govitecan can also play a more crucial role due to its higher response rate.

Overall, for all 529 patients enrolled in this trial, the median progression-free survival for the patients with Sacituzumab govitecan was 4.8 months. (95% CI, 4.1 to 5.8), while for the patients with chemotherapies (hazard ratio for disease progression or death, 0.43; 95% CI, 0.35 to 0.54), the median progression-free survival was 1.7 months (95% CI, 1.5 to 2.5). Besides, the median overall survival for the patients with Sacituzumab govitecan and chemotherapy (hazard ratio, 0.51; 95% CI, 0.41 to 0.62) was 11.8 months and 6.9 months, respectively indicated a significant difference [14]. In terms of efficacy, we can conclude that for the whole population enrolled in this ASCENT trial, Sacituzumab govitecan is better than previous chemotherapies than progression-free survival, overall survival and response rate.

In addition, from the data of the ASCENT trial, the exploratory biomarkers were also collected and analyzed to evaluate the association between Trop-2 expression and germline BRCA1/2 mutation

status. There are 468 patients with mTNBC who have already received two or more prior chemotherapies or with one or more metastases and are randomly assigned to receive sacituzumab govitecan or treatment of physician choice until disease progression or side effects were found. A validated immunohistochemistry assay and histochemical scoring were used to evaluate the Trop-2 expression level and collected BRCA1/2 mutation status at baseline. From the result of all 468 patients, 290 patients had Trop-2 expression. Among them, 64% (n=151) patients received sacituzumab govitecan and 60% (n=139) patients received treatment of physician choice. For the different Trop-2 levels (high, medium, low), the median progression-free survival of patients with sacituzumab govitecan was 6.9, 5.6, and 2.7 months. For the patients with treatment of physician choice, the median progression-free survival was 2.5, 2.2 and 1.6 months for the high, medium, and low Trop-2 expression group. Interns of median overall survival, the data were 14.2, 14.9 and 9.3 months corresponding to high, medium and low Trop-2 expression levels for patients with Sacituzumab govitecan. While for the patients with treatment of physician choice, median overall survival was 6.9, 6.9 and 7.6 months, respectively. Besides, the objective response rate was also high for patients with Sacituzumab govitecan compared with patients with treatment of physician choice (44%, 38%, and 22% versus 1%, 11%, and 6%) [15].

For the patients with high and medium Trop-2 expression levels, Sacituzumab govitecan shows an obvious advantage compared with previous chemotherapies. For the small group with a low Trop-2 expression level, Sacituzumab govitecan did not play a significant role. It also proves that Sacituzumab govitecan is essential in targeting Trop-2 antigen for treating triple-negative breast cancer [15].

3.2 Phase 1/2 clinical trial of Sacituzumab govitecan in treatment of metastatic Platinum-Resistant Urothelial Carcinoma

Apart from treating triple-negative breast cancer, Sacituzumab govitecan is also a novel option for Metastatic Platinum-Resistant Urothelial Carcinoma (PRUC) patients. PRUC is another aggressive cancer, and the only known treatment is combination chemotherapy [16]. However, chemotherapy's therapeutic effect is poor, with median overall survival only 15 months, and the 5-year survival was only 15% [17]. Fortunately, Sacituzumab govitecan showed sound clinical effects and low toxicity in treating PRUC [18]. In the IMMU-132 clinical trials, the investigators reported that for the three patients who had a clinically evident response, overall survival was 7.5+to 11.4+ months and the progression-free survival was 6.7 to 8.2 months. In addition, only two patients were found in grade 3 toxicities. As for the grade 4 adverse reaction, the investigators did not observe grade 4 nonhematologic toxicities [19]. Compared with the regular chemotherapy, the median progression-free survival was prolonged, which showed that Sacituzumab govitecan has a significant advantage in treating PRUC.

3.3 Phase 1/2 clinical trial of Sacituzumab govitecan in treatment of Non–Small-Cell Lung Cancer

Like metastatic Platinum-Resistant Urothelial Carcinoma, non-small-cell lung cancer is difficult to cure by regular treatment, no matter combination chemotherapy, molecularly targeted therapy or immunotherapy, because of the low response rate [20]. However, Sacituzumab govitecan once again proved its clinical value through high efficacy and low side effects when treating non-small-cell lung cancer. The researchers conducted IMMU-132 in a single-arm multicenter trial in patients who developed the metastatic NSCLC. As a result, they demonstrated that the primary endpoints were safety and objective response rate (ORR). Plus, the researchers used progression-free survival and overall survival as secondary endpoints. In this experiment, the total number of patients was fifty-four. Among the response-assessable population (n = 47), the ORR was 19%. They also observed that the median response duration was 6.0 months (95% CI, 4.8 to 8.3 months) clinical benefit rate (was 43%. Compared with the traditional treatment, Sacituzumab govitecan increased the response rate and prolonged the survival of patients, which demonstrated that this drug has excellent clinical effectiveness.

4. Adverse events during Sacituzumab govitecan treatment

Although compared with standard care chemotherapy, Sacituzumab govitecan has shown significant benefits in overall survival and progression-free, but the toxic effects of Sacituzumab govitecan, especially myelosuppression and diarrhea, are more common than chemotherapy. For example, in the IMMU-132-01 trial among 108 patients with mTNBC who received Sacituzumab govitecan: 67%of patients experienced nausea, 62% of patients experienced diarrhea, 55% of patients experienced fatigue and neutropenia (64%) and anemia (50%) [21]. Under the premise that the average number of dosing cycles is 9.6 (18.7 doses), the most common AEs evaluated as grande three or higher are neutropenia, anemia, and the decrease of white blood cell count. Serious AEs occurred in 35 patients (32%) [6]. The most severe adverse events were febrile neutropenia (7%), vomiting (6%), and nausea (4%). It is worth noting that 48 of 108 patients (44%) were due to AEs. The treatment was temporarily stopped, the most common being neutropenia, and three patients (2.8%) needed to stop treatment. During the treatment, four people died [22].

It is preposterous to discuss adverse reactions if we do not consider the dose. So, the relationship between adverse reaction and dose is significant. In the study of SG in small cell lung cancer, the researchers found some grade >3 adverse events, including neutropenia (34%), fatigue (13%), diarrhea (9%), and anemia (6%) [23]. In the study, the investigators administered more than 590 doses (over 295 cycles) in the patients with a median of 10 doses (≥ 5 cycles) per patient, including two patients who received >60 doses (>30 cycles). As a result, ten patients received hematopoietic cytokine, but only after grade 3 events had occurred. So, it is unlikely that the rates were influenced by neutropenia or febrile neutropenia. Neutropenia was the main indication for dose reductions.

In the ASCENT Phase III trial, the most common AEs related to around 60% of neutropenia, diarrhea and nausea, nearly half chance of hair loss and fatigue and over 30% of anaemia. However, in the ASCENT Phase III trial, Sacituzumab govitecan did not show severe cardiovascular toxicity, and there were no deaths related to treatment. However, compared with Phase I and phase II clinical trials, the discontinuation rate of Sacituzumab govitecan-related AEs was 4.7%, which was nearly double the previous rate [23]. The above data shows that patients' adverse reactions cannot be ignored in treatment, and future studies need to solve the problem of side effects further.

5. Conclusion

Sacituzumab govitecan, as an effective drug with low side effects, represents a promising new treatment for many patients who entered metastatic malignancies stage (especially triple-negative breast cancer). This review demonstrated about components and mechanisms of Sacituzumab Govitecan and three relevant clinical trials data analyses. Compared with traditional chemotherapy drugs, Sacituzumab govitecan has an excellent therapeutic effect in many tumours in clinical trials. However, the most common adverse reactions observed in mTNBC patients treated with Sacituzumab govitecan are nausea, neutropenia, and diarrhea, like chemotherapy. Proper improvement and management of adverse reactions related to Sacituzumab govitecan are necessary for patients to adhere to treatment and stabilize the treatment cycle while maintaining patients' overall quality of life. Several studies of Sacituzumab govitecan involving breast cancer patients are also underway, including evaluating the drug as either neoadjuvant therapy (for example, NCT04230109) or adjuvant treatment for early triple-negative breast cancer; or using Sacituzumab govitecan with a PARP inhibitor (for example, NCT04039230). There are also clinical trials about advanced triple-negative breast cancer and hormone receptor-positive and HER2-negative metastatic breast cancer (TROPiCS-02 [NCT03901339]). At the same time, Sacituzumab govitecan needs further clinical testing to improve drug safety and combine with other effective treatments to maximize the elimination of cancer cells to provide better treatment options for patients such as triple-negative breast cancer.

References

[1] Syed YY. Sacituzumab Govitecan: First Approval. Drugs. 2020; 80 (10): 1019 - 1025.

[2] Goldenberg DM, Sharkey RM. Antibody-drug conjugates targeting TROP-2 and incorporating SN-38: A case study of anti-TROP-2 Sacituzumab govitecan. MAbs. 2019; 11 (6): 987 - 995.

[3] Goldenberg DM, Sharkey RM. Antibody-drug conjugates targeting TROP-2 and incorporating SN-38: A case study of anti-TROP-2 Sacituzumab govitecan. MAbs. 2019; 11 (6): 987 - 995.

[4] Kciuk M, Marciniak B, Kontek R. Irinotecan-Still an Important Player in Cancer Chemotherapy: A Comprehensive Overview. Int J Mol Sci. 2020; 21 (14): 4919.

[5] Weiss J, Glode A, Messersmith WA, Diamond J. Sacituzumab govitecan: breakthrough targeted therapy for triple-negative breast cancer. Expert Rev Anticancer Ther. 2019; 19 (8): 673 - 679.

[6] Starodub AN, Ocean AJ, Shah MA, et al. First-in-human trial of a novel anti-trop-2 antibody-SN-38 conjugate, sacituzumab govitecan, for the treatment of diverse metastatic solid tumors. Clin Cancer Res. 2015; 21: 3870 – 3878.

[7] Bardia A, Mayer IA, Diamond JR et al. Efficacy and Safety of Anti-Trop-2 Antibody Drug Conjugate Sacituzumab Govitecan (IMMU-132) in Heavily Pretreated Patients with Metastatic Triple-Negative Breast Cancer. J Clin Oncol 2017, 35 (19): 2141 – 8.

[8] Fenn KM, Kalinsky K. Sacituzumab govitecan: antibody-drug conjugate in triple-negative breast cancer and other solid tumors. Drugs Today (Barc). 2019 Sep; 55 (9): 575 - 585.

[9] Bardia A, Hurvitz SA, Tolaney SM, Loirat D, Punie K, Oliveira M, Brufsky A, Sardesai SD, Kalinsky K, Zelnak AB, Weaver R, Traina T, Dalenc F, Aftimos P, Lynce F, Diab S, Cortés J, O'Shaughnessy J, Diéras V, Ferrario C, Schmid P, Carey LA, Gianni L, Piccart MJ, Loibl S, Goldenberg DM, Hong Q, Olivo MS, Itri LM, Rugo HS; ASCENT Clinical Trial Investigators. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. N Engl J Med. 2021 Apr 22; 384 (16): 1529 - 1541.

[10] Spring LM, Nakajima E, Hutchinson J, Viscosi E, Blouin G, Weekes C, Rugo H, Moy B, Bardia A. Sacituzumab Govitecan for Metastatic Triple-Negative Breast Cancer: Clinical Overview and Management of Potential Toxicities. Oncologist. 2021 Oct; 26 (10): 827 - 834.

[11] Logothetis C, Dexeus FH, Finn L, et al. A prospective randomized trial comparing MVAC and CISCA chemotherapy for patients with metastatic urothelial tumors. J Clin Oncol 1990; 8: 1050 - 5.

[12] von der Maase H, Sengelov L, Roberts JT, et al. Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patients with bladder cancer. J Clin Oncol 2005; 23: 4602 - 8.

[13] Cardillo TM, Govindan SV, Sharkey RM, et al. Sacituzumab govitecan (IMMU132), an anti-Trop-2/SN-38 antibody-drug conjugate: characterization and efficacy in pancreatic, gastric, and other cancers. Bioconjug Chem 2015; 26: 919 - 31. 9.

[14] Ambrogi, F., Fornili, M., Boracchi, P., Trerotola, M., Relli, V., Simeone, P., La Sorda, R., Lattanzio, R., Querzoli, P., Pedriali, M., Piantelli, M., Biganzoli, E., & Alberti, S. (2014). Trop-2 is a determinant of breast cancer survival. PloS one, 9 (5), e96993.

[15] Faltas B, Goldenberg DM, Ocean AJ, Govindan SV, Wilhelm F, Sharkey RM, Hajdenberg J, Hodes G, Nanus DM, Tagawa ST. Sacituzumab Govitecan, a Novel Antibody--Drug Conjugate, in Patients with Metastatic Platinum-Resistant Urothelial Carcinoma. Clin Genitourin Cancer. 2016 Feb; 14 (1): e75 - 9.

[16] Masters GA, Temin S, Azzoli CG, et al: Systemic therapy for stage IV non-small-cell lung cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 33: 3488 - 3515, 2015.

[17] Seligson JM, Patron AM, Berger MJ, Harvey RD, Seligson ND. Sacituzumab Govitecan-hziy: An Antibody-Drug Conjugate for the Treatment of Refractory, Metastatic, Triple-Negative Breast Cancer. Ann Pharmacother. 2021 Jul; 55 (7): 921 - 931.

[18] Syed YY. Sacituzumab Govitecan: First Approval. Drugs. 2020 Jul; 80 (10): 1019 - 1025.

[19] Gray JE, Heist RS, Starodub AN, Camidge DR, Kio EA, Masters GA, Purcell WT, Guarino MJ, Misleh J, Schneider CJ, Schneider BJ, Ocean A, Johnson T, Gandhi L, Kalinsky K, Scheff R, Messersmith WA, Govindan SV, Maliakal PP, Mudenda B, Wegener WA, Sharkey RM, Goldenberg DM. Therapy of Small Cell Lung Cancer (SCLC) with a Topoisomerase-I-inhibiting Antibody-Drug Conjugate (ADC) Targeting Trop-2, Sacituzumab Govitecan. Clin Cancer Res. 2017 Oct 1; 23 (19): 5711 - 5719.

[20] Bardia, A., Rugo, H. S., Horne, H., Wegener, W. A., Goldenberg, D. M., & O'Shaughnessy, J. (2018). Abstract OT2-07-05: a phase III, randomized trial of sacituzumab govitecan (IMMU-132) vs treatment of physician choice (TPC) for metastatic triple-negative breast cancer (mTNBC).

[21] Bardia, A., Hurvitz, S. A., Tolaney, S. M., Loirat, D., Punie, K., Oliveira, M., ... & Rugo, H. S. (2021). Sacituzumab govitecan in metastatic triple-negative breast cancer. New England Journal of Medicine, 384 (16), 1529 - 1541.

[22] Dieras, V., Weaver, R., Tolaney, S. M., Bardia, A., Punie, K., Brufsky, A., ... & Carey, L. (2021). Subgroup analysis of patients with brain metastases from the phase 3 ASCENT study of sacituzumab govitecan versus chemotherapy in metastatic triple-negative breast cancer. CANCER RESEARCH, 81 (4).

[23] Bardia, A., Tolaney, S. M., Punie, K., Loirat, D., Oliveira, M., Kalinsky, K., Zelnak, A., Aftimos, P., Dalenc, F., Sardesai, S., Hamilton, E., Sharma, P., Recalde, S., Gil, E. C., Traina, T., O'Shaughnessy, J., Cortes, J., Tsai, M., Vahdat, L., Diéras, V., … Hurvitz, S. A. (2021). Biomarker analyses in the phase III ASCENT study of sacituzumab govitecan versus chemotherapy in patients with metastatic triple-negative breast cancer. Annals of oncology: official journal of the European Society for Medical Oncology, 32 (9), 1148 – 1156.