EE392

# NUMBER NEEDED TO TREAT (NNT) COMPARING SACITUZUMAB GOVITECAN AND SINGLE-AGENT CHEMOTHERAPY IN RELAPSED OR REFRACTORY METASTATIC TRIPLE-NEGATIVE BREAST CANCER

**Gabriel Marasco[1], Rafael Anunciação[2], Flávia Andreghetto[2], Pedro Aguiar[3,4]**

1. ORIGIN Health; 2. Gilead Sciences Brazil; 3. Clinic Oncologist, Grupo Oncoclínicas; 4. Oncology Fellowship Preceptor, Faculdade de Medicina do ABC



## Conclusion

- The study found that sacituzumab govitecan (SG) has a low NNT compared to single-agent chemotherapy for both progression-free survival (PFS) and overall survival (OS) endpoints in patients with refractory metastatic triple negative breast cancer (mTNBC)
- The NNT using restricted mean survival time ($NNT_{RMST}$) was lower than NNT using the inverse of absolute risk reduction ($NNT_{ARR}$), which indicates the importance of considering the effect of SG during the follow-up period
- The results for intention-to-treat (ITT) and without brain metastasis (WBM) populations were very similar, highlighting the consistent benefit of SG for both populations
- These findings communicate an alternative perspective on the effectiveness of healthcare intervention and can be used to inform decisions among physicians, healthcare managers and payers around treatment strategies and resource allocation for patients with refractory metastatic triple-negative breast cancer

## Plain Language Summary

- This study presented an alternative approach to quantify the magnitude of benefit for an innovative treatment class, conducted in the context of a highly aggressive disease of refractory metastatic triple negative breast cancer
- Our study reinforced that measures which can adequately summarize the treatment effect of a new treatment and be easily conveyed to healthcare stakeholders are essential for decision-making

**References:** 1. Carlos Souto Maior Borba MA, de Mendonça Batista P, Falcão Almeida M, do Carmo Rego MA, Brandão Serra F, Barbour Oliveira JC, Nakajima K, Silva Julian G, Amorim G. Treatment patterns and healthcare resource utilization for triple negative breast cancer in the Brazilian private healthcare system: a database study. Sci Rep. 2023 Sep 22;13(1):15785; 2. Plasilova ML, Hayse B, Killelea BK, et al. Features of triple-negative breast cancer: Analysis of 38,813 cases from the national cancer database. Medicine (Baltimore). 2016;95(35):e4614; 3. Gonçalves H, Guerra MR, Duarte Cintra JR, Fayer VA, Brum IV, Bustamante Teixeira MT. Survival Study of Triple-Negative and Non–Triple-Negative Breast Cancer in a Brazilian Cohort. Clin Med Insights Oncol. 2018;12; 4. American Cancer Society. 2021. Triple-negative Breast Cancer. https://www.cancer.org/cancer/breast-cancer/about/types-of-breast-cancer/triple-negative.html; 5. Reinert T, Pellegrini R, Rol R, Werutsky G, Barrios CH. Estimation of the Number of Brazilian Women Living With Metastatic Breast Cancer. JCO Glob Oncol. 2020 Sep;(6):307–12; 6. The ASCO post (2021). FDA Grants Regular Approval to Sacituzumab Govitecan-hziy for Pretreated Patients With Triple-Negative Breast Cancer. https://ascopost.com/issues/may-25-2021/fda-grants-regular-approval-to-sacituzumab-govitecan-hziy-for-pretreated-patients-with-triple-negative-breast-cancer/;7. Bardia A, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. N Engl J Med. 2021;384(16):1529-41; 8. Bardia A, Rugo HS, Tolaney SM, Loirat D, Punie K, Oliveira M, Brufsky A, Kalinsky K, Cortés J, Shaughnessy JO, Diéras V, Carey LA, Gianni L, Piccart-Gebhart M, Loibl S, Yoon OK, Pan Y, Hofsess S, Phan SC, Hurvitz SA. Final Results From the Randomized Phase III ASCENT Clinical Trial in Metastatic Triple-Negative Breast Cancer and Association of Outcomes by Human Epidermal Growth Factor Receptor 2 and Trophoblast Cell Surface Antigen 2 Expression. J Clin Oncol. 2024 Feb 29:JCO2301409; 9. Yang Z, Yin G. An alternative approach for estimating the number needed to treat for survival endpoints. PLoS One. 2019 Oct 18;14(10):e0223301.

**Acknowledgments:** This study was funded by Gilead Sciences, Inc. Editing and production assistance were provided by Origin Health, and funded by Gilead Sciences, Inc.

**Disclosures:** GM is a senior HEOR consultant at Origin Health. RA and FA declare that they both hold shares of stocks in Gilead Sciences, Inc. PA has no financial interests or relationships to disclose.

**Correspondence:** Rafael Anunciação, rafael.anunciacao@gilead.com

## Background

- Triple negative breast cancer (TNBC) represents 15–20% of all diagnosed breast cancers worldwide and is characterized by the absence of the estrogen receptor, progesterone receptor, and human epidermal growth receptor 2 (HER2).[1]
- TNBC is linked to a worse prognosis, an aggressive clinical course, increased rates of metastasis, typically visceral, and low survival rates.[2,3] Overall survival (OS) among patients with metastatic TNBC (mTNBC) remains low, with a five-year OS rate of 12%.[4]
- An observational study conducted in Brazil indicated that 16% of all breast cancer patients have TNBC. Furthermore, in the same study, the median OS of patients with mTNBC was 16 months, and the 5-year OS rate was 5.5%, indicating the poorest prognosis for this disease. These local findings resonate with previous global data, further emphasizing the persistent challenges in effectively managing mTNBC patients.[5]
- Sacituzumab govitecan (SG) is a novel antibody-drug conjugate (ADC) that targets Trop-2, and it consists of an anti-Trop-2 antibody linked to SN-38 via a hydrolyzable linker[6]. In the phase 3 ASCENT trial, SG has demonstrated a significant survival improvement over chemotherapy (shown in **Figure 3** and **Figure 4**), with a manageable safety profile in the second-line or greater mTNBC setting.[7,8]
- The number needed to treat (NNT) is an absolute effect measure that has been used to assess the beneficial and harmful effects of medical interventions. NNT represents the number of patients who need to be treated with a particular intervention for 1 person to benefit compared to an alternative treatment.[9]
- Among the methodologies, the use of the inverse of absolute risk reduction (ARR) and restricted mean survival time (RMST) emerge as pivotal estimation procedures employed in this type of assessment. Despite of many advantages, $NNT_{ARR}$ may not adequately capture the treatment effect over time, while $NNT_{RMST}$ has the potential to better quantify NNT for survival endpoints since it reflects the treatment effect over a follow-up period instead of just a single time point.[9]

## Objective

- To assess the relative benefit of SG versus single-agent chemotherapy of physician's choice (eribulin, vinorelbine, capecitabine, or gemcitabine) in patients with relapsed or refractory mTNBC, using the NNT methodology.

## Methods

- The ASCENT study's data (NCT02574455) were reviewed, specifically the progression-free survival (PFS) and OS at 12 months among the intention-to-treat (ITT) population, which included patients with stable brain metastases and patients without brain metastasis (WBM).
- The PFS and OS curves from ASCENT trial[7] were digitized using the Engauge Digitizer tool and processed in statistical software R.
- The NNT was calculated using the $NNT_{RMST}$ method for ITT and WBM populations. Additionally, we also considered the $NNT_{ARR}$ in this analysis in the same scenarios.

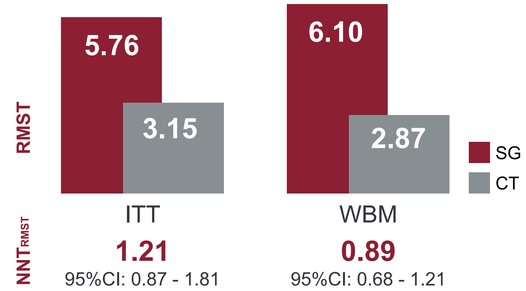
## Limitations

- $NNT_{ARR}$ disregards the process of events and censors throughout the follow-up period, failing to reflect average survival time.
- Identified as a more suitable method to quantify the treatment effect in this study, $NNT_{RMST}$ measures the area under the Kaplan-Meier (KM) curve or the area above the cumulative incidence curve from 0 to a specific time point. Instead, this approach lacks the ability of capturing the relevance of endpoints, conveying information about the cost-effectiveness of the treatments and the need of a prespecified follow-up time.
- This analysis estimated the individual patient data (IDP) using flexsurv R package, which could lead to haziness due to variation of trial population characteristics and/or censored data from ASCENT trial, parametric model assumptions, or specific model selection.

## Results

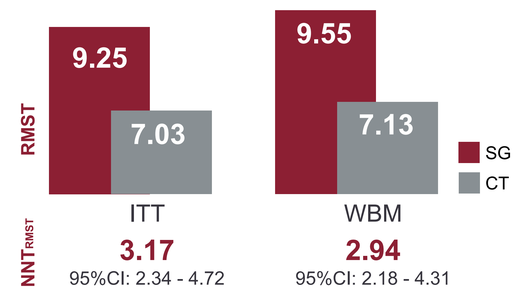
- Comparing SG versus single-agent chemotherapy, the $NNT_{RMST}$ results for PFS endpoint in the ITT and WBM populations were as follows: 1.21 (95% Confidence Interval (CI) 0.87 to 1.91) and 0.89 (95% CI 0.68 to 1.21), respectively. **(Figure 1)**
- For OS, the $NNT_{RMST}$ results obtained in ITT and WBM were 3.17 (95% CI 2.34 to 4.72) and 2.94 (95% IC 2.18 to 4.31), respectively. **(Figure 2)**
- Furthermore, using the $NNT_{ARR}$ method, summarized results for PFS were 9.72 and 7.25, while for OS were 3.85 and 3.56, respectively in ITT and WBM populations. Detailed results for the respective ARR and CI can be found in the tables below **Figure 1** and **Figure 2**.

**Figure 1. Progression-free survival: comparison of $NNT_{RMST}$ between ITT and WBM populations.**



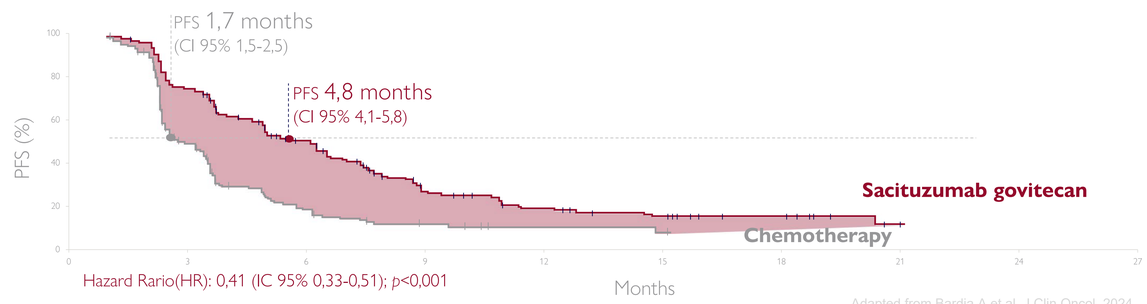

| | PFS | | |
|---|---|---|---|
| Population | SG | CT | $NNT_{ARR}$ |
| ITT | 15.86% | 5.57% | 9.72 |
| WBM | 15.03% | 1.23% | 7.25 |

**Figure 2. Overall survival: comparison of $NNT_{RMST}$ between ITT and WBM populations.**



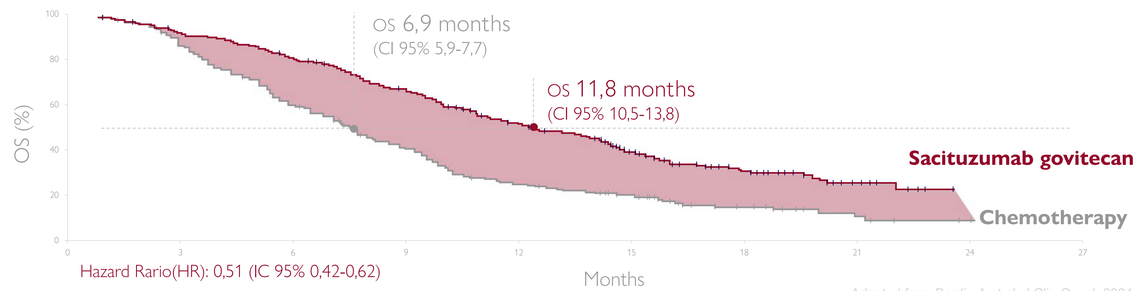

| | OS | | |
|---|---|---|---|
| Population | SG | CT | $NNT_{ARR}$ |
| ITT | 48.53% | 22.57% | 3.85 |
| WBM | 51.54% | 23.47% | 3.56 |

**Figure 3. Progression-free Survival (PFS) among ITT Patients**




Adapted from Bardia A et al. J Clin Oncol. 2024

**Figure 4. Overall Survival (OS) among ITT Patients**




Adapted from Bardia A et al. J Clin Oncol. 2024