

Peer Review File

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Reviewer A Comments:

Thanks for your work in the field of TNBC and for submitting this editorial commentary on sacituzumab govitecan for publication. Kindly find some comments and suggestions below which could possibly improve the accurateness of the manuscript.

Comment 1. OR should read ORR.

Reply 1: We modified as requested.

Comment 2. It could be considered atypical to show HR for the overall population, while only giving the medians for the primary PFS and OS analyses.

Reply 2: We agree with the reviewer. We delete the information for HR

Comment 3. Consider to state 'no known baseline brain metastases' for the primary analysis population.

Reply 3: We modified the phrase at page 2 lines 7 and 8.

Comment 4. Some linguistic improvement should be considered (PFS instead of the PFS; end(o)points, clinical benefit instead of the clinical benefit, common frequent, were instead of was).

Reply 4: We correct typos and languages as requested.

Comment 5. Please clarify that proportions for AE's of any CTCAE grades are mentioned when giving most common AEs, or at least specify CTCAE when focusing on grade 3.

Reply 5: We modified the text as requested.

Comment 6. It should be avoided to mention that the efficacy differed between primary analysis population and all patients, since any difference in activity among these groups was not assessed.

Reply 6: We delete the sentence as requested.

Comment 7. The trial recruited patients irrespective of Trop2 expression. Therefore, the statement 'patients with mTNBC positive to Trop-2' is incorrect.

Reply 7: We modified the sentence as requested.

Comment 8. The statement from third line onward is incorrect, also patients in second line received SG in ASCENT (this was possible if there was a DFI<12 months after (neo)adjuvant chemotherapy), and this is also foreseen in the FDA and EMA label

(irrespective of the DFI).

Reply 8: We modified the sentence as requested at page 3 lines 1 and 2.

Comment 9. The section on access in Italy is less understandable from my point of view. Access to SG is currently not only limited due to country approvals/reimbursement decision, but also due to limited availability. I would consider to rewritten or shorten this section, and focus on the fact that access is currently limited or unavailable in the majority of countries.

Reply 9: We added this information at page 4 lines 8 and 9.

Comment 10. It is a good point to mention the high cost of the drug, but the first sentence of this section does not fit well with the rest of this paragraph.

Reply 10: We anticipated the sentence in the previous paragraph.

Comment 11. References should be edited, e.g., reference 5 is unclear. Combinations with SG can also not be part of a current treatment algorithm since these are not approved.

Reply 11: We removed the sentence.

Comment 12. Some subset analyses of ASCENT could be added (e.g., biomarker analysis *Annals of Oncology* 2021).

Reply 12: We added this info at page 2 lines 21 and 22.

Reviewer B Comments:

This editorial describes the results of the phase III ASCENT trial which compared sacituzumab govitecan-hziy (SG) vs. standard chemotherapy in patients with metastatic triple-negative breast cancer. The authors summarize the results of the trial which showed that treatment with SG was associated with a significant improvement in median progression-free survival and overall survival compared with standard chemotherapy. Additionally, they highlight the tolerable safety profile of this antibody drug conjugate that targets Trop-2.

Comment 1. I am unclear what are the major points of this commentary. The piece needs more structure and convey clearly what is the implications of the results. Is it to describe the impact of the results to a clinician's practice? Is the focus on the slowness of drug approval in Italy?

Reply 1: Despite the toxic effects of SG are superior to that of chemotherapy, if well manage, they determine a low incidence of treatment discontinuation. Then, we want to point out that despite differences in SG use can emerged in different countries for the lack of drug availability and delay in the guideline approval, it is important that all patients can have the opportunity to be treated with this drug also in earliest lines of treatment. We added this phrase at the end of manuscript.

Several sentences are awkwardly written, please see following the suggested corrections:

Comment 2: Page 2: They demonstrated that patients with mTNBC pretreated with at least two lines of treatment, experienced a significant superiority of sacituzumab govitecan over chemotherapy in terms of survival

Page 2: Progression-free and overall survival were significantly longer with SG than with single agent chemotherapy among patients with mTNB.

Delete this sentence as it is repetitive.

Reply 2: We rewrote the first sentence and we delete the second sentence as requested.

Comment3: Page 3: “The results of this study have changed the clinical practice of patients with mTNBC positive to Trop-2 from the third line of treatment and beyond.”

Delete “positive to Trop2” as known Trop 2 expression was not required to determine patient eligibility.

Reply 3: It has been done.

Comment 4: Page 4: Given the promising activity of this drug alone from the third line and behind, we expected even more efficacy of the drug also in previous lines of treatment alone or in combination with other drugs such as Pembrolizumab, Atezolizumab, Talazoparib has already done in ongoing trials.

This sentence needs to be rewritten as it is unclear. Behind should be beyond.

Reply 4: It has been done.

Comment 5: Page 4: Unfortunately, due to the fact that different countries follow different given by regulatory agencies...

Is there a word missing in this sentence after the second different?

Reply 5: We added the word guidelines.

Comment 6: Page 4: It is even more important in the mTNBC subgroup given the late stage of this aggressive disease and the patients necessity to be cured in the best appropriate way.

This sentence needs to be rewritten as metastatic breast cancer is not a curable condition.

Reply 6: We corrected the phrase.

Comment 7: Page 5: Recently, at San Antonio Breast Cancer Conference 2021, Hope Rugo proposed the use of SG in an algorithm for the second line of treatment in metastatic TNBC alone or in combination with new antibody drug conjugate, chemotherapy or in patients with high tumor mutational burden or high MSI in combination with checkpoint inhibitors (5).

Check Dr. Rugo’s presentation on her proposed algorithm to treat metastatic TNBC. This sentence is confusing and needs to be clearer as to how to sequence treatment for

patients with metastatic TNBC. Also, there is a misspelling of “coniugate”.

Reply 7: We removed the sentence.

Comment 8: Page 5: 5. San Antonio Breast Cancer Symposium (SABCS) 2021, San Antonio, TX, USA.

This citation is incomplete. I am unable to find this reference to Dr. Rugo’s presentation at SABCS 2021.

Reply 8: We removed the citation.