Peer Review File

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Reviewer A:

The purpose of this article is to comment on: Martinez-Marti A, et al. COAST: An open label, randomized, phase II, platform study of durvalumab alone or in combination with novel agents in patients with locally advanced, unresectable, stage III NSCLC. ESMO meeting 2021.

The Comments provide a general overview of the background and mechanism of action of Monalizumab and Oleclumab. The authors reviewed relevant trials that used these medications with positive results. Discussion about immune system, its synergism and potentially increasing the benefits of immune checkpoint inhibitor is relevant and a widely discussed topic. Figure 1 is a good illustration to review the mechanism of action of Monalizumab and Oleclumab.

Comments

(Lines 40-44) Reference to Durvalumab in combination with chemotherapy and significantly improved median OS. In the Poseidon trial the Durvalumab + Tremelimumab + chemotherapy arm did not reach statistical significance for OS. It was the Durvalumab + Tremelimumab +chemo that reached OS benefit. The other reference is with the Caspian Trial, but this follows small cell histology, thus out of focus with the goal of the article which is NSCLC.

I don't feel either reference (POSEIDON and CASPIAN trials) support the statement of durvalumab in combination with chemotherapy has demonstrated significant overall survival in NSCLC.

Table 1 contains information pertaining the CASPIAN Trial. I would limit studies relevant to NSCLC.

(Lines 56-60) Monalizumab in H&N patients in phase I/II with cetuximab. This comment stretches the relation to the COAST study. In COAST, we have NSCLC histology and

Monalizumab is combined with an immune checkpoint inhibitor. The COAST trial is evaluating the synergism between ICI and Monalizumab. This statement weakly supports this trial.

Minor comment grammatical corrections needed in : Lines 45, 147

- It has been made clear in Table 1 that only the combination of durvalumab + tremelimumab and chemotherapy versus chemotherapy alone demonstrated a significant mOS benefit.
- The CASPIAN trial (SCLC) has been deleted now (Table 1 and main text including corresponding reference).
- The POSEIDON trial has now been published in more detail (new reference 6 is included); very robust data clearly indicate that the combination of durvalumab and the novel agents tremelimumab plus chemotherapy significantly increase mOS when compared with chemotherapy alone. For the sake of accuracy this trial needs to be mentioned.
- The CASPIAN trial has been deleted in Table 1 and the References Section.
- Discussion of monalizumab in head-and-neck cancers has been omitted in the main text (including corresponding reference).
- We corrected one typo, the second one could not be found.

Reviewer B:

Wolfram et al reviewed 'ESMO Meeting 2021, #LBA42'. The COAST trial has not been published. Therefore, it would be difficult to discuss reason of discrepancy of mPFS of durvalumab in the PACIFC and the COAST studies based on the conference data (Line 141-145). I consider the discussion should be limited to NKG2, adenosine receptors and new agents.

- The COAST trial has been published at WCLC 2021 as an "extensive abstract". In addition, the discussant during the meeting provided additional comments with regard to this trial. It should also be noted that the observed mPFS discrepancies (COAST versus PACIFIC) triggered a huge and lively discussion during the meeting as the reported mPFS values are set in stone and will not change in any further publication. Therefore, we regard the finding as significant and do not want to omit it.