Peer Review File

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Reviewer A:

Authors described available data evaluating efficacy and safety of immune checkpoint inhibitors either as monotherapy or in combination for elderly lung cancer patients. The manuscript was well organized and seems to be useful for respiratory oncologists.

I have one major comment.

Authors insisted that studies are urgently needed to clarify the effect of ICIs in the elderly population. In a recent review of NSCLC patients >75 years treated with ICI, there is a need for more evidence showing the benefit of ICIs (Cancers (Basel). 2020 Jul 21;12(7):1995). Until several years ago, a single third-generation cytotoxic anticancer drug (docetaxel, vinorelbine, or gemcitabine) was recommended for NSCLC without molecular targets such as EGFR and ALK. What kind of trials (cytotoxic anticancer drug monotherapy vs ICI monotherapy etc) do authors need in order to decide the standard regimen in elderly NSCLC patients?

ANSWER

It's a really interesting comment.

In my opinion, two clinical trials conducted by IFCT (French cooperative thoracic intergroup) are relevant to answer.

For patients ≥ 75y with treatment-naïve advanced NSCLC, the control arm should be CARBOPLATIN AUC 6 every 4 weeks with weekly PACLITAXEL 90mg/m² (E. Quoix, Lancet, 2011 sep 17;378(9796):1079-88). Compared to single chemo agent, this regimen demonstrated an OS benefit (10.3 months vs 6.2m) and should be compared with single agent immunotherapy or combination (chemo + IO or combination IO). This regimen is used as control arm in ELDERLY trial.

In second or further line, there is no standard of care in geriatric population but we could use the result of the MODEL trial evaluating switch maintenance in elderly patients with advanced NSCLC. This phase III trial demonstrated a prolonged PFS (not in OS) using switch maintenance, an early second line, with PEMETREXED (non squamous NSCLC) or GEMCITABINE (E. Quoix Eur J Cancer. 2020 Oct;138:193-201) and demonstrated the feasibility of these two regimens in elderly.

Minor comments:

1. line 94 etc.: 64,5 years -> 64,5 years; 53,8% -> 53.8%
2. line 127: AOK study -> OAK study
3. line 151, 283: ARTIC -> ARCTIC
4. line 152: aNSCL -> aNSCLC
5. line 173: CheckMate-17 -> CheckMate 017
6. line 174, 181, 214, etc.: & Al or & al -> et al might be better?
7. line 159: Among 10.452 patients -> Among 10,452 patients
8. line 263: Checkmate-227 -> Checkmate 227
9. line 285: CheckMate-9LA -> CheckMate 9LA
10. line 366-368: ref 'https://clinicaltrials.gov/ct2/show/NCT03351361' might be added.

Reviewer B:

This is a fascinating review article about the efficacy and safety of immune checkpoint inhibitors (ICIs) in elderly lung cancer patients. This review includes all major clinical trials about ICI monotherapy as well as the combination therapy ICI and cytotoxic chemotherapy. The authors also mentioned the retrospective analysis and ICIs in ED-SCLC. Minor revisions are needed for the publication.

Minor revisions:

1. A period is a generally accepted decimal separator for scientific writing. (L94, 64,5 years; L94, 53,8%; L108, 17,7 months,,, and so on)
2. In L117, 0.1.02 is not appropriate.
3. In L173, Checkmate-17 should be CheckMate-017.
4. Did you mention Figure 1 in the article?
5. Figure 1 is hard to understand. What is the difference of both Favor? What did the arrowheads mean?