

Peer Review File

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Reviewer A

Comment 1: Real world data regarding outcomes with osimertinib is not entirely novel but is valuable to show these data in a different clinical environment. The inclusion of a wide PS as used in regular clinical practice is particularly helpful.

Response 1: Agreed

Comments 2: The inclusion of site of presentation is also useful to see. This is an issue that is well known for lung cancers and well researched previously for barriers to early presentation but it is still valuable to review this in the context of the covid pandemic.

Response 2: Agreed

Comment 3: The impact of Covid on survival whilst on treatment is important to discuss although given the small numbers infected drawing any conclusions is impossible. I would like to see the proportion of individuals included in the study who were vaccinated as that maybe a confounder - in particular those hospitalised vs not hospitalised.

Response: We have revised the Discussion limitations section to highlight that while vaccination status was not routinely collected in clinic charts, the prevalence of COVID-19 amongst the studied cohort (10.8%) was similar to that observed in the general population of British Columbia (7.5%) during the studied time period and only one patient died from COVID-19. We feel this can provide reassurance to patients that the risk of SARS-CoV-2 infection while receiving anti-cancer therapies can be minimized with strict infection control procedures.

Page 15. Line 470-481.

Comment 4: My main question though is why the group from January 2019 to at least February 2020 are included in the same analysis? I recognise many of these individuals may have had some of their treatment during the pandemic but certainly not all and their route and barriers to presentation would also be different. It would be interesting to see those results as a separate cohort. Did they present differently? Did their outcomes alter as they were actually much more likely to be able to effectively isolate as if diagnosed and established on treatment pre the pandemic they would likely have to attend hospital less frequently than those initiating treatment in the pandemic. Did some have their treatment finished or pass away before the pandemic even started and are therefore more of a control arm?

Response 4: As suggested by the reviewers, we have modified the inclusion criteria. The 47 patients diagnosed with EGFR mutated advanced NSCLC prior to March 11 2020 are now excluded. As this is a small number of patients, statistical comparisons of patients diagnosed with EGFR mutated advanced NSCLC before (n=47) and after (n=231) this time point is not possible.

Reviewer B

Comment 5: The authors included those patients who were diagnosed before the COVID-19 pandemic. I think the authors should use the data after the COVID-19 pandemic, or compare the data before and after the COVID-19 pandemic, if they want to discuss the influence of COVID-19 on lung cancer treatment. I understand that the COVID-19 pandemic led to the delayed diagnosis of lung cancer, which resulted in the high rate of patients with poor PS.

Therefore, I recommend the authors to set the appropriate inclusion period.

Response 5: Please see response #4. We agree with both reviewers and have revised the analysis to include only patients diagnosed after March 10, 2020.

Comment 6: The authors discussed the relationship between poor PS and worse outcomes. I think the authors should discuss this point referencing the NEJ001 phase II study (J Clin Oncol. 2009; 27(9): 1394-1400) which included 22 patients with PS of 3-4, instead of the NEJ032B (reference 6 in the current manuscript).

Response 6: The manuscript has been amended to include this reference.

Page 5, Lines 156-160.

Comment 7: The observed finding of elderly patients aged ≥ 75 as a risk factor for shorter OS is important. Therefore, the authors should add the demographic distribution according to age in Table 1. Hopefully, this should be expressed like age < 65 , $65-75$, ≥ 75 .

Response: Agreed. Table 1 has been amended in accordance to this suggestion.

Line: Please see Table 1

Comment 8: The running title should include the term “COVID-19” or “COVID-19 pandemic”, such as “First-line osimertinib during COVID-19 pandemic”.

Response 8: The running title has been changed as requested.

Page 1, Line 24

Comment 9: The title of “COVID-19 disease (Line 357)” would is not appropriate. I think “COVID-19” would be better.

Response 9: We have modified the text as requested.

Page 12, Line 375