Peer Review File

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Round 1

Reviewer A

Comment 1: Table 1 may be split into two tables (ALK, ROS1, and the other fusions) for better representation. Also, the contents in Table 1 can be presented in more meaningful order (i.e., chronological order, or therapy types, etc.).
Reply 1: Thank you very much for your advice, we had split Table 1 into two tables and presented them in chronological order.
Changes in the text: Page5-6, line 75-84.

Comment 2: It would be helpful for the readers if the authors added an illustration to show the timeline of the development of the targeted drug.
Reply 2: Thank you for your constructive comments, we had added an illustration to show the timeline of the development of the targeted drug.
Changes in the text: Page7, line 85-86.

Minor comment 1: p. 11, lines 188-193: Add a reference for the result.
Reply 1: Thank you very much for your advice, we had added a reference for the result.
Changes in the text: Page14, line 225-232.

Minor comment 2: p. 13, line 217-221: Add reference for the result;
Reply 2: Thank you for your positive comments, we had added a reference for the result.
Changes in the text: Page15-16, line 260-264.

Minor comment 3: p. 20 line 371-375: Add references for other rare fusion genes;
Reply 3: Thank you very much for your advice, we had added a reference for the result.
Changes in the text: Page 23, line 421-422.

Reviewer B:

Comment 1: In the section about ALK-fusions, we learn that, in addition to Crizotinib, three more ALK TKIs may be used in the first-line setting for patients in ALK-fusions in NSCLC. These are Alectinib, Brigatinib and Ceritinib. I think it would be highly valuable to the readers if the authors could provide an overview of which ALK TKIs are used in the first-line setting in different parts of the world. For example, in Europe, it is common to use either Alectinib or Brigatinib in the first-line setting but not other ALK TKIs. The choice of ALK TKI in the first-line setting largely dictates which other ALK TKIs may be used at disease progression. Therefore, on overview of ALK TKI usage in the first-line setting in different parts of the world would be highly beneficial for the readers. The same applies for which drugs are used in the first-line setting for other gene-fusions.
Reply 1: Thank you very much for your valuable comments. Because we did not find

literature on the use of related drugs in different regions, we did not analyze drugs are used in the first-line setting in different parts of the world. However, we see that some of the literature has subgroup analysis of Asian and non-Asian population, so we added some outcomes and overview of the first-line drugs use according to Asian and non-Asian population. I hope these would be beneficial for the readers.
Changes in the text: Page 9, line 123-130; Page10, line141-146; Page 157-161; Page 12, line 186-190; Page 13, line 205-208; Page 14, line 221-222; Page 15, line 245-249; Page 17, line287-288, 302-305; Page 18, line 309-310.

Comment 2: The introduction could be improved. Currently it gives the impression that all patients with ALK fusions receive Crizotinib which is not accurate. In general, the introduction could be made shorter and broader with less specific information since the authors state the details in the different sub-sections of the review article.
Reply 2: Thank you very much for your positive comments, we had made some changes to the introduction. We deleted the inappropriate and controversial parts, and roughly described the types of drugs used by various genes.
Changes in the text: Page 3, line 45-47, 51-59.

Round 2

Comment: The authors have addressed my concerns. I have one minor comment remaining. In the introduction, authors have added “Among them, ensartinib was first approved by National Medical Products Administration (NMPA) as a second-line drug for the treatment of crizotinib resistance”. The authors should either comment on results of other ALK TKIs following Crizotinib resistance or delete this sentence since it currently only put focus on Ensartinib in the state of Crizotinib resistance.
Reply: Thank you for your constructive comments, we also found this sentence was not appropriate in this part, so we had deleted the sentence “Among them, ensartinib was first approved by National Medical Products Administration (NMPA) as a second-line drug for the treatment of crizotinib resistance” in our paper.