Peer Review File

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For the comment from Reviewer A:

Comment: Only one comment, the Histopathological and Genetic Characteristics section, is perhaps too long and difficult to read for a clinician, although it may be suitable for pathologists, it should be kept in mind for whom the article is intended.

Reply 1: We are grateful for your suggestion. The section on histopathological and genetic characteristics is indeed longer and more complex than the other chapters. In fact, this part is one of the contents we want to highlight, because SBC lacks specific clinical manifestations and has typical pathological and molecular characteristics. In addition, SBC is well known as a rare disease with good prognosis, but we found that there are still very few patients with distant metastasis. Our next work will explore the histopathological features or molecular markers of poor prognosis, so this part was described in detail. Of course, besides clinician, we also hope that our article can provide a reference for pathologists to understand this rare disease in more detail. We have simplified our manuscript as much as possible and marked the modified parts in red.

For the comment from Reviewer B:

Comment 1: (page 10 line 199-201) The authors described "SBC is often … and coexists with other subtypes of ductal carcinoma in situ (31)." However, this description may be misleading or inappropriate. The previous study (ref 31) has shown that in situ and invasive components shared the same immune-profile and genetic alteration.

Reply 1: Thanks for your suggestion. We are sorry that the description here was inappropriate. We re-studied the previous study (ref 31) and revised the description to "SBC often has an associated intraductal component (32)."

Changes in the text:

In addition, similar to other subtypes of ductal carcinoma, SBC often has an associated intraductal component (32). (See Page10, Lines201-202)

Comment 2: (page 13 line 262-263) As immunohistochemical markers of secretory carcinoma, the authors could add the following two markers: MUC4 [PMID: 26517645, 28548128] and SOX10 [PMID: 28548128].

Reply 2: Thanks for your kind suggestion. We did not include these two markers in the common positive markers of SBC, mainly considering that although all patients with SBC were positive for MUC4 and SOX10 immunohistochemical staining in the study of Krings et al. [PMID: 28548128], other researches did not reflect the significant relationship between these two markers and SBC. After your reminder, we think that this objective fact can be shown in the article to make this part more complete, so we

have modified it in the new version.

Changes in the text:

In addition, Krings et al. (38) founded that all patients with SBCs expressed MUC4 and SOX10, previously described in the MASCs (39,40), and put forwarded that these two markers may provide an additional diagnostic tool useful in the differential diagnosis of SBC. The validity of MUC4 and SOX10 as diagnostic markers of SBC needs to be further verified by large sample study. (See Page14, Lines276-280).

Comment 3: (page 24 line 493-496) The authors described "As a novel therapeutic strategy, … NTRK fusion-positive tumor, including MASCs, congenital mesoblastic nephroma, infantile fibrosarcoma, mammary analogue secretory carcinoma, and many other tumors in different organs, …." In this sentence, the following words are duplicated: "MASC" and "mammary analogue secretory carcinoma".

Reply 3: Thanks for your suggestion very much. It was our carelessness that caused the repetition of expressions in the text. We have deleted the repeated parts in the revised manuscript.

Changes in the text:

As a novel therapeutic strategy, TRK inhibitor (TKI) targeted therapy for patients with NTRK fusion-positive tumor, including MASCs, congenital mesoblastic nephroma, infantile fibrosarcoma, and many other tumors in different organs…. (See Pages24-25, Lines508-511).