Peer Review File

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To reviewer 1:

Comment 1: As the authors already stated in the Discussion, this reviewer thinks that the major limitation of this study is that the number of cases is too small. Has there been a check of the minimum number of cases that can statistically guarantee the results?

Reply 1: As the reviewer pointed out, the limitation is that the number of cases is small in this analysis. Since our department was established in August 2009, the cause is that the number of cases has not yet been accumulated sufficiently. Though the minimum number of cases that can be statistically guaranteed is not checked in detail, a preliminary experiment was conducted on TIL, and it was verified that statistical analysis could be performed with the number of cases this time, and immunohistochemistry staining was started.

Comment 2: Is it possible to determine whether CD8 and CD103 are co-expressed in TILs? What percentage of TILs or CTLs express CD103? Or were there investigations into this topic?

Reply 2: In this analysis, it is difficult to determine whether CD8 and CD103 are co-expressed in TIL. However, CD103 (tumoral) was expressed in 1.5-97.5% of TIL, with a median of 80%.

Comment 3: Where do the authors think the source of TILs existing in the lymph node metastasis is? Lymphocytes residing in lymph nodes do not play any role?

Reply 3: It is thought that the precursor CTL existing in the lymph node receives antigen presentation from antigen-presenting cells and is activated and proliferated in the lymph node. Although it can be confirmed from in vitro data that lymphocytes in lymph nodes have cytotoxic activity against cancer cells, it is considered that cancer cells that have acquired an immune escape mechanism can metastasize to lymph nodes.

To reviewer 2:

Comment 1: How many patients received adjuvant therapy? Were there any patients with neoadjuvant treatment?

Reply 1: Seven of 50 patients received adjuvant chemotherapy. There were 2 cases of UFT and 5 cases of CDDP + VNR. None of the patients received neoadjuvant chemotherapy.

Changes in the text. Lines 18-20 in Page 11 were added.

Comment 2: The observation period in one patient was 16 days, please comment.

Reply 2: A patient with a 16-day observation period died suddenly from another illness at home.

Changes in the text. Lines 18-19 in Page 21 were added.

Comment 3: Discussion section summary: The authors cannot conclude that adjuvant chemotherapy is advisable in patients with low CD103+ from their results.

Reply 3: As the reviewers mentioned, the results do not allow us to conclude that adjuvant chemotherapy is recommended for patients with low CD103-positive lymphocytes, so we deleted the sentences

Changes in the text. Lines 15-17 in Page22 were deleted.

Comment 4: Page 14, line 12-17: the authors should comment in how far the lymph nodes should be evaluated for their immune milieu if not resected with respect to the mentioned intratumoral heterogeneity of PD-L1 expression.

Reply 4: The PD-L1 expression of cancer cells is heterogeneous and is affected by the immunological tumor microenvironment, but in our analysis, the PD-L1 expression of cancer cells in primary tumors and metastatic lymph nodes correlates. If the lymph nodes are not resected, the PD-L1 expression of the primary cancer cells may reflect to some extent the expression of lymph node metastases.

Changes in the text. Lines 4-6 in Page 17 were added.

Comment 5: The authors should comment on the “tumor cell score” or change to tumor proportion score as this is used more frequently in context of PD-L1 analysis.

Reply 5: We wrote the tumor cell scores for the PD-L1 expression adopted this time in methods

Changes in the text. Lines 11-13 in Page 10.

Comment 6: The figure size is small and of poor quality, for instance Figure 3A wich is of highest interest) without any option to review in detail

Reply 6: As the reviewers mentioned the size of the figure was small, so I enlarged all the figures as much as possible.

Comment 7: Did the authors deduce any clinical strategy concerning treatment decision from their findings?

Reply 7: CD103 + TIL is thought to contribute to cancer immunity, the efficacy of ICIs may be expected in cases with marked tumor infiltration of CD103+ lymphocytes (Lines 15,16 in Page 22).