Author's response to reviews

Title: The pretreatment albumin to globulin ratio predicts chemotherapeutic outcomes in patients with unresectable metastatic colorectal cancer

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Reviewer: Dr. Yasunaru Sakuma

Major Compulsory Revisions

1. We added more detailed information for the patient characteristics, such as the body mass index (BMI) and performance status (PS), in Table 1.
2. We added laboratory data, such as the cholinesterase and cholesterol levels, and evaluated the correlations between the pretreatment AGR and serum markers, such as cholinesterase/cholesterol. The results are shown in Table 3. We also evaluated the correlations between the survival and serum markers, such as cholinesterase/cholesterol. The results are shown in Tables 4 and 5. We have no data for transferrin/pre-albumin. We also evaluated the neutrophil to lymphocyte ratio (NLR) and Glasgow prognostic score (GPS), which are also inflammatory markers recognized to correlate with the prognosis of patients with various malignancies. The results are shown in Tables 4 and 5. In the univariate analysis, both the AGR and NLR had significant relationships with the OS. However, in the multivariate analysis, only AGR had a significant relationship with the OS.
3. The frequency of molecular targeted therapy did not differ between the two groups. The average relative dose intensity also did not differ between the two groups. These results are shown in Table 3.
4. We have no data for the cytokine levels. Therefore, we could not evaluate these parameters.

Minor Essential Revisions

1. Patients with low AGR are considered to have a tendency to display rapid progression of the tumor. Therefore, it is recommended for such patients to
receive an intensive regimen.

2. We referred to the fact that the patients did not have bowel obstruction, anemia or other complications before chemotherapy in the “Methods” section.

Reviewer: Dr. Minoru Fukuchi

Major Compulsory Revisions

1. In the Introduction, we added a comment focused on patients with colorectal cancer.

2. We performed the multivariate analysis of PFS and OS again, adding other useful markers, such as the histological type, number of organs affected by metastasis, peritoneal dissemination, NLR and GPS.

3. We evaluated the neutrophil to lymphocyte ratio (NLR) and Glasgow prognostic score (GPS), which are also inflammatory markers recognized to correlate with the prognosis of patients with various malignancies. The results are shown in Tables 4 and 5. The pretreatment AGR was found to be an independent prognostic factor for the PFS and OS.

4. We used a ROC curve to determine the appropriate cut-off value for AGR. Based on the results, the appropriate cut-off value was 1.246. Therefore, we set 1.25 as the cut-off value.