Reviewer 1

The authors performed an interesting study to evaluate the influence of hTERT rs2736100 polymorphism on mRNA expression levels and telomere length in gastric cancer patients and 5 cell lines, and the association of this polymorphism with gastric cancer risk in a Korean population. Despite of reduced number of gastric cancer samples (only 35) for hTERT mRNA and telomere length quantification, the results showed that A-allele carriers present lower hTERT mRNA expression and shortened telomere length in both gastric cancer tissue and cell lines. While the CC homozygous showed both parameters increased in intestinal-type gastric cancer. On contrary, there was no association of this polymorphism with gastric cancer risk in the population evaluated, which seems contradictory.

Minor comments:

1- Materials and Methods: Measurement of telomere length and hTERT expression in gastric cancer tissues and cell lines. In this subsection was reported that the telomere length was examined in 35 gastric cancer tissues, while hTERT mRNA transcript expression was examined in 35 non-cancerous gastric mucosae. Why this discrepancy, since both analyzes should be performed in tumor tissue? The author should clarify this issue.

   Answer: As the reviewer indicated, *hTERT* mRNA transcript expression was examined in 35 gastric cancer tissues. This description has been corrected.

2- The legend of Figure 1 should be corrected: “the PCR product of G-type allele” should be corrected for “the PCR product of C-type allele”.

   Answer: As the reviewer recommended, the legend of Figure 1 has been corrected.

Reviewer 2

This manuscript presents the interrelationship between telomere length and TERT expression between normal epithelium and gastric cancer. In intestinal type gastric cancer, tumor telomere length was found to be shorter and hTERT mRNA expression decreased in patients with the rs2736100 allelotype in intron 2 of TERT. However, this polymorphism was not found to be associated with gastric cancer risk. Well written and well presented there are just a few questions raised in my review of this paper.

1. Were all the tissues and blood specimens used from the gastric cancer patients from prechemo/radiotherapy?
   Answer: None of the patients received chemotherapy or radiation therapy before surgery. We have added this sentence to the subsection “Samples” of the “Materials and Methods” section (Page 7, line 7).

2. In the results section, the last section of paragraph 2 in the Subsection Influence of rs2736100 polymorphism on telomere length and hTERT mRNA expression discusses the association of hTERT expression with the genotype of the studied SNP and how it is impacted by GKN1 treatment, particularly with regard to significant down regulation of TERT expression especially in those with C/A or A/A allelotypes. However, it isn’t clear from Figure 2 whether the change in expression following GKN1 treatment is actually different in the cell lines based on their allelotype. This might be clarified by determining if the delta between pre and post treatment TERT expression levels is really different for each of the cell lines grouped by allelotype.
   Answer: Thank you for providing an important comment. As described in “Results” section, the *hTERT* mRNA expression levels were increased in AGS and MKN1 cells with C/C homozygote and were reduced in KATO-III cells with A/A homozygote, compared to MKN-45 and SNU-638 cells with C/A heterozygote (Fig. 2B). When we analyzed the effect of GKN1 on *hTERT* mRNA expression, non-treated gastric cancer cells were used as a control. The effects of GKN1 were presented as the fold changes of *hTERT*

expression in GKN1-treated cells relative to non-treated controls (Fig. 2, Page 9). Statistically, we found that GKN1 treatment significantly down-regulated *hTERT* mRNA expression in all gastric cancer cells compared to non-treated cells, especially in MKN-45 and SNU-638 cells with C/A heterozygote and KATO-III cells with A/A homozygote (Fig. 2A & C), suggesting that GKN1 may be involved in the regulation of *hTERT* mRNA expression by affecting rs2736100 polymorphism. However, further studies are strongly needed to identify the exact molecular mechanisms by which GKN1 regulates the rs2736100 polymorphism (page 15).

3. Similarly, in Figure 2, the Y axis is not the same scale and does not align between 2 b and 2c. This would clarify these points as well.
   Answer: As the reviewer suggested, the Y axis in Figure 2 has been aligned.

Reviewer 3

In this manuscript, Byung Joon Choi et al. analyzed the rs2736100 polymorphism, determining its involvement in the regulation of hTERT expression and telomere length. Furthermore, the authors examined its link to gastric cancer risk in a Korean population. The result is of novelty and enhanced our knowledge on the regulation of hTERT expression. This manuscript is well organized and the language is good. Taken together, this manuscript is acceptable for publication in World Journal of Gastroenterology.

Answer: Thank you very much for your positive review.

Editor

U1: reduce duplication

Answer: It has been corrected. Please refer to “Page 10, line 8”.

U2: Concise

Answer: It has been corrected. Please refer to “Page 17, line 3”.

U3: Statistical significance did not show.

Answer: We examined the expression of *hTERT* gene in 5 gastric cancer cell lines without and with GKN1 treatment. Statistical significance has been shown in Figure 2A.