Peer Review File

Article Information: https://dx.doi.org/10.21037/jgo-22-931

Reviewer A
GENERAL

This is a retrospective study of neoadjuvant imatinib therapy (NAT) for gastrointestinal stromal tumors (GISTs). The authors analyzed 211 GIST patients who underwent surgical resection and postoperative adjuvant imatinib therapy (AT) and compared survivals between patients with and without NAT. The data per se are valuable because GISTs are rare tumors. However, the poor design of this study has made it difficult for this reviewer to interpret the results. It is for this reason that this reviewer thinks the manuscript is unsuitable for publication in Annals of Translational Medicine.

SPECIFIC
Comment 1: The NAT group included 46 patients (65%) who were classified into the "unknown" risk. This may be the reason why the mitotic index was not assessable in surgical specimens collected after NAT. If this is so, the indication for NAT in the present study is questionable.
Reply 1: We apologize for the unintentional mistake during analyzing. Actually, only 22 patients (31%) who were classified into the "unknown" risk in the NAT group. We have modified our text as advised (see Page 7, line 135, and Table 1). Inadequate baseline pre-NAT mitotic index is inevitable in most NAT studies [1],which was referred to in limitation paragraph (see Page 13, line 275). This was likely underestimated due to potential high-risk cases in the NA-risk part of NAT group. Even without mitotic count, when we adjusted the NAT effects for other prognostic key covariates such as tumor size, location, and AT by Cox regression and IPTW, the results showed that neoadjuvant imatinib (NAT) might be more beneficial than classic, postsurgical AT in terms of DRFS. Thank you.
Changes in the text:

Page 7, line 133: Consequently, in the absence of mitotic count, the NAT group (Group B) consisted of 22 patients (31.0%) with high-risk tumors only based on tumor size and location (21 tumors of size >10 cm, 1 tumor of size >10 cm and rupture, and 27 tumors of size >5 cm with nongastic origin) (Table 1, Table S2a and S2b).
Page 13, line 274: However, this study had some inherent deficits due to its retrospective nature.
Comment 2: The authors compared survivals between patients with NAT (NAT group) and those without NAT (upfront surgery group). The latter included 25 patients (18%) with low-risk GISTs. As the prognosis of this population is very good, this comparison is scientifically inappropriate. In addition, why did these patients undergo AT postoperatively?
Reply 2: Thank you for noticing. This part of low-risk patient received AT postoperatively usually according to the joint decision of the surgeon and medical oncologic physician. But the exact cause was not indicated in the medical records. Even so, the NAT group was found to have better outcomes in DRFS compared to the AT group.
Comment 3: This reviewer could not understand why the authors separately showed disease-free

survival, local recurrence-free survival, and distant recurrence-free survival. This has made the findings complicated and clinically meaningless.

Reply 3: Thank you for noticing. The outcomes of interest in the current study were distance recurrence-free survival (DRFS), local recurrence-free survival (LRFS), and overall survival (OS) (see Page 5, line 88). Our recent retrospective analysis of rectal GIST demonstrated that LRFS was more closely associated with surgical quality than neoadjuvant imatinib, whereas DRFS was independently associated with NAT. Instead of recurrence-free survival, we felt that DRFS and LRFS would be more indicative of the effect of neoadjuvant imatinib on localized GISTs. Some other studies also used DRFS as an outcome measure to evaluate the effect of neoadjuvant treatment [2-4].

Comment 4: The exclusion criteria are difficult to comprehend (p.4).

Reply 4: Thank you for your suggestion. The exclusion criteria have been revised accordingly. We have modified our text as advised (see Page 4, line 76). Thank you.

Changes in the text: The exclusion criteria were as follows: (I) patients with an initial diagnosis of metastatic disease or (II) patients with no perioperative administration of imatinib.

Comment 5: “Exposure and outcomes” failed to correctly explain groups A and B (p.4).

Reply 5: Thank you for your suggestion. The description of groups A and B has been revised accordingly. We have modified our text as advised (see Page 4, line 82). Thank you.

Changes in the text: Group A included patients who underwent UR and AT for a recommended duration of 1 or 3 years if the tumor parameters met the norms of intermediate or high risk according to the modified National Institutes of Health (NIH) consensus criteria. Group B included patients who underwent NAT, surgical resection, and AT, with the administration of perioperative imatinib for a recommended duration of 3 years.

Reviewer B

Comment 1: Considering the retrospective nature of the study/analyses, there should be further acknowledgment of the significant limitations of the analyses particularly with respect to lack of clear understanding of baseline patient risk categories between the 2 groups. The effect of duration of adjuvant therapy in a retrospective setting could be influenced by the time to progression or death and hence may be a questionable covariate as it may be greatly confounded in a retrospective setting. Although the findings from the analyses could be hypothesis generating, great caution should be exercised not to generalize any of the findings. There should be further discussions with respect to the opposite trends observed in gastric GIST, or with respect to LRFS and OS favoring Group A, and as to why patients with inadequate baseline risk characterization (eg, baseline pre-NAT mitotic index) were included in this retrospective study/analysis. Although authors have made further attempts to correct for significant differences in baseline characteristics, there is still known or unknown confounders impacting the final results or conclusions considering the retrospective nature of this analysis. Below please find some of the major comments which need to be addressed

Reply 1: We wish to cordially thank this reviewer for the extremely good and useful advice: “The effect of duration of adjuvant therapy in a retrospective setting could be influenced by the time to progression or death and hence may be a questionable covariate as it may be greatly confounded in a retrospective setting.” We followed this suggestion and have re-run the full statistical models of Cox regression and inverse probability of treatment weighting, turning the one of covariates from

duration of AT to whether AT (see Page 8, line 159 and 170 and Table 4). With respect to the opposite trends observed in gastric GIST, additional discussion was performed (see Page 11, line 231). With respect to why patients with inadequate baseline pre-NAT mitotic index were included in the study, additional discussion was performed (see Page 10, line 214 and page 13, line 271). The "limitation" paragraph was re-written accordingly (see Page 13, line 266).
Change in text: Page 8, line 159 and 170 and Table 4; Page 11, line 231; Page 10, line 214 and page 13, line 271; Page 13, line 266.

Abstract Section
Comment 2: Abstract should clearly indicate that this is a retrospective study.
Reply 2: Thanks for your advice. We now added "a retrospective study" in "Methods" section (see Page 2, line 26).
Change in text: Methods: This is a retrospective study at a high-volume center.
Comment 3: Please ensure other comments related to results/discussion/conclusion are addressed in the abstract
Reply 3: Yes. We have revised the entire text in response to the comments, and we have also updated the abstract. Thank you for the meticulous effort (see Page 2, line 23).

Methods Section
Comment 4: The recommended duration of imatinib treatment requirement appear to be significantly different between treatment A and treatment B (1 or no less than 3 years for intermediate to high risk for A vs no less than 3 years for intermediate to high risk; please comment as to why different set of AT requirements.
Reply 4: Thank you for noticing. Adjuvant imatinib is recommended for at least three years after resection of a high-risk GIST, and one year of an intermediate-risk GIST [5-8]. SSG XVIII trial, in which patients were randomized to one versus three years of adjuvant imatinib, OS was improved with three years, as compared with one year, of therapy, suggesting an actual increase in cure[9]. Consequently, we proposed different duration of AT based on estimation of recurrence risk following resection of a GIST.
Comment 5: Please provide further information if all the statistical analyses set a priori or some of them performed/added based on the results
Reply 5: Thank you for noticing. Our statistical analyses were set a priori. Based on the results of our previous study [10], we planned to conduct a cox regression model and to use inverse probability of treatment weighting to confirm the robustness of the main result of COX regression. As the observed number of events related to tumor was small, we restricted the number of covariates corrected and clarified the reason (see Page 8, line 161).
Comment 6: The definition of Group B under methodology section 2.2 is not consistent with the other places within the manuscript including Section 3.1 or Figure 1
Reply 6: Thank you for your suggestion. The definition of Group B has been revised accordingly. We have modified our text as advised (see Page 4, line 84; Page 6, line 128, figure 1). Thank you.
Change in text: Group B included patients who underwent NAT, surgical resection, and AT, with the administration of perioperative imatinib for a recommended duration of 3 years (12).
Comment 7: Although the number of OS events may not be sufficient, the multivariate analysis for OS should have been included for consistency and to further know whether the opposite trend on

OS in favor of Group A was still maintained

Reply 7: Thank you for your suggestion. Multivariate analysis for OS has been implemented and it shows a consistent trend in favor of Group B, although not statistically significant. (see Page 8, line 173; table 4).

Change in text: while tumor size ≤5 cm was associated with better LRFS (P = 0.072) and OS (P = 0.078) with marginal significance (Table 4).

Results Section

Comment 8: In Figure 1, provide the number of patients with gastric vs non-gastric in the initial round N=922 since the selection process may have been biased towards to selection of more non-GIST GIST

Reply 8: Thank you for your suggestion. The distribution of anatomical location of GIST in the hospital cohort (N=922) and the study cohort (N=211) was implemented. (see Figure S1 and Table S1).

Change in text: A total of 922 patients with GIST were identified (Figure 1, S1and Table S1).

Comment 9: Provide the number of patients in Group B that were available for risk stratification based on NIH consensus. Further discuss as to why a large portion of pts in Group B (65%) could not be risk stratified and why they were still included in the data set. Consequently, this should be discussed as one the major shortcomings of this retrospective analysis as patient baseline risk category could not be assessed and hence could have ultimately confounded the analysis results or findings

Reply 9: Thank you for suggestion. We specified the proportion of high-risk patients in Group A and B accordingly (see Page 7, line 134). Also, we have added discussion regarding insufficient risk stratification (see Page 10, line 217). Furthermore, we have rewritten the limitation with adequate description on the retrospective nature, how it affected the estimates, and how we tried to corrected (see Page 13, line 268).

Change in text:

Page 7, line 134: Consequently, in the absence of mitotic count, the NAT group (Group B) consisted of 49 patients (69.0%) with high-risk tumors only based on tumor size and location (21 tumors of size >10 cm, 1 tumor of size >10 cm and rupture, and 27 tumors of size >5 cm with nongastic origin) (Table S2a and S2b).

Page 10, line 217: As in other neoadjuvant studies (20), we did not obtain accurate mitotic information before the preoperative administration of imatinib in Group B.

Page 13, line 268: However, this study had some inherent deficits due to its retrospective nature.

Comment 10: Under section 3.2, there should be a mention of DCR, PR, SD for Group A.

Reply 10: Thank you for noticing. Group A used imatinib postoperatively only. In this case, there was no tumor for response assessment. As a result, there was no mention of DCR, PR, SD for Group A.

Comment 11: Under section 3.3, there should be further clarification as to what is meant by "in the entire cohort"

Reply 11: Thank you for suggesting. We have added a clear supplementary notes of "n = 211" after "in the entire cohort" (see Page 8, line 155).

Change in text: In the entire cohort (n = 211), the median DRFS, LRFS, and OS were not reached

Comment 12: The 5-year landmark analyses with respect LRFS, DRFS, and OS showed no clear difference between groups with stronger trend for OS in favor of Group A; there should be further

discussions around OS findings which did not support the non-gastric DRFS findings
Reply 12: Thank you for suggesting. According to comment 7, a multivariate analysis for OS has been implemented and showed a corrected trend for OS in favor of NAT. Further discussions around OS findings were added accordingly (see Page 10, line 212).
Change in text: Despite a minor numerical advantage for Group A in 5-year OS, the log rank test revealed no difference in OS between the two groups (see Table 2, Figure S3B).

Comment 13: Table 1 column heading should indicate which is Group A or B; similarly in other tables or figures
Reply 13: Thank you for suggestion. We have modified column headings in table 1/2 and supplementary tables, in which Group A or B is clearly indicated.
Change in text: Table 1, Table 2, Table S2a, Table S3, Table S4, Table S5b, Table S9, Table S10.
Comment 14: The choice of term used to refer to the surgery is different for Group A vs Group B; For Group B it is referred to as "surgery" however for Group A as "resection". please use the same word if appropriate otherwise provide further information as to the differences between the nature of the surgery performed for Group A vs Group B; it is sometimes unclear as to whether the difference between Group A and Group B in terms of treatment received is only the addition of NAT. There seems to be differences in the duration of AT received and here is also the concern around the type of surgery received, raising questions with respect to the validity, reliability and rigor of this retrospective study/analysis
Reply 14: Thank you very much for your careful review and detailed instruction. Both “resection” and “surgery” mean removal of the primary lesion of GIST. We have unified the wording as resection as suggested.
Change in text: Page 2, line 31; Page 2, line 39; Page 4, line 67; Page 9, line 195; Table 1/2; Table S3, Table S4, Table S5b, Table S9, Table S10.
Comment 15: Figure S1, it is not clear as to what the decrease from baseline in SLD signifies, is it with respect to prior surgery (ie, post NAT prior to surgery) or is it the best overall response. If it is the latter, please also provide the comparative figure for Group A
Reply 15: Thank you for your suggestion. Figure S1 now is labeled as Figure S2. New Figure S2 signified the decrease in SLD from baseline to post NAT prior surgery, and it is now been modified (see the legend of Figure S2) accordingly. On the other hand, Group A did not receive any imatinib before surgery, so there was no comparative figure for Group A.
Change in text: Figure S2

Comment 16: In section 3.4, the mutational index was not included due to it being affected by NAT. Please comment as to why the mutational index based on tumor biopsy pre-NAT could not be used or was not available. Please comment as to why patients with inadequate baseline risk stratification were included in this retrospective analysis.
Reply 16: Thank you for your notice. I guess the “mutational index ” refers to “mitotic index”. Regarding to “mitotic index” in NAT group, the reason why it was not available was given in an early paragraph (see Page 7, line 133). And the reason why it still be included in the study was discussed in the discussion and particularly in “limitation” section (see Page 11, line 220; Page 13, line 276).
Change in text:

Page 7, line 133: The grading by mitotic count was not accurate in regular biopsy [11], and NAT had evidence of pathologic treatment effect, which did not yield accurate mitotic information[1].

Page 11, line 220: As in other neoadjuvant studies [1], we did not obtain accurate mitotic information before the preoperative administration of imatinib in Group B.

Page 13, line 276: In the absence of an accurate mitotic index in Group B, the proportion of high-risk patients was similar for the two groups (Table 1). The originally high mitotic index might be masked by neoadjuvant imatinib, resulting in an underestimation of the true proportion of high-risk individuals in the NAT group.

Comment 17: There should be further clarification as to how the effect of AT was assessed considering lack of group with no AT treatment a priori. If AT is being treated as a continuous covariate, there should be further acknowledgement that the positive correlation may have been driven by the fact that patients with shorter time to progression could have received a shorter duration of AT and vice versa. Hence, in a retrospective setting, covariate evaluation with respect to the effect of duration of AT on DRFS, LRFS, or even OS could be highly confounded. The only settings in which the effect different durations of AT on relapse free survival can be accurately addressed is a randomized control setting in which a priori patients are assigned to different durations of treatment.

Reply 17: Thank you very much for your professional advice. We have consulted a statistician. Similar to your viewpoint, he stated that if AT is analyzed as a continuous covariate, it could operate as a mediating variable, hence distorting the link between NAT and DRFS. Accordingly, we conducted a statistical reanalysis using AT as a categorical variable, including multivariate analysis and sensitivity analysis (see Page 9, line 174; Page 9, line 187; Table 3, Table 4). In addition, we have examined the association between outcomes and AT discontinuation (see Table S3, S4).

Change in text:

Page 9, line 174: In the multivariate analysis, neoadjuvant treatment (HR = 0.23, 95% CI = 0.056–0.96, P = 0.044), tumor size ≤5 cm (P = 0.014), and adjuvant imatinib (P = 0.046) were associated with better DRFS

Page 9, line 187: After adjusting for tumor size, location, and AT, patients who received NAT had a better DRFS than those who received UR (HR = 0.26, 95% CI = 0.076–0.905, P =.048; Table S8).

Comment 18: In section 3.5, it should be mentioned that in Gastric GIST, there was a trend in favor of Group A even though it was found no statistically significant. Considering the small sample size and multiplicity of tests, it is likely that some of the findings were driven by chance and not due to the effect of NAT in either direction.

Reply 18: Thank you for suggestion. We mentioned the phenomenon and explained the possible reason in the discussion section (see Page11, line 239).

Change in text: In addition, a trend in favor of Group A was observed in gastric GIST. A possible reason might be that gastric GIST in Group B was characterized by a larger tumor size (Table S9) and more high-risk tumors (Table S10) than in Group A.

Comment 19: In section 3.6, the effect of duration of AT on DRFS would be difficult to assess retrospectively considering the fact that the duration of treatment could be affected by the time to progression of the disease. Similarly with respect to the effect of NAT on DRFS, it would be important to find out the reasons as to why some patients received or were assigned NAT followed by surgery and AT instead of UR followed by AT. If there are specific reasons/preferences for this assignment, that could most likely undermine the use of retrospective analyses to assess NAT effect.

The gold standard to assess the effect of important parameters such as neoadjuvant treatment effect or duration of treatment on key efficacy parameters is a randomized controlled study.

Reply 19: Thank you for your suggestion. According to Comment 17, we have conducted statistical reanalysis including sensitivity analyses. Regarding the assignment of NAT or UR, it was a joint decision by multidiscipline team and the patient, reflecting a treatment setting in a real world. The reason why RCT was difficult to conduct was explained in limitation section (see Page 13, line 282).

Change in text: The gold standard to assess the effect of neoadjuvant treatment is an RCT. However, neoadjuvant therapy sometimes is necessary for GIST, particularly located at the esophagogastric junction and in the duodenum and rectum, to achieve complete resection and avoid extensive organ disruption. For ethical reasons, the random assignment of participants is not permitted under this circumstance. Thus, the guideline recommendation of neoadjuvant treatment for GIST is based on phase II single-arm trials or retrospective series (1-6).

Discussion Section

Comment 20: Throughout the discussion there seems to be general statements with regards to the advantage of addition of NAT with respect DRFS. The statements need to be specific (ie, non-gastric GIST) and balanced (eg, opposite trend observed in gastric GIST, or with respect to LRFS or OS).

Reply 20: Thank you for your suggestion. We specified the advantage of addition of NAT with respect DRFS in the nongastric GIST in discussion and conclusions sections accordingly (see Page 9, line 198; Page 14, line 294).

Change in text:

Page 9, line 198: The multivariate analysis by the Cox proportional-hazards model and sensitivity analysis by IPTW revealed that NAT was associated with better DRFS (HR = 0.232, 95% CI = 0.0166–0.806, P = 0.022), especially in patients with nongastric GISTs (HR = 0.131, 95% CI = 0.017–0.989, P = 0.049).

Page 14, line 294: The findings suggested that NAT decreased the risk of metastasis, especially in patients with nongastric GISTs, compared with UR and AT.

Comment 21: In second paragraph, NAT was only associated with better DRFS in non-gastric GIST as the trend was reversed in gastric GIST. Therefore, the general statement is not correct and needs to specify and include additional information regarding the trend observed in gastric GIST

Reply 21: Thank you for noticing. As mentioned above, we emphasized the advantage of addition of NAT with respect DRFS in nongastric location. Also we have discussed thoroughly in the third paragraph in discussion section (see Page 11, line 237).

Change in text:

For gastric GIST, only five events were observed in our study. It was difficult to assess the treatment effect in this subset of patients. In addition, a trend in favor of Group A was observed in gastric GIST. A possible reason might be that gastric GIST in Group B was characterized by a larger tumor size (Table S9) and more high-risk tumors (Table S10) than in Group A. The marked disparate distribution of tumor size and risk classification between two groups in gastric GIST is known as “confounding by indication.” Joseph et al. defined “confounding by indication” bias in the association between a treatment and its intended outcome due to disease seriousness for the treatment decision [12]. Our findings were unable to invalidate the association between NAT and DRFS in stomach GIST. The majority of proximal gastric GIST are KIT-mutant tumors [13], which also require function preservation. NAT have a key role in the therapy of proximal gastric GIST and dismal gastric GIST with sensitive mutation. In clinical practice, NAT dismiss in gastric GIST may

be deceiving. Further exploration on the link between NAT and DRFS in gastric GIST is needed.

Comment 22: The authors indicate that the mutational status was not reliable based on the effect of NAT on the rates. It is not sufficiently clear as to why mitotic index determination could not be made based on tumor biopsies obtained prior to the start of treatments (ie, NAT) and furthermore considering the lack of availability of this key baseline information why patients were included in this retrospective analysis.

Reply 22: Thank you for suggestion. As mentioned above, with respect to why patients with inadequate baseline pre-NAT mitotic index were included in the study, additional discussion was performed (see Page 10, line 214 and page 13, line 271). The "limitation" paragraph was re-written accordingly (see Page 13, line 266).

Comment 23: With respect to the result of DRFS benefit of NAT in non-gastric GIST, considering lack of supporting evidence with respect to KM curve for OS or the 5-year survival, it raises questions regarding the clinical relevance/significance of this finding or as to whether it is real; there should be further discussion addressing the heterogeneous results of the study/analyses

Reply 23: Thank you for suggestion. It has been explained in Reply 7 and Reply 12.

Comment 24: For Table 4, please also add OS even though the events are limited. It is important include for consistency and also to see if the opposite trend observed in favor of Group is also present in the multivariate analysis setting.

Reply 24: Thank you for suggestion. It has been explained in Reply 7.

Comment 25: Considering that the duration of AT duration of AT may have been affected by the time to progression, it is questionable if inclusion of AT duration in the multivariate model in a retrospective setting is appropriate. Please repeat multivariate model excluding AD treatment duration.

Reply 25: Thank you for suggestion. It has been explained in Reply 17.

Comment 26: As part of shortcomings and limitations or confounding factors of the study/analyses all of the issues raised should be mentioned or adequately addressed.

Conclusions Section

Reply 26: Thank you. Limitation has been rewritten (see Page 13, line 275).

Comment 27: As part of the conclusions, it should be clearly indicated that higher DRFS with NAT was only observed in non-gastric GIST and that the opposite trend (although not statistically significant) was observed in gastric GIST. Furthermore, it should be highlighted that a trend in favor of Group A was observed for LRFS and OS. Therefore, the overall findings of the study cannot support the use of NAT and no statements regarding the duration of AT can be made due to conflicting/inconsistent results, number of confounding factors, and retrospective nature of the study.

Reply 27: Thank you. This study had some inherent deficits due to its retrospective nature. Although we corrected for several key confounders using Cox regression model and IPTW, the potential for unknown confounders still remains. We have thoroughly acknowledged the shortcomings in limitation section. We are cautious in the wording of our conclusions. (see Page 14, line 293).

1. Iwatsuki, M.; Harada, K.; Iwagami, S.; Eto, K.; Ishimoto, T.; Baba, Y.; Yoshida, N.; Ajani, J.A.; Baba, H. Neoadjuvant and adjuvant therapy for gastrointestinal stromal tumors. Annals of gastroenterological surgery 2019, 3, 43-49, doi:10.1002/ags3.12211.
2. Consortium, I.-S.T. Association of Event-Free and Distant Recurrence–Free Survival With Individual-Level Pathologic Complete Response in Neoadjuvant Treatment of Stages 2 and 3 Breast Cancer: Three-Year Follow-up Analysis for the I-SPY2 Adaptively Randomized Clinical Trial. JAMA oncology 2020, 6, 1355-1362, doi:10.1001/jamaoncol.2020.2535 %J JAMA Oncology.
3. Wiltshire, K.L.; Ward, I.G.; Swallow, C.; Oza, A.M.; Cummings, B.; Pond, G.R.; Catton, P.; Kim, J.; Ringash, J.; Wong, C.S.; et al. Preoperative radiation with concurrent chemotherapy for resectable rectal cancer: Effect of dose escalation on pathologic complete response, local recurrence-free survival, disease-free survival, and overall survival. International Journal of Radiation Oncology*Biology*Physics 2006, 64, 709-716, doi:https://doi.org/10.1016/j.ijrobp.2005.08.012.
4. Yu, N.Y.; Iftimi, A.; Yau, C.; Tobin, N.P.; van 't Veer, L.; Hoadley, K.A.; Benz, C.C.; Nordenskjöld, B.; Fornander, T.; Stål, O.; et al. Assessment of Long-term Distant Recurrence-Free Survival Associated With Tamoxifen Therapy in Postmenopausal Patients With Luminal A or Luminal B Breast Cancer. JAMA oncology 2019, 5, 1304-1309, doi:10.1001/jamaoncol.2019.1856 %J JAMA Oncology.
5. National Comprehensive Cancer Network (NCCN) Clinical Practice guidelines in Oncology: Gastrointestinal Stromal Tumors (GISTs) (Version 1.2022) . Available online: https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf (accessed on 30, October).
6. Li, J.; Ye, Y.; Wang, J.; Zhang, B.; Qin, S.; Shi, Y.; He, Y.; Liang, X.; Liu, X.; Zhou, Y.; et al. Chinese consensus guidelines for diagnosis and management of gastrointestinal stromal tumor. Chin J Cancer Res 2017, 29, 281-293, doi:10.21147/j.issn.1000-9604.2017.04.01.
7. Ye, Y.J.; Qin, S.K.; Shen, L.; Cao, H.; He, Y.L.; Liang, H.; Li, Y.; Li, J.; Zhang, B.; Wang, J.; et al. Guidelines of Chinese Society of Clinical Oncology on Diagnosis and Treatment of Gastrointestinal Stromal Tumor (2020 version); People's Medical Publishing House: 2021.
8. Casali, P.G.; Blay, J.Y.; Abecassis, N.; Bajpai, J.; Bauer, S.; Biagini, R.; Bielack, S.; Bonvalot, S.; Boukovinas, I.; Bovee, J.; et al. Gastrointestinal stromal tumours: ESMO-EURACAN-GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of oncology : official journal of the European Society for Medical Oncology 2021, doi:10.1016/j.annonc.2021.09.005.
9. Joensuu, H.; Eriksson, M.; Hall, K.S.; Reichardt, A.; Hermes, B.; Schutte, J.; Cameron, S.; Hohenberger, P.; Jost, P.J.; Al-Batran, S.E.; et al. Survival Outcomes Associated With 3 Years vs 1 Year of Adjuvant Imatinib for Patients With High-Risk Gastrointestinal Stromal Tumors: An Analysis of a Randomized Clinical Trial After 10-Year Follow-up. JAMA Oncol 2020, 6, 1241-1246, doi:10.1001/jamaoncol.2020.2091.
10. Ling, J.Y.; Ding, M.M.; Yang, Z.F.; Zhao, Y.D.; Xie, X.Y.; Shi, L.S.; Wang, H.M.; Cao, W.T.; Zhang, J.W.; Hu, H.B.; et al. Comparison of outcomes between neoadjuvant imatinib and upfront surgery in patients with localized rectal GIST: An inverse probability of treatment weighting analysis. Journal of surgical oncology 2021, 124, 1442-1450, doi:10.1002/jso.26664.
11. Kobara, H.; Mori, H.; Rafiq, K.; Fujihara, S.; Nishiyama, N.; Chiyo, T.; Matsunaga, T.; Ayaki, M.; Yachida, T.; Kato, K.; et al. Analysis of the amount of tissue sample necessary for mitotic count

and Ki-67 index in gastrointestinal stromal tumor sampling. Oncology reports 2015, 33, 215-222, doi:10.3892/or.2014.3608.
12. Allan, V.; Ramagopalan, S.V.; Mardekian, J.; Jenkins, A.; Li, X.; Pan, X.; Luo, X. Propensity score matching and inverse probability of treatment weighting to address confounding by indication in comparative effectiveness research of oral anticoagulants. Journal of comparative effectiveness research 2020, 9, 603-614, doi:10.2217/cer-2020-0013.
13. Sharma, A.K.; de la Torre, J.; IJzerman, N.S.; Sutton, T.L.; Zhao, B.; Khan, T.M.; Banerjee, S.; Cui, C.; Nguyen, V.; Alkhuziem, M.; et al. Location of Gastrointestinal Stromal Tumor (GIST) in the Stomach Predicts Tumor Mutation Profile and Drug Sensitivity. Clinical Cancer Research 2021, 27, 5334-5342, doi:10.1158/1078-0432.CCR-21-1221 %J Clinical Cancer Research.