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Letter to the Editor: Reconsidering the routine use of adjuvant somatostatin analogs in type I gastric neuroendocrine tumors after endoscopic treatment

Ozturk B *et al*. Adjuvant SSA therapy in type I gastric NETs

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Abstract

Yang *et al* recently published an article in *World Journal of Gastroenterology* reported that adjuvant somatostatin analog (SSA) therapy following endoscopic treatment significantly reduced the risk of tumor progression in patients with type I gastric neuroendocrine tumors (G-NETs). While these findings suggest a potential therapeutic benefit, several methodological and clinical considerations require clarification before routine use of adjuvant SSA can be endorsed. Differences in follow-up times between progressive and non-progressive groups could lead to inaccurate conclusions on progression-free survival, warranting further confirmation, particularly for indolent tumors prone to late recurrence. Moreover, well-differentiated grade 1 type I G-NETs are characterized by low metastatic potential and excellent survival, and current guidelines primarily recommend SSA therapy for unresectable, recurrent, or metastatic disease. Importantly, the study did not comprehensively report distant metastases or long-term survival outcomes, limiting the assessment of clinically meaningful benefit. Furthermore, the safety profile of prolonged SSA therapy warrants careful consideration in this favorable-risk population. These issues should be addressed before routine adjuvant SSA therapy is broadly adopted.

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Key Words: Type I gastric neuroendocrine tumor; Somatostatin analog; Prognosis; Side effects

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Core Tip: Type I gastric neuroendocrine tumors are usually indolent and are associated with low metastatic potential. Although adjuvant somatostatin analog therapy

following endoscopic resection can reduce recurrence risk, its routine use in low-risk patients should be carefully evaluated considering the scarce survival data and potential treatment-related adverse effects.

TO THE EDITOR

We read with interest the recent article published in the *World Journal of Gastroenterology* by Yang *et al*[1] who evaluated the role of adjuvant somatostatin analogs (SSAs) following endoscopic treatment for type I gastric neuroendocrine tumors (G-NETs). The authors highlight that the combination of endoscopic treatment and SSA use reduces the risk of disease progression and recurrence (hazard ratio = 0.38, 95%CI: 0.17-0.90, P = 0.027). While the study addresses an important treatment question, several methodological and clinical issues require further clarification before routine adjuvant SSA treatment can be recommended in this context.

First, the difference in follow-up time between groups can complicate the interpretation of progression-free survival. The median follow-up time in the progressive group was significantly shorter than the non-progressive group. Differences in follow-up time can introduce potential bias and inaccuracy when confirming progression-free survival, particularly for indolent tumors susceptible to late recurrence. However, such differences do not necessarily invalidate progression-free survival findings if appropriate time-to-event analyses are applied[2,3]. A more methodologically relevant comparison should assess follow-up times between the treatment groups (*i.e.*, endoscopic resection alone *vs* resection plus SSAs), as any difference at this level would directly influence the validity of endpoints used for the study conclusions.

Second, the incidence of metastasis is low in well-differentiated grade 1 G-NETs. Therefore, adjuvant SSA therapy is not routinely considered as the standard treatment in this subgroup. SSA therapy is generally used for unresectable and metastatic disease[4-6]. According to the European Society for Neuroendocrine Tumors 2023 guidelines, SSA therapy is primarily recommended for unresectable, multifocal, or

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recurrent disease that is unsuitable for endoscopic or surgical management, rather than for routine adjuvant therapy after complete resection[6]. While the reduction in metachronous gastric lesions is clinically meaningful, it remains unclear whether this translates into a reduction in distant metastasis, an improvement in disease-specific survival, or an increase in overall survival. Yang *et al*[1] did not comprehensively report on distant metastatic events or survival outcomes. Without a demonstratable impact on distant metastasis or survival, the clinical relevance of routine adjuvant SSA therapy remains uncertain. Given the mostly indolent nature and excellent prognosis of type I G-NETs, the clinical benefit of adjuvant SSA therapy might not appear to be significant, further supporting a conservative surveillance-based strategy[2,7,8].

Lastly, although SSAs are generally well tolerated, long-term treatment can be associated with side-effects, including metabolic disorders, gallstones, and gastrointestinal symptoms[9,10]. In patients with indolent type I G-NETs, the risk-benefit balance of treatment is particularly important. Reporting adverse event rates, gallstone formation rates, metabolic changes, and treatment discontinuation rates would considerably improve clinical applicability.

In conclusion, Yang *et al*[1] provide valuable data suggesting a potential protective effect of adjuvant SSAs following endoscopic treatment of type I G-NETs. Nevertheless, follow-up imbalance, limited reporting of distant and survival outcomes, and the absence of detailed safety data warrant cautious interpretation. Clarification of these issues is essential before routine adjuvant SSA use can be justified in this favorable-risk population.

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Footnotes

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