

The Consensus of Imaging Assessment on Treatment Response in Gastrointestinal Stromal Tumor (GIST)

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Gastrointestinal Stromal Tumor (GIST) is the most common mesenchymal tumor of the GI tract, and has evolved rapidly over the past several years. The current treatment guidelines from the European Society of Medical Oncology (ESMO), the National Comprehensive Cancer Network (NCCN), and other published guidelines are aligned in recommendation for GIST management. In localized disease, there is a general agreement that when GIST presents as a small (≤ 2 cm) nodule in the esophagus, stomach or duodenum, the recommended approach is to perform endoscopic ultrasound as a baseline, and subsequent follow-up (ESMO guidelines)⁽¹⁾. Larger nodules (>2 cm) carry a higher risk for aggressive behavior and a biopsy should be performed followed by excision if a GIST diagnosis is made. For rectal GIST, endoscopic ultrasound and MRI assessment followed by biopsy and wide excision is the standard approach, regardless of tumor size⁽¹⁾. In advanced disease, imatinib 400 mg daily is the standard of care for inoperable patients, metastatic GIST or as an adjuvant treatment after complete resection of metastatic disease.

Radiologists play an important role in staging, risk management and follow up of treatment. Contrast-en-

hanced abdominal and pelvic CT scan is the technique of choice for staging and follow-up. MRI should be used in rectal GIST as it provides better preoperative staging information. PET or PET-CT/MRI is not routinely required but may be useful for early detection of tumor response during neoadjuvant treatment.

There are many tumor response assessment criteria recommended in the literature, such as SWOG, WHO, RECIST 1.0, RECIST 1.1, PERCIST and Choi, and each one has its own benefit and drawback. Among these criteria, the two most popular used in GISTs are RECIST and Choi's response criteria. Majority of experts agree that "size response" alone, as defined by Response Evaluation Criteria In Solid Tumors (RECIST) is not the optimum surrogate marker after imatinib therapy. There are patients whose tumors do not decrease size, but in fact show response to treatment by FDG-PET scan, and have prolonged stable disease. Data shows that such patients gain the same benefit from imatinib with equivalent rates of overall survival (OS) compared with patients whose tumors exhibit size response. This opinion is supported by data from the B2222 trial⁽²⁾, as well as by studies conducted by Benjamin *et al.*⁽³⁾, and Le Cesne *et al.*⁽⁴⁾

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Choi *et al.*⁽⁵⁾ investigated alternative measures of response. This study resulted in a new criteria based on CT findings. Choi's criteria for partial response (PR) are defined as over 10% decrease in tumor size, compared to 30% decrease by RECIST criteria, or over 15% decrease in tumor density. It has been suggested that the prognostic value of response determined by Choi's criteria after treatment by imatinib is more useful than that determined by RECIST criteria. In contrast, Choi's criteria in progressive disease (PD) are defined as over 10% increase in tumor size, compared to 20% increase by RECIST criteria. However, the overall survival (OS) does not seem to significantly different comparing both criteria for PD⁽⁶⁾.

The study conducted by Benjamin *et al.*⁽³⁾ (n = 98) specifically sought to determine whether Choi's criteria could predict progression free survival (PFS) better than RECIST criteria⁽³⁾. Investigators concluded that patients who met Choi's good response criteria at the 2 months stage displayed significantly better PFS than patients not meeting the criteria ($p = 0.0002$). In addition, in the group where response was assessed by RECIST criteria, no significant correlation with PFS was observed ($p = 0.1$). In comparison, GIST response rate to imatinib by Choi's criteria was higher than RECIST criteria (83% vs. 46%), and similar to FDG-PET (83% vs. 83%), which was used as a gold standard in this study.

Some investigators prefer RECIST criteria to as-

sess response to imatinib treatment. In the EORTC Intergroup 62005 study⁽⁴⁾, patients who exhibited "stable disease" by RECIST criteria at 6 months had similar clinical outcome to "responders" (complete response and partial response) at 6 months. Therefore, Imatinib should be terminated only in the "progressive disease" group determined by RECIST criteria. This pattern of response was also seen in the B2222 study by Blanke *et al.*⁽⁷⁾

Consensus

To compare baseline and follow-up studies for evaluation response to treatment in GISTs, the Thai Radiology Association for Liver and GI Diseases, recommend interpreters using similar CT protocol technique, and the same equipment to measure the size and density of compared lesions. In Thai context, using RECIST criteria alone may have negative impact to some patients, whom imatinib is still beneficial, but the use has to be terminated because of the size progression, regardless of density. On the other hand, Choi's criteria on progressive disease (PD) using only 10% increase in size compared to 20% increase by RECIST criteria, may also result in premature termination of imatinib treatment.

In spite of ongoing controversial issues on GIST response to treatment assessment, the consensus is to apply Choi's criteria for imaging evaluation of response to treatment in GIST with a small modification for PD.

Table 1. Response assessment: RECIST versus Choi's criteria.

	RECIST 1.1	Choi
CR	<ul style="list-style-type: none"> ● Disappearance of all lesions ● No new lesions 	<ul style="list-style-type: none"> ● Disappearance of all lesions ● No new lesions
PR	<ul style="list-style-type: none"> ● Decrease in tumor size $\geq 30\%$ ● No new lesions ● No PD of non-target lesions 	<ul style="list-style-type: none"> ● Decrease in tumor size $\geq 10\%$ or decrease in tumor density $\geq 15\%$ on CT ● No new lesion ● No PD of non-measurable lesions
SD	<ul style="list-style-type: none"> ● Does not meet criteria for CR, PR or PD ● No symptomatic deterioration attribute to tumor progression 	<ul style="list-style-type: none"> ● Does not meet criteria for CR, PR or PD ● No symptomatic deterioration attribute to tumor progression
PD	<ul style="list-style-type: none"> ● Increase in tumor size $\geq 20\%$ ● Unequivocal progression of non-target lesions overall ● New lesion 	<ul style="list-style-type: none"> ● Increase in tumor size $\geq 10\%$ and does not meet PR criteria by tumor density ● New lesion ● New intratumoral nodules or increase in size of the existing intratumoral nodules

In the PD criteria, the recommendation is to use 20% increased size, not 10% as indicating in Choi's criteria.

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