Published in final edited form as:

AJR Am J Roentgenol. 2017 December ; 209(6): 1278–1284. doi:10.2214/AJR.17.18018.

Alternative Response Criteria and Clinical Risk Factors for Assessing Tumor Response in Patients With Metastatic Renal Cell Carcinoma Who Are Receiving Salvage Therapy

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Abstract

Objective—The purpose of this study is to compare the prognostic value of various solid tumor response criteria as well as the additive value of clinical risk factors in patients with advanced renal cell carcinoma (RCC).

Materials and Methods—Two sets of CT scans (pretreatment scans and scans obtained 1–3.5 months after treatment) were reviewed for 57 patients with metastatic RCC treated with pazopanib in the salvage setting. Tumor response on the posttherapy scan was evaluated using Response Evaluation Criteria in Solid Tumors (RECIST) and Choi, modified Choi (mChoi), MASS (Morphology, Attenuation, Size, and Structure), and 10% threshold criteria. In addition, combined Memorial Sloan-Kettering Cancer Center (MSKCC) risk factors plus imaging criteria were used to define response groups. Response evaluations using these criteria were correlated with overall survival (OS) and progression-free survival (PFS), with use of the log-rank test.

Results—Patients classified as having progressive disease (PD) on the basis of RECIST, mChoi, and MASS criteria had a significantly worse OS than patients with stable disease (SD) and partial response (PR). With the addition of MSKCC risk factors, all groups with PD defined by combined criteria had significantly worse OS. For 37 patients with no or one MSKCC risk factor, response groups defined by Choi, mChoi, MASS, and 10% threshold criteria did not differ in PFS or OS. However, among 20 patients with two to three MSKCC risk factors, those classified as having PR had longer PFS than did those with SD and had longer OS than did those with PD.

Conclusion—For patients with advanced RCC for which prior therapies have failed, the prognostic value of various imaging-based tumor response criteria differs on the basis of the MSKCC clinical risk status.

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Based on a presentation at the Radiological Society of North America 2015 annual meeting, Chicago, IL.

Keywords

clinical risk factors; pazopanib; renal cell carcinoma; salvage therapy; tumor response criteria

Accurate assessment of tumor response is an essential component of oncologic therapy. Traditionally, radiologic evaluation of tumor response depends on tumor size (e.g., as with the widely adopted Response Evaluation Criteria in Solid Tumors [RECIST]) [1]. These criteria were developed in the era of cytotoxic therapy, and numerous trials have validated their utility in predicting overall survival (OS) and progression-free survival (PFS) for patients treated with cytotoxic agents [2].

Molecularly targeted antiangiogenic agents have revolutionized the treatment of certain malignancies, such as metastatic renal cell carcinoma (RCC), that often have a poor response to conventional chemotherapy [3]. Antiangiogenic agents frequently have a cytostatic effect, resulting in decreased tumor vascularity and necrosis, rather than a cytotoxic effect. A decrease in tumor diameter of more than 30% is uncommon for RCC treated with molecularly targeted agents [4]. A total of 44–70% of patients experience a best response of stable disease (SD), according to RECIST [5, 6]. Nonetheless, patients treated with these agents often receive significant clinical benefit in spite of minimal tumor shrinkage [7]. Thus, more refined methods of evaluating tumor response are necessary.

Concerns regarding the utility of RECIST for assessing tumor response to targeted therapy were first raised by Choi et al. [8] in an evaluation of gastrointestinal stromal tumor (GIST) treated with imatinib. Most patients with GIST receive clinical benefit after treatment with imatinib; however, 75% of these patients achieve only SD according to RECIST [8]. On the basis of their observation that the CT attenuation of these tumors often decreases after treatment, Choi and colleagues proposed a new set of response criteria in which partial response (PR) was defined as either a decrease of more than 10% in unidimensional tumor size or a decrease of more than 15% in tumor attenuation on contrast-enhanced CT. Compared with RECIST, the Choi criteria were found to have stronger correlation with survival among patients with GIST. Subsequently, these findings were replicated for additional tumor types, such as RCC [9, 10].

These findings led other researchers to propose alternative criteria that incorporated changes in both the size and attenuation of tumors. For example, Nathan et al. [11] suggested that modified Choi (mChoi) criteria, in which both a decrease of more than 10% in tumor size and a decrease of more than 15% in tumor attenuation are needed for classification of PR, were a better predictor of PFS. Smith et al. [12] found that prolonged PFS and OS had a stronger correlation with Morphology, Attenuation, Size, and Structure (MASS) criteria (Table 1). Two groups have reported that the 10% threshold criteria, in which a decrease of more than 10% in tumor size qualifies as PR, is predictive of longer PFS and OS [13, 14].

In addition to imaging-based criteria, pre-therapy clinical schemas, such as the Memorial Sloan-Kettering Cancer Center (MSKCC) risk model, help oncologists stratify the clinical outcome of patients with RCC [15, 16]. Smith et al. [17] reported that the highest accuracy in predicting PFS is achieved when MSKCC risk factors are incorporated into imaging-

based response criteria. Their study examined patients treated with first-line anti-vascular endothelial growth factor therapy.

The purpose of this study is to determine which of these criteria best correlate with PFS and OS in patients with advanced RCC. We also examine whether clinical risk factors have additional prognostic value when combined with imaging-based criteria.

Materials and Methods

This retrospective study was approved by the institutional review board at the University of Texas MD Anderson Cancer Center, with a waiver of informed consent provided.

Subjects

A total of 112 consecutive adult patients with metastatic RCC who had been treated with pazopanib (Votrient, GlaxoSmithKline) in the genitourinary medical oncology clinic at our institution between November 1, 2009, and November 1, 2011, were included. The patients had been part of a clinical study examining the efficacy of pazopanib therapy after disease progression occurred during treatment with other targeted therapies [18]. Therefore, all patients had received one or more prior targeted therapies, including sorafenib, sunitinib, bevacizumab, temsirolimus, everolimus, or a combination of temsirolimus and everolimus; some patients had also received prior chemotherapy or cytokines.

Inclusion criteria were contrast-enhanced CT scans obtained 4 weeks before and at least 4 weeks after initiation of pazopanib therapy, adequate follow-up during treatment with pazopanib (i.e., with at least one clinic visit occurring at MD Anderson Cancer Center every 3 months), and treatment with pazopanib as a single agent during the interval between pretherapy and posttherapy scans. Note that the pretherapy scan usually showed disease progression during previous therapy, except when the previous therapy was discontinued because of adverse effects.

Exclusion criteria included lack of contrast-enhanced CT scans ($n = 22$), lack of posttherapy CT scans ($n = 14$), widely differing phases of contrast enhancement ($n = 4$) between the pretherapy and posttherapy scans (e.g., delayed images acquired through the chest), or minimal-volume disease (i.e., lung nodules only or lymph nodes < 1.5 cm; $n = 9$). Patients were also excluded if pazopanib was initiated more than 1 month before the pre-therapy scan ($n = 2$) or was discontinued more than 1 month before the posttherapy scan ($n = 4$).

All patients were followed until discontinuation of pazopanib therapy, either as a result of adverse effects ($n = 5$) or progressive disease ($n = 52$), as assessed during the clinical outcome study [18] per RECIST 1.1. The median duration of pazopanib therapy was 139 days (mean, 283 days; range, 36–1321 days). The median duration of follow-up after initiation of pazopanib therapy was 279 days (mean, 462 days; range, 53–1521 days).

Patients underwent MDCT (with LightSpeed 16, LightSpeed VCT, or LightSpeed Plus scanners [all by GE Healthcare]) performed after injection of 125 or 150 mL of nonionic iodinated contrast material (ioversol [Optiray 350, Mallinckrodt] or iodixanol [Visipaque 320, GE Healthcare]), in accordance with our routine clinical protocol. Images of the chest

and images of the abdomen and pelvis were acquired approximately 30 seconds and 70 seconds, respectively, after IV contrast administration. Patients with CT scans from outside institutions were included, provided the timing of contrast administration was similar to that used in our institutional protocol. Axial images reconstructed at a 2.5-mm slice thickness were used when available; for seven patients, only 5-mm slice reconstructions were available. For each patient, the same slice thickness was examined for pretherapy and posttherapy scans.

Tumor Measurement

Two fellowship-trained abdominal radiologists (who had 1 year of postfellowship experience exclusively interpreting oncologic scans) independently examined two sets of CT scans performed before and after initiation of pazopanib therapy, which were displayed on a PACS (iSite, Philips Healthcare). Radiologists were blinded to patient outcomes and clinical data.

Representative tumors were selected on axial images according to RECIST 1.1 (i.e., up to two lesions per organ and five lesions per patient) [1]. Osseous lesions with a soft-tissue component larger than 1 cm were included, whereas sclerotic lesions were excluded. Parenchymal lung lesions were not measured because of limitations regarding assessment of central necrosis caused by cavitation and partial volume effects [12]. For each lesion, the longest diameter was measured, and ROIs were manually drawn along the lesion margin for measurement of mean attenuation values (Figs. 1A and 1B). Visual assessment was done to determine the presence or absence of central necrosis (used for MASS criteria).

Response Assessment

Tumor response on the posttherapy scan was evaluated with RECIST, Choi, mChoi, MASS, and 10% threshold criteria (Table 1). Patients were assigned to PR, SD, and PD response categories on the basis of these criteria (Fig. 1). For criteria that included tumor attenuation, the mean CT attenuation for all measured lesions in a given patient was used.

Tumor response was also evaluated using combined criteria incorporating MSKCC risk factors and imaging-based response classification (Table 1). MSKCC poor-risk factors for previously treated patients include anemia (hemoglobin level, ≤ 13 mg/dL [for male patients] and ≤ 11.5 mg/dL [for female patients]), a high calcium level (> 10 mg/dL), and a poor Karnofsky Performance Status (KPS) score (< 80) [16].

Statistical Analyses

Variance component analysis was performed to assess interreader variability for measurements of tumor size and attenuation. Compared with inter-patient variability and random error, the interreader variability was negligible. Therefore, the mean of the measurements of the two readers was used for further analyses.

For each set of criteria, PFS was defined as the time from the initial posttreatment CT scan to disease progression on the basis of the criteria or death from any cause. Analyses of PFS included patients classified as having PR or SD on the basis of the posttreatment scan. OS was defined as the time from the posttreatment CT scan to death from any cause.

OS and PFS summary statistics according to the five response evaluation criteria were calculated using the Kaplan-Meier method. Patients were classified as having PR, SD, or PD according to each set of criteria, and comparisons were performed using the log-rank test. When the overall test result was statistically significant, post hoc pairwise comparisons were performed (for PR vs SD, PR vs PD, and SD vs PD). All tests were two-sided, and $p = 0.05$ was considered to denote statistical significance. Statistical analyses were performed using statistical software (SAS, version 9, SAS Institute).

Results

A total of 152 lesions in 57 patients (39 men and 18 women) were measured. The median patient age was 60 years (range, 22–78 years). The median interval between the pretherapy CT scan and initiation of pazopanib therapy was 1 day (range, 1–22 days), whereas that between the pre- and posttherapy scans was 65 days (range, 30–125 days). The median number of prior targeted therapies received was two (range, one to five therapies). Some patients had been previously treated with chemotherapy ($n = 14$) or cytokines ($n = 10$).

Tumors were located in the lymph nodes ($n = 58$), kidney ($n = 19$), liver ($n = 18$), pancreas ($n = 15$), adrenal glands ($n = 18$), retro-peritoneum ($n = 9$), abdominal wall or muscle ($n = 6$), bone ($n = 3$), heart ($n = 2$), pleura ($n = 2$), and mediastinum ($n = 1$).

Forty-eight patients had tumors of the clear cell histologic subtype, one patient had the papillary subtype, eight patients had other subtypes (e.g., sarcomatoid or undifferentiated), and no patient had the chromophobe or medullary subtype. Eighteen patients had a low KPS score (< 80), six patients had a high serum calcium level, and 43 patients had anemia. The number of patients who had zero, one, two, or three MSKCC poor-risk factors was 10, 27, 18, and two, respectively.

No patients had disappearance of all lesions (i.e., a complete response) noted on the posttherapy scan. Table 2 shows the number of patients in each response group, as classified by the various imaging-based response criteria, in addition to the median PFS and OS for each group.

Response Classification and Overall Survival

There was a significant interaction between the response group (PR, SD, or PD) and OS with use of RECIST, mChoi, and MASS criteria (Table 2). In other words, when RECIST, mChoi, and MASS criteria were used for assessment, the response groups had different OS durations. As an example, Figure 2A shows the Kaplan-Meier curves for response groups according to mChoi criteria. Because the overall test result was statistically significant, pairwise comparisons were performed, which showed that patients categorized as having PD by RECIST, mChoi, and MASS criteria had significantly shorter OS, compared with patients with SD or PR. No difference in OS was noted for the SD and PR groups, on the basis of mChoi and MASS criteria. With RECIST, no patients were included in the PR category.

When combined (i.e., imaging plus MSKCC) criteria were used to define response groups, all combined criteria were significantly correlated with OS (Table 2). As an example, Fig.

2B shows the Kaplan-Meier curves for response groups according to mChoi plus MSKCC criteria. For all criteria, PR and SD groups differed from PD groups, but not from each other, with regard to OS.

Response Classification and Progression-Free Survival

A trend toward longer PFS was noted for patients with PR, compared with those with SD, with use of the mChoi or 10% threshold criteria ($p = 0.064$, for both) (Table 2 and Fig. 3A). PR and SD groups, as defined by Choi or MASS criteria, did not show a significant difference in PFS. Analyses of PFS were not significantly affected by the addition of MSKCC risk factors because only patients with PR or SD were included in these analyses. The addition of MSKCC factors increased the number of patients classified as having PD but did not affect the classification of PR versus SD.

Memorial Sloan-Kettering Cancer Center Favorable-Risk and Poor-Risk Groups

To determine whether the prognostic value of the various response criteria varied depending on clinical risk factors, subgroup analyses were performed for the MSKCC favorable-risk group (which had no or one risk factor) and the poor-risk group (which had two or three risk factors). Table 3 shows the results for the 37 patients with no or one MSKCC risk factor. No significant difference in PFS was noted for patients with PR or SD defined by the Choi, mChoi, MASS, or 10% threshold criteria, although a trend was noted for mChoi and 10% criteria ($p = 0.08$ and 0.065 , respectively) (Fig. 3B). No significant difference in OS was found for the PR, SD, or PD groups defined by Choi, mChoi, MASS, or 10% threshold criteria, although a trend was noted for MASS criteria ($p = 0.062$). Patients with PD on the basis of RECIST had shorter OS compared with patients with SD ($p = 0.033$).

Table 4 shows the results for the 20 patients in the poor-risk category. For all criteria, patients classified as having PR had a longer PFS when compared with those classified as having SD (all p values < 0.03). Examples for mChoi criteria are shown in Figure 3C. There was a significant effect of response classification on OS for all criteria (all p values < 0.02), except for the 10% threshold criteria, which neared significance at $p = 0.053$. For Choi criteria, post hoc pairwise comparisons showed that patients with PR had a longer OS than did those with SD or PD ($p = 0.01$) and that OS for patients with SD and PD did not differ ($p = 0.52$). For mChoi and MASS criteria, patients with PR had longer OS than did those with PD ($p < 0.0005$), and no significant difference was noted between patients with SD and PR or between patients with SD and PD ($p > 0.2$), possibly because of the small sample sizes.

Discussion

Various criteria incorporating changes in both the size and attenuation of tumors have been proposed to overcome the limitations of RECIST (e.g., Choi, mChoi, MASS, and 10% threshold criteria). For the group of patients receiving salvage therapy in the present study, we found that these criteria were not as sensitive for predicting PFS, as had been previously reported for patients who were targeted therapy naive [11–14]. Among these, the criteria that required a 10% decrease in size to qualify as PR (i.e., mChoi and 10% threshold criteria) were more sensitive in identifying those patients who were likely to have prolonged PFS (p

= 0.064). This finding speaks to the mild tumor shrinkage that often results from targeted therapies.

When we narrowed our focus to assess the group with clinically poor risk only, however, all criteria were able to predict a subgroup of patients that had prolonged PFS within this group. This finding is in contrast to findings for the favorable-risk group, for which response groups defined by the various criteria did not differ in survival. This suggests that the prognostic value of imaging-based tumor response criteria may vary depending on the clinical risk status of the patient.

RECIST had high sensitivity for predicting patients who were likely to have shorter overall survival. This finding may be explained by the stringency of RECIST for classifying PD (i.e., tumor growth of > 20% is likely to lead to shorter survival). The addition of MSKCC risk factors to imaging-based criteria resulted in a larger number of patients being assigned to the PD category (Table 2) and a statistically significant correlation with OS, for all criteria. This is not surprising given that MSKCC risk factors were developed as prognostic indicators of overall survival for patients with RCC [15, 16].

In the present study, the MSKCC poor-risk classification (i.e., presence of two to three risk factors) was almost synonymous with a low KPS score. Eighteen of 20 patients with a poor-risk classification according to clinical factors (and, therefore, classified as having PD according to combined criteria) had a KPS score of less than 80. All patients with a KPS score of less than 80 were classified as belonging to the MSKCC poor-risk category. Thus, poor performance status before initiation of therapy was predictive of shorter survival after treatment.

Numerous studies have shown the importance of performance status in the prognosis of metastatic RCC [15, 18–20]. A high baseline KPS score before first-line therapy was predictive of which patients were more likely to receive second-line therapy [21]. The type of second-line therapy, on the other hand, did not affect survival (i.e., there was no difference in OS between patients treated with second-line vascular endothelial growth factor inhibitors vs second-line mammalian target of rapamycin inhibitors) [21]. This suggests that performance status may be a surrogate marker of underlying tumor biology, particularly in the salvage therapy setting.

In contrast to the shorter survival noted for patients classified as having PD, no significant difference in OS was noted for patients with SD or PR, for all criteria. This is important to consider when interpreting results of prior research studies that have found differences in OS between groups with and without treatment response (hereafter known as responders and nonresponders, respectively), after assignment of patients in the PR group to the responder category and patients with SD or PD to the nonresponder category, as in studies by Goh et al. [22], Krajewski et al. [14], and Thian et al. [23]. This dichotomized classification may not be an accurate representation of patients with SD, whose survival is often more similar to that of patients with PR than to patients with PD. Combining patients with SD and PD into one category (i.e., the nonresponder category) also decreases the statistical significance of

the PD group. This may explain why Thian et al. [23] did not find a correlation with OS when using RECIST or Choi criteria.

The similar clinical outcome for patients with PR and SD suggests that we should re-define what constitutes response, at least for patients treated with targeted agents in the salvage therapy setting. In the era of cyto-toxic therapy, a good response was defined arbitrarily as the disappearance or shrinkage of all lesions by at least 30%. This standard does not seem to be applicable to malignancies treated with targeted agents, however, and much work has focused on finding a better way to define PR [9–14]. One method may be to consider previous PR and SD categories as the responder group. This in fact reflects current clinical practice, particularly in the salvage setting, where patients often continue receiving therapy as long it is tolerable and they do not have disease progression.

The limitations of the present study include its retrospective design, modest sample size, and heterogeneous patient population that had been previously treated with a variety of therapies. In our attempt to include as much data as possible, we included patients who had CT scans obtained at outside institutions, provided that portal venous phase images were available. Thus nonuniform imaging technique is an additional limitation.

In conclusion, imaging-based response criteria and clinical risk factors have additive roles in predicting the clinical outcome of patients with advanced RCC, particularly in the salvage therapy setting. Patients who had PD on the basis of RECIST, mChoi, and MASS criteria had significantly shorter survival durations. Of note, there was no difference in OS between patients with PR and those with SD for any of the criteria, suggesting the possibility of combining patients with SD and patients with PR into a responder group.

Performance status is an important clinical risk factor and an indirect measure of tumor biology. Not surprisingly, patients identified as having poor risk on the basis of clinical factors had decreased survival durations. Within the poor-risk group, however, patients with a favorable response (PR) on the basis of imaging criteria had longer PFS than did patients with SD. Imaging criteria were less prognostic in the favorable-risk group. Thus, the prognostic value of imaging-based tumor response criteria may differ depending on the clinical risk status of the patient, particularly in the salvage setting.

Acknowledgments

We thank Sooyoung Shin, for assistance with data collection, and Robert Benjamin, for manuscript review.

N. M. Tannir is a consultant for Novartis, Bristol-Myers Squibb, Exelixis, GlaxoSmithKline, and Nektar but received no funding for this study.

This study used the services of the Cancer Center Support Group Biostatistics Resource Group, which is supported by award P30CA016672.

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Fig. 1.

51-year-old man with renal cell carcinoma and solitary hepatic metastasis. Axial contrast-enhanced CT images show ROIs drawn along margin of lesions (*white line*) to measure mean attenuation. Longest diameter of each lesion (*double-headed arrows*) was measured. **A**, CT image shows 5.5-cm left liver lesion with mean attenuation of 67 HU before therapy. **B**, CT image obtained after 2 months of treatment with pazopanib shows lesion has developed central necrosis and measures 6.3 cm (15% increase in longest diameter) and has mean attenuation of 42 HU (–37% change in attenuation). Response assessment for this patient would depend on criteria used, i.e., patient would be classified as having stable disease by Response Evaluation Criteria in Solid Tumors, partial response by Choi or Morphology, Attenuation, Size, and Structure criteria, and progressive disease by modified Choi or 10% threshold criteria.

Fig. 2.

Representative Kaplan-Meier curves for overall survival (OS) of adult patients with renal cell carcinoma. E = number of events (death), N = number of total patients.

A, Response groups defined using modified Choi (mChoi) criteria. Partial response (PR) and stable disease (SD) groups overlap and have longer survival than patients with progressive disease (PD).

B, Response groups defined by combined mChoi and Memorial Sloan-Kettering Cancer Center (MSKCC) risk factors. Addition of MSKCC risk factors increases the number of patients classified as having PD. There is slight separation of PR and SD groups, although not significant.

Fig. 3.

Representative Kaplan-Meier curves for progression-free survival (PFS) of adult patients with renal cell carcinoma. E = number of events (disease progression), N = number of total patients.

A, Kaplan-Meier curves for response groups defined using modified Choi (mChoi) criteria. Patients with partial response (PR) had trend toward longer PFS than patients with stable disease (SD).

B, Kaplan-Meier curves for response groups defined using mChoi criteria for patients in favorable-risk group. Graph shows PR and SD curves are further separated; however, p value is less significant because of smaller number of patients.

C, Kaplan-Meier curves for response groups defined using mChoi criteria for patients in poor-risk group. Patients with PR have longer PFS than do patients with SD.

Various Response Criteria

Table 1

Response	RECIST	Choi Criteria	Modified Choi Criteria	MASS Criteria	10% Threshold Criteria	Combined MSKCC and Imaging Criteria
PR	Decrease in sum of LD 30%	Decrease in sum of LD 10% or decrease in mean attenuation ^a 15%	Decrease in sum of LD 10% and decrease in mean attenuation ^a 15%	Decrease in sum of LD 20% or development of central necrosis ^b	Decrease in sum of LD 10%	0–1 Risk factors plus imaging-based PR classification
SD	Sum of LD decreases by < 30% or increases by < 20%	Sum of LD decreases by < 10% or increases by < 10% and does not meet criteria for PR on basis of attenuation	Does not meet criteria for PR or PD	Does not meet criteria for PR or PD	Does not meet criteria for PR or PD	0–1 Risk factors plus imaging-based SD classification
PD	Increase in sum of LD 20% or new lesions	Increase in sum of LD 10% and does not meet criteria for PR on basis of attenuation	Increase in sum of LD 10%	Lesion becomes more enhanced ^c or increase in sum of LD 20% in the absence of central necrosis	Increase in sum of LD 10%	2–3 Risk factors or imaging-based PD classification

Note—For all criteria, the development of new lesions denotes progressive disease (PD). RECIST = Response Evaluation Criteria in Solid Tumors, MASS = Morphology, Attenuation, Size, and Structure, MSKCC = Memorial Sloan-Kettering Cancer Center, PR = partial response, LD = longest diameters (of all selected lesions in a patient), SD = stable disease, PD = progressive disease.

^aMean attenuation of all selected lesions in a patient.

^bAs determined by subjective assessment

^c“More enhanced” is a designation indicating central filling in of or new enhancement of a previously hypoattenuating mass.

Table 2
Response Classification by Imaging-Only Criteria and Combined Imaging and Memorial Sloan-Kettering Cancer Center (MSKCC) Criteria

Criteria	Partial Response			Stable Disease			Progressive Disease			Log-Rank Test <i>p</i> ^a	
	No. of Patients	Median OS (y)	Median PFS (y)	No. of Patients	Median OS (y)	Median PFS (y)	No. of Patients	Median OS (y)	Median PFS (y)	PFS ^g	OS
RECIST	0	—	—	48	1.82	0.23	9	0.34	0	—	0.0002
Choi	37	1.42	0.25	10	1.6	0.08	10	0.47	0	0.96	0.092
mChoi	18	2	0.69	25	1.82	0.19	14	0.46	0	0.064	0.0089
MASS	24	1.38	0.32	24	3	0.16	9	0.34	0	0.96	0.0009
10% Threshold	21	2.58	0.59	25	1.6	0.17	11	0.47	0	0.064	0.1137
RECIST and MSKCC	0	—	—	33	3	0.27	24	0.47	0.04	—	< 0.0001
Choi and MSKCC	24	2.58	0.32	7	3	0.17	26	0.68	0.01	0.72	0.0009
mChoi and MSKCC	11	> 2.58 ^b	1.94	18	3	0.21	28	0.68	0.01	0.08	0.0005
MASS and MSKCC	16	2.58	0.32	17	> 1.82 ^b	0.25	24	0.47	0.04	0.68	0.0001
10% Threshold and MSKCC	14	> 1.38 ^b	0.69	15	3	0.19	28	0.68	0.01	0.26	0.0005

Note—Dash (—) denotes that a value could not be calculated because of lack of data. OS = overall survival, PFS = progression-free survival, RECIST = Response Evaluation Criteria in Solid Tumors, mChoi = modified Choi, MASS = Morphology, Attenuation, Size, and Structure.

^aLog-rank test for PFS is performed between PR and SD groups only.

^bNot reached.

Table 3
Response to Therapy in Memorial Sloan-Kettering Cancer Center (MSKCC) Favorable-Risk Group (With 0–1 MSKCC Risk Factors) (*n* = 37)

Criteria	Partial Response			Stable Disease			Progressive Disease			Log-Rank Test <i>p</i> ^a	
	No. of Patients	Median OS (y)	Median PFS (y)	No. of Patients	Median OS (y)	Median PFS (y)	No. of Patients	Median OS (y)	PFS ^a	OS	
RECIST	0	—	—	33	2.78	—	4	0.93	—	0.033	
Choi	24	2.24	0.32	7	2.78	0.17	6	1.55	0.72	0.35	
mChoi	11	NR	1.94	18	2.78	0.21	8	1.55	0.08	0.13	
MASS	16	2.24	0.32	17	NR	0.25	4	0.93	0.68	0.062	
10% Threshold	14	NR	0.69	15	2.78	0.19	8	1.55	0.065	0.16	

Note—Dash (—) denotes that a value could not be calculated because of lack of data. OS = overall survival, PFS = progression-free survival, RECIST = Response Evaluation Criteria in Solid Tumors, mChoi = modified Choi, MASS = Morphology, Attenuation, Size, and Structure, NR = not reached.

^aLog-rank test for PFS is performed between PR and SD groups only.

Response to Therapy in Memorial Sloan-Kettering Cancer Center (MSKCC) Poor-Risk Group (2–3 MSKCC Risk Factors) (*n* = 20)**Table 4**

Criteria	Partial Response				Stable Disease				Progressive Disease				Log-Rank Test <i>p</i> ^a	
	No. of Patients	Median OS (y)	Median PFS (y)	No. of Patients	Median OS (y)	Median PFS (y)	No. of Patients	Median OS (y)	No. of Patients	Median OS (y)	PFS	OS	PFS	OS
RECIST	—	—	—	15	0.63	—	5	0.19	5	0.19	—	0.005		
Choi	13	0.67	0.16	3	0.13	0	4	0.19	4	0.19	0.011	0.004		
mChoi	7	0.67	0.42	7	0.29	0.06	6	0.19	6	0.19	0.024	0.018		
MASS	8	0.67	0.32	7	0.29	0.06	5	0.19	5	0.19	0.028	0.017		
10% Threshold	7	0.67	0.42	10	0.24	0.01	3	0.19	3	0.19	0.008	0.053		

Note—Dash (—) denotes that a value could not be calculated because of lack of data. OS = overall survival, PFS = progression-free survival, RECIST = Response Evaluation Criteria in Solid Tumors, mChoi = modified Choi, MASS = Morphology, Attenuation, Size, and Structure.

^aLog-rank test for PFS is performed between PR and SD groups only.