Changes in Tumor Density in Patients with Advanced Hepatocellular Carcinoma Treated with Sunitinib

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Statement of translational relevance

The identification of new anticancer agents brings many clinical challenges, including accurately assessing their clinical efficacy. The antitumor activity of targeted agents, such as sunitinib, sorafenib, and imatinib, may comprise changes in tumor vascularization, cavitation, and necrosis that do not significantly affect tumor size and are captured as stable disease using Response Evaluation Criteria in Solid Tumors (RECIST). We evaluated changes in tumor density on computed tomography scans using Choi criteria as a surrogate endpoint for sunitinib activity in a phase II study of patients with hepatocellular carcinoma (HCC). Compared with conventional RECIST-based measures, reductions in tumor density correlated notably better with improved time to progression. Our findings suggest that radiological endpoints in addition to RECIST, or as an alternative to RECIST, need to be validated and integrated into HCC clinical trial design.
Abstract

Purpose: Response Evaluation Criteria in Solid Tumors (RECIST) may underestimate the efficacy of targeted therapies. In hepatocellular carcinoma (HCC) studies with sunitinib, RECIST-defined response rates are low, although hypodensity on computed tomography (CT) scans occurs more frequently. This exploratory analysis investigated tumor density as a surrogate endpoint of sunitinib activity in a phase II HCC study.

Experimental Design: Patients received sunitinib 50 mg/d (4 wks on/2 wks off). Tumor size and density were assessed on CT scans using RECIST and Choi criteria, the latter of which classify a partial response as a ≥15% reduction in tumor density or a ≥10% reduction in tumor size. The overall percentage volume of tumor necrosis was calculated with volumetric reconstruction. Tumor perfusion parameters were assessed using perfusion CT scans with specific acquisition.

Results: Among 26 evaluable patients, one achieved a partial response and 22 had tumor stabilization by RECIST. In analysis of tumor density, 17/26 patients (65.4%) were responders by Choi criteria. Volumetric assessment showed major tumor necrosis (≥30% of tumor volume) in 10/21 patients (47.6%). Among four patients evaluated, tumor blood flow was reduced by 58.8% and blood volume by 68.4% after 4 wk of treatment. The median time to progression (TTP) was 6.4 mo. Patients with responses by Choi criteria had a significantly longer TTP (7.5 mo) compared with non-responders (4.8 mo; hazard ratio 0.33, two-sided \( P = 0.0182 \)).

Conclusions: Tumor density assessment suggested that radiological endpoints in addition to RECIST may be considered to capture sunitinib activity in HCC.
Introduction

Surrogate efficacy parameters, such as tumor response, are decisive factors during phase II trials for “go/no-go” decisions on launching large-scale clinical trials designed to demonstrate progression-free survival (PFS) and overall survival (OS) advantages. Response Evaluation Criteria in Solid Tumors (RECIST) are a well-established tool for assessment of tumor response to cytotoxic chemotherapy in clinical trials (1). However, their limitations in assessing the antitumor activity of targeted therapies and antiangiogenic agents are increasingly being recognized (2). Unlike cytotoxic agents that may induce rapid tumor shrinkage, targeted therapies are acknowledged to yield sustained tumor stabilization and delay tumor progression. Furthermore, antiangiogenic agents can also reduce tumor vascularization, provoke areas of necrosis, and sometimes cause cavitations in solid tumors. These peculiar features have been reported with imatinib, sorafenib, and sunitinib in several tumor types, including non-small cell lung cancer (3), renal cell carcinomas (RCC) (4), gastrointestinal stromal tumors (GIST) (5–7), and hepatocellular carcinoma (HCC) (8, 9). Changes in tumor vascularization, cavitation, and necrosis may have no major effect on tumor size and are frequently captured as stable disease using RECIST. As stable disease is not considered a reliable surrogate endpoint of antitumor activity in clinical trials, using RECIST for development decisions carries a risk of prematurely terminating the development of active drugs.

Several additional radiologic assessments aiming to provide more sensitive measures of response to therapy have been proposed, including high-frequency ultrasonography, dynamic contrast-enhanced magnetic resonance imaging (DC-MRI), and 18-fluorodeoxyglucose positron emission tomography (18FDG-PET) scanning (6). Interestingly, computed tomography (CT) scans not only provide information on tumor size (10), but can also supply accurate tissue density measurements. Choi et al. were the first to propose CT assessment criteria based on tumor density in patients with imatinib-treated GIST and defined a partial response as a ≥15% decrease in tumor density or a ≥10% decrease in one-dimensional size on a contrast-enhanced CT scan (5, 6). These
criteria yielded a response rate almost double that of RECIST and were also significantly more predictive of time to tumor progression (TTP) and OS in GIST (5, 6), compared with RECIST.

The oral, multitargeted tyrosine kinase receptor inhibitor sunitinib is licensed for use in imatinib-refractory/-intolerant GIST and advanced RCC and provides a high rate of clinical responses in these diseases (11). Sunitinib is being investigated in several other tumor types, and was recently studied in 37 patients with advanced, unresectable HCC in a phase II, single-arm trial (12). Most patients had Child-Pugh A status (83.8% Child Pugh A; 16.2% Child Pugh B) and stage C Barcelona Clinic Liver Cancer classification (92.0%). Assessment by RECIST found only one partial response, giving an overall response rate of 2.7%; 13 patients had stable disease for ≥3 mo, resulting in a disease control rate of 37.8%.

Although the number of RECIST-defined objective responses was low in this trial (12), investigators observed that sustained tumor stabilization was usually associated with decreased tumor density on CT scans (13). This led us to conduct an ancillary study to quantify changes in tumor density on CT scans prior to and after treatment with sunitinib, in an attempt to identify patients who benefit from sunitinib therapy.
Patients and Methods

Study design and per-protocol assessments

The design and per-protocol results of this single-arm, multicenter trial (NCT00247676) have been described extensively in a recent publication (12).

This trial was approved by institutional review boards at all participating centers (in France, South Korea, and Taiwan), and all patients provided written informed consent. Eligible patients were aged ≥18 y with histologically proven HCC not amenable to curative surgery, life expectancy ≥3 mo, RECIST-defined measurable disease, Child-Pugh Class A or B without ascites, Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, and adequate organ function. Patients were not eligible if they had prior systemic therapy for HCC (including sorafenib) or liver transplantation. Prior treatment with lipiodol (or any other local therapy) was only permitted if patients had subsequent disease progression or recurrence that was accompanied by the development of at least one new measurable lesion.

Patients self-administered sunitinib orally at a starting dose of 50 mg daily for 4 wk, followed by 2 wk off treatment, in 6-wk cycles until disease progression, unacceptable toxicity, or consent withdrawal. Dose reductions to 37.5 mg and then to 25 mg were allowed in patients with clinically significant toxicities.

CT scans were performed at screening, after the first 4 wk on treatment, and then every 6 wk (i.e., after each 4-wk sunitinib treatment period). Efficacy analyses included all patients receiving sunitinib for at least one 4-wk treatment period.

Radiologic analyses

At the end of the study, CT scan images were centralized for review by an independent radiologist (MZ) at Beaujon University Hospital (Clichy, France), who was blinded to the clinical data. One or two target lesions were defined at baseline and were followed up, regardless their initial density. The tumor was delineated and the density in the overall lesions was measured. Tumor density was
defined at baseline and compared with that observed at subsequent tumor evaluations. Imaging techniques are further defined in Supplementary Appendix S1 (available online only). Correlative efficacy evaluations included tumor response according to changes in tumor density, volumetric measurement of tumor necrosis and the entire tumor, and tumor perfusion in a limited number of patients. These analyses were not initially planned in the study protocol and were exploratory. For determination of changes in tumor density and volumetric measurement of tumor necrosis, ≥1 dominant hepatic mass ≥2 cm was selected at baseline and followed every cycle.

Two-dimensional tumor density was assessed using CT attenuation coefficients as described by Choi et al. in GIST (5, 6). These defined partial response as a decrease in tumor density (measured in Hounsfield units [HU]) of ≥15% on CT or a decrease in tumor size (sum of the largest diameters of target lesions as defined in RECIST, cm) of ≥10% (Supplementary Table S1, online only) (6).

Three-dimensional evaluation of tumor necrosis was also performed. Tumor necrosis was defined as tumoral tissue that did not enhance on multiphasic CT examinations after contrast medium injection. We derived methods used for the measurement of liver volumetry and regeneration as described elsewhere (14, 15) to obtain a volumetric reconstruction of the tumor and of its inner volume of necrosis on CT scan. This was done by manually delineating the tumor and necrotic areas (Advantage Windows software version 4.2, GE Healthcare, WI). A section thickness of 5 mm (without overlaps) was used for volumetry. The percentage volume of necrosis in the whole tumor was then calculated, with major and minor necrosis defined as ≥30% and ≥15% necrosis, respectively.

To establish whether changes in tumor density were due to hypovascularization, tumor blood perfusion parameters were determined by carrying out exploratory perfusion CT scans with specific acquisition in four patients. Using the deconvolution method for the perfusion CT, the following hemodynamic perfusion parameters were analyzed in regions of interest: blood flow, blood volume, mean transit time, arterial index, and permeability surface as described elsewhere (16).
Statistical analysis

Methods of calculation for comparison of tumor density and volumetric measurement of tumor necrosis before and after treatment were performed using the Wilcoxon Signed Rank Test (in which significance is defined by two-sided $P$ values < 0.05).

Time-to-event endpoints were summarized using the Kaplan-Meier method and comparison of Kaplan-Meier curves used the log-rank (Mantel-Cox) test.

Results

Assessment of changes in tumor density

All 37 patients were followed until disease progression and/or occurrence of death. In total, 6/11 patients (54.6%) not included in the ancillary study to quantify changes in tumor density had progressed at the time of analysis, compared with 16/26 patients (61.5%) who were included. No significant differences in terms of RECIST response rate or PFS were detected in the 11 excluded patients compared with 26 patients who were included in this analysis. Twenty-six patients had CT scans available for assessment of tumor density, and their baseline characteristics are shown in Table 1. The remaining 11 patients were not evaluable for tumor density for the following reasons: density measurements could not be performed due to software incompatibility ($n = 5$), adequate imaging not available at first evaluation ($n = 5$), and target lesions <2 cm ($n = 1$).

In total, 46 target lesions in 26 patients were measured (median 2 lesions/patient, range 1–4) at baseline and after cycle 1. The median number of treatment cycles was three (range 1–7). As some patients discontinued after cycle 1, 32 target lesions (19 patients) were evaluated after cycle 2, 28 (16 patients) after cycle 3, and 21 (11 patients) after cycle 4.

Using the best response at any cycle as an endpoint, no significant change in tumor size (as measured based on largest diameters) from baseline (mean size 54.5 ± 8.1 mm; $P = 0.7$) to the time
of best response (mean size $54.3 \pm 8.3$ mm) was detectable amongst evaluable lesions
(Supplementary Fig. S1, online only).

Figs. 1A and B represent scans from a patient who displayed no change in tumor diameter after 4 wk of treatment, but a significant ($P < 0.05$) decrease in tumor density that coincided with normalization of $\alpha$-fetoprotein levels. This patient experienced 33 mo of disease control.

Most changes in whole tumor density seemed to occur early, as illustrated in Fig. 1C. Median tumor density at baseline was 86.0 HU (range 39–162) and decreased significantly to 55.0 HU (range 27–147) after cycle 1 ($P < 0.001$). Median tumor densities after cycles 2, 3, and 4 were 68.0 HU (range 27–155), 76.5 HU (range 40–178), and 70.0 HU (range 40–141), respectively. None of these values differed significantly from baseline values ($P > 0.05$). Density seemed to increase markedly after cycle 3, as mean values were significantly higher after cycles 3 and 4, compared with the first cycle evaluation ($P < 0.01$ and 0.05, respectively).

**Volumetric changes in tumor density in whole tumors**

Since measurement of tumor density could be affected by subjectively positioning an area of interest on tumor slides, we analyzed changes in tumor density in three dimensions. Twenty-one patients had a total of 32 tridimensional measurable lesions evaluable for changes in tumor volume. No significant changes in mean tumor volume were observed from baseline ($295.0 \pm 587.0$ mm$^3$) to the time of best tumor response ($321.8 \pm 573.5$ mm$^3$; $P = 0.58$).

At baseline, the mean volume of tumor necrosis was $44.5 \pm 9.2$ mm$^3$ ($15.1\% \pm 21.6$ of tumor volume) and increased significantly to $129.4 \pm 70.3$ mm$^3$ ($40.2\% \pm 30.5$ of tumor volume) after cycle 1 ($P = 0.001$). Major necrosis ($\geq 30\%$ of tumor volume) was observed in $10/21$ patients ($47.6\%$), while minor necrosis ($\geq 15\%$ of tumor volume) was induced in $13$ patients ($61.9\%$).
Assessment of tumor perfusion on CT scan

To determine whether changes in tumor density were due to reductions in tumor vascularization, additional investigations using perfusion CT scans were performed in four patients. Among these patients, all of whom had RECIST-defined stable disease, blood flow was reduced by 58.8% (range 39.3–71.1%) and blood volume by 68.4% (range 58.1–74.3%) after 4 wk of sunitinib treatment, compared with baseline. Figure 2 shows CT scans performed before and after 4 wk of sunitinib treatment, showing a significant decrease in tumor density suggestive of a large area of tumor necrosis. Three-dimensional reconstruction of hepatic vascularization before and after sunitinib revealed a number of changes in macro- and microvascularization, with devascularized areas and the occurrence of large blood spaces. Perfusion CT scans performed before and after sunitinib in the same patient showed a significant decrease in blood flow, as indicated in Figures 2E and F by the blue areas. As shown in Figure 2, perfusion parameters including blood volume and blood flow appeared to increase by 34.7% and 14.8%, respectively, in non-tumor liver tissues during sunitinib treatment.

Response assessed by Choi criteria versus RECIST

Figure 3 illustrates changes in tumor size according to RECIST (panel A) or variations in tumor density (panel B) measured by CT scan at baseline and after 4 wk of sunitinib treatment in all evaluable patients. Among 26 patients evaluated in this trial, one (3.8%) presented a partial response, 22 (84.6%) had tumor stabilization, and three (11.5%) experienced disease progression according to RECIST. Based on Choi criteria (5), 17/26 evaluable patients (65.4%) were responders. The remaining 9/26 patients (34.6%) were considered non-responders and included one patient with stable disease and eight with tumor progression.

Table 2 compares best response by RECIST versus response by Choi criteria in the 26 evaluable patients at the time of first evaluation. In total, 16/22 patients who had a best response of stable disease by RECIST were responders according to Choi criteria, while six patients with RECIST-defined
stable disease were non-responders using Choi criteria. Three patients had progressive disease according to both criteria.

**Activity assessed by RECIST or Choi criteria versus time to progression**

Among the 26 evaluable patients in this study, the median time to progression (TTP) was 6.4 mo by RECIST, with 10 patients presenting new lesions as a cause of progression, six patients having an increase of ≥20% in tumor size, and 10 patients remaining stable. The median TTP of patients with a partial response or tumor stabilization by RECIST was 7.5 mo and was significantly higher than the 0.9-mo TTP observed in patients with a best response of progressive disease (hazard ratio [HR], 0.21; 95% confidence interval [CI], 0.001–0.48; two-sided $P = 0.0153$). This confirms that progression by RECIST predicts a poor outcome in HCC. The outcome of 17 patients with responses according to Choi criteria was compared with that of the nine patients classed as non-responders (Fig. 4). Patients with a response according to Choi criteria experienced a significantly longer median TTP (7.5 mo), compared with non-responders (4.8 mo; HR, 0.33; 95% CI, 0.04–0.75, two-sided $P = 0.0182$). No significant difference in median OS was observed between Choi responders (9.3 mo) and non-responders (4.8 mo, HR, 0.70; 95% CI, 0.3–1.6; $P = 0.56$).

**Discussion**

The aims of phase II trials include detecting indications of antitumor activity and providing information that can be used for further clinical development. Phase II studies with sunitinib in HCC were designed using response rate according to RECIST as a primary conservative endpoint for efficacy. However, regardless of doses and schedules used in the recently reported phase II trials, response rates of sunitinib in HCC were generally <10%, which is below the 20% threshold usually acknowledged to define active anticancer agents (12, 17–19). Despite limited changes in HCC tumor sizes, striking appearances of large areas of tumor hypodensity were frequently reported during treatment with sunitinib. Using dynamic contrast-enhanced magnetic resonance imaging, Zhu et al.
(17) reported that sunitinib significantly reduced intratumor vascularization, leading to significant changes in the transfer constant $K_{\text{trans}}$, a surrogate endpoint for vessel leakage, in patients with partial responses or sustained tumor stabilization. In our study using contrast-enhanced CT scans, we also reported sunitinib-associated changes in inner tumor density accompanied by reduced tumor blood flow and volume that suggest the occurrence of extensive tumor necrosis. In this population of patients with unresectable liver cancer, it was not possible to obtain pathological specimens that would have confirmed the presence of tumor necrosis. Instead, tumor blood flow analysis provided a non-invasive method to evaluate the effect of sunitinib on tumor vascularization in a small subset of patients. Limited changes in tumor size with possible reduction in tumor density were also observed with sorafenib, despite additional evidence showing that this drug improved survival of patients with HCC (8, 9, 20, 21). In the phase III SHARP and Asia-Pacific trials, RECIST-defined response rates with sorafenib were 2% and 3.3%, respectively (20, 21), which are in the same order of magnitude as response rates with sunitinib in this study (12). These clinical reports with multitargeted inhibitors seem to indicate that changes in intratumor vascularization did not modify overall tumor size and were not associated with significant tumor shrinkage, resulting in limited numbers of objective responses according to RECIST.

Lack of enhancement and/or decreased tumor density has been previously used in transarterial chemoembolization and local ablation to define responders and non-responders. This method was shown to provide early evidence of clinical activity (22), and has also been used to monitor activity of targeted agents. Choi et al. (6) first reported changes in tumor density in patients with GIST tumors treated with imatinib. They showed that a $\geq 15\%$ reduction of tumor density or a $\geq 10\%$ reduction in tumor size correlated better with PFS than RECIST. Another approach, revisiting RECIST using modified criteria (mRECIST), has been recommended by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases (23). Both mRECIST and Choi criteria recognize that changes in overall tumor size, as measured by the largest tumor diameters, may not be appropriate for evaluating the antitumor effects of antiangiogenic
agents in HCC, and consider the occurrence of hypodense areas. Additionally, Response Evaluation Criteria in Cancer of the Liver (RECICL) proposed by the Liver Cancer Study Group of Japan captures tumor necrosis based on two-dimensional measurements (24). These novel criteria should be incorporated prospectively in future clinical trials and validated as surrogate endpoints for survival parameters.

In our trial, we showed that sunitinib was capable of inducing a reduction of \( \geq 15\% \) in tumor density or a \( \geq 10\% \) reduction in tumor size in 65.4\% of patients. Likewise, the study reported by Koeberle et al. (19) using sunitinib 37.5 mg on a continuous daily dosing schedule also found responses in 62\% of patients according to Choi criteria, whereas RECIST captured an objective response rate of only 2\%. In our study, perfusion CT scans also showed an early reduction in blood flow to the tumor site after 1 mo of treatment with sunitinib, indicative of direct and rapid effects on tumor vasculature. Similarly, in a phase II study using bevacizumab, Zhu et al. reported a significant decrease in tumor perfusion parameters including blood flow and blood volume within 2 wk after bevacizumab administration in patients with advanced HCC (25).

Interestingly, using Choi criteria, modifications in density seemed to occur early, with best responses observed at the first imaging assessment in 20/26 evaluable patients and after cycle 2 in the remaining six patients, despite a best response of tumor stabilization by RECIST. In our experience, Choi criteria were associated with a better outcome, as reflected by a marked increase in TTP among responders versus non-responders. Although the number of patients in this study was limited, these data also strongly suggest that endpoints evaluating intratumor vascularization, such as the measurement of tumor density, would be more appropriate to capture the effects of sunitinib than RECIST. As two-dimensional decreases in tumor density seem to correlate favorably \( (P = 0.04) \) with volumetric reconstructions of areas of tumor necrosis in our study (data not shown), two-dimensional measurements are likely more appropriate for future trials, due to their greater ease of use. However, the small sample size and unplanned nature of the analyses reported here need to be taken into account. At this time, measurements of tumor density remain exploratory endpoints in a
limited number of patients, and further work is needed to determine whether density changes correlate with clinical efficacy in HCC in larger clinical trials.

Among 26 patients evaluated in this trial, 22 (84.6%) had tumor stabilization according to RECIST. In the absence of a control group, one may consider that disease stabilization might have been related to the presence of indolent disease. Although cross-study comparisons should be interpreted with care, it may be useful to note that our study population primarily comprised patients with Barcelona Clinic Liver Cancer (BCLC) stage C disease (92.3%) (12), and was similar to that of the SHARP trial (81.6% of patients with BCLC stage C disease) in which TTP in the placebo group was only 2.8 mo (20, 21). Moreover, PFS in the present study showed that more than 50% of patients had progressed at 6 mo, suggesting that patients entered in this trial had disease forms associated with poor prognosis.

Criteria for progression are not unequivocally defined using Choi criteria. Therefore, in this study, we were unable to define PFS or TTP according to Choi criteria. Considering that 10 patients presented new lesions as a cause of progression, six patients had an increase of ≥20% in tumor size, and 10 patients remained stable according to RECIST, it is likely that RECIST and Choi criteria would converge in defining similar rates of progression. Importantly, while we cannot define PFS according to Choi criteria in this trial, our data suggest that early occurrence of response by Choi criteria at the first tumor evaluation defines patients who will experience a better outcome with sunitinib therapy. This early identification of responders is also supported by the immediate divergence of the TTP curves in Figure 4.

In summary, these analyses provide further evidence that conventional imaging strategies relying on changes in tumor dimensions may not be sufficient to capture the antitumor activity of targeted antiangiogenic agents in HCC. Additional or alternative endpoints to RECIST-defined objective response need to be validated and integrated into HCC clinical trial design.
Disclosure of Potential Conflicts of Interest

S. Faivre has received honoraria from Pfizer Inc, Bayer, Schering, Merck Serono, and Sanofi-Aventis, and has had a consultant/advisory role with Amgen. J.-Y. Douillard and E. Raymond have had a consultant/advisory role with Pfizer Inc. Y.-K. Kang has received honoraria from and has had a consultant/advisory role with Pfizer Inc and Bayer. A.-L. Cheng has received honoraria from and has had a consultant/advisory role with Pfizer Inc. S. Lanzalone, X. Lin, and M.J. Lechuga are employees of Pfizer Inc.

Acknowledgments

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References


Fig. 1. Changes in tumor density in hepatocellular carcinoma (HCC) during treatment with sunitinib. Scans at baseline (A, example of a patient with a treatment-naive 39-mm tumor lesion, density 93±8 Hounsfield units [HU]) and after 4 wk of treatment (B, same patient, lesion size 37 mm, density 45±28 HU) are shown for a patient’s tumor (arrows) that displayed no change in diameter after therapy, but a significant ($P < 0.05$) decrease in tumor density. Median tumor density for all evaluable patients decreased significantly after cycle 1 relative to baseline and increased to near baseline levels after cycle 3 (C). The number of target lesions was 46 at baseline (26 patients), 46 after cycle 1 (26 patients), 32 after cycle 2 (19 patients), 28 after cycle 3 (16 patients), and 21 after cycle 4 (11 patients).

Fig. 2. Representative changes in the tumor vascularization during treatment with sunitinib in patients with hepatocellular carcinoma. Computed tomography (CT) scans showing tumor density and inner tumor vascularization, respectively, at baseline (A and C) and after 4 wk of sunitinib therapy (B and D). After sunitinib treatment, decreased tumor density (B, arrow) was associated with changes in the inner tumor vascularization (D), with occurrence of wide blood spaces (arrow). Perfusion CT scans performed at the same time points (baseline [E] and after 4 wk of treatment [F]) showed a decrease in tumor blood flow after sunitinib therapy (arrows and blue areas).

Fig. 3. Waterfall plot of changes in tumor size using sums of largest diameters of target lesions (RECIST; A) or mean tumor density change in target lesions (B), after 4 wk of sunitinib treatment ($n = 26$ evaluable matched patients).

Fig. 4. Median time to progression according to Choi criteria.
FIG 4

Median time to progression

- Choi responder ($n = 17$): 7.5 mo
- Choi non-responder ($n = 9$): 4.8 mo

Hazard ratio: 0.33
(95% CI, 0.04–0.75)
$P = 0.0182$
Table 1. Baseline characteristics of patients included in tumor imaging assessments.

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<th>Patient characteristic</th>
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<td>Median age, years (range)</td>
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*Complete portal vein thrombosis: n=2; partial portal vein thrombosis: n=11.
BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group.
Table 2. Best response by RECIST versus response by Choi criteria in 26 evaluable patients.

<table>
<thead>
<tr>
<th>Choi criteria, n (%)</th>
<th>RECIST, n (%)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Partial response</td>
<td>Stable disease</td>
<td>Progressive disease</td>
<td></td>
</tr>
<tr>
<td>Partial response</td>
<td>17 (65.4)</td>
<td>1 (3.8)</td>
<td>16 (61.5)</td>
<td>–</td>
</tr>
<tr>
<td>Stable disease</td>
<td>1 (3.8)</td>
<td>–</td>
<td>1 (3.8)</td>
<td>–</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>8 (30.8)</td>
<td>–</td>
<td>5 (19.2)</td>
<td>3 (11.5)</td>
</tr>
</tbody>
</table>
Changes in Tumor Density in Patients with Advanced Hepatocellular Carcinoma Treated with Sunitinib

Sandrine Faivre, Magaly Zappa, Valérie Vilgrain, et al.

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