

Choi response criteria for early prediction of clinical outcome in patients with metastatic renal cell cancer treated with sunitinib

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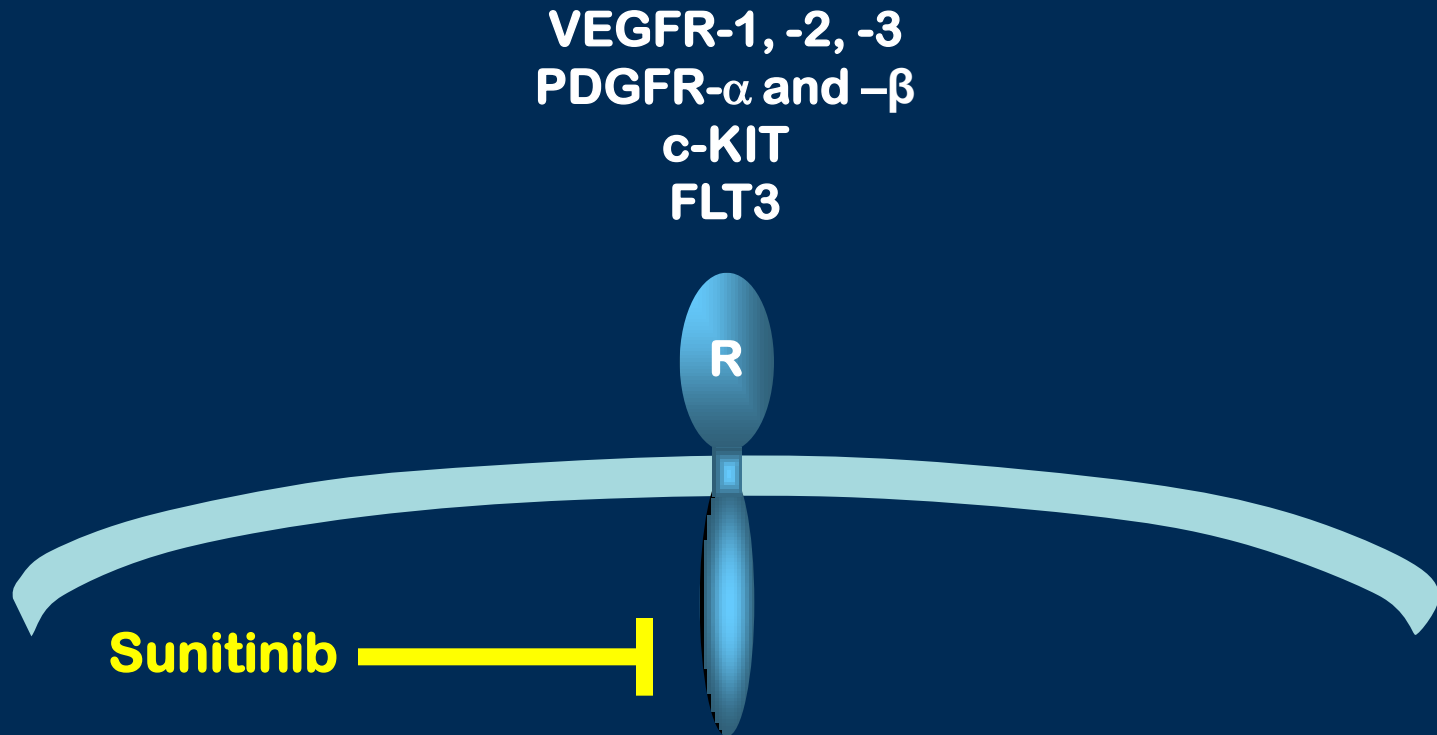
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VU university medical center



Sunitinib in renal cell cancer

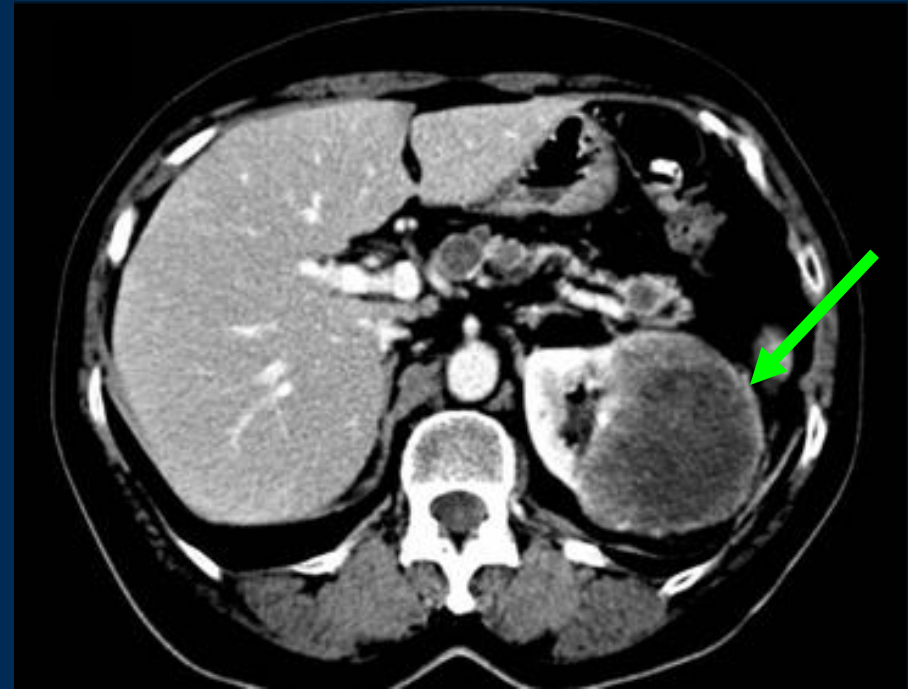
Sunitinib malate (Sutent®) has been approved for the treatment of advanced renal cell cancer (RCC)



Sunitinib-induced tumor necrosis



At baseline



During sunitinib treatment

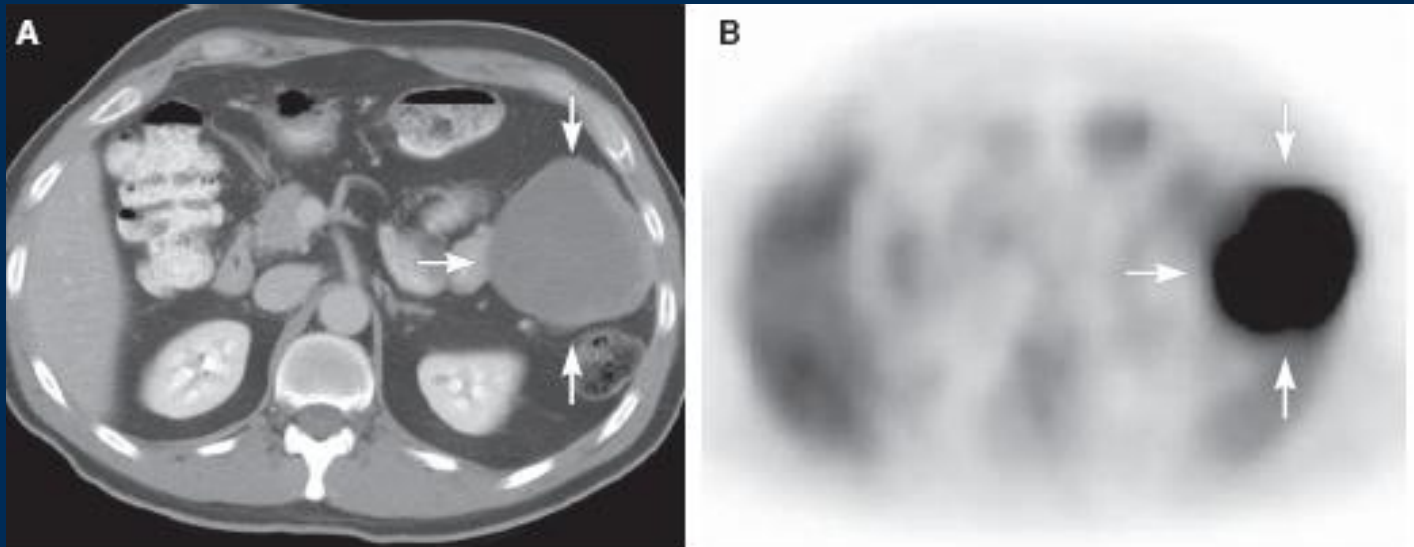
Evaluation of sunitinib treatment

- Objective responses may be underestimated by Response Evaluation Criteria In Solid Tumors (RECIST), since sunitinib can cause tumor necrosis without a marked decrease in tumor size

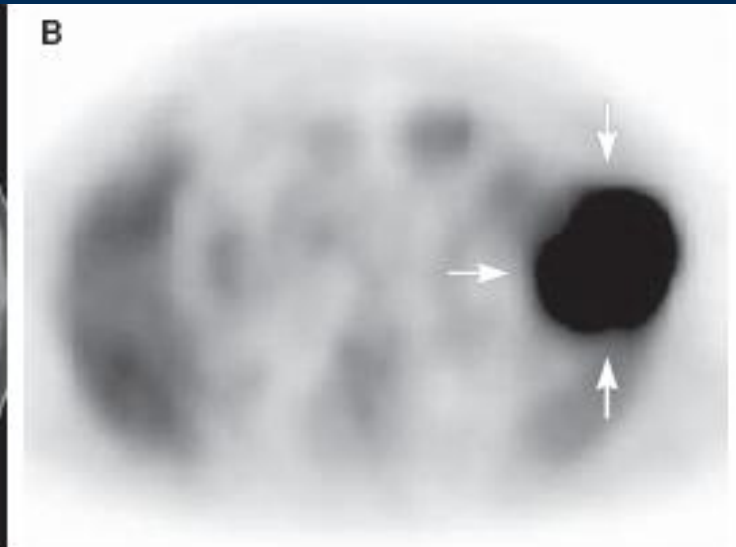
Evaluation of sunitinib treatment

- Objective responses may be underestimated by Response Evaluation Criteria In Solid Tumors (RECIST), since sunitinib can cause tumor necrosis without a marked decrease in tumor size
- Criteria defined by Choi *et al.* for response evaluation include tumor density and may be of value to early predict sunitinib efficacy

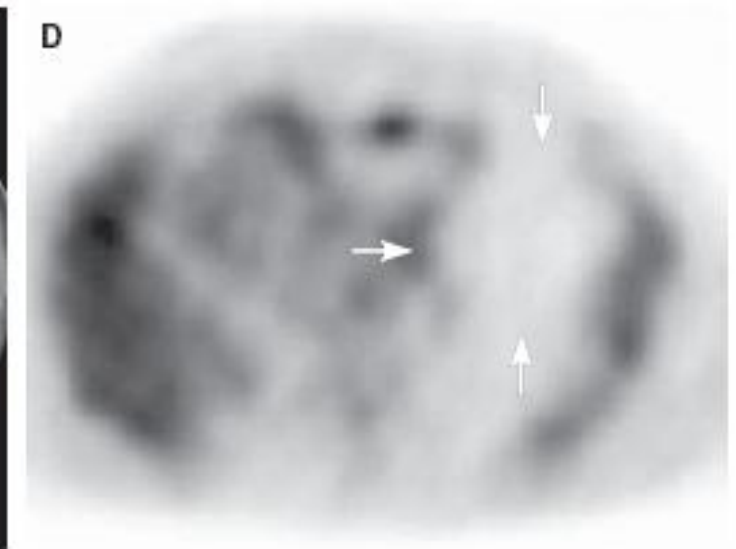
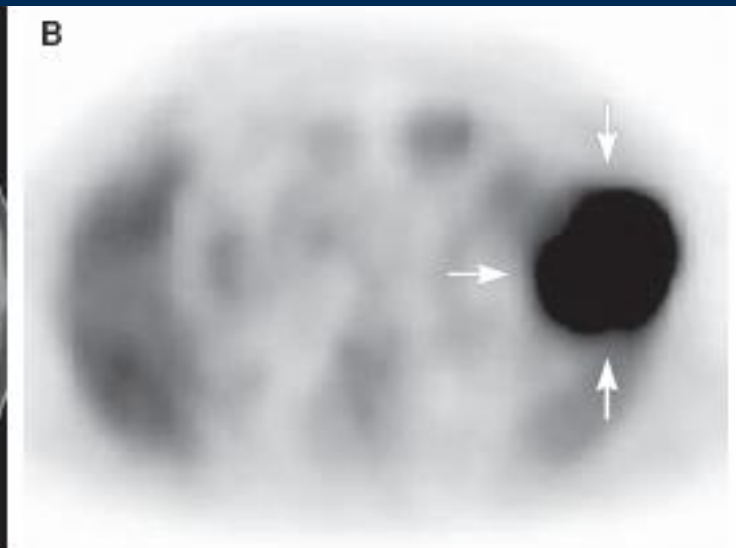
Imatinib treatment in GIST



Imatinib treatment in GIST



Imatinib treatment in GIST



Response assessment: RECIST *versus* Choi criteria

RECIST

Choi criteria

CR Disappearance of all lesions
No new lesions

Disappearance of all lesions
No new lesions

PR Decrease in tumor size $\geq 30\%$

No new lesions

No PD of non-target lesions

Decrease in tumor size $\geq 10\%$ or
decrease in tumor density $\geq 15\%$
on CT

No new lesions

No PD of non-measurable lesions

SD Does not meet criteria for CR, PR
or PD

No symptomatic deterioration
attributed to tumor progression

Does not meet criteria for CR, PR
or PD

No symptomatic deterioration
attributed to tumor progression

PD Increase in tumor size $\geq 20\%$

New lesions

Increase in tumor size $\geq 10\%$ and
does not meet PR criteria by
tumor density

New lesions

Response assessment: RECIST *versus* Choi criteria

RECIST	Choi criteria
CR Disappearance of all lesions No new lesions	Disappearance of all lesions No new lesions
PR Decrease in tumor size $\geq 30\%$ No new lesions No PD of non-target lesions	Decrease in tumor size $\geq 10\%$ or decrease in tumor density $\geq 15\%$ on CT No new lesions No PD of non-measurable lesions
SD Does not meet criteria for CR, PR or PD No symptomatic deterioration attributed to tumor progression	Does not meet criteria for CR, PR or PD No symptomatic deterioration attributed to tumor progression
PD Increase in tumor size $\geq 20\%$ New lesions	Increase in tumor size $\geq 10\%$ and does not meet PR criteria by tumor density New lesions

Response assessment: RECIST *versus* Choi criteria

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New lesions

Objectives

- **To evaluate Choi criteria for early prediction of sunitinib efficacy in patients with metastatic renal cell cancer (mRCC)**
- **To compare the predictive value of Choi criteria and that of RECIST for progression-free (PFS) and overall survival (OS)**

Methods

- 55 mRCC patients treated with sunitinib were included
- Patients underwent routine helical CT scans of the chest and abdomen at baseline and during treatment
- Tumor assessment was determined according to RECIST and Choi criteria
- According to Choi criteria the longest tumor diameter required was ≥ 15 mm; density was determined in Hounsfield Units (HU) on CT scans
- Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method
- Log rank test was used to test the differences between survival curves

Tumor lesions for the efficacy analysis

	n
Eligible lesions for analysis	
RECIST	225
Choi criteria	173

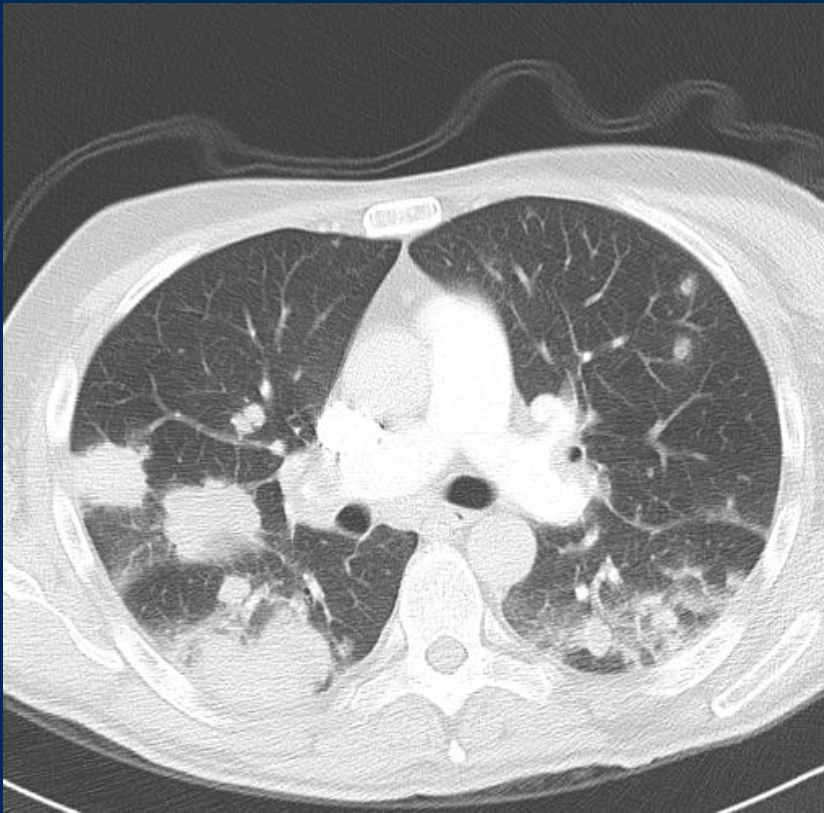
Tumor lesions for the efficacy analysis

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RECIST	225
Choi criteria	173
Exclusion according to both RECIST and Choi criteria	26
Bone metastasis	11
Primary tumor	10
Brain metastasis	5

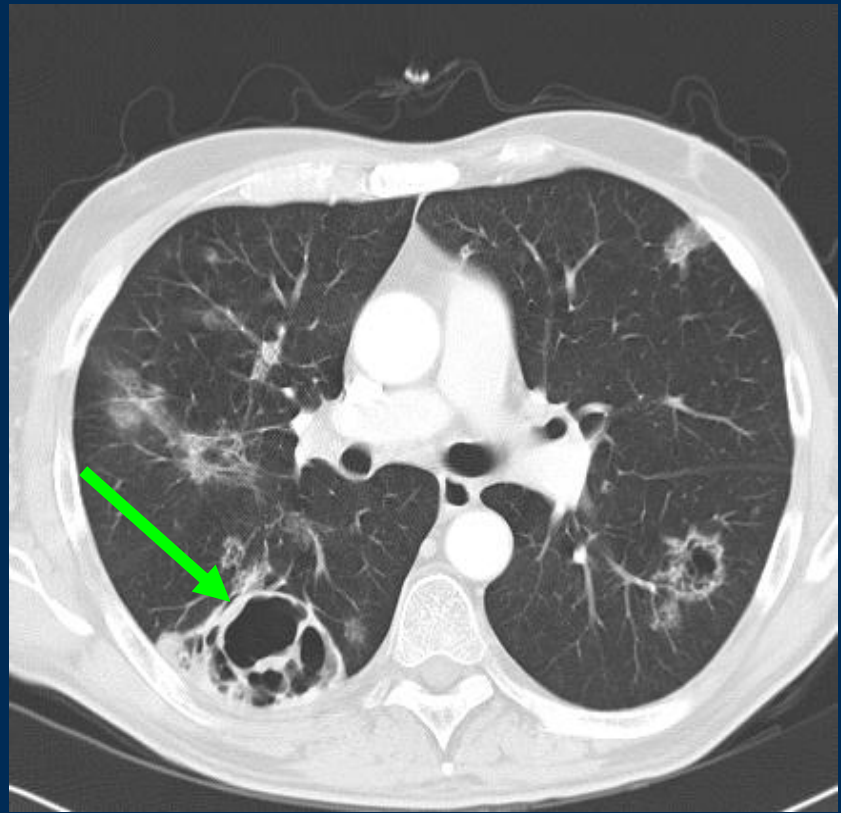
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Eligible lesions for analysis	
RECIST	225
Choi criteria	173
Exclusion according to both RECIST and Choi criteria	26
Bone metastasis	11
Primary tumor	10
Brain metastasis	5
Exclusion according to Choi criteria only	52
Tumor lesion at baseline ≥ 10 mm, < 15 mm	38
Air-containing cavity at evaluation	8
Beam-hardening artifact obscuring helical CT density (e.g. metal-containing parts)	6

Sunitinib can induce air-containing cavitations in lung metastases

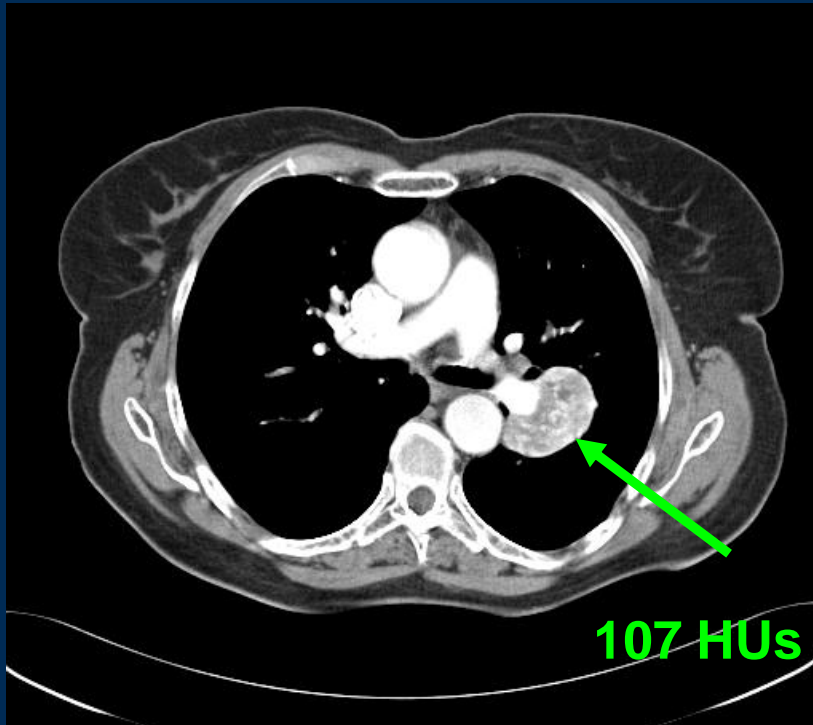


At baseline

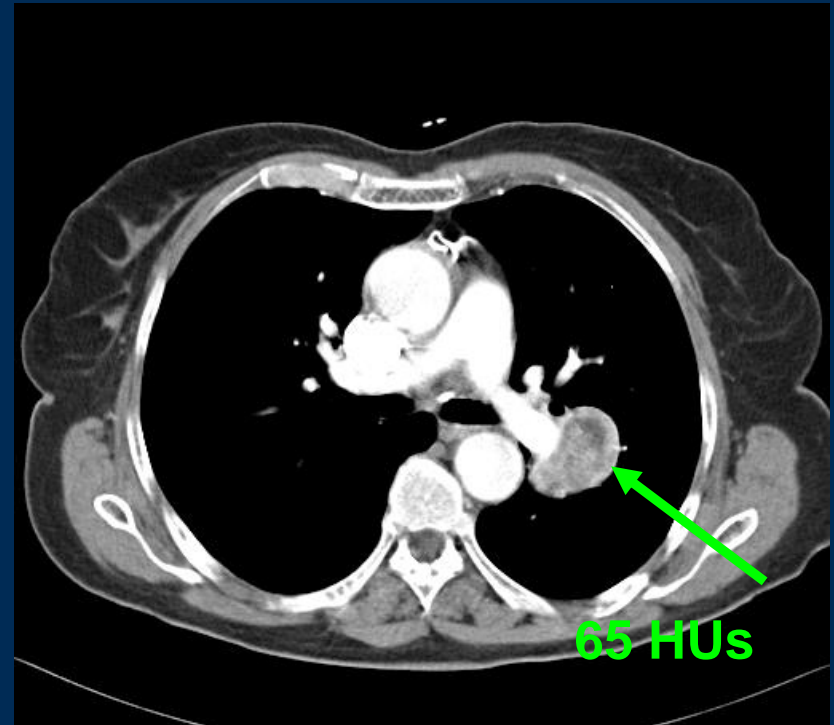


At first evaluation

Sunitinib can induce a decrease in tumor density



At baseline



At first evaluation

Median tumor density decreased from 66 HUs to 47 HUs ($p \leq 0.001$)

Response evaluation

Choi criteria

First evaluation*

n (%)

PR	36 (65)
SD	6 (11)
SD \geq 12 weeks	n.a.
PD	13 (24)

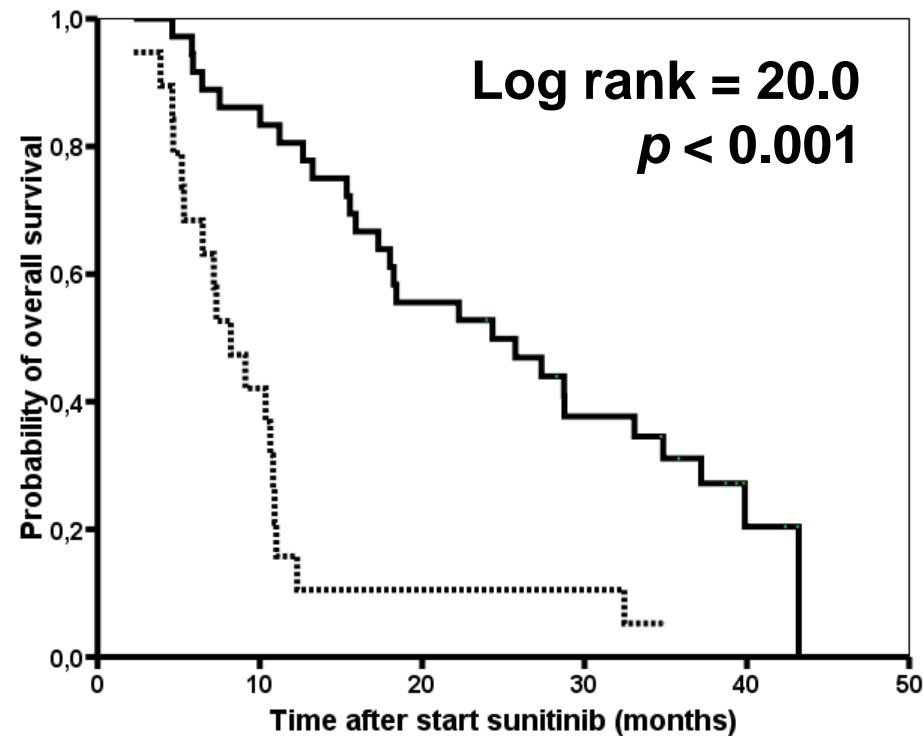
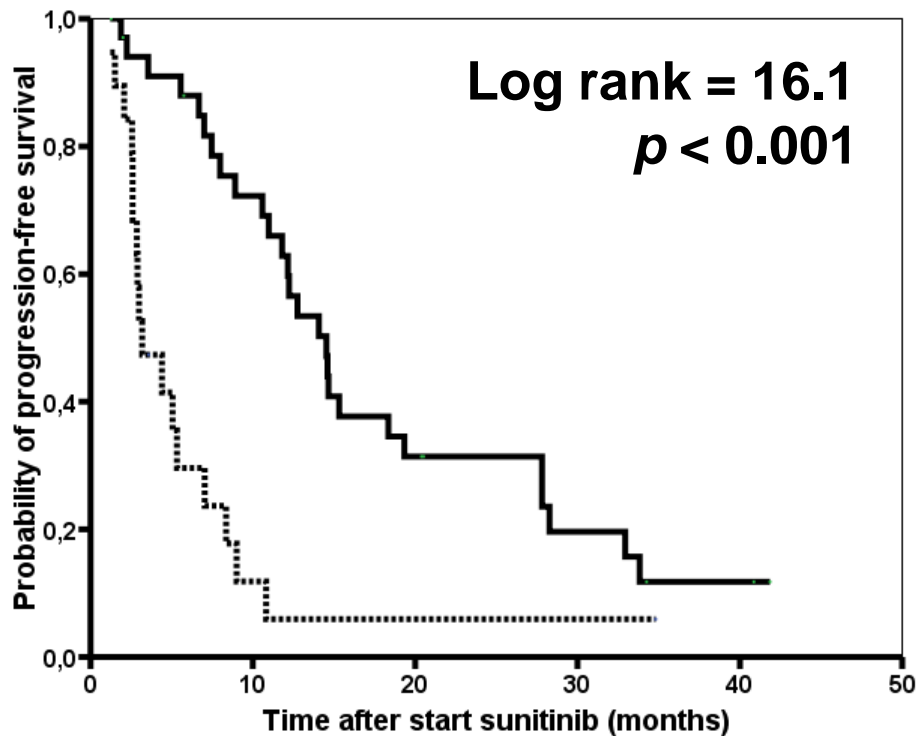
* *First evaluation was done after a median of 2 months*

Response evaluation

	<u>Choi criteria</u>	<u>RECIST</u>	
	First evaluation* n (%)	First evaluation* n (%)	Best response n (%)
PR	36 (65)	7 (13)	17 (31)
SD	6 (11)	38 (69)	28 (51)
SD ≥ 12 weeks	n.a.	n.a.	24 (44)
PD	13 (24)	10 (18)	10 (18)

* First evaluation was done after a median of 2 months

Choi criteria can be used to early predict clinical outcome



— Responder (PR)
.... Non-responder (SD + PD)

Survival analyses

	PFS median (months)	OS median (months)
Choi criteria	LR = 16.1, $p < 0.001$	LR = 20.0, $p < 0.001$
PR (n = 36)	14.5	25.4
SD + PD (n = 19)	3.2	10.4
RECIST at first evaluation	LR = 0.2, $p = 0.685$	LR = 1.7, $p = 0.191$
PR (n = 7)	18.3	27.4
SD + PD (n = 48)	9.0	13.2

LR = log rank

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RECIST clinical benefit	LR = 63.2, $p < 0.001$	LR = 18.8, $p < 0.001$
PR + SD \geq 12 weeks (n = 41)	12.2	22.3
SD < 12 weeks + PD (n = 13)	2.6	7.2

LR = log rank

Conclusions

- **Choi criteria can be easily applied on contrast-enhanced CT scans**
- **Reliability of Choi criteria is limited in patients with:**
 - most lesions ≥ 10 mm and < 15 mm
 - a small number of lesions
 - heterogenous lesions
 - hypodense lesions at baseline
 - differences in i.v. contrast

Conclusions

- **Choi criteria have a significantly better predictive value than RECIST for PFS and OS at first evaluation in patients with PR**
- **In patients with clinical benefit, RECIST has predictive value similar to Choi criteria**
- **Use of Choi criteria in tumors defined as SD or PD will not change the management of sunitinib-treated mRCC patients**

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