Incontri
di aggiornamento
del Dipartimento
Oncologico

mRCC: walking through the first line

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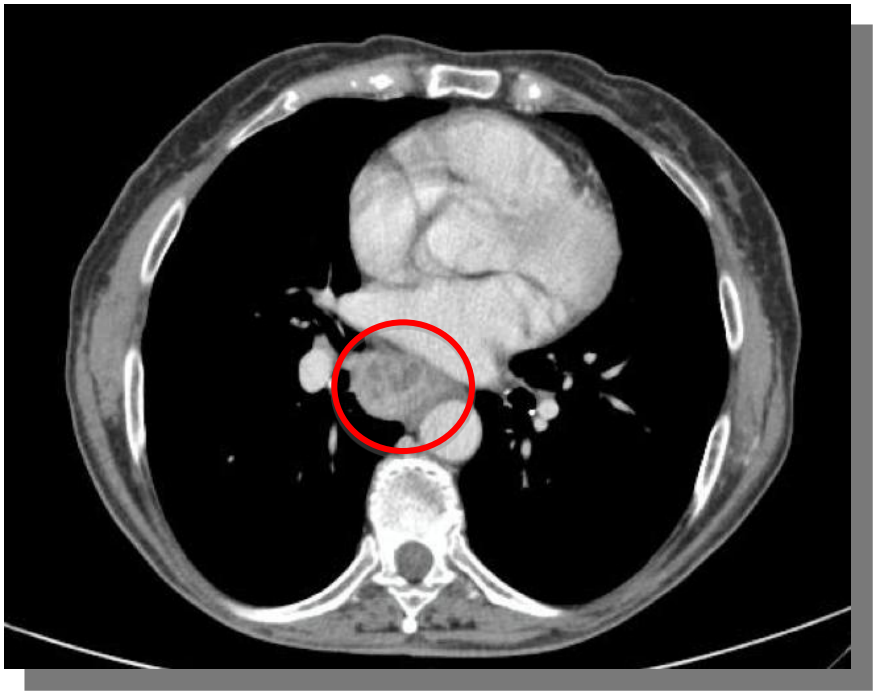
Aiom
Associazione Italiana di Oncologia Medica

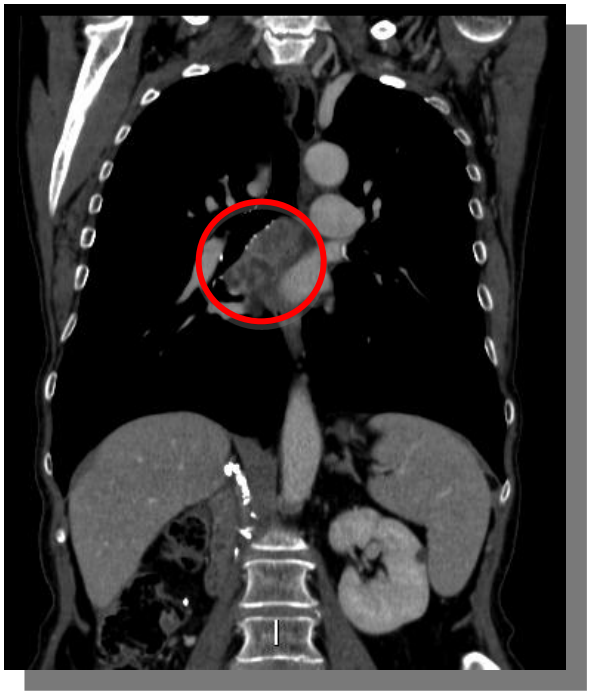
CLINICAL PRESENTATION

- Woman, **67 years old** at diagnosis, ECOG PS 0, no comorbidities

Which treatment in first-line?

- March 2012: on CT-scan appearance of **mediastinal lymph nodes**
- **Biopsy: metastasis of clear cell renal cell carcinoma**



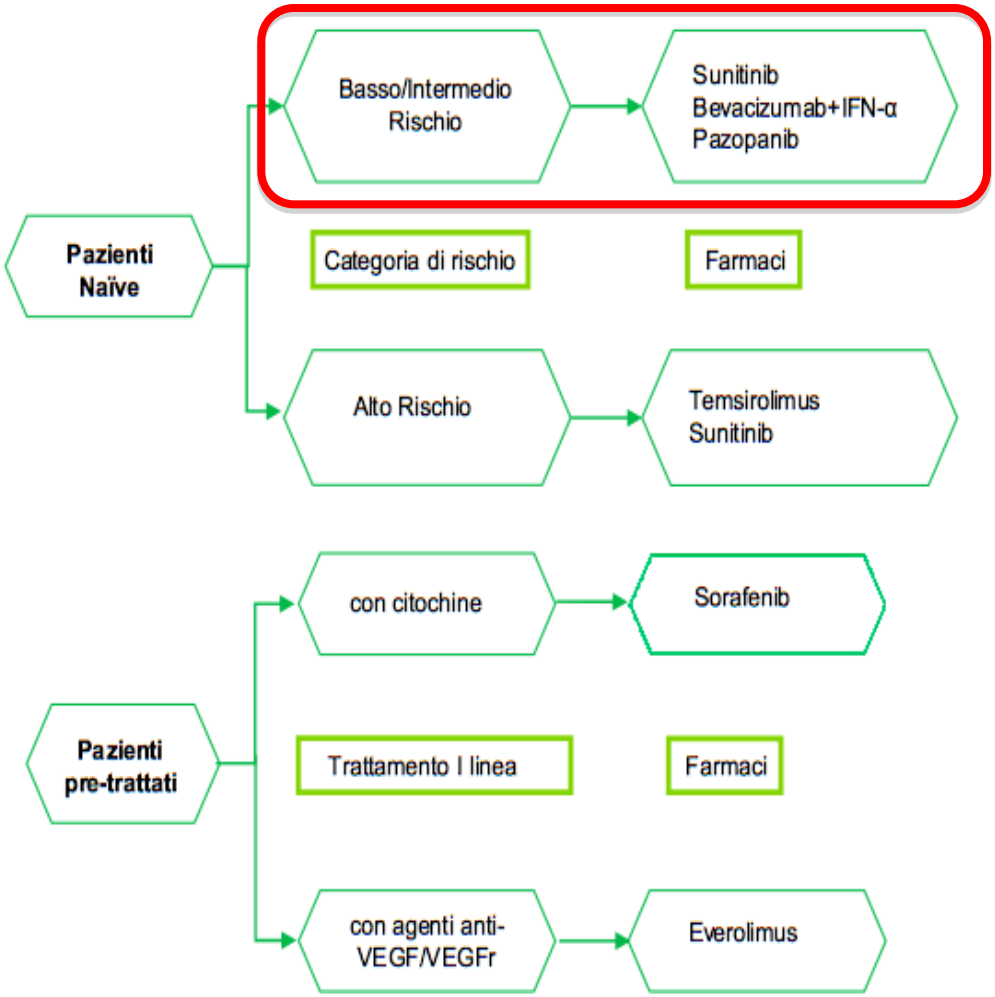


mRCC: AIOM GUIDELINES

Risk Criteria for VGFR-targeted therapy
(Prognostic factors for poor OS)

KPS <80
Diagnosis to therapy <1 year
Anaemia
Hypercalcaemia
Neutrophilia
Elevated LDH

0 factors: Favourable risk
1-2 factors: Intermediate risk
≥3 factors: Poor risk



Heng DYC et al. J Clin Oncol. 2009;27:5794-9.
R.J. Motzer, J Clin Oncol, 20 (1): 289-296, 2002

AIOM guidelines *2014*

HOW TO CHOOSE THE FIRST-LINE TREATMENT IN mRCC?

QUALITY OF LIFE

COMORBIDITIES

TOLERABILITY PROFILE

TOXICITY RISK FACTORS

MSKCC RISK CLASSIFICATION

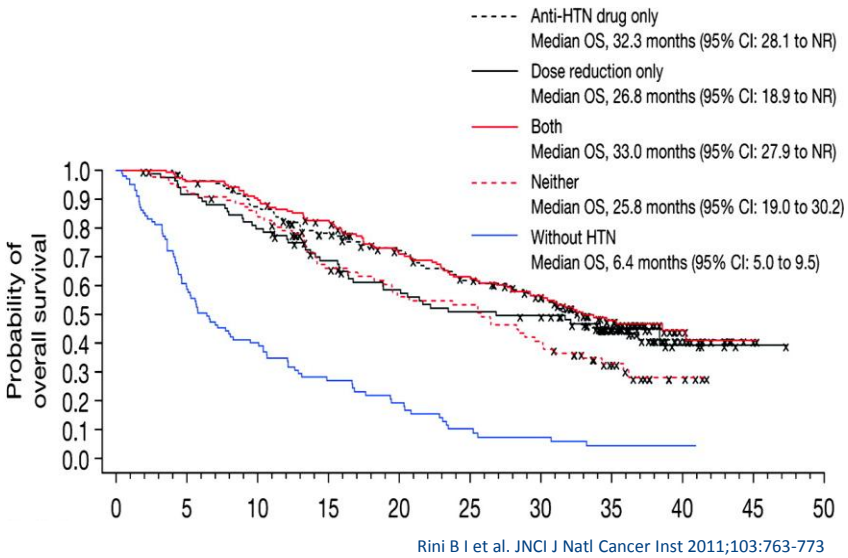
NEED OF TUMOR SHRINKAGE?

QUALITY OF EVIDENCE

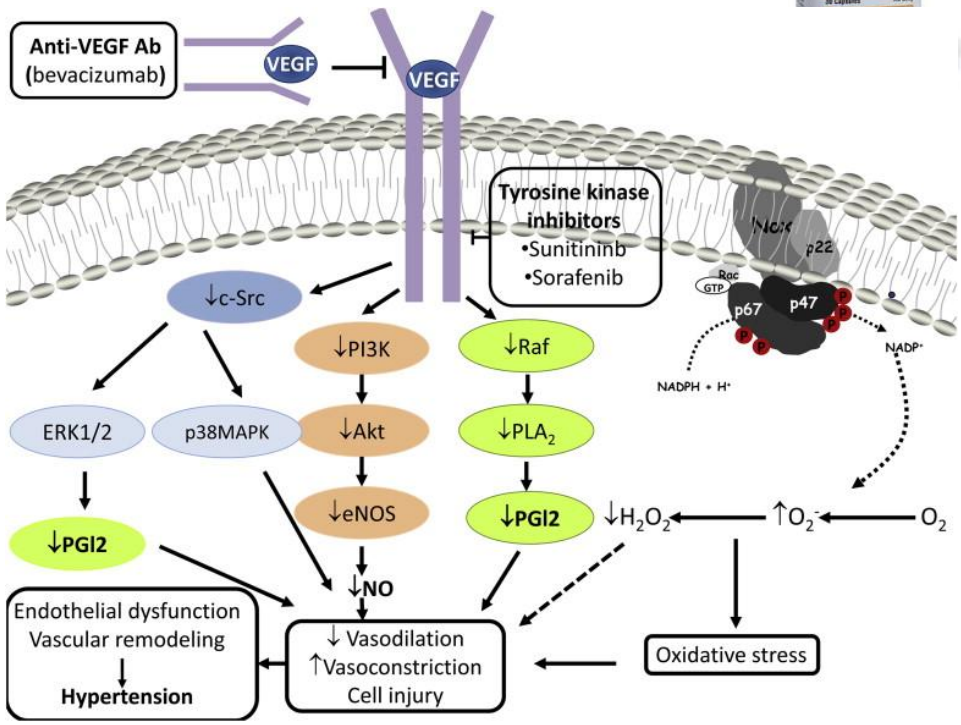
RANDOMIZED CLINICAL TRIALS' RESULTS

First-line treatment: SUNITINIB

Hypertension as a potential biomarker of sunitinib-related efficacy



Rini B I et al. JNCI J Natl Cancer Inst 2011;103:763-773



Cycle 1
50 mg/die
4/6 wks

Cycle 2
50 mg/die
4/6 wks

Cycle 3
50 mg/die
4/6 wks

Cycle 4
50 mg/die
4/6 wks

HYPERTENSION

HAND-FOOT SYNDROME G3

FATIGUE G2

April 2012

First-line treatment: SUNITINIB

Alternative scheduling

- **Retrospective review of 21 pts at CCF on Sutent 4/2 changed to 2/1 schedule due to toxicity** (Najjar et a. abstract #406).

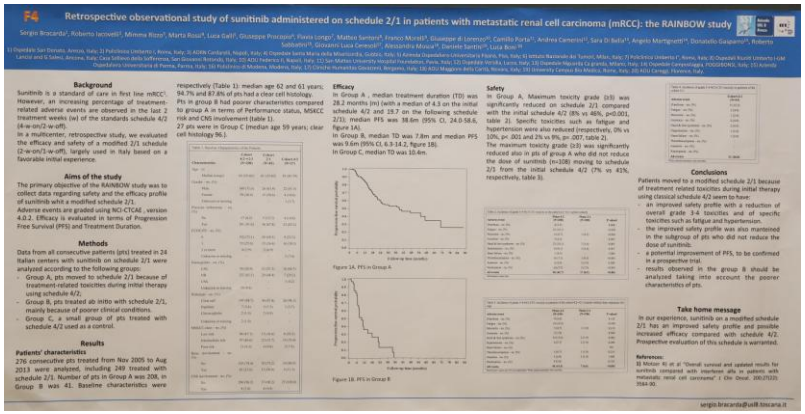
	4/2 Schedule		2/1 Schedule		No. w/ less tox on 2/1[1]	P[2]
	All grade	Grade 3+	All grade	Grade 3+		
Fatigue	11 (53%)	7 (33%)	10 (48%)	3 (14%)	7 (33%)	.04
Diarrhea	7 (34%)	3 (15%)	9 (43%)	1 (5%)	5 (24%)	.75
Hand-foot	7 (34%)	6 (29%)	3 (14%)	-0-	7 (33%)	.04
Thrombocytopenia	4 (20%)	2 (10%)	1 (5%)	-0-	4 (19%)	0.12
Worst grade	**21 (100%)**	**20 (95%)**	**21 (100%)**	**7 (33%)**	**14 (67%)**	**.001**

[1] Refers to any grade change in toxicity
[2] Wilcoxon signed-rank test comparing significance of increased or decreased any grade toxicity on 2/1 vs. 4/2 regimen

- **Median overall treatment duration on the 4/2 schedule was 13.5 months and median overall treatment duration on the 2/1 schedule was 24.4 months.**

Brian I. Rini, ASCO GU 2013

Retrospective Observational Study of Sunitinib administered in a 2/1-2/1 Schedule (2 weeks on-1 week off for an overall cycle length of 6 weeks) in patients with metastatic Renal Cell Carcinoma (mRCC): RAINBOW Study.


Retrospective observational study of sunitinib administered on schedule 2/1 in patients with metastatic renal cell carcinoma (mRCC): the RAINBOW study

Cycle 1 50 mg/die 4/6 wks → **Cycle 2** 50 mg/die 4/6 wks → **Cycle 3** 50 mg/die 4/6 wks → **Cycle 4** 50 mg/die 4/6 wks

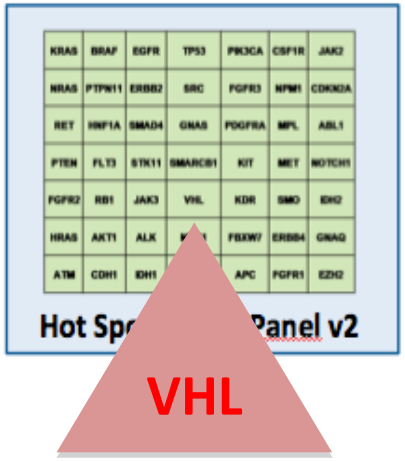
HAND-FOOT SYNDROME G3

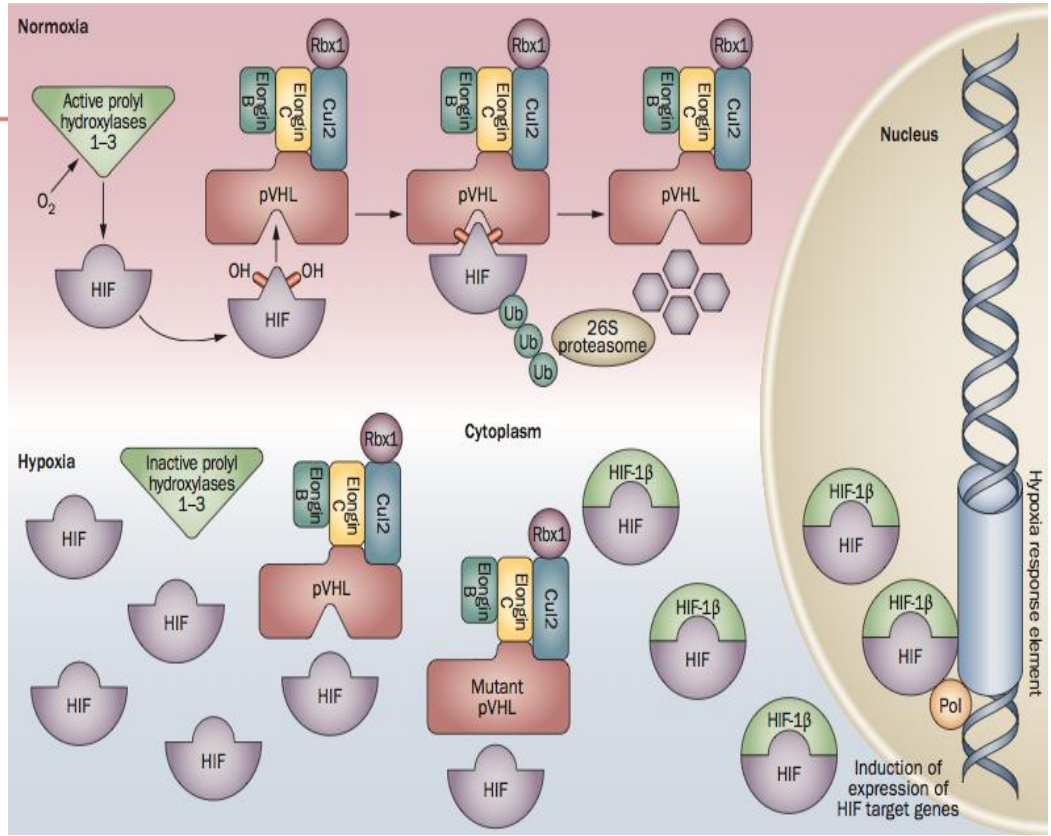
FATIGUE G2

April 2012

COMPLETE REMISSION

Materials and Methods





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4/6 wks

Cycle 2
50 mg/die
4/6 wks

Cycle 3
50 mg/die
4/6 wks

Cycle 4
50 mg/die
4/6 wks

Cycle 5
50 mg/die
2:1/2:1 wks

Cycle 9
50 mg/die
2:1/2:1 wks

RP

RP

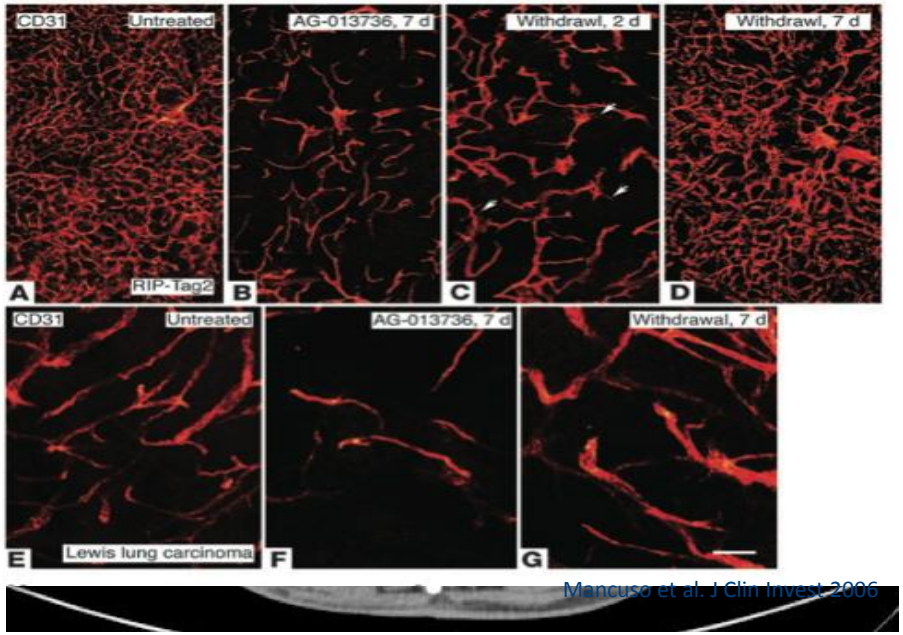
CR

April 2012

July 2013

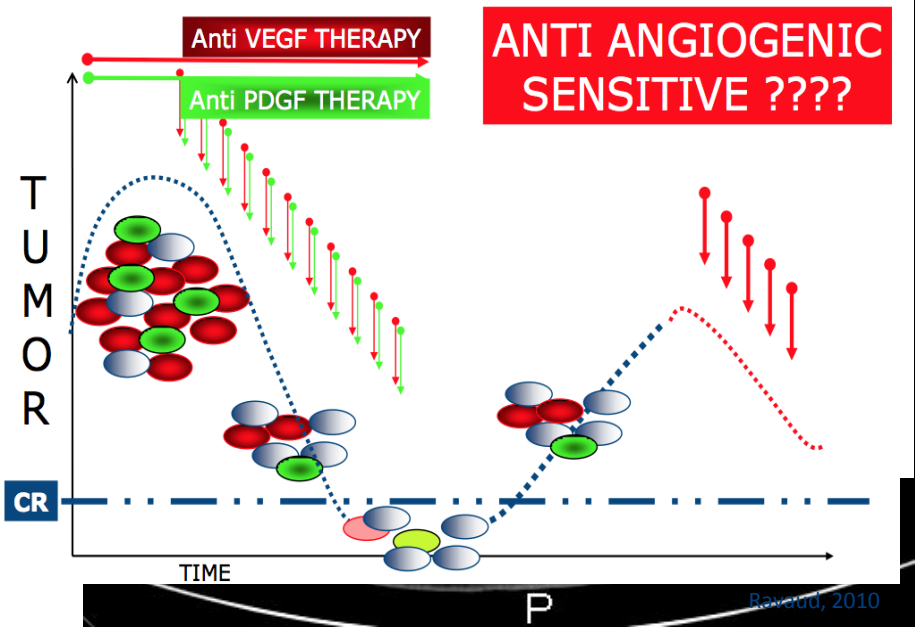
COMPLETE REMISSION

Rapid vascular regrowth in tumors after reversal of VEGF inhibition



Mancuso et al. J Clin Invest 2006

Maintenance after CR: development of VEGF-resistance



Reynaud, 2010

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50 mg/die
4/6 wks

Cycle 2
50 mg/die
4/6 wks

Cycle 3
50 mg/die
4/6 wks

Cycle 4
50 mg/die
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Cycle 5
50 mg/die
2:1/2:1 wks

Cycle 9
50 mg/die
2:1/2:1 wks

RP

RP

CR

April 2012

July 2013

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

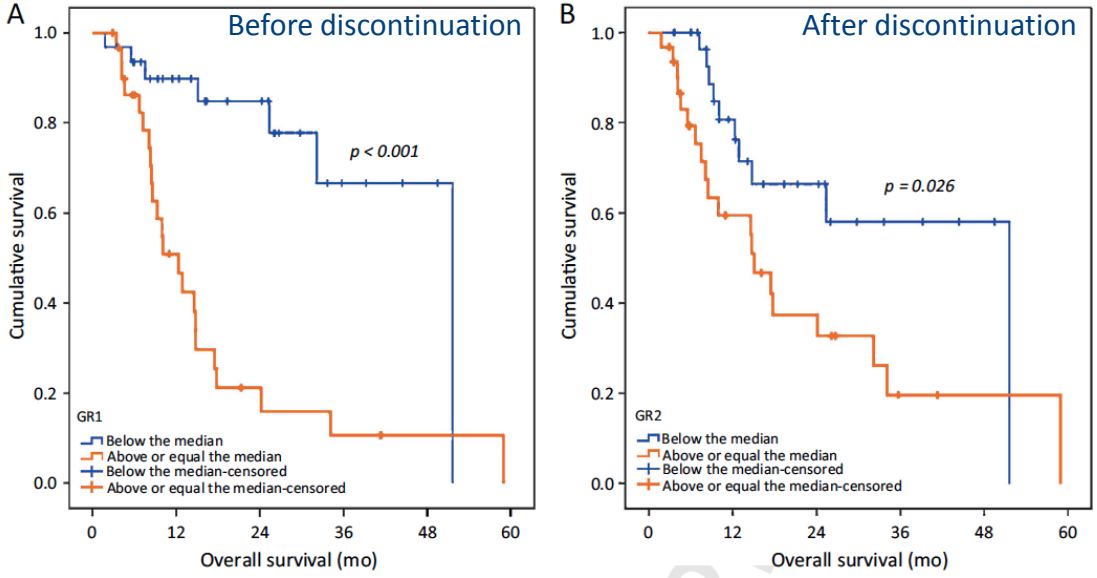
European Association of Urology

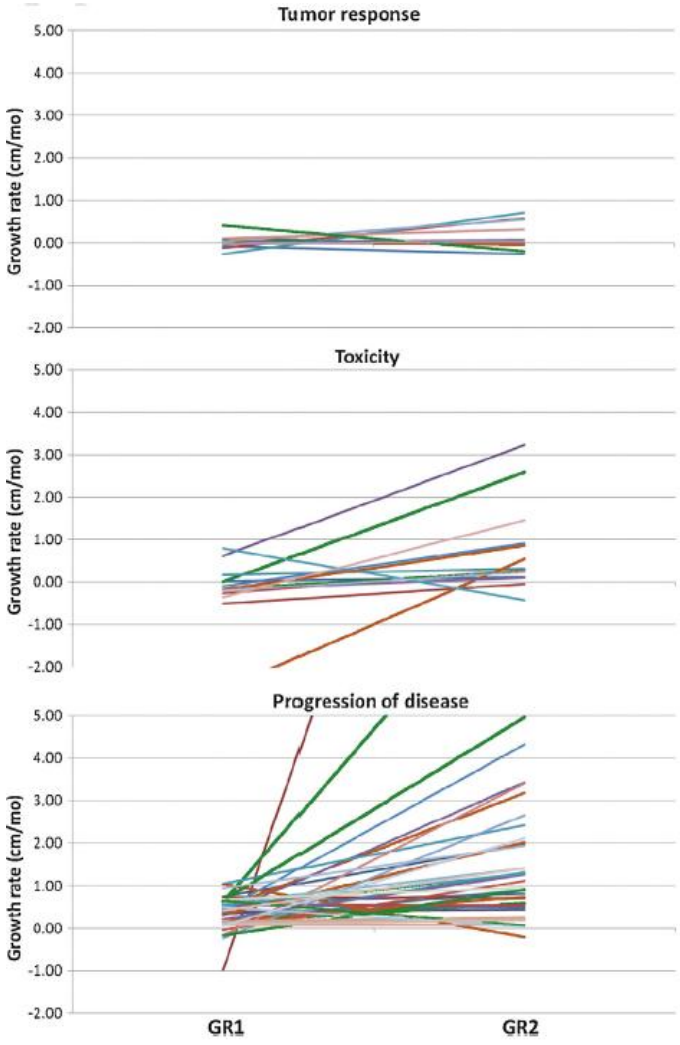
Platinum Priority – Kidney Cancer
Editorial by XXX on pp. x–y of this issue

Evidence and Clinical Relevance of Tumor Flare in Patients Who Discontinue Tyrosine Kinase Inhibitors for Treatment of Metastatic Renal Cell Carcinoma

Roberto Iacovelli [a,b,], Francesco Massari [a,c], Laurence Albiges [a], Yohann Loriot [a], Christophe Massard [a], Karim Fizazi [a], Bernard Escudier [a]*

[a] Medical Oncology Department, Institut Gustave Roussy, Villejuif, France; [b] Department of Radiology, Oncology and Human Pathology, Sapienza University of Rome, Rome, Italy; [c] Department of Medical Oncology, University of Verona, Verona, Italy

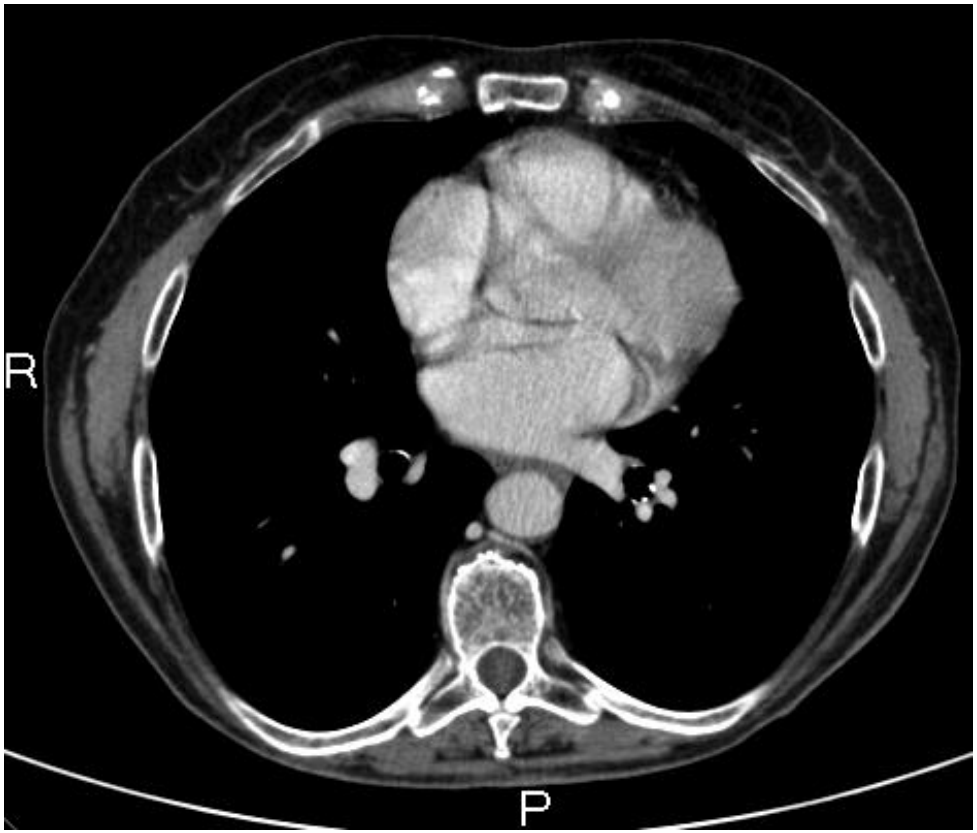




TKI discontinuation results in acceleration of tumor GR and induces TF, which can negatively affect the prognosis of mRCC patients.

Iacovelli R, Massari F et al., Eur. Urol. 2014, article in press

AFTER ONE YEAR…



Cycle 9
50 mg/die
2:1/2:1 wks

FOLLOW UP

CR

CR

July 2013

November 2014

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