Corso interattivo

Therapy Management

nel carcinoma renale

Roma – 19 MAGGIO 2009

3° Caso clinico

Effetti Gastroenterici

Maria Sofia Rosati

Effetti gastroenterici

	Frequenza*	Reazioni avverse	Tutti i gradi n(%)	Grado 3 n(%)	Grado 4 n(%)
Effetti gastrointestinali di sunitinib in mRCC	Molto comune	Diarrea	83 (49,1%)	5 (3,0%)	0 (0%)
	Molto comune	Nausea	84 (49,7%)	2 (1,2%)	0 (0%)
	Molto comune	Stomatite	70 (41,4%)	6 (3,6%)	0 (0%)
	Molto comune	Dispepsia	69 (40,8%)	1 (0,6%)	0 (0%)
	Molto comune	Vomito	52 (30,8%)	2 (1,2%)	0 (0%)
	Molto comune	Stipsi	34 (20,1%)	0 (0,0%)	0 (0%)
	Molto comune	Glossodinia	25 (14,8%)	0 (0,0%)	0 (0,0%)
	Molto comune	Dolore addominale*	17 (10,1%)	2 (1,2%)	0 (0%)
	Comune	Flatulenza	16 (9,5%)	0 (0%)	0 (0%)
	Comune	Distensione addominale	9 (5,3%)	0 (0%)	0 (0%)
	Comune	Secchezza della bocca	9 (5,3%)	0 (0%)	0 (0%)

*molto comune (> 1/10), comune (> 1/100 a < 1/10), non comune (> 1/1.000 a < 1/100), raro (> 1/10.000 a 1/1.000), molto raro (< 1/10.000).

Quadro clinico-anamnestico alla diagnosi

Luglio 2008

- R.E., 65 aa, uomo
- Pensionato, ex elettricista
- Fumatore
- Coniugato, 2 figli

Anamnesi Patologica e Comorbidità:

- IDDM in trattamento
- Colelitiasi (assume ac. ursodesossicolico ciclicamente)

La diagnosi di mRCC

Anamesi Patologica Oncologica:

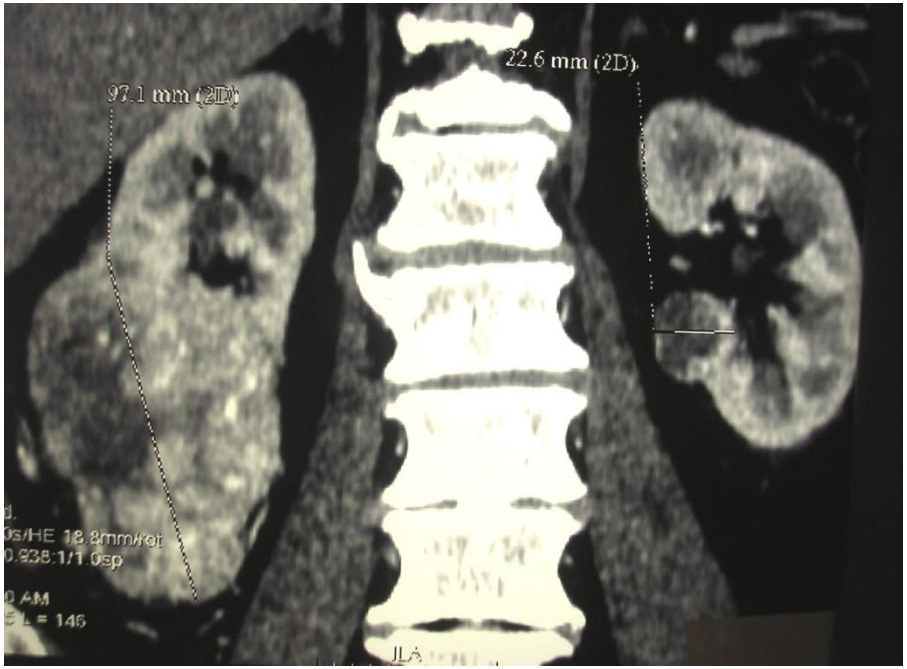
- Giugno 2008: Linfedema severo dell'arto superiore sx, intensamente dolente associato ad ipofunzionalità dello stesso.
- Si reca in PS su consiglio del proprio MC dove viene eseguito un esame etg color-doppler aa sup sx che evidenzia la presenza di un grossolano pacchetto linfonodale sovraclaveare e contestuale TVP giugulare-succlavia
- Si ricovera ed esegue TC TB

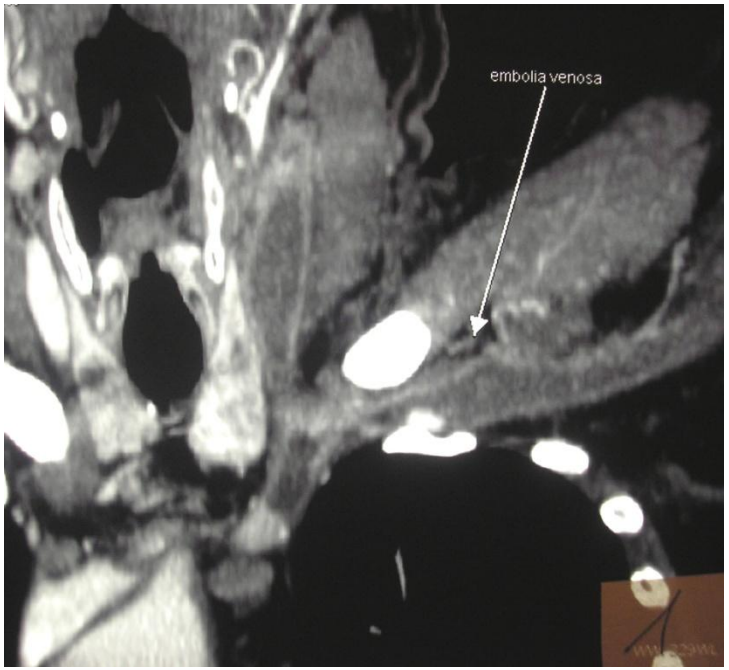
TC basale

TC TB: “Estesa embolia della vv giugulare, succlavia e confluente del TV sx con adenopatie sovraclaveari contigue; EP subsegmentaria arteriosa e venosa del segmento posterobasale del LID; grossolane adenopatie ilo-mediastiniche e lesioni secondarie polmonari in pz con massa discariocinetica renale dx e piccola lesione analoga renale sx. Colecisti normodistesa con minimo ispessimento delle pareti infundibolari esente da calcoli calcifici. Coledoco lievemente ectasico”

STADIO IV

TC Basale





Domanda 1

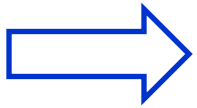
DOMANDA 1: Come procedere?

a. Accertamento bioptico
b. Nessun accertamento
c. Ulteriore approfondimento strumentale

Domanda 1

DOMANDA 1: Come procedere?

“Biopsia escissionale del linfonodo sovraclaveare sx”

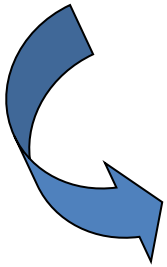


Metastasi linfonodale; origine compatibile con carcinoma renale a cellule chiare

Ulteriori accertamenti strumentali

Luglio 2008, SCINTIGRAFIA OSSEA TB: "Negativa"

Luglio 2008, ECOGRAFIA TIROIDEA: tiroide nei limiti per dimensioni a struttura finemente disomogenea



Luglio 2008: TSH 0,24 uU/ml, FT3 3 pg/ml, FT4 9.8 pg/ml, AbTg 60 U/l

Luglio 2008, ECOCARDIOGRAMMA: nei limiti, FE 4Ch: 63%

Ulteriori accertamenti clinico-strumentali

- KPD 80%
- Livelli di Hb: 12.4 g/dL
- LDH (297 mU/mL)
- Calcemia: 9.63 mg/dL
- Bilirubina tot 0.89 mg/dL (diretta 0.17 mg/dL)
- Glicemia 109 mg/dL

Domanda 2

DOMANDA 2 : Quale terapia proporre?

a. Bevacizumab + IFN
b. Sunitinib
c. Chirurgia
d. Sorafenib
e. Temsirolimus
f. HD IL-2
g. IFN

La scelta terapeutica

La nostra decisione:

Il 28.07.2008 il paziente inizia terapia con

Sunitinib secondo schedula classica

50 mg/die per 4 settimane ogni 6 settimane.

Tossicità

Primo ciclo ben tollerato, solo astenia lieve, tono dell'umore depresso, caratteristica colorazione giallastra della cute. Continua LMWH per TVP. Riduce insulina.

22.9.2008, 3 sett II ciclo riferisce comparsa di nausea intensa non associata a vomito, iporessia e stipsi; dolori diffusi flu-like (K: 4 mEq/L, Na: 146 mEq/L, Bilirubina tot 1.32 mg/dL, Ac. urico 9.2 mg/dL)

7.10.2008 EGDS: lieve iperemia della mucosa gastrica

Prosegue lansoprazolo 30 mg/die, acido ursodesossicolico 250 mg/die e sucralfato 1 gr os/die con modesta remissione dei sintomi gastrici.

Domanda 3

DOMANDA 3 : Come proseguire?

a. Sunitinib 50 mg/die 4q6w
b. Sunitinib 37.5 mg/die 4q6w
c. Sunitinib 25 mg/die 4q6w
d. Sospendere temporaneamente
e. Sospendere e cambiare trattamento

Considerazioni

British Journal of Cancer (2008) 99, 259 – 265

www.bjcancer.com

Predictive factors for severe toxicity of sunitinib in unselected patients with advanced renal cell cancer

AAM van der Veldt[1], E Boven[1], HH Helgason[2], M van Wouwe[1], J Berkhof[3], G de Gast[2], H Mallo[2], CN Tillier[1], AJM van den Eertwegh[1] and JBAG Haanen[*,2]

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Sunitinib has been registered for the treatment of advanced renal cell cancer (RCC). As patient inclusion was highly selective in previous studies, experience with sunitinib in general oncological practice remains to be reported. We determined the efficacy and safety of sunitinib in patients with advanced RCC included in an expanded access programme. ECOG performance status > 1, histology other than clear cell and presence of brain metastases were no exclusion criteria. Eighty-two patients were treated: 23% reached a partial response, 50% had stable disease, 20% progressed and six patients were not evaluable. Median progression-free survival (PFS) was 9 months and median overall survival (OS) was 15 months. Importantly, 47 patients (57%) needed a dose reduction, 35 (43%) because of treatment-related adverse events, 10 (12%) because of continuous dosing, and two because of both. Stomatitis, fatigue, hand–foot syndrome and a combination of grade 1–2 adverse events were the most frequent reasons for dose reduction. In 40 patients (49%), there was severe toxicity, defined as dose reduction or permanent discontinuation, which was highly correlated with low body surface area, high age and female gender. On the basis of age and gender, a model was developed that could predict the probability of severe toxicity.

British Journal of Cancer (2008) **99,** 259–265. doi:10.1038/sjbjc.6604456 www.bjcancer.com
Published online 1 July 2008

Keywords: renal cell cancer; sunitinib; toxicity; dose reduction; non-clear cell histology

maschio, età: 65, BSA: 1.54

La scelta terapeutica

La nostra decisione:

Si decide di ridurre la dose di Sunitinib a

37,5 mg/die per 4 settimane ogni 6 settimane.

Tossicità

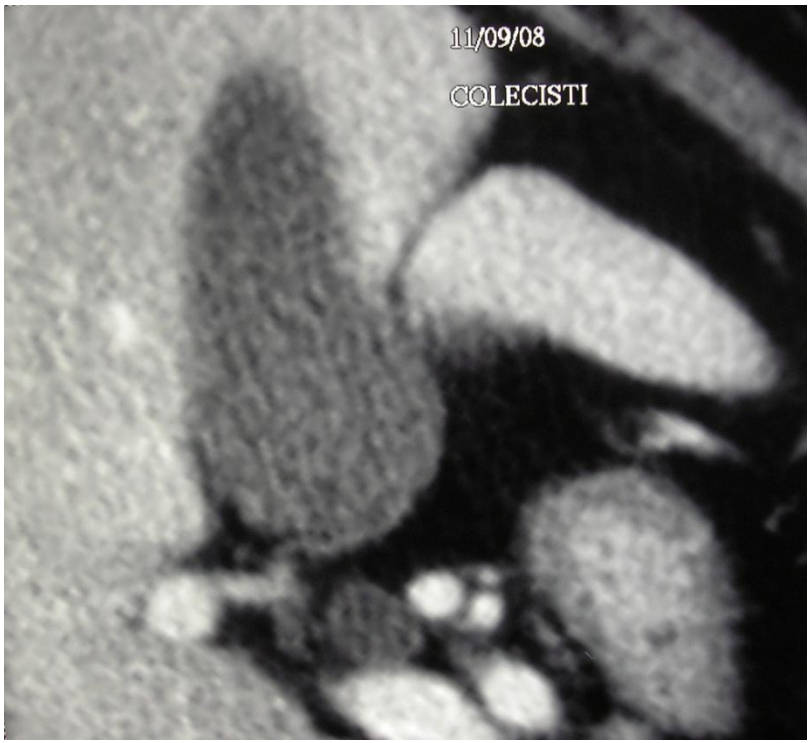
- Il paziente riprende Sunitinib 37.5 mg/die (sospeso ac. ursodesossicolico poiché bilirubina nei limiti)
- Il 2 gg del III ciclo presenta dolore addominale intenso associato a vomito. All'EO idrope della colecisti (punto cistico e Murphy +), l' addome intensamente dolente e dolorabile; cute e sclere intensamente itteriche. Iperpiressia: 38.8°C

Bilirubina tot 8.5 mg/dL (dir. 4,56)
Amilasi 208 U/L, Lipasi 345 U/L
LDH 547 mU/ml
FA 2140 mU/ml
PA nei limiti
Azotemia 109 mg/dl
Creatinina 2.80 mg/dl

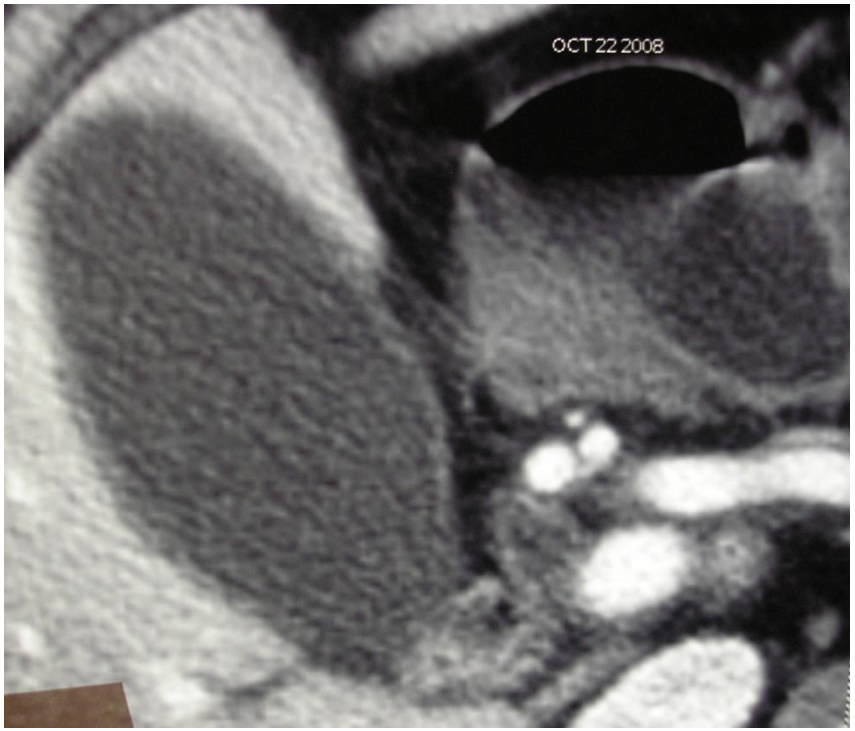
Accertamenti strumentali

"TC TB: idrope della colecisti con netto ispessimento delle pareti infundibolari e del cistico in assenza di calcoli calcifici. Coledoco ectasico sino alla papilla dove si rileva ispessimento delle pareti della via biliare principale. Reperti addominali invariati."

PRIMA



DOPO



Gestione del paziente

- Ricoverato presso il Reparto di medicina intraprende terapia di supporto idro-elettrolitico, terapia antalgica e prosegue acido ursodesossicolico e terapia antibiotica

- Remissione dei sintomi 10 gg successivi.
- Alla dimissione: indici di funzionalità epatica ai limiti superiori, peggioramento del PS, dispnea moderata e tosse stizzoza non remittente con codeina

Domanda 4

DOMANDA 4: Come proseguire?

a. Proseguire Sunitinib

b. Cambiare linea

c. BSC

La scelta terapeutica

La nostra decisione:

BSC

Conclusioni

•Il paziente ha sviluppato versamento pleurico, eseguito toracentesi e talcaggio pleurico.

• E' deceduto il 27/12/2008

Osservazioni

- Se la storia clinica del pz fosse iniziata a Dicembre 2008, la nostra scelta terapeutica sarebbe cambiata?

- Pochi studi sul sunitinib riportano, tra gli effetti collaterali, colecistiti o altre patologie acute a carico delle vie biliari: sarebbero opportuni altri studi? In relazione all'aumento della bilirubina e degli acidi urici è giustificato un uso profilattico dell'acido ursodesossicolico?

- Il paziente diabetico necessita di una maggiore attenzione nell'approccio con sutent?

Osservazioni

Acalculous Cholecystitis in a Patient with Metastatic Renal Cell Carcinoma Treated with Sunitinib

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Clinical Genitourinary Cancer,
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Abstract

A 62-year-old woman was treated with sunitinib as a second-line therapy for metastatic clear-cell renal carcinoma. She was given oral sunitinib 50 mg once daily, 4 weeks on followed by 2 week off. During the fourth week of her first cycle, the patient was admitted to our hospital because of an acute-onset, right upper quadrant pain associated with nausea and vomiting. She was diagnosed with acute acalculous cholecystitis, which was treated with broad-spectrum antibiotics, and sunitinib therapy was discontinued. A follow-up computed tomography scan of the abdomen revealed a complete resolution of gallbladder changes. Our patient did not have major risk factors for developing an acalculous cholecystitis except for a relative immunosuppressed state secondary to her advanced renal cancer. The Naranjo Adverse Drug Reaction Probability Scale score for this event was 5, indicating a probable association of the event with sunitinib. Because the use of sunitinib is expanding in clinical practice, we want to alert the oncology community about this uncommon and life-threatening complication in patients receiving sunitinib or another agent with antiangiogenic activity.

Case Report

A 62-year-old woman was treated with sunitinib as a second-line therapy

Osservazioni

Annals of Oncology Advance Access published March 6, 2008

letter to the editor

Annals of Oncology

Remission of diabetes while on sunitinib treatment for renal cell carcinoma

introduction

Sunitinib is an oral inhibitor of tyrosine kinases, including vascular endothelial growth factor receptor (VEGFR) and platelet-derived growth factor receptor (PDGFR), and has been associated with higher response rates and longer progression-free survival in patients with metastatic renal cell

with 28 680 U/l (<9.5 U/l). Intensive multiple-dose insulin therapy using a basal-bolus approach was started (42 IU daily). Vaccinations were stopped because of disease progression in November 2005 and sunitinib treatment was started in January 2006 (37.5 mg daily). Gradually, the insulin dose could be tapered off until September 2006 (Figure 1), from that time point on the patient was euglycemic without insulin. There was a slight increase in weight during these 8 months (74 to 74.9 kg). Initially, the response to sunitinib treatment was stable disease (according to Response Evaluation Criteria in Solid Tumors criteria), but in February 2007 the computed tomography scan showed progressive disease and the treatment with sunitinib was stopped.

The patient's glycemic control including postprandial

A. Templeton[1]*, M. Brändle[2], T. Cerny[1] & S. Gillessen[1]

Ringraziamenti Speciali

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