



Challenges From Treatment and From Disease

Rare Complications of Systemic mRCC Treatment

**Sergio Bracarda MD
U.O.C. Oncologia Medica
Dipartimento di Oncologia USL-8
Istituto Toscano Tumori (ITT)
Ospedale San Donato,
Arezzo, Italy**

Rare Complications of Systemic mRCC Treatment

Which Real Issue for this Talk ?

Not simply «Rare Complications», such as:

- a Terrible (..and never previously seen) Blue Painting Area in the Fifth Finger Nail of the Left Hand under treatment with «TRASHITINIB» ... -

The Journal of Terrible Things. 2013; 1:1-5

But surely ...

RARE ***and RELEVANT*** ***Complications*** of Systemic mRCC Treatment

Rare Complications of Systemic mRCC Treatment

- ✓ **Which Cut-Off to define «Rare» these Complications?**

< 2-3% of Treatment Related Adverse Events

- ✓ **And which selection ?**

Only NCI-CTC Grade 3-4 (*Rare but Relevant ..*)

Rare Complications of Systemic mRCC Treatment

Sorafenib:	Grade 3-4	Clinically Relevant ?
✓ <i>Fatigue</i>	3%	<i>not</i>
✓ <i>Bleeding</i>	3%	<i>yes</i>

Sunitinib:	Grade 3-4	Clinically Relevant ?
✓ <i>Mucositis</i>	2%	<i>yes</i>
✓ <i>HyperCreatininemia</i>	1%	<i>yes</i>
✓ <i>< LVEF</i>	3%	<i>yes</i>

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Pazopanib:

Grade 3-4

Clinically Relevant ?

✓ *HyperBilirubinemia* 3%

yes *

**especially in pts with with increased ALT (12%) and AST (7%)*

Axitinib:

Grade 3-4

Clinically Relevant ?

✓ *Hb elevation .. 10%* (any grade)

not (Sorafenib. 1%)

✓ *Arthralgia*

1%

not

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Temsirolimus:	Grade 3-4	Clinically Relevant ?
✓ <i>HyperTrygliceridemia</i>	3% (Ev < 1%)	so and so
✓ <i>Mucositis</i>	1%	yes
Everolimus:	Grade 3-4	Clinically Relevant ?
✓ <i>HyperCholesterolemia</i>	4% (Tems 1%)	so and so
✓ <i>Mucositis</i>	1%	yes

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Bev. + IFN:	Grade 3-4	Clinically Relevant ?
✓ <i>Proteinuria</i>	7% (<i>rare overall, not for Bev..</i>)	yes
✓ <i>ATE / VTE</i>	2% (<i>Arterial / Venous</i>)	yes
✓ <i>GI Perforation</i>	1.1%	yes

How to Manage these Rare (but Gr. 3-4) Complications ?

- ✓ *Mucositis* (Sun, Ev, Tem) *Topical and Lidocaine Solutions, Transient suspension*
- ✓ *HyperCreatininemia* (Sun) *Dose reduction
Transient suspension
Anti-Hypertensive Drug Optimization*
- ✓ *Proteinuria* (Bev.) *Discontinue for grade 4.
restart at recovery*
- ✓ *Hb Elevation* (Axitinib) *Observation; eventual phlebotomy*
Di Lorenzo 2011; Seruga 2009; Cohen 2012

How to Manage these Rare (but Gr. 3-4) Complications ?

- ✓ *ATE / VTE (Bev.)* *Proper Drug selection in high-risk Pts for vascular events. Drug prophylaxis?*
- ✓ *HyperBilirubinemia (Pazopanib,* *Strict monitoring of Liver enzymes*
Immediate drug removal
- ✓ *HyperTrygliceridemia (Tems.)* *No dose reductions. Start Diet and Fibrates if >1000mg/dl.*
- ✓ *HyperCholesterolemia (Everol.)* *No dose reductions. LifeStyle modifications Statins use ?*

Di Lorenzo 2011; Seruga 2009; Cohen 2012

Ranking the Rare but Relevant Events ! :

-- The Hit Parade --

1. ATE / VTE

Really relevant, but almost exclusively related to Bevacizumab

2. HyperBilirubinemia

Really relevant; because expression of a serious impairment of liver function

3) Mucositis

Less relevant and not so «Rare». However, if under-evaluated, possible cause of:

- Reduced Drug-Compliance (and less activity) &*
- General Well Being deterioration (less eating & drinking)*

Di Lorenzo 2011; Seruga 2009; Cohen 2012

Rare but Relevant (RbR) Complications: Conclusions

Dear Doctor, please remember:

- ✓ *Every Patient is different from the Others:*
- ✓ *Looking for the «right Drug for the right Patient», **to reach the Maximum with any Drug***

Consider Also:

*The possibility of RbR (Rare but Relevant) Toxicities ,
especially in the case of Relevant Comorbidities (e.g. vascular, liver diseases) !!*

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THANKS !
DANKE !
MERCI !
GRAZIE !

