Challenges From Treatment and From Disease

Rare Complications of Systemic mRCC Treatment

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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» … -


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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Grade 3-4</th>
<th>Clinically Relevant?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sorafenib:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>3%</td>
<td>not</td>
</tr>
<tr>
<td>Bleeding</td>
<td>3%</td>
<td>yes</td>
</tr>
<tr>
<td>Sunitinib:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucositis</td>
<td>2%</td>
<td>yes</td>
</tr>
<tr>
<td>HyperCreatininemia</td>
<td>1%</td>
<td>yes</td>
</tr>
<tr>
<td>&lt; LVEF</td>
<td>3%</td>
<td>yes</td>
</tr>
</tbody>
</table>

Eighth European International Kidney Cancer Symposium  
Budapest, 03-04May 2013
# Rare Complications of Systemic mRCC Treatment

**Pazopanib:** Grade 3-4 Clinically Relevant?

<table>
<thead>
<tr>
<th>Complication</th>
<th>Grade</th>
<th>Relevant</th>
</tr>
</thead>
<tbody>
<tr>
<td>HyperBilirubinemia</td>
<td>3%</td>
<td>yes *</td>
</tr>
</tbody>
</table>

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

**Axitinib:** Grade 3-4 Clinically Relevant?

<table>
<thead>
<tr>
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<th>Grade</th>
<th>Relevant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb elevation</td>
<td>10%</td>
<td><strong>not</strong> (Sorafenib, 1%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>1%</td>
<td><strong>not</strong></td>
</tr>
</tbody>
</table>
## Rare Complications of Systemic mRCC Treatment

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<th>Medication</th>
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<th>Clinically Relevant ?</th>
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</thead>
<tbody>
<tr>
<td><strong>Temsirolimus:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HyperTrygliceridemia</td>
<td>3% (Ev &lt; 1%)</td>
<td>so and so</td>
</tr>
<tr>
<td>Mucositis</td>
<td>1%</td>
<td>yes</td>
</tr>
<tr>
<td><strong>Everolimus:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HyperCholesterolemia</td>
<td>4% (Tems 1%)</td>
<td>so and so</td>
</tr>
<tr>
<td>Mucositis</td>
<td>1%</td>
<td>yes</td>
</tr>
</tbody>
</table>
### Rare Complications of Systemic mRCC Treatment

<table>
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<th>Bev. + IFN:</th>
<th>Grade 3-4</th>
<th>Clinically Relevant?</th>
</tr>
</thead>
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<tr>
<td>Proteinuria</td>
<td>7% (rare overall, not for Bev.)</td>
<td>yes</td>
</tr>
<tr>
<td>ATE / VTE</td>
<td>2% (Artherial / Venous)</td>
<td>yes</td>
</tr>
<tr>
<td>GI Perforation</td>
<td>1.1%</td>
<td>yes</td>
</tr>
</tbody>
</table>
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.

- HyperCholesterololemia (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 !