METASTATIC RENAL CANCER

CLINICAL CASE PRESENTATION

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DISCLOSURE

Honoraria for advisory board: Bristol-Myers Squibb, Pfizer
Honoraria for speaking: Astellas
Honoraria for congress and travel support: Bristol-Myers Squibb
CLINICAL CASE

Social history

• 48 years old man
• Active smoker 50 pack-years, regular alcohol consumption (about 1 L of beer per day)
• Tunnel worker

Past medical history

• Treated hypertension (G2)
• No others relevant past medical or surgical history

No family history of cancer
Clinical presentation

- 1-month history of microscopic haematuria and 3-month history of G1 right flank pain
- PS ECOG 0 - Karnofsky performance status (KPS) 100%
- Normal clinical examination, no palpable abdominal mass

Laboratory examinations

- Haemoglobin 100 g/L; normal serum creatinine, lactate dehydrogenase, C-reactive protein, serum-corrected calcium, leukocyte and platelet counts

Abdominal ultrasonography (performed by the urologist)

- Right renal mass with invasion of the pelvicalyceal system

ECOG, Eastern Cooperative Oncology Group; PS, performance status
STAGING

Contrast-enhanced (CT) scan of chest, abdominal and pelvis:

• **Right renal mass** 7.6x7.7 cm with invasion of pelvicalyceal system (suspected renal cell cancer)
• **Suspected** retroperitoneal lymph node metastases
• **Multiple** small lung metastases

CT, computed tomography
## RISK ASSESSMENT

<table>
<thead>
<tr>
<th>Variables</th>
<th>IMDC</th>
<th>MSKCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin &lt; LLN</td>
<td>X 100 g/L</td>
<td>X</td>
</tr>
<tr>
<td>KPS &lt;80%</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Calcium &gt; ULN</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Time from diagnosis to treatment &lt; 1 year</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>LDH &gt; 1.5 ULN</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Platelet count &gt; ULN</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Neutrophil count &gt; ULN</td>
<td>X</td>
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### IMDC Risk Score

<table>
<thead>
<tr>
<th>IMDC Risk Score</th>
<th>Risk group</th>
<th>Median survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Favorable</td>
<td>43.2 months</td>
</tr>
<tr>
<td>1-2</td>
<td>Intermediate</td>
<td>22.5 months</td>
</tr>
<tr>
<td>≥3</td>
<td>Poor</td>
<td>7.8 months</td>
</tr>
</tbody>
</table>

IMDC score, International Metastatic RCC Database Consortium score; KPS, Karnofsky performance status; LDH, lactate dehydrogenase; LLN, lower limit of normal; ULN, upper limit of normal

*Heng et al. Lancet Oncol. 2013*
Symptomatic patient with suspected renal cell cancer (differential diagnosis: urothelial carcinoma of the pelvicalyceal system), lymph node and lung metastases

Stage IV; cT3 cN1 cM1

If renal cell cancer the IMDC score is 1 (Intermediate Risk)
Q1. What is the next step?

1. Biopsy and Systemic treatment
2. Systemic treatment without biopsy
3. Biopsy and observation
4. Cytoreductive nephrectomy and systemic therapy
5. Cytoreductive nephrectomy and observation
6. Cytoreductive nephrectomy and resection of lung metastases
Cytoreductive nephrectomy controversial after CARMENA trial.

Histological diagnosis:

- Clear cell renal cell carcinoma with rhabdoid features
- WHO/ISUP 2016: grade 4
- Retrocaval lymph node: metastasis of clear cell carcinoma
- Stage (UICC, 8th edition): pT3a, pN1 (1/1), V1, Pn0, R0

No postoperative complications
Rapid cancer progression in the lungs and IMDC risk group remains intermediate.

CT, computed tomography; IMDC, International Metastatic RCC Database Consortium.
Q2. What treatment would you recommend?

1. Pembrolizumab + axitinib
2. Avelumab + axitinib
3. Sunitinib
4. Ipilimumab + nivolumab
5. Cabozantinib or pazopanib or tivozanib
6. Bevacizumab + INF
7. Atezolizumab + bevacizumab
TREATMENT

ccRCC

Good risk

Standard:
- Sunitinib [I, A]
- Pazopanib [I, A]
- Bevacizumab + IFN [I, A]
- Tivozanib [II, A; MCBS 1]a

Option:
- High-dose IL2 [III, B]
- Bevacizumab + low-dose IFN [III, B]

Intermediate risk

Standard:
- Nivolumab + ipilimumab [I, A; MCBS 3]a

Option:
- Cabozantinib [II, A; MCBS 3]a
- Sunitinib [I, B]
- Pazopanib, [I, B]
- Tivozanib [II, B; MCBS 1]a
- Bevacizumab + IFN [II, C]

Poor risk

Standard:
- Nivolumab + ipilimumab [I, A; MCBS 3]a

Option:
- Cabozantinib [II, B; MCBS 3]a
- Sunitinib [II, C]
- Pazopanib, [II, C]
- Temsirolimus [I, C]

INF, interferon
TREATMENT

First-line ipilimumab 1 mg/kg + nivolumab 3 mg/kg every 3 weeks for 4 doses followed by nivolumab 3 mg/kg every 2 weeks

Cycle 1 d1
- Blood tests OK
- No symptoms

Cycle 2 d1
- Blood tests OK
- No symptoms

Cycle 3 d1
- Blood tests OK
- No symptoms

1 week before cycle 4
- Blood tests ?
- Diarrhoea

Blood test before every cycle: CBC w/differential, AST, ALT, ALP, bilirubin test, serum urea, creatinine, Ca, Mg, Na, K, Cl, LDH, glucose, amylase, lipase, TSH

ALP, alkaline phosphatase; ALT, alanine amino transferase; AST, aspartate amino transferase; CBC, complete blood count; LDH, lactate dehydrogenase; TSH, thyroid stimulating hormone
ADVERSE EVENT

Before 4\textsuperscript{th} dose of ipilimumab + nivolumab (week 11):

Diarrhoea with 3-4 liquid stools per day (G2), no fever, no nausea

- Baseline investigations:
  
  Mild hypokalemia (3.0 mmol/L) with normal liver, thyroid and renal function, full blood count, and CRP

  Negative viral PCR, general culture, no parasites, no \textit{Clostridium difficile}

- Symptomatic treatment:
  
  Oral fluids and loperamide
  
  Avoiding high fibre/lactose diet
  
  Potassium supplementation by mouth


CRP, \textit{C}-reactive protein; PCR, polymerase chain reaction
CHEST, ABDOMINAL AND PELVIC CT SCAN

Before treatment

After 11 weeks

CT, computed tomography
ADVERSE EVENT

2 days after….
Diarrhoea with 7-9 liquid stools per day (G3), nausea G2, dehydration, mild abdominal pain without peritonism. No haemodynamic instability

- Hospitalisation and fluids + electrolytes supplementation
- Abdominal CT scan without complications

CT, computed tomography
Q3. What treatment would you recommend?

1. Oral prednisolone 0.5-1 mg/kg
2. Oral budenoside 9 mg/day
3. IV (methyl)prednisolone 1-2 mg/kg + sigmoido/colonoscopy
4. Infliximab 5 mg/kg
5. Infliximab 5 mg/kg + IV (methyl)prednisolone 1-2 mg/kg
6. Loperamide 4 mg first dose then 2 mg after each loose stool (max 16 mg/day) without steroids or anti-inflammatory drugs
IMMUNE-RELATED GASTROINTESTINAL TOXICITY

Management:

- Hospitalisation and fluids + electrolytes supplementation
- IV methylprednisolone 2 mg/kg reduced to 1 mg/kg after 3 days for improvement
- Colonoscopy: acute colitis with severe inflammation
- After improvement switch to oral prednisolone and wean over 4 weeks

After 5 weeks, no immune-related toxicity

Q4. What would you recommend?

1. Resume ipilimumab and nivolumab without dose adjustment
2. Resume with nivolumab only
3. Resume with ipilimumab only
4. Delay therapy (1 month)
5. Observation only
6. Switch to VEGF-targeted agent

VEGF, vascular endothelial growth factor
LAST FOLLOW-UP VISIT

Stable complete remission after observation 6 months after the last treatment
Q5. What treatment would you recommend in case of progression?

1. Any TKI
2. Ipilimumab and nivolumab
3. Nivolumab
4. Pembrolizumab + axitinib
5. Nivolumab re-challenge
6. Lenvatinib + everolimus

TKI, tyrosine kinase inhibitor
What treatment would you recommend in case of progression?

TKI, tyrosine kinase inhibitor

Escudier et al. Ann Oncol 2019
THANK YOU FOR YOUR ATTENTION

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