New agents in the treatment of liver cancer

Deep Dive into Liver Cancer – Session IV, 5th DiCE Masterclass 2020

21-10-2020

Jeroen Dekervel - MD PhD
Disclosures

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- **Travel grants:** Ipsen, Servier, Roche
As a comparison: colon cancer

- Very early stage → surgical resection

- Early stage without involved lymph nodes → surgical resection + sometimes chemotherapy

- Lymph nodes involved but no distant metastasis → surgical resection + chemotherapy

- Distant metastasis → chemotherapy
Hepatocellular carcinoma

- Take into account **disease stage** (like colon cancer)

- Take into account (often) **impaired liver function**

- Take into account (often) impaired **patient performance status**
Surgeon
Nurse specialist
Oncologist
Pathologist
Radiologist
Radiation therapist
Interventional radiologist
Hepatologist
Transplant surgeon
Chemotherapy
Tyrosine Kinase Inhibitors
Sorafenib in Advanced Hepatocellular Carcinoma

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Median survival without treatment: 5 – 8 months

FIRST LINE

Sorafenib / Nexavar

+ 2.8 months vs no treatment
Median survival without treatment: 5 – 8 months

<table>
<thead>
<tr>
<th>FIRST LINE</th>
<th>SECOND LINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sorafenib / Nexavar</td>
<td>Regorafenib / Stivarga</td>
</tr>
<tr>
<td>Lenvatinib / Lenvima</td>
<td>Cabozantinib / Cabometyx</td>
</tr>
<tr>
<td>+ 2.8 months vs no treatment</td>
<td>+ 2.2 months vs no 2nd line</td>
</tr>
<tr>
<td>Equal to sorafenib</td>
<td>Ramucirumab / Cyramza*</td>
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<tr>
<td></td>
<td>+ 1.2 months vs no 2nd line</td>
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* If aFP > 400
<table>
<thead>
<tr>
<th>Common</th>
<th>Serious</th>
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<tbody>
<tr>
<td>Diarrhoea</td>
<td>Thrombosis</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Bleeding</td>
</tr>
<tr>
<td>Induced hypertension</td>
<td>Heart failure</td>
</tr>
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<td>Hepatotoxicity</td>
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</tr>
<tr>
<td>Skin changes</td>
<td>GI tract fistula formation</td>
</tr>
<tr>
<td>Nausea</td>
<td>Intestinal perforation</td>
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<tr>
<td>Increased thyroxine dosage requirement</td>
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<tr>
<td>Changes in taste</td>
<td></td>
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<tr>
<td>Weight loss</td>
<td></td>
</tr>
<tr>
<td>GRADE 1: Mild</td>
<td>GRADE 2: Moderate</td>
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<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
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Immunotherapy
Breakthrough of the Year
Cancer Immunotherapy
T cells on the attack
83 yo male patient treated with Nivolumab/Opdivo

- 04/2019: aFP 400800 ug/l
- 07/2019: aFP 150 ug/l
- 09/2019: aFP 5 ug/l
Median survival without treatment: 5 – 8 months

**FIRST LINE**
- Sorafenib / Nexavar
  + 2.8 months vs no treatment
- Lenvatinib / Lenvima
  Equal to sorafenib
- Nivolumab / Opdivo
  Not better than sorafenib

**SECOND LINE**
- Regorafenib / Stivarga
  + 2.8 months vs no 2nd line
- Cabozantinib / Cabometyx
  + 2.2 months vs no 2nd line
- Ramucirumab / Cyramza*
  + 1.2 months vs no 2nd line

* If aFP > 400
100 people with HCC treated with immunotherapy

Solution?

- **Find test** to identify those 15% that benefit
- **Combine** immunotherapy with other drug to increase efficacy
HCC

Antiangiogenic treatments

Vascular normalisation

Immune checkpoint inhibitors

Increased treatment response
Median survival without treatment: 5 – 8 months

**NEW FIRST LINE**

<table>
<thead>
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<th>Effect vs no treatment</th>
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<tbody>
<tr>
<td>Atezolizumab + Bevacizumab / Tecentriq + Avastin</td>
<td>42% less risk of death vs sorafenib</td>
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Side effects immunotherapy
- New
- Diverse
- Rare
- Managable
New agents in the treatment of HCC: summary

Developing drugs for patients with hepatocellular carcinoma has proven to be difficult due to chemoresistance of the disease, impaired liver function and/or functional status.

Tyrosine kinase inhibitors were the first drugs to lengthen life of HCC patients, albeit with modest effect.

Immunotherapy have dramatic effects in this disease, but identifying those likely to benefit remains the challenge.

Very recently, a combination treatment of immunotherapy and anti-angiogenesis has become the new standard of care for treatment of HCC.