Presurgical Feasibility of Bevacizumab for Nephrectomy-Eligible, Treatment-Naïve Patients with Metastatic Renal Cell Carcinoma

Presentation discussed in this issue:

Abstract

Slides from the presentation

**Phase II Presurgical Feasibility Study of Bevacizumab in Untreated Patients with Metastatic Renal Cell Carcinoma**

**Jonasch E et al.**
# Introduction

- The role of cytoreductive nephrectomy (CN) for mRCC is not well established
  - Two randomized clinical trials demonstrated improved survival of patients who underwent nephrectomy in addition to treatment of metastases with immunotherapy (*NEJM* 2001;345:1655; *Lancet* 2001;358:966)
  - Little attention has been given to the timing of nephrectomy relative to systemic therapy
- Objectives of this single-site prospective study in patients with newly diagnosed, untreated mRCC with intermediate- and poor-risk features:
  - Determine safety of CN after antiangiogenic therapy with bevacizumab (bev)
  - Compare clinical outcomes attained with bev pretreatment to those of nephrectomy followed by antiangiogenic therapy
  - Determine whether bev pretreatment can select for benefit from CN


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# Phase II, Non-Randomized, Single-Institution Study

<table>
<thead>
<tr>
<th>Eligibility</th>
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<tr>
<td>Histologically/cytologically confirmed metastatic clear cell RCC, with a resectable primary tumor in place</td>
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<thead>
<tr>
<th>Treatment</th>
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<tr>
<td><strong>1st Cohort (n=23): Bev 10mg/kg q14d x 4 + Erlotinib 150 mg qd</strong></td>
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<tr>
<td><em><em>2nd Cohort</em> (n=27): Bev 10mg/kg q14d x 4</em>*</td>
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**Week 8:** restage

**Week 10** (4wk after last bev dose and 2wk after last erlotinib dose for 1st cohort): cytoreductive nephrectomy if no clinical or radiographic progression and if performance status is adequate

**Week 14:** Restage and restart therapy if disease stable or regressed

* Study amended after report of no benefit to addition of erlotinib in randomized phase II setting (*JCO* 2007)

**Perioperative Outcome and Complications**

- No report of intraoperative or perioperative complications attributable to study drug
- At four weeks postoperatively, 9 patients (20.9%) had delayed wound healing
  - No treatment delay (n = 5)
  - 20-21 days treatment delay (n = 2)
  - Grade 3, delayed wound healing, preventing resumption of trial therapy (n = 2)
  - Surgical intervention for fascial dehiscence three months after restarting bev therapy (n = 1)
- Postoperative death due to prolonged/challenging operation and deemed unrelated to study drug (n = 2)
- Median overall hospital stay = 5 days


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**Clinical Outcomes**

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Patients (n = 50)</th>
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<tr>
<td><strong>Nephrectomy rate</strong></td>
<td>84%</td>
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<tr>
<td>Median progression-free survival* (PFS)</td>
<td>11.0 months</td>
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<td>Median overall survival (OS)</td>
<td>25.4 months</td>
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<tr>
<td>Median response duration</td>
<td>8.3 months</td>
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<tr>
<td>Overall response (OR)</td>
<td></td>
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<tr>
<td>Complete response (CR)</td>
<td>12%</td>
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<tr>
<td>Partial response (PR)</td>
<td>10%</td>
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</table>

*Time to disease progression from time of first treatment*

Waterfall Plot of Best Response in Primary Tumor Site to Presurgical Bevacizumab for mRCC

52% (23/45 patients with first restaging scans) had primary tumor reduction


Discussion and Conclusions

- Presurgical treatment of mRCC with bevacizumab therapy yields clinical outcomes comparable to post-surgical treatment with antiangiogenic therapy but may result in wound-healing delays
  - Nephrectomy rate = 84%
  - Rate of delay in wound healing = 20.9%
  - Primary tumor regression rate = 52%
- In intermediate- and poor-risk populations, the observed PFS outcomes fall within the prospectively anticipated range for PFS, and OS is comparable to those from studies in the front-line setting
  - Median PFS: 11.0 mos; Median OS: 25.4 mos
- This study was unable to define the role of presurgical systemic therapy for selecting appropriate patients for CN due to lack of randomization and small sample size
- Prospective randomized trials exploring the definitive clinical benefit of this treatment approach are warranted