Selection and timing of nephrectomy for metastatic kidney cancer

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Disclosures

- None
Objectives

- Kidney cancer epidemiology
- Risk stratification for metastatic disease
- Evidence for cytoreductive nephrectomy
- New data in the era targeted therapy
- Potential selection criteria
Kidney Cancer Epidemiology

Nationally, in 2018:
- 65,370 cases
- 14,970 deaths

In NC, in 2017
- 2,054 cases
- 474 deaths
Diverse Presentation

41 yo male
Adrenal met
ECOG 0
No symptoms
NL labs

70 yo female
Lung mets
ECOG 1
Pain/\downarrow weight
Bulky LAD
\uparrow LDH

55 yo male
Lung met
ECOG 2-3
Pain/Swelling
\downarrow Hb
\uparrow LDH
Risk Stratification - PS

ECOG and Disease Specific Survival

- ECOG 0: 26.7 months
- ECOG 1: 13.8 months
- ECOG 2/3: 6.8 months

Median Survival

% Survival

Months
Risk Stratification - MSKCC

- Performance status
- LDH > 1.5 nl
- Hb < nl
- Calcium > 10
- Dx to Tx < 1 yr

Motzer, JCO, 2002
Risk Stratification – IMDC/Heng

- Performance Status
- Hb < nl
- Calcium > UL nl
- Dx to Tx < 1 yr
- Neutrophil > UL nl
- Platelets > UL nl

Heng, Lancet Oncology, 2014
The Age of Cytoreductive Nephrectomy

Nephrectomy Followed by Interferon Alfa-2b Compared with Interferon Alfa-2b Alone for Metastatic Renal-Cell Cancer

Robert C. Flanigan, M.D., Sydney E. Salmon, M.D., Brent A. Blumenstein, Ph.D., Scott I. Bearman, M.D., Vivek Roy, M.D., Patrick C. McGrath, M.D., John R. Caton, Jr., M.D., Nikhil Munshi, M.D., and E. David Crawford, M.D.

11.1 vs. 8.1 month OS advantage (p=0.05)
Immunotherapy vs. Targeted Therapy
Ongoing Treatment Trends

Ferry et al, Tsao et al.
## CN in the Targeted Therapy Era

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Population</th>
<th>Survival Benefit</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choueiri et al., J Urol, 2011</td>
<td>645 patients (multi-institutional)</td>
<td>Median survival: 19.8 vs. 9.4 months (HR 0.44, 95% CI 0.32-0.59)</td>
<td>Marginal benefit for poor risk and poor performance status</td>
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<tr>
<td>Heng et al., Eur Urol, 2014</td>
<td>1,658 patients in IMDC</td>
<td>Median survival: 20.6 vs. 9.5 months (HR 0.60, 95% CI 0.52-0.69)</td>
<td>No benefit in patients with 4+ IMDC risk criteria (ie, poor risk)</td>
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<tr>
<td>Hanna et al., JCO, 2016</td>
<td>15,390 patients in NCDB</td>
<td>Median survival: 17.1 vs. 7.7 months (HR 0.45, 95% CI 0.40-0.50)</td>
<td>Benefit ↓ with shorter survival; improved survival if TT first</td>
</tr>
<tr>
<td>Mathieu et al., Uro Onc, 2015</td>
<td>351 patients from 18 hospitals</td>
<td>Median survival: 38.1 vs. 16.4 months</td>
<td>No benefit for poor risk and poor performance status</td>
</tr>
</tbody>
</table>
CARMENA Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma

- Phase III RCT, non-inferiority trial
- Intermediate & Poor Risk
- 450 patients from 2009-2017
CARMENA Trial

- Disease control
  - Any: 61.8 vs 74.6%
  - >12 weeks: 36.6 vs. 47.9%

- Perioperative Outcomes
  - 2% 30-day mortality
  - 15.9% Clavien III+
  - 39.0% Any complication
  - Grade III+: 32.8 vs 42.7%

HR 0.89 (0.71-1.10)

HR 0.82 (0.67-1.00)
CARMENA Trial

Poor accrual and early closure

“Patients unwilling to be randomized between surgical and non-surgical option.”

“Manny patients I saw either ‘obviously’ need a nephrectomy or ‘obviously’ needed oncology.”

Sickest subgroup / “palliative” nephrectomy

Stewart et al., Eur Urol, 2016
SURTIME Trial

- 99 patients from 19 institutions
- CN then sunitinib vs. 3 cycles sunitinib then CN

Bex, ESMO, 2017
Selecting Patients for CN

- Determinants of Perioperative Morbidity/Mortality

- Favorable vs. Intermediate vs. Poor Risk

- Additional considerations
  - Bleeding/pain
  - Histology (sarcomatoid/non-clear cell)
  - Estimate tumor burden removed
  - Burden/symptoms of non-lung metastases
Return of the Golden Age?

Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma

Robert J. Motzer, M.D., Bernard Escudier, M.D., David F. McDermott, M.D., Saby George, M.D., Hans J. Hammers, M.D., Ph.D., Sandhya Srinivas, M.D., Scott S. Tykodi, M.D., Ph.D., Jeffrey A. Sosman, M.D., Giuseppe Procopio, M.D., Elizabeth R. Plimack, M.D., Daniel Castellano, M.D., Toni K. Choueiri, M.D., et al., for the CheckMate 025 Investigators

Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma

Robert J. Motzer, M.D., Nizar M. Tannir, M.D., David F. McDermott, M.D., Osvaldo Arén Frontera, M.D., Bohuslav Melichar, M.D., Ph.D., Toni K. Choueiri, M.D., Elizabeth R. Plimack, M.D., Philippe Barthélémy, M.D., Ph.D., Camillo Porta, M.D., Saby George, M.D., Thomas Powles, M.D., Frede Donskov, M.D., Ph.D., et al., for the CheckMate 214 Investigators
Summary

- Sunitinib only is non-inferior for patients with intermediate and poor risk disease.

- Deferred cytoreductive nephrectomy is non-inferior for patients with intermediate risk disease.
Take Home Points

- Cytoreductive nephrectomy likely remains the standard for favorable risk disease

- Initial systemic therapy may be advisable for intermediate/poor risk disease

- New opportunities for enhanced risk stratification and selection for cytoreductive nephrectomy
QUESTIONS/COMMENTS?

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