IMMUNE CHECKPOINT INHIBITORS DEBATE:
BIOPSY VS. NO BIOPSY (CON)

Ilya G. Glezerman, MD
Memorial Sloan Kettering Cancer Center, New York, NY
Weill Cornell Medical College, New York, NY
Ilya Glezerman, MD

Albany Medical College
Medicine Residency @BIMC, New York, NY
Nephrology Fellowship @ BIMC, New York, NY
Associate Attending Physician@ MSKCC, New York, NY
Associate Professor of Medicine@ WCMC, New York, NY

• Clinical focus: Onco-Nephrology
• Research focus: Kidney Toxicities of Chemotherapy and Checkpoint Inhibitors
Disclosures

I have no financial disclosures
Objectives (Please list at least 2 Objectives)

Use case vignettes to:
- Highlight clinical course of AIN related to CPI
- Review potential complications of the kidney biopsy in a setting of CPI kidney toxicity
Clinical Vignette #1

- 48 yo male with Metastatic Gastric Cancer
- Receiving FOLFOX + nivolumab-S/P two cycles
- Presented for the next Cycle but noted to have elevated Creatinine
- UA: protein 100, LE trace, WBC 6/HPF
- No N/V/D
- Received IVF but renal function cont to worsen
- No obstruction on imaging
- Nephrology service consulted and pt was suspected to have CPI induced AIN
- Steroid taper initiated with rapid resolution of AKI
- Unfortunately, Pt passed away 8 months after the resolution of AKI
Clinical Vignette #2

58 yo female with h/o Breast Ca
- On neoadjuvant treatment with Carboplatin/Taxol and pembrolizumab (s/p 2 Cycles)
- Developed AKI (baseline Scr 0.7 mg/dL) with Scr 1.8 mg/dL
- Denies N/V/D
- No obstruction on imaging
- UA significant for pyuria

Kidney Biopsy:
Tissue submitted for light microscopy consist of three (3) cores of renal cortex and medulla and four (4) cores of renal medulla and one (1) fragment of urothelium – AIN on microscopy
- Developed gross hematuria
- Admitted for observation
Kidney Biopsy Complications in Patients with AKI

Post Biopsy Complications in Hospitalized Patients


<table>
<thead>
<tr>
<th>Complication</th>
<th>N (%)</th>
<th>95% CI of Proportion</th>
<th>Median (Interquartile Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>159</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood transfusion for biopsy-related bleeding a</td>
<td>12 (8 [4 to 15])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiographic intervention to stop bleeding</td>
<td>3 (2 [1 to 5])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematoma a-b</td>
<td>11 (7 [14 to 12])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death in 30 d a</td>
<td>4 (3 [1 to 6])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reimaging after biopsy to check for bleeding a</td>
<td>31 (20 [14 to 26])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drop in hemoglobin g/dl</td>
<td>0.8 (0.4, 1.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin drop &gt;1</td>
<td>60 (59 [51 to 47])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin drop &gt;2</td>
<td>15 (10 [6 to 15])</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Postbiopsy Complications in Hospitalized Patients with Acute Kidney Disease

- Transfusion: 8 (4–13%)
- Angiographic Intervention: 7 (4–12%)
- Hematoma: 2 (1–5%)
- Reimaging: 20 (14–26%)
Biopsy Complications in Non-Hospitalized Patients

Biopsy Findings in Immune Therapy Associated Acute Kidney Injury

- Study of 138 pts with AKI in setting of CPI use
  - 60 pts underwent Biopsy
  - 93% AIN

- Study of 429 pts with AKI in setting of CPI use
  - 151 pts underwent Biopsy
  - 82.3% AIN
Treatment of Immunotherapy Associated AKI

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI) for Complete Renal Recovery</th>
<th>Odd Ratio (95% CI) for Predictors of Renal Recovery after ICP/IAK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 yrs)</td>
<td>1.54 (0.77-3.19)</td>
<td>1.19 (0.67-1.88)</td>
</tr>
<tr>
<td>Female</td>
<td>0.89 (0.44-1.79)</td>
<td>0.94 (0.44-2.01)</td>
</tr>
<tr>
<td>Combination ICP therapy</td>
<td>1.44 (0.68-3.04)</td>
<td>1.95 (0.83-4.63)</td>
</tr>
<tr>
<td>Fold increase in baseline SC</td>
<td>1.00 (0.66-1.16)</td>
<td>0.63 (0.36-1.11)</td>
</tr>
<tr>
<td>Concomitant IAE with AKI</td>
<td>0.41 (0.17-0.95)</td>
<td>0.38 (0.13-0.96)</td>
</tr>
<tr>
<td>Concomitant Drug</td>
<td>2.51 (1.13-5.56)</td>
<td>2.66 (1.14-6.19)</td>
</tr>
<tr>
<td>Treated with glucocorticoids</td>
<td>4.14 (1.14-14.91)</td>
<td>5.55 (1.41-21.01)</td>
</tr>
</tbody>
</table>

Cortazar F et al. JASN 2020
Response to Corticosteroids-Diagnostic?

Renal Outcomes Biopsy vs No Biopsy
Treatment Delay and Risk of Non-Recovery

Figure S4: Predictors of Renal Recovery among Patients Treated with Corticosteroids

<table>
<thead>
<tr>
<th>Variable</th>
<th>Uncorrected OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
<th>Lower Odds Of Recovery</th>
<th>Higher Odds Of Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.01 (0.86-1.19)</td>
<td>1.01 (0.86-1.19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>1.21 (1.06-1.39)</td>
<td>1.21 (1.06-1.39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1.01 (0.85-1.21)</td>
<td>1.01 (0.85-1.21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comorbidities</td>
<td>3.02 (1.05-8.59)</td>
<td>3.02 (1.05-8.59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR (per 10 mL/min)</td>
<td>0.97 (0.94-0.99)</td>
<td>0.97 (0.94-0.99)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>0.87 (0.73-1.03)</td>
<td>0.87 (0.73-1.03)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment duration</td>
<td>0.50 (0.32-0.80)</td>
<td>0.50 (0.32-0.80)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concurrent ATN at basalization</td>
<td>1.25 (0.99-1.58)</td>
<td>1.25 (0.99-1.58)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concurrent other AEs</td>
<td>1.17 (0.99-1.40)</td>
<td>1.17 (0.99-1.40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR &lt; 30 mL/min at initiation</td>
<td>1.27 (1.01-1.60)</td>
<td>1.27 (1.01-1.60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR &lt; 10 mL/min at initiation</td>
<td>2.00 (1.74-2.31)</td>
<td>2.00 (1.74-2.31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment dose (days)</td>
<td>1.50 (1.03-2.19)</td>
<td>1.50 (1.03-2.19)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Gupta S et al. J of Immunother Cancer 2021
Cortazar F et al. JASN 2021
Approach to Immunotherapy Induced AKI

Clinical Suspicion for ICI-AKI
(>2x baseline serum Cr)
High risk features present: CKD; Combination ICI therapy; PPIs, NSAIDs

Nephrotic Range Proteinuria? >3g/d
Or Oliguria? <500ml urine/day
Or Hematuria w/ dysmorphic features?

Consider Kidney Biopsy

Empirical trial of Steroids
Prednisone 1mg/kg/day
for 1-2 weeks duration

*Complete or **partial recovery?

Consider Kidney Biopsy

Continue to monitor kidney function; ICI rechallenge on individual basis with oncologist.

*Complete recovery: Return of Scr to < 0.26mg/dl above baseline
**Partial recovery: Return of Scr to > 0.26mg/dl but less than twice baseline

Abbreviations: CKD, Chronic Kidney Disease; Cr, Creatinine; PPI, Proton Pump Inhibitor; NSAIDs; Nonsteroidal anti-inflammatory drugs