Androgen Receptor Expression in Renal Cell Carcinoma: A New Actionable Target?

New Frontiers in Urologic Oncology

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Disclaimers

• No disclosures
Objectives

• To discuss the role of androgen receptor (AR) expression in renal cell carcinoma (RCC).

• To present an exploratory analysis of AR expression from a single institutional cohort of patients.
Introduction

• RCC is the most common type of kidney cancer and the most lethal urological malignancy.
• Many cases of metastatic RCC are resistant to conventional systemic therapies including chemotherapy.
• Thus, continued understanding on the molecular mechanisms of RCC progression is needed in finding novel therapies in the fight against RCC.
Introduction

• The mechanism of AR involvement in carcinogenesis is poorly understood.

• Studies have suggested AR inhibits the tumor suppressor P53 in hepatocellular carcinoma and activates G protein signaling cascades in ovarian cancer. \(^1,2\)

• Other studies have shown AR could promote RCC metastasis via modulation of the HIF2a-VEGF pathway. \(^3\)

• These newly identified mechanisms may provide us with newer therapeutic approaches in RCC progression.
Purpose

• We assess AR expression at the protein level in archival RCCs of various histologies.
Methods

• We identified 66 patients with RCC surgically treated at Moffitt Cancer Center from 2003 through 2015.

• Formalin-fixed paraffin-embedded blocks were retrieved from Pathology and representative slides were selected for tissue microarray (TMA) construction by sampling three cores of 1-mm diameter per each case.
Methods

• Immunohistochemical (IHC) staining was then performed with the Ventana Discovery XT automated system (Ventana Medical Systems, Tucson, AZ) using a anti-AR rabbit monoclonal primary antibody (Ventana SP107 rabbit mab; Rocklin, CA, USA). Slides were counterstained with Hematoxylin, dehydrated and cover slipped as per normal laboratory protocol.

• Binary expression status [Negative (0) vs. positive ($\geq 1+$ in at least 1% of tumor cells)] was generated for statistical analysis.

• Survival outcomes were evaluated using the Kaplan Meier method. Logistic regression and Cox proportional hazard was used to assess prognostic associations.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year), median (IQR)</td>
<td>60 (53-69)</td>
<td>66</td>
<td>100</td>
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<tr>
<td>BMI (kg/m²), median (IQR)</td>
<td>29.5 (24.3-32.6)</td>
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<td>Tumor size (cm), median (IQR)</td>
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<tr>
<td>Follow-up (month), median (IQR)</td>
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<td>16</td>
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<td>Tumor necrosis</td>
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<td>47</td>
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<td>Tumor thrombus</td>
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Results

• In total, 56.1% of tumors expressed AR:
  – 66.7% in clear cell
  – 44.2% in non-clear histologies
Results

- Five-year OS was 86.3 and 70.6%, respectively (log-rank $p=0.040$)

HR = 0.35 (0.12-0.99), $p = 0.050$
Results

- Five-year CSS was 89.5 and 70.6% for AR positive and negative tumors (log-rank p=0.072)

HR = 0.35 (0.11-1.15), p = 0.084
Results

• Five-year PFS was 71.5 and 49.6% for AR positive and negative tumors (log-rank p=0.064)

HR = 0.44 (0.18-1.07), p = 0.072
# Results

<table>
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<th>T3/4 (29 events)</th>
<th>OR (univariate)</th>
<th>p</th>
<th>OR (multivariate)</th>
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<td>Negative</td>
<td>0.11 (0.03-0.33)</td>
<td>&lt;0.001</td>
<td>0.10 (0.03-0.38)</td>
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<td><strong>Histology</strong></td>
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<tr>
<td>Clear</td>
<td>2.6 (0.86-7.95)</td>
<td>0.091</td>
<td>1.43 (0.35-5.85)</td>
<td>0.620</td>
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<td>&lt;2</td>
<td>18.6 (2.26-152.3)</td>
<td>0.007</td>
<td>22.5 (2.26-223.8)</td>
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Conclusions

- Our preliminary results indicate that AR expression appears to be a marker of indolent disease in RCC.

- Inhibition of hormonal signaling may be putative in treatment therapies against this cancer type.

- Whether AR plays a key role in RCC progression and what possible mechanisms may be involved remain to be defined.

- Larger, prospective studies are needed to validate these results.
References

