PD39-05: Prevalence and Landscape of Actionable Genomic Alterations in Renal Cell Carcinoma

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Introduction

• Actionable genomic alterations include somatic mutations and structural alterations that predict response to targeted therapy

• Defining the landscape of actionable alterations in RCC may identify therapeutic targets and inform targeted therapy trials

• **OBJECTIVE:** describe the prevalence and landscape of actionable alterations and the corresponding evidence supporting the alteration as predictive of response to targeted therapy in RCC
Methods

• Institutional clinical sequencing database queried to include tumor samples sequenced across all cancers

• Actionable alterations with clinical/biologic evidence supporting an association with response to targeted therapy stratified by level of evidence using an oncology knowledge database (OncoKB)\(^1\)

\(^1\)Chakravarty et al. *JCO PO*. 2017
1. **FDA-recognized** biomarker predictive of response to an **FDA-approved drug** in this indication.

2. **Standard care** biomarker recommended by the NCCN or other expert panels predictive of response to an **FDA-approved drug** in this indication.

3A. **Compelling clinical evidence** supports the biomarker as being predictive of response to a drug in this indication.

3B. **Standard care** or **investigational** biomarker predictive of response to an **FDA-approved** or **investigational** drug in another indication.

4. **Compelling biological evidence** supports the biomarker as being predictive of response to a drug.
Targetable alterations in Renal Cell Carcinoma (n=753)

- Clear cell
  - Mutation: 58/448 (13%)
  - CNV: 9/65 (14%)
  - Fusion: 2/43 (4%)
  - Multiple: 24/197 (12%)

Levels of evidence:
- LEVEL_1
- LEVEL_2
- LEVEL_3A
- LEVEL_3B
- No aberration

Type of alteration:
- Mutation
- MSI
- CNV
- VUS
- Fusion
- Multiple
• **SUMMARY**
  
  – The prevalence of actionable alterations in RCC is 12%
  
  – Type of alteration varies by histologic subtype
    
    • Clear cell RCC $\rightarrow$ acquired somatic mutations
    
    • Papillary RCC $\rightarrow$ copy number variations
    
    • Chromophobe RCC $\rightarrow$ MSI/fusion (rare)

• **NEXT STEPS**
  
  – Validation of results (TCGA, TRACERx)
  
  – Clonality of alterations
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