Memorial Sloan Kettering Cancer Center

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

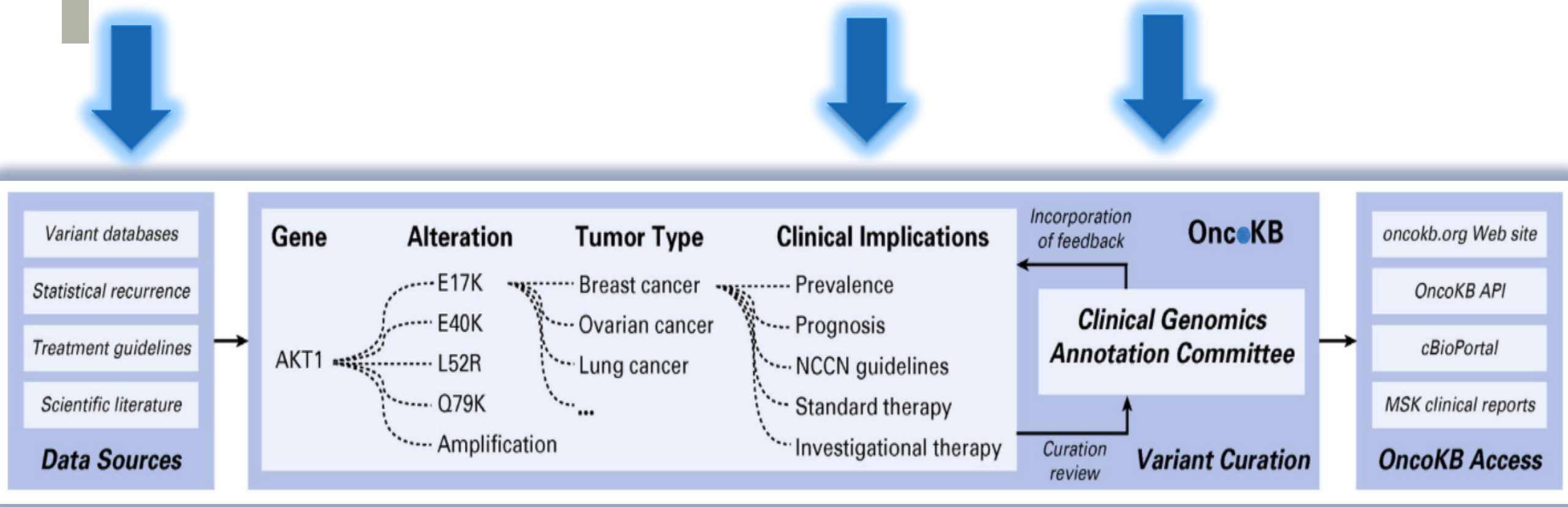
Methods

- 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]

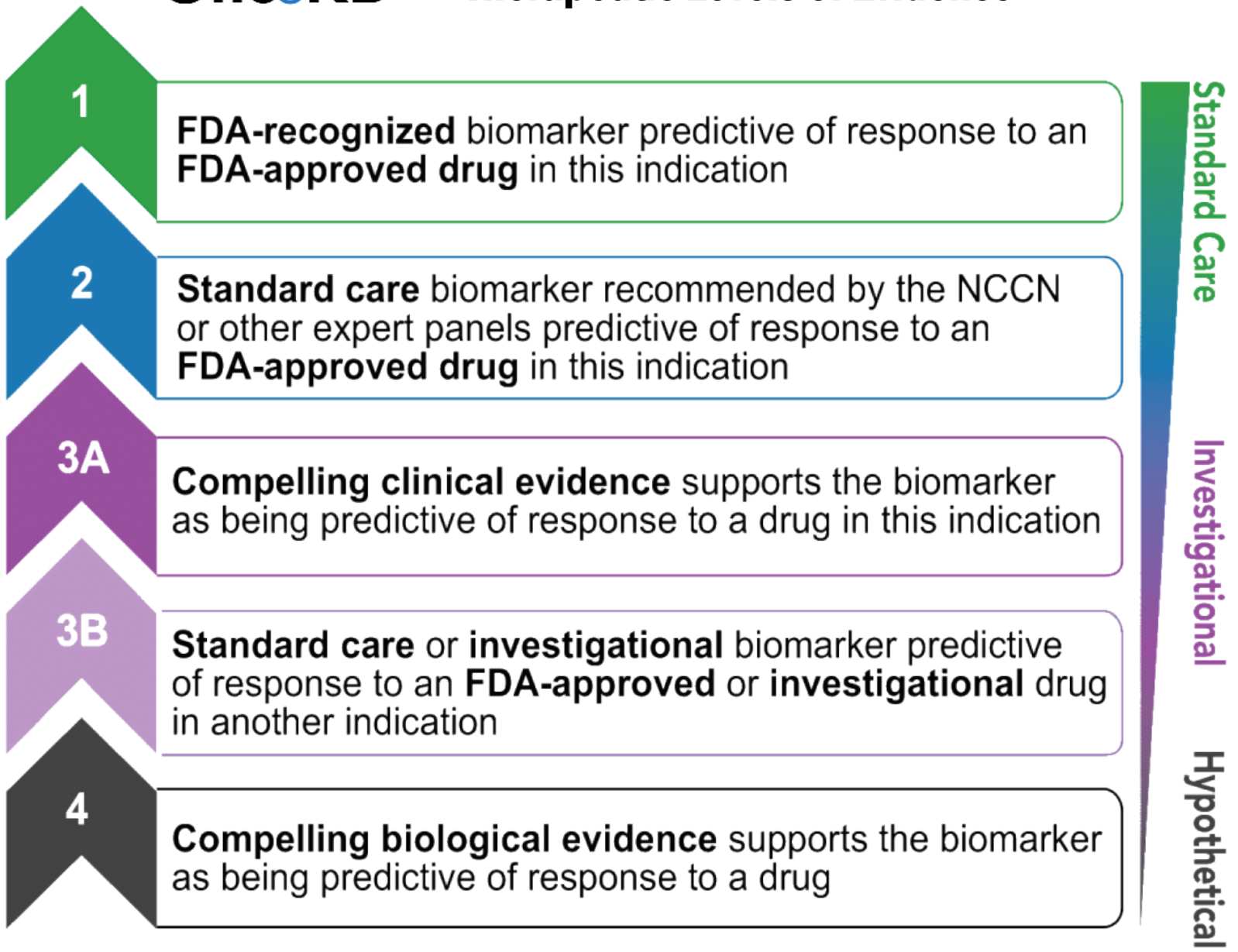
[1]Chakravarty et al. *JCO PO.* 2017

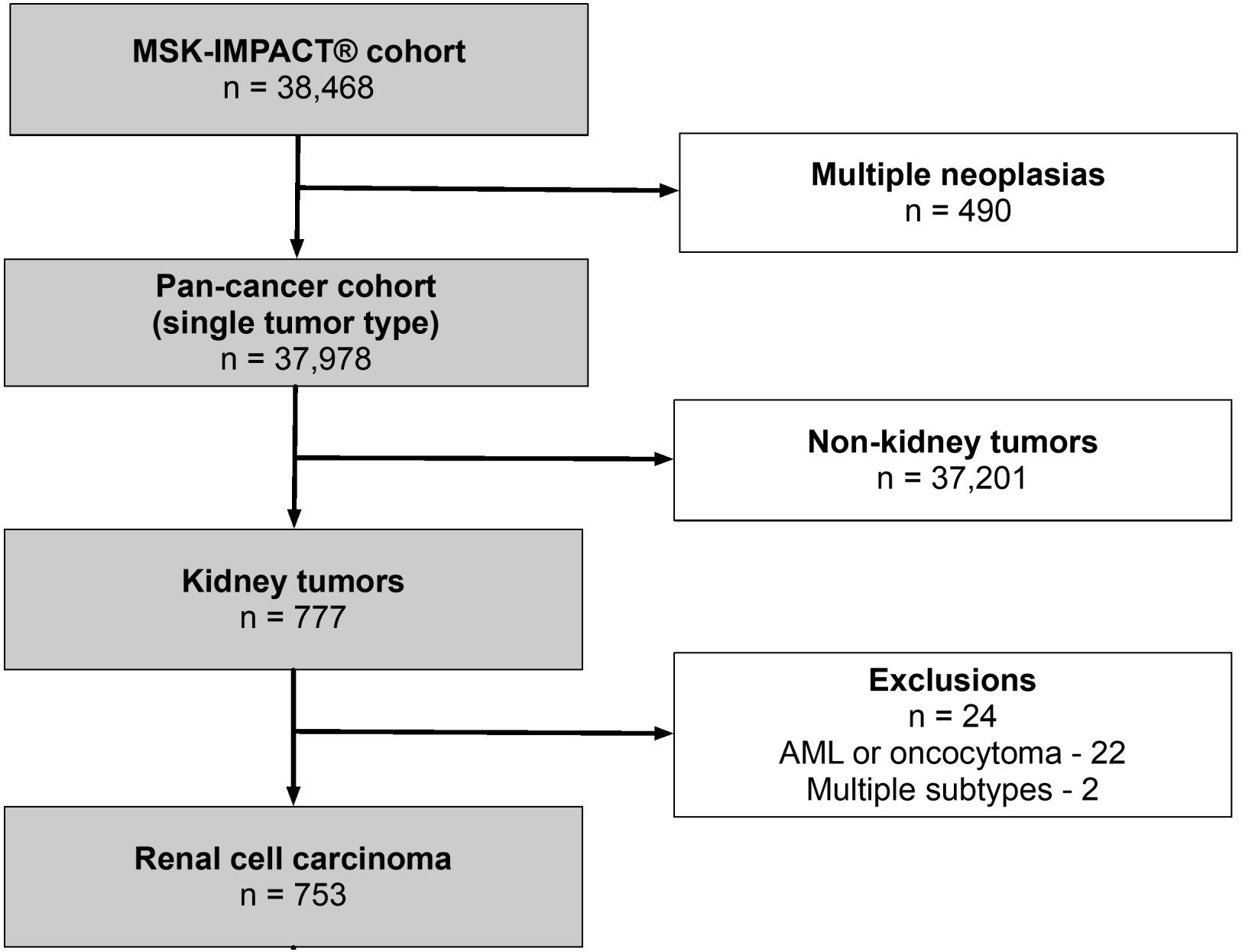
OncoKB Workflow



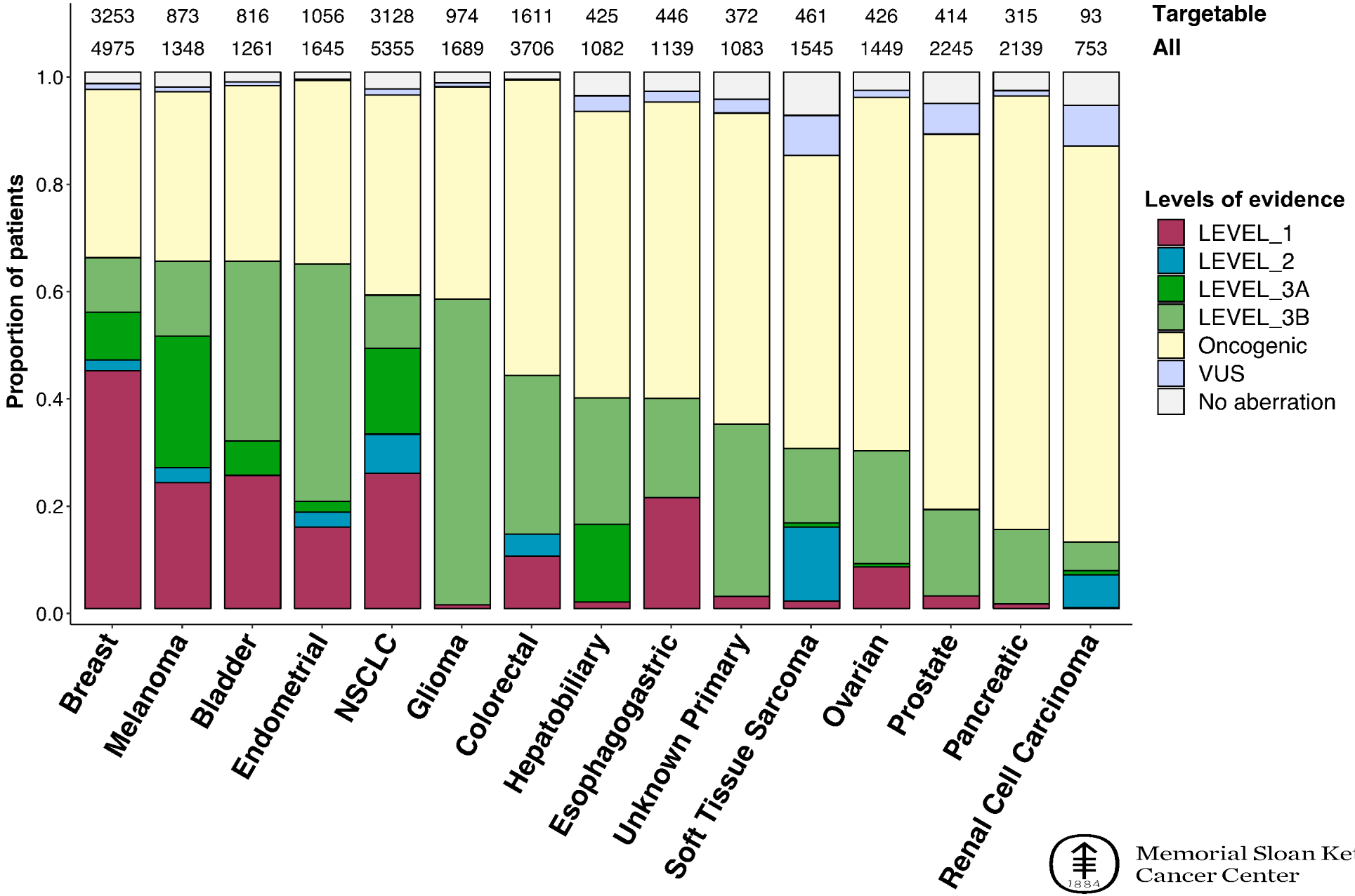
Chakravarty et al. *JCO PO.* 2017

OncoKB Therapeutic Levels of Evidence




MSK-IMPACT® cohort
n = 38,468
Multiple neoplasias
n = 490
Pan-cancer cohort
(single tumor type)
n = 37,978
Non-kidney tumors
n = 37,201
Kidney tumors
n = 777
Exclusions
n = 24
AML or oncocytoma - 22
Multiple subtypes - 2
Renal cell carcinoma
n = 753

Pan-cancer MSK-IMPACT cohort
Targetable alterations by cancer type (15 most common)



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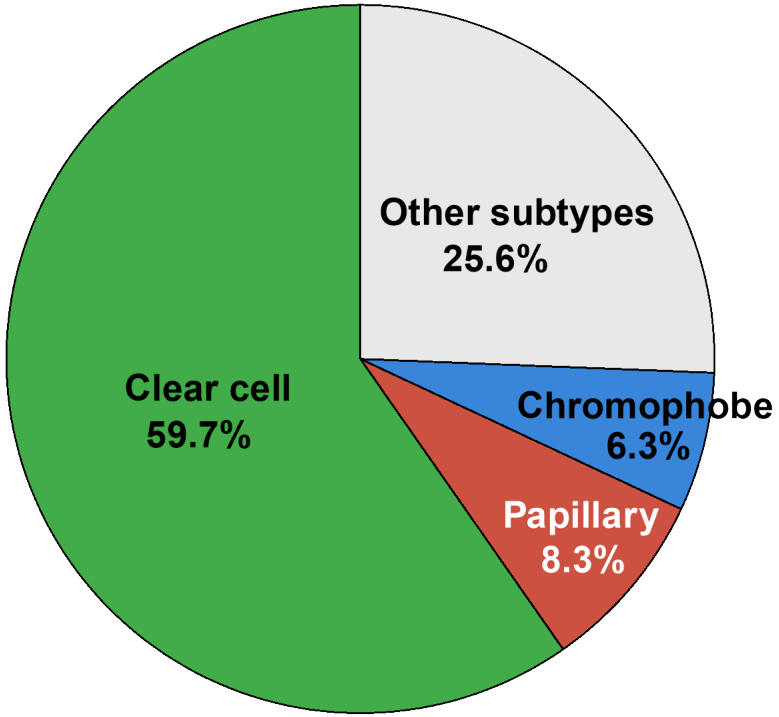
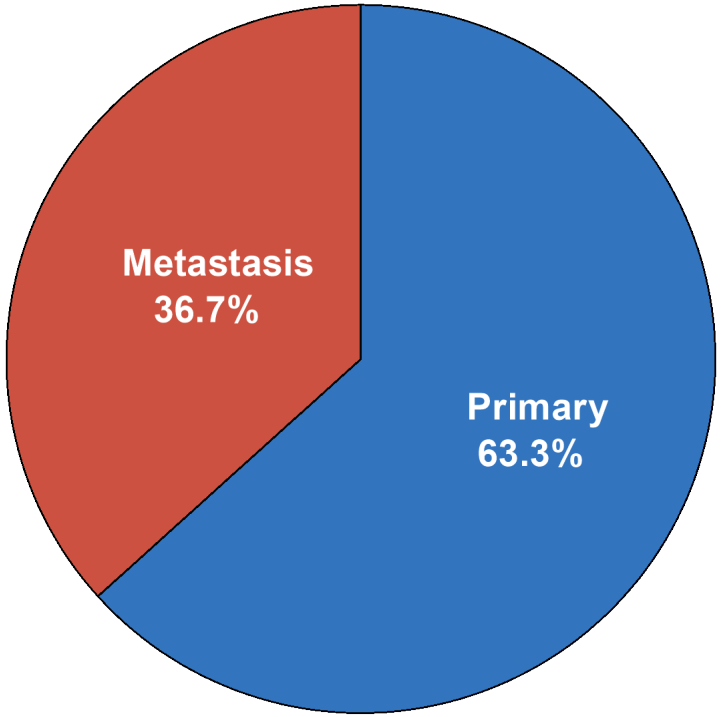
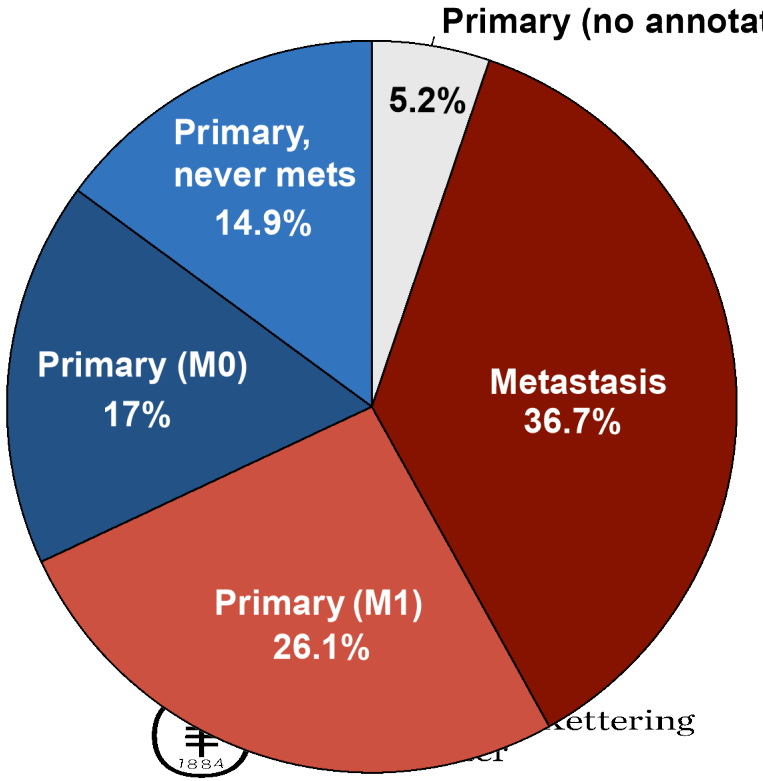
RCC histologic subtypes



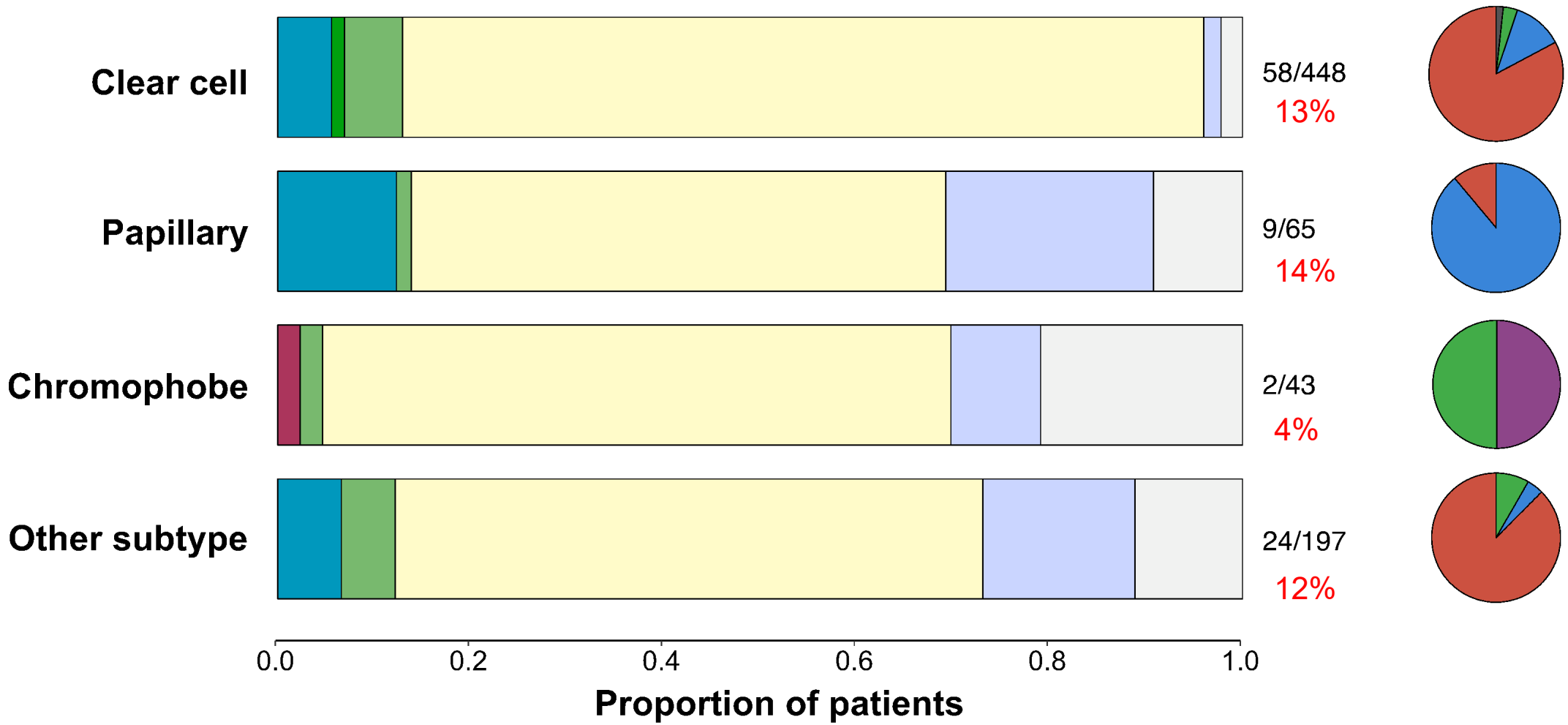
Sample type



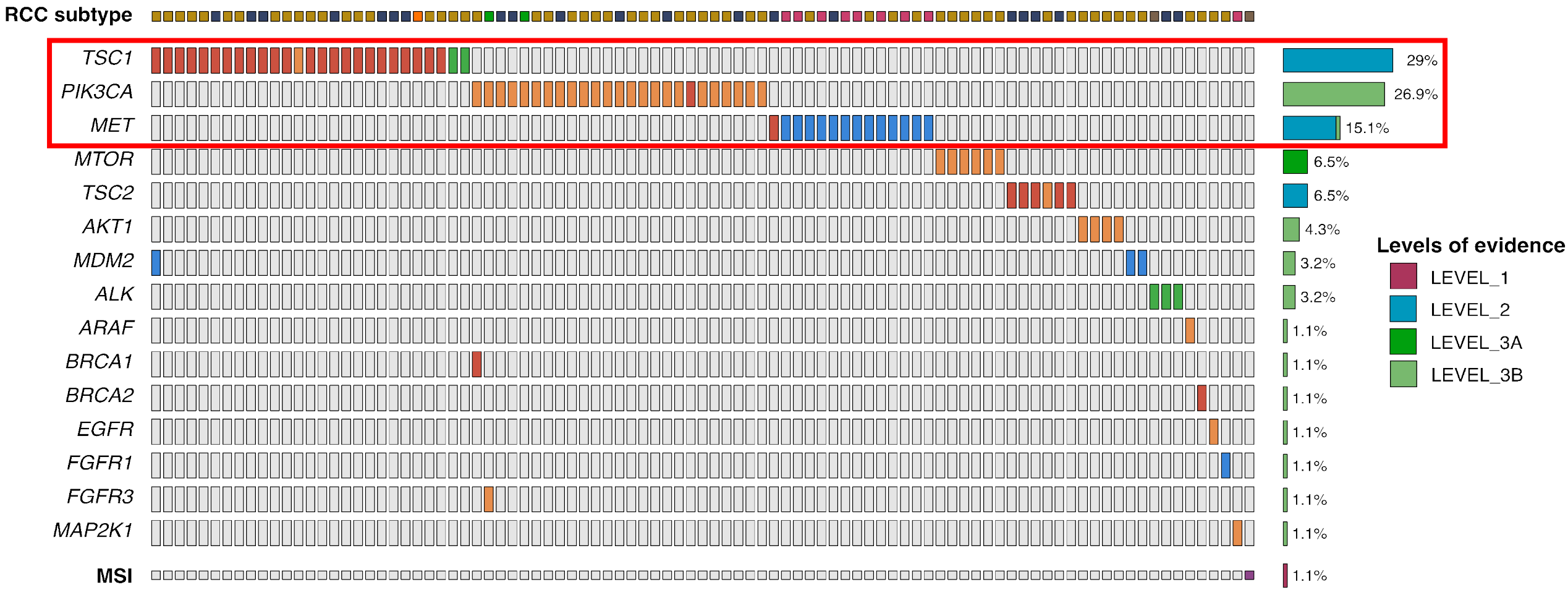
Clinical annotations



Targetable alterations in Renal Cell Carcinoma (n=753)



Targetable alterations in RCC



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- SUMMARY
  - The prevalence of actionable alterations in RCC is 12%
  - Type of alteration varies by histologic subtype
    - Clear cell RCC → acquired somatic mutations
    - Papillary RCC → copy number variations
    - Chromophobe RCC → MSI/fusion (rare)

- NEXT STEPS
  - Validation of results (TCGA, TRACERx)
  - Clonality of alterations

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