# Levels of Evidence



Refseq Refsea Genome DNA Gene Chromosome Transcript Protein Position Version DNA Sub Protein Sub Variant Variant Somatic **PMIDs** Classification & Position & Position Type Consequence (Optional) The cancer type, suggested ontology from NCI Thesaurus or Oncotree. The NCI Cancer Type Term Browser relates NCI Thesaurus codes to ICD9/10, SNOMED or UMLS. Biomarker Diagnostic, Prognostic, Predictive Class Therapeutic **Known Associated Drugs or Drug Classes** Context (Optional) **Effect of Variant in Therapeutic Context:** Effect Resistant, Responsive, Not-Responsive, Sensitive, Reduced-Sensitivity (Optional) Somatic Cancer Variant Interpretation Schema (ex.from CanDL): Tier1: Alteration has matching FDA approved or NCCN recommended therapy. Tier2: Alteration has matching therapy based on evidence from clinical trials, Level of

case reports, or exceptional responders.

Tier3: Alteration predicts for response or resistance to therapy based on evidence from pre-clinical data (in vitro or in vivo models).

Tier4: Alteration is a putative oncogenic driver based on functional activation of a pathway

Sub-Level of Evidence

Evidence

Prospective/retrospective trials/studies/metadata analysis, expert opinion, case reports, preclinical data, inferential data

# Global Alliance for Genomics & Health

Allele Descriptive

Allele Interpretive

## Tier I: Variants of **Strong Clinical Significance**

Therapeutic, prognostic & diagnostic

#### **Level A Evidence**

FDA-approved therapy guidelines

#### **Level B Evidence**

Well-powered studies experts in the field

# AMP/CAP/ASCO

### Tier II: Variants of **Potential Clinical Significance**

Therapeutic, prognostic & diagnostic

#### Level C Evidence

FDA-approved therapies for different tumor types or investigational therapies

Multiple small published studies with some

#### **Level D Evidence**

Preclinical trials or a few case reports without

# Tier III: Variants of **Unknown Clinical Significance**

significant allele frequency in the general or specific subpopulation databases, or pan-cancer or tumor-specific variant

No convincing published evidence of cancer

## Tier IV: Benign or **Likely Benign Variants**

Observed at significant allele frequency in the general or specific

No existing published evidence of cancer





