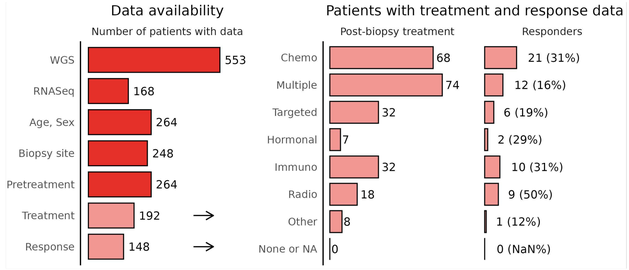
The Genomic and Actionability Landscape of AYA Cancer

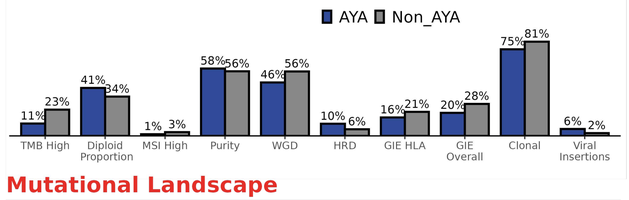
Website: https://www.hartwigmedicalfoundation.nl
Tools: https://github.com/hartwigmedical/hmftools
Database: https://www.hartwigmedicalfoundation.nl/en/data/database/

CC BY NC: This license enables reusers to distribute, remix, adapt, and build upon the material in any medium nor format for noncommercial purposes only, and only so long as attribution is given to the creator.

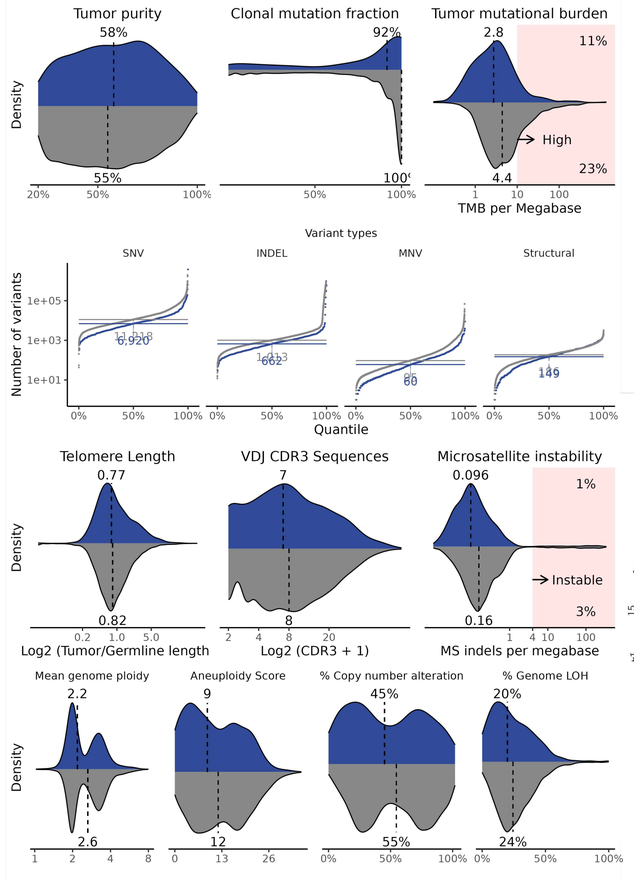
Cohort Metadata



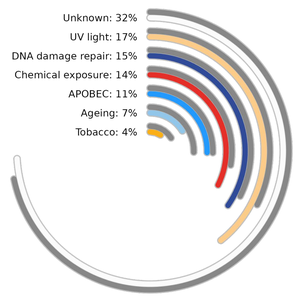
Tumor Characteristics

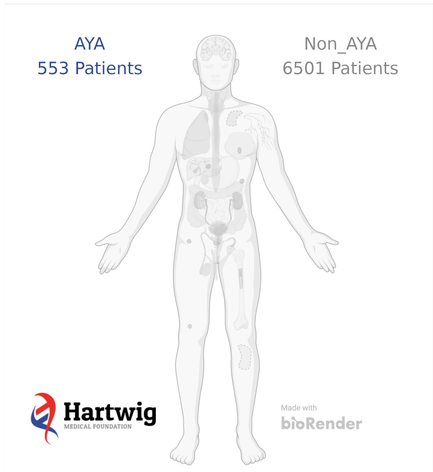


Mutational Landscape

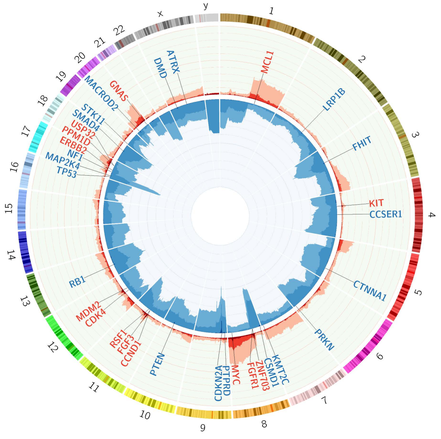


Processes Underlying Mutations

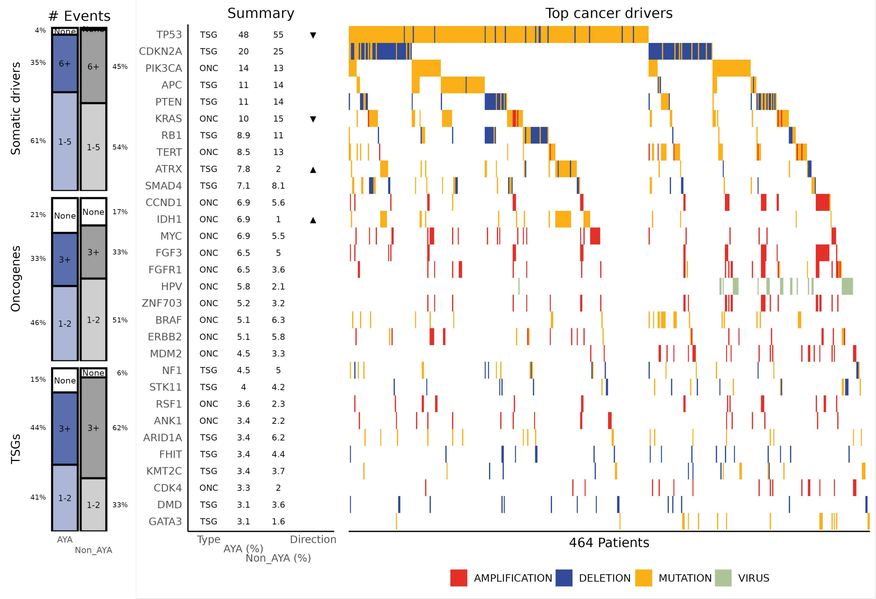




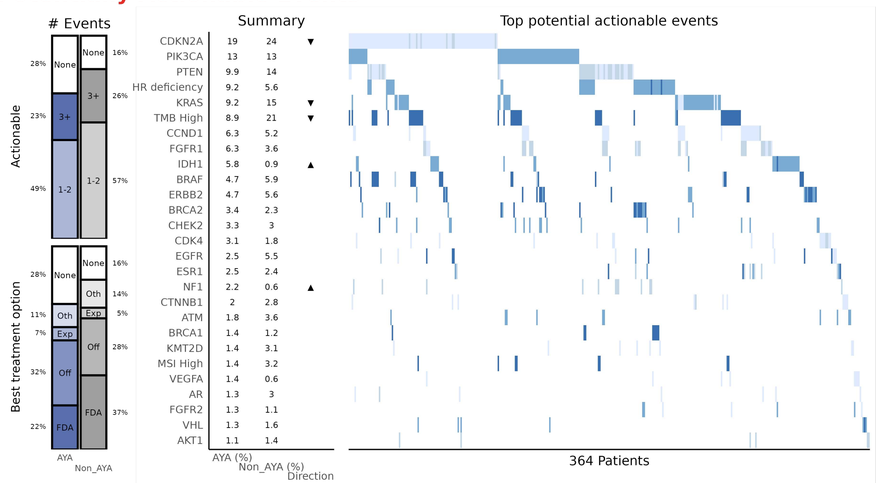
Copy Number Alteration Profile



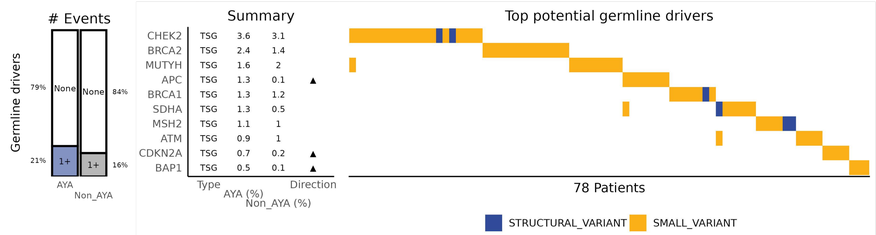
Cancer Driver Landscape



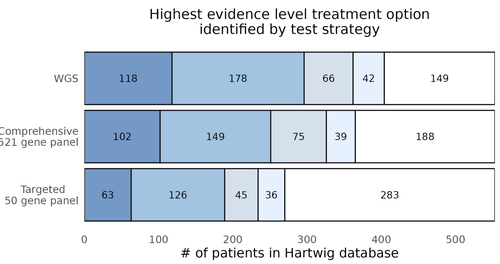
Potentially Actionable Events

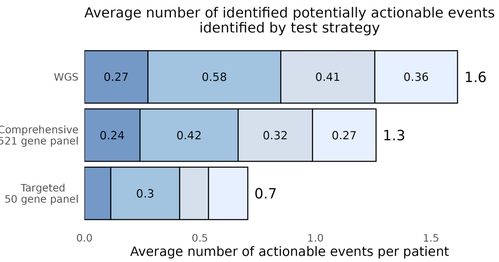


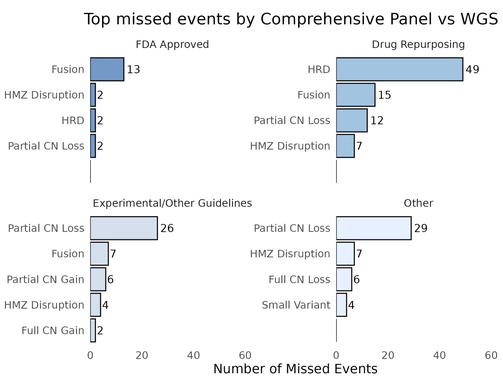
Germline Predisposition

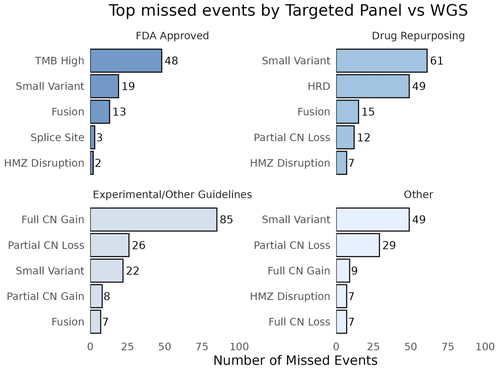


WGS vs Panel Coverage









Panel annotations and abbreviations

Cohort Metadata: WGS - whole genome sequencing, RNASeq - RNA Sequencing, Chemo - Chemotherapy, Targeted - Targeted Therapy, Hormonal - Hormonal Therapy, Immuno - Immunotherapy, Radio - Radiotherapy.
Treatments - some samples received multiple types of treatment. Patients have both pre and post biopsy treatment available. Responders - Complete or partial response based on RECIST criteria.
Tumor Characteristics: TMB - tumor mutational burden, MSI - microsatellite instable, WGD - whole genome doubling, GIE - genetic immune escape, HLA - human leukocyte antigen, LOH - loss of heterozygosity, HRD - homologous recombination deficiency.
Mutational Landscape: SNV - single nucleotide variant, INDEL - insertion or deletion, Structural - structural variant, MNV - multiple nucleotide variant, VDJ - variable–diversity–joining, CDR - Complementarity-determining regions.
Processes Underlying Mutations: Processes estimated based on single base substitutions and trinucleotide contexts. Signatures were fit using deconstructSigs in R with cosmic version 3.4 and grouped based on proposed aetiology.
Copy Number Alteration Profile: Inner ring shows the percentage of tumours with homozygous deletion (dark blue), LOH and significant loss (copy number < 0.6× sample ploidy; blue) and near copy neutral LOH (light blue).
Outer ring shows percentage of tumours with high level amplification (>3× sample ploidy; dark red), moderate amplification (>2× sample ploidy; red) and low level amplification (>1.4 × sample ploidy; light red).
Frequently observed high-level driver gene amplifications (red) and homozygous deletions (blue).

Cancer Driver Landscape, Germline Disposition: Events - events per tumor, TSG - tumor suppressor gene, ONC - oncogene. Summary %'s based on all samples, oncoplots only show samples with atleast 1 event.
Potentially Actionable Events: References Jackson Clinical Knowledgebase database. # Events: FDA - FDA approved, Off - Drug Repurposing, Exp - Experimental/Other Guidelines, Oth - Any other event.
TMB high - tumor mutational burden > 10 mutations per megabase, MSI high - > 4 microsatellite inserts per megabase, Rest * - All remaining potentially actionable events.

Acronym: AYA
DOIDs included: Many
Date created from database: 2024-11-08

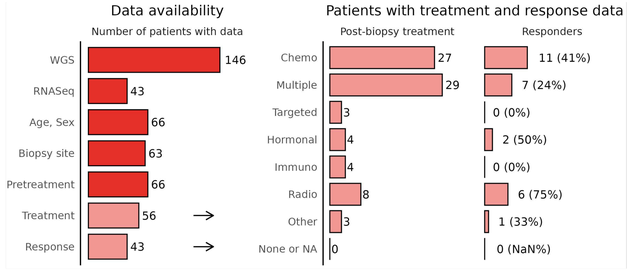
WGS vs Panel Coverage Summary: In-silico coverage study comparing WGS to comprehensive and targeted panels across various genomic biomarkers. WGS actionable biomarkers identified by the Jackson Clinical Knowledgebase (CKB) used as a baseline, and panel coverage determined by rules below:
-Signatures: TMB High and MSI High captured by comprehensive panel (no HRD); only MSI High covered by targeted panel.
-Small variants/splice sites: Coverage measured by comparing genomic coordinates of events to panel BED input files.
-Copy number: Events for panel genes with min copy number < 0.5 or max copy number > 6 assumed covered.
-Other events: Fusions, HMZ (Homozygous) Disruptions, Viral inserts, HLA type assumed not captured by panels.
** See documentation for further details on the WGS vs Panel coverage study.

The Genomic and Actionability Landscape of Breast AYA Cancer

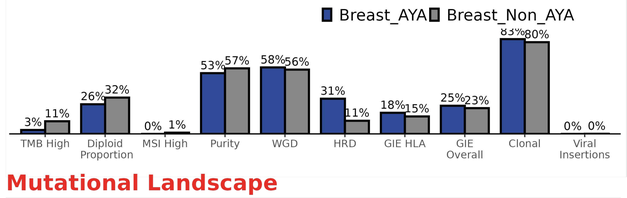
Website: https://www.hartwigmedicalfoundation.nl
Tools: https://github.com/hartwigmedical/hmftools
Database: https://www.hartwigmedicalfoundation.nl/en/data/database/

CC BY NC
CC BY NC: This license enables reusers to distribute, remix, adapt, and build upon the material in any medium nor format for noncommercial purposes only, and only so long as attribution is given to the creator.

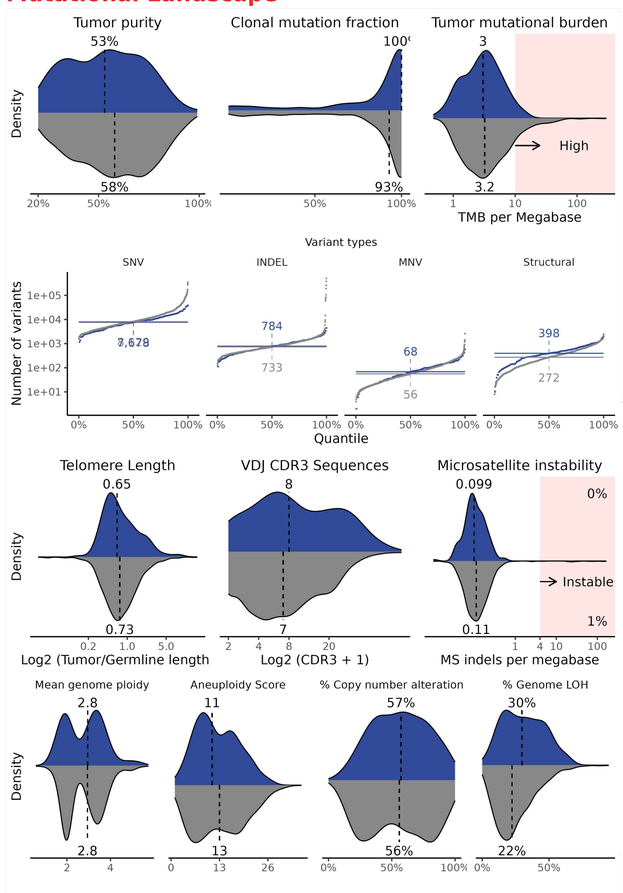
Cohort Metadata



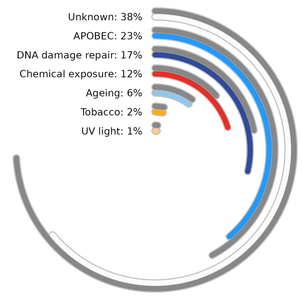
Tumor Characteristics

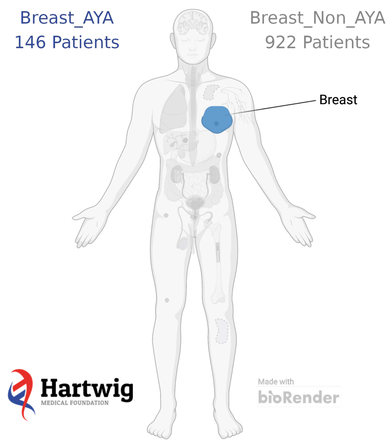


Mutational Landscape

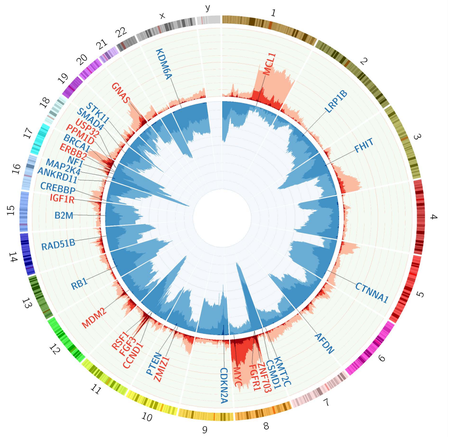


Processes Underlying Mutations

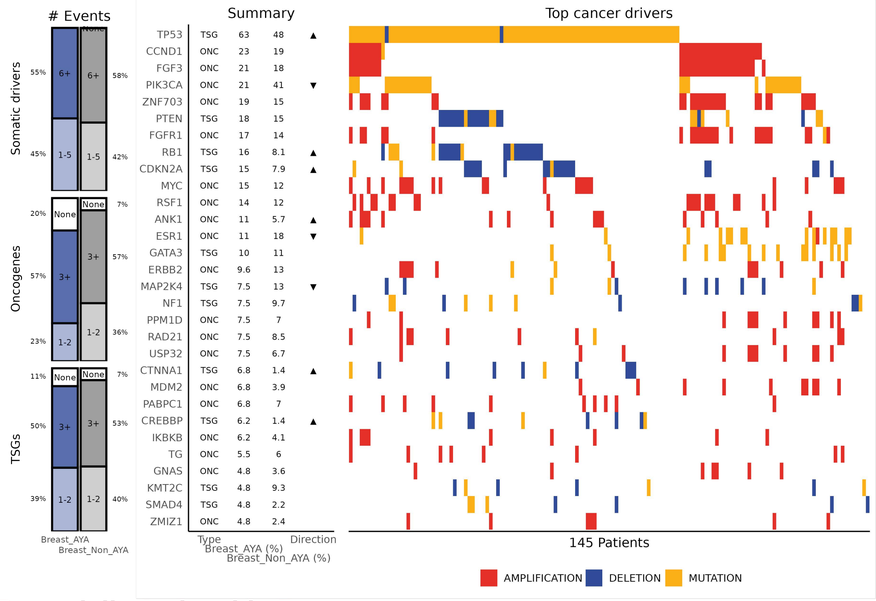




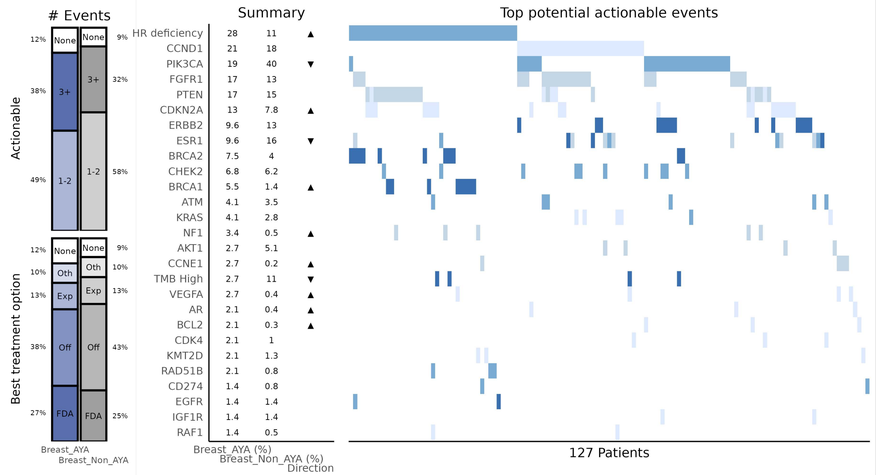
Copy Number Alteration Profile



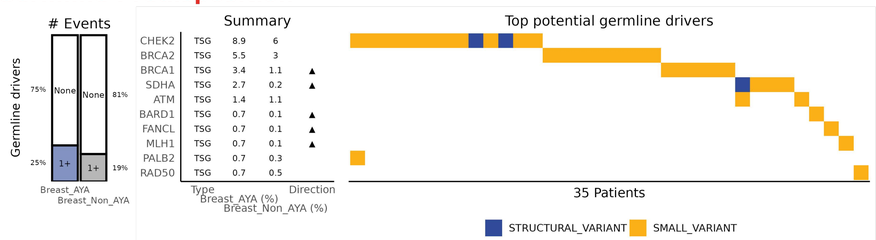
Cancer Driver Landscape



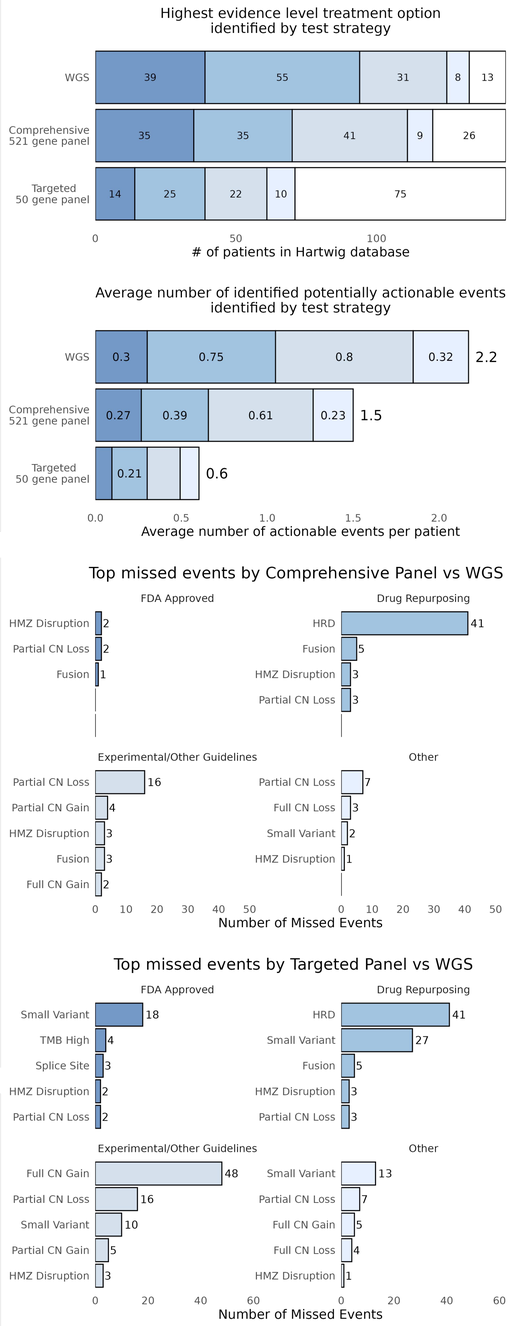
Potentially Actionable Events



Germline Predisposition



WGS vs Panel Coverage



Panel annotations and abbreviations

Cohort Metadata: WGS - whole genome sequencing, RNASeq - RNA Sequencing, Chemo - Chemotherapy, Targeted - Targeted Therapy, Hormonal - Hormonal Therapy, Immuno - Immunotherapy, Radio - Radiotherapy.
Treatments - some samples received multiple types of treatment. Patients have both pre and post biopsy treatment available. Responders - Complete or partial response based on RECIST criteria.
Tumor Characteristics: TMB - tumor mutational burden, MSI - microsatellite instable, WGD - whole genome doubling, GIE - genetic immune escape, HLA - human leukycte antigen, LOH - loss of heterozygosity, HRD - homologous recombination deficiency.
Mutational Landscape: SNV - single nucleotide variant, INDEL - insertion or deletion, Structural - structural variant, MNV - multiple nucleotide variant, VDJ - variable-diversity-joining, CDR - Complementarity-determining regions.
Processes Underlying Mutations: Processes estimated based on single base substitutions and trinucleotide contexts. Signatures were fit using deconstructSigs in R with cosmic version 3.4 and grouped based on proposed aetiology.
Copy Number Alteration Profile: Inner ring shows the percentage of tumours with homozygous deletion (dark blue), LOH and significant loss (copy number < 0.6× sample ploidy; blue) and near copy neutral LOH (light blue).
Outer ring shows percentage of tumours with high level amplification (>3× sample ploidy; dark red), moderate amplification (>2× sample ploidy; red) and low level amplification (>1.4 × sample ploidy; light red).
Frequently observed high-level driver gene amplifications (red) and homozygous deletions (blue).

Cancer Driver Landscape, Germline Disposition: Events - events per tumor, TSG - tumor suppressor gene, ONC - oncogene. Summary %'s based on all samples, oncoplots only show samples with atleast 1 event.
Potentially Actionable Events: References Jackson Clinical Knowledgebase database. # Events: FDA - FDA approved, Off - Drug Repurposing, Exp - Experimental/Other Guidelines, Oth - Any other event.
TMB high - tumor mutational burden > 10 mutations per megabase, MSI high - > 4 microsatellite inserts per megabase, Rest * - All remaining potentially actionable events.

Acronym:
DOIDs included: 1612,60076,60080,60081,3459,60075,3007,60079,50938
Date created from database: 2024-11-08

WGS vs Panel Coverage Summary: In-silico coverage study comparing WGS to comprehensive and targeted panels across various genomic biomarkers. WGS actionable biomarkers identified by the Jackson Clinical Knowledgebase (CKB) used as a baseline, and panel coverage determined by rules below:
-Signatures: TMB High and MSI High captured by comprehensive panel (no HRD); only MSI High covered by targeted panel.
-Small variants/splice sites: Coverage measured by comparing genomic coordinates of events to panel BED input files.
-Copy number: Events for panel genes with min copy number < 0.5 or max copy number > 6 assumed covered.
-Other events: Fusions, HMZ (Homozygous) Distruptions, Viral inserts, HLA type assumed not captured by panels.
** See documentation for further details on the WGS vs Panel coverage study.