PEVO^data

# PEVO basket trial, combining immunotherapy with an epidrug in squamous cell carcinomas

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Gábor Balogh

## Introduction

PEVO: <u>Pe</u>mbrolizumab <u>Vo</u>rinostat:

– Combination Therapie:
  ▶ combining multiple drugs in one therapy approach
– Basket trial:
  ▶ including multiple cancer "types" in one study approach (i.e. different sites of origins)
– Individualised/personalised medicine:
  ▶ designing an individual, patient suited therapy approach on the basis of known biomarkers

## Introduction

Combining immunotherapy with an epidrug: -> increasing the ORR (overall response rate)

– Pembrolizumab:

- ▶ immunodrug, Checkpoint inhibitor
- ▶ humanized antibody used in cancer immunotherapy that treats melanoma, lung cancer, head and neck cancer, Hodgkin lymphoma, stomach cancer, and cervical cancer.
- ▶ targets the programmed cell death protein/ligand interaction (PD-1/PD-L1) between lymphocytes and cells (binds and blocks PD-1 located on lymphocytes)

# Introduction

– Vorinostat:

  ▶ epidrug
  ▶ Histone deacetylase inhibitors (HDI)
  ▶ Vorinostat's inhibition of histone deacetylases results in the accumulation of
    acetylated histones and proteins, including transcription factors crucial for the
    expression of genes

# PEVO trial study design

Patientinclusion:



PEVO<sup>SQ</sup> inclusions

✓ Inclusions completed Early May 2022

Cumulated inclusions
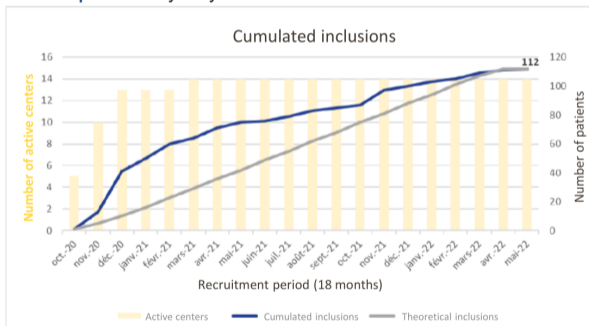
**further reading:**

E de Guillebon et al.:

Combining immunotherapy with an epidrug in squamous cell carcinomas of different locations: rationale and design of the PEVO basket trial biomarkers following the pembrolizumab and vorinostat treatment

**Snakemake:**

DAG:

**Pipelines:**



| RNAseq | |
|---|---|
| **Task** | **Tool** |
| trimming | Trimgalore |
| quality check | fastqc |
| mapping | STAR |
| counting alignments for each FLAG | samtools flagstat |
| mark duplicates | picard markdup |
| variant calling | bcf-tools mpileup/ varscan2 |
| variant annotation | ensemble vep + SnpEff |
| variant interpretation | Annovar |
| gene counting | featurecounts |
| fusions | fusioncatcher + arriba |
| sequence classification | Kraken2 |
| circular rnas | ciri2 |

| WES | |
|---|---|
| **Task** | **Tool** |
| trimming | Trimgalore |
| quality check | fastqc |
| mapping | BWA-MEM |
| counting alignments for each FLAG | samtools flagstat |
| mark duplicates | picard markdup |
| ( Base Quality Score Recalibration | GATK - BQSR ) |
| variant calling | deepvariant + bcf-tools + lofreq neusomatic + mutect2 + lofreq_somatic |
| variant annotation | ensemble vep |
| variant interpretation | Annovar |
| cnv calling | cn.Mops  Excavator 2  cnv_kit |
| coverage | mosdepth |
| sequence classification | Kraken2 |

**preliminary results:**

– WES-SNP
  - ▶ somatic:
      - ▶ lofreq_somatic
      - ▶ neusomatic
      - ▶ mutect_2
      - ▶ dragen_somatic

**preliminary results:**

– WES-SNP
  ► somatic:
    ► lofreq_somatic
    ► neusomatic
    ► mutect_2
    ► dragen_somatic
  ► germline:
    ► deepvariant
    ► bcf_tools
    ► lofreq
    ► dragen_germline

**somatic SNPs:**



Venn Diagram for snps:
mutect2_somatic_filtered, lofreq_somatic, dragenNEW_somatic, neusomatic_passed_filtered

Legend:
- mutect2_somatic_filtered
- lofreq_somatic
- dragenNEW_somatic
- neusomatic_passed_filtered

**somatic SNPs:**



SNP found by different callers

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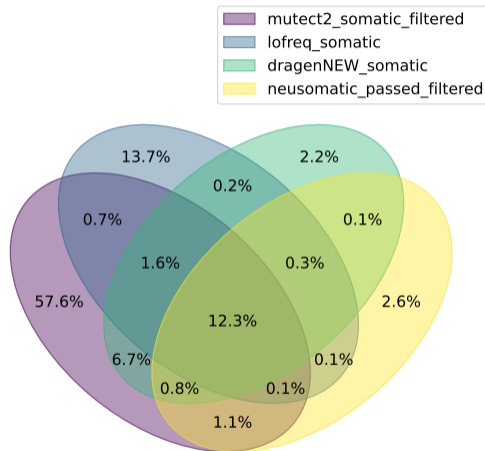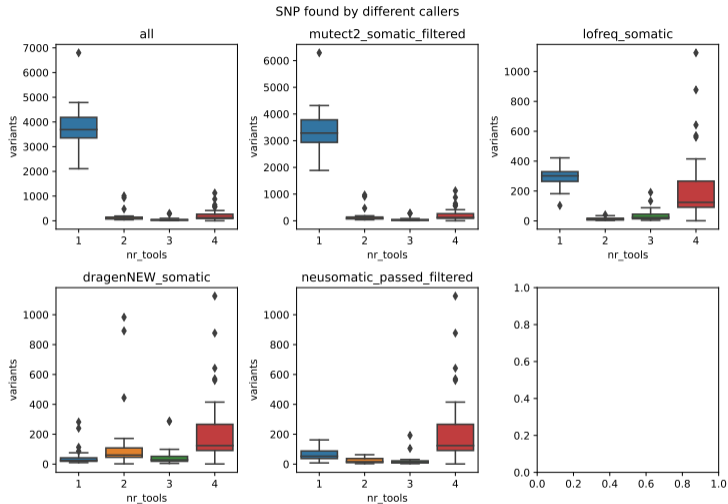
**germline SNP:**



Venn Diagram for snps:
lofreq, dragenNEW_germline, bcf_bed, deepvariant_passed_filtered

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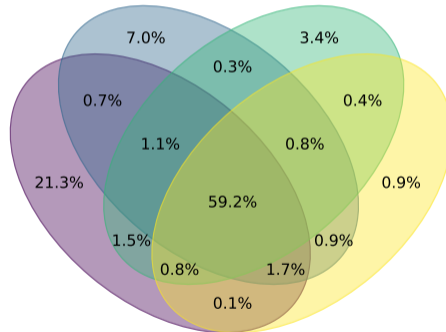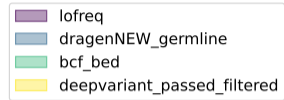
**germline SNP:**



SNP found by different callers, germline
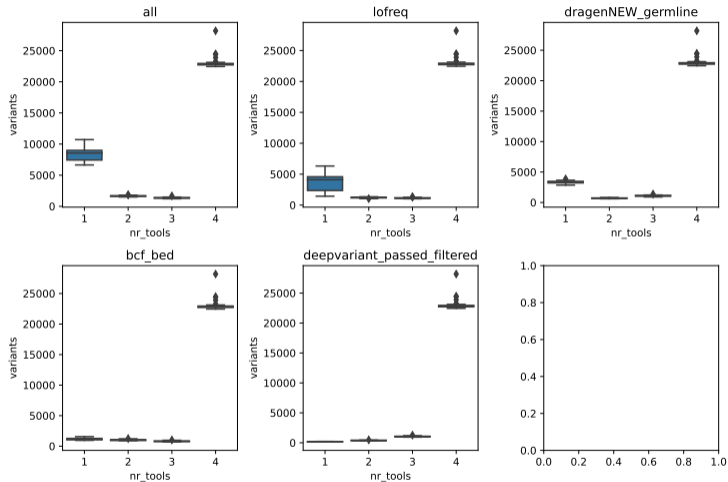
**Fusion tools:**
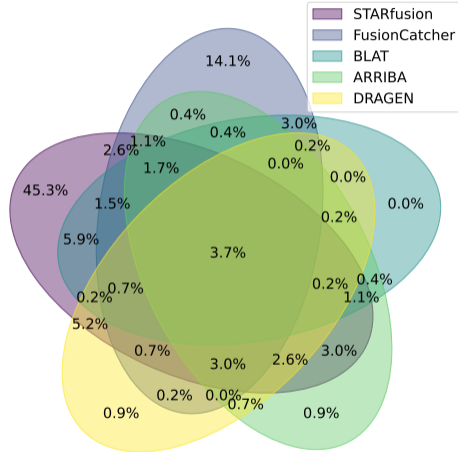
– StarFusion
– FusionCatcher
– Arriba
– Dragen

**Fusion tools:**

– StarFusion
– FusionCatcher
– Arriba
– Dragen
– all of them are validated with FusionInspector
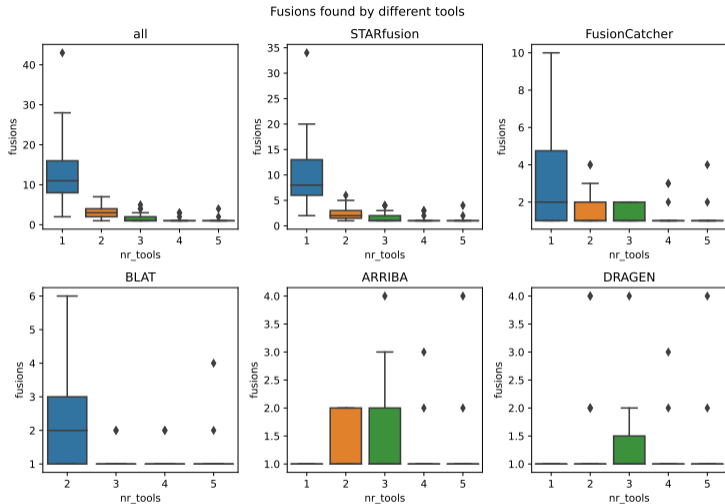– semiautomated BLAT verification

**preliminary results:**



Venn Diagram for Fusions:
STARfusion, FusionCatcher, BLAT, ARRIBA, DRAGEN

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**preliminary results:**



Fusions found by different tools

# Thank You!

**Gábor Balogh**

IZBI Leipzig
Department for Computer Science

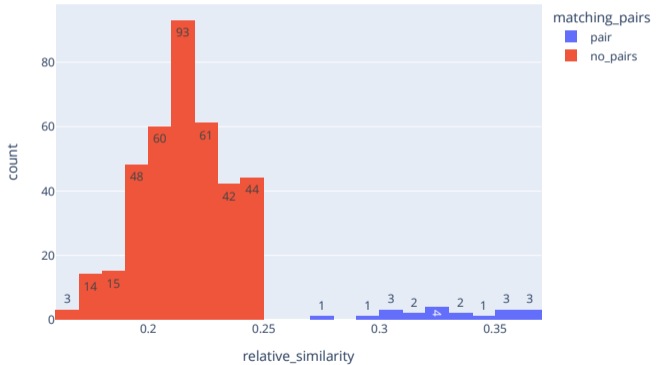gabor@bioinf.uni-leipzig.de

https://www.bioinf.uni-leipzig.de

**our preliminary results:**

TIS-DNA – TIS-RNA sample pairing:

relative shared variants between DNA and RNA

**our preliminary results:**

DNA BLD-TIS sample pairing:

relative shared variants between BLD and TIS