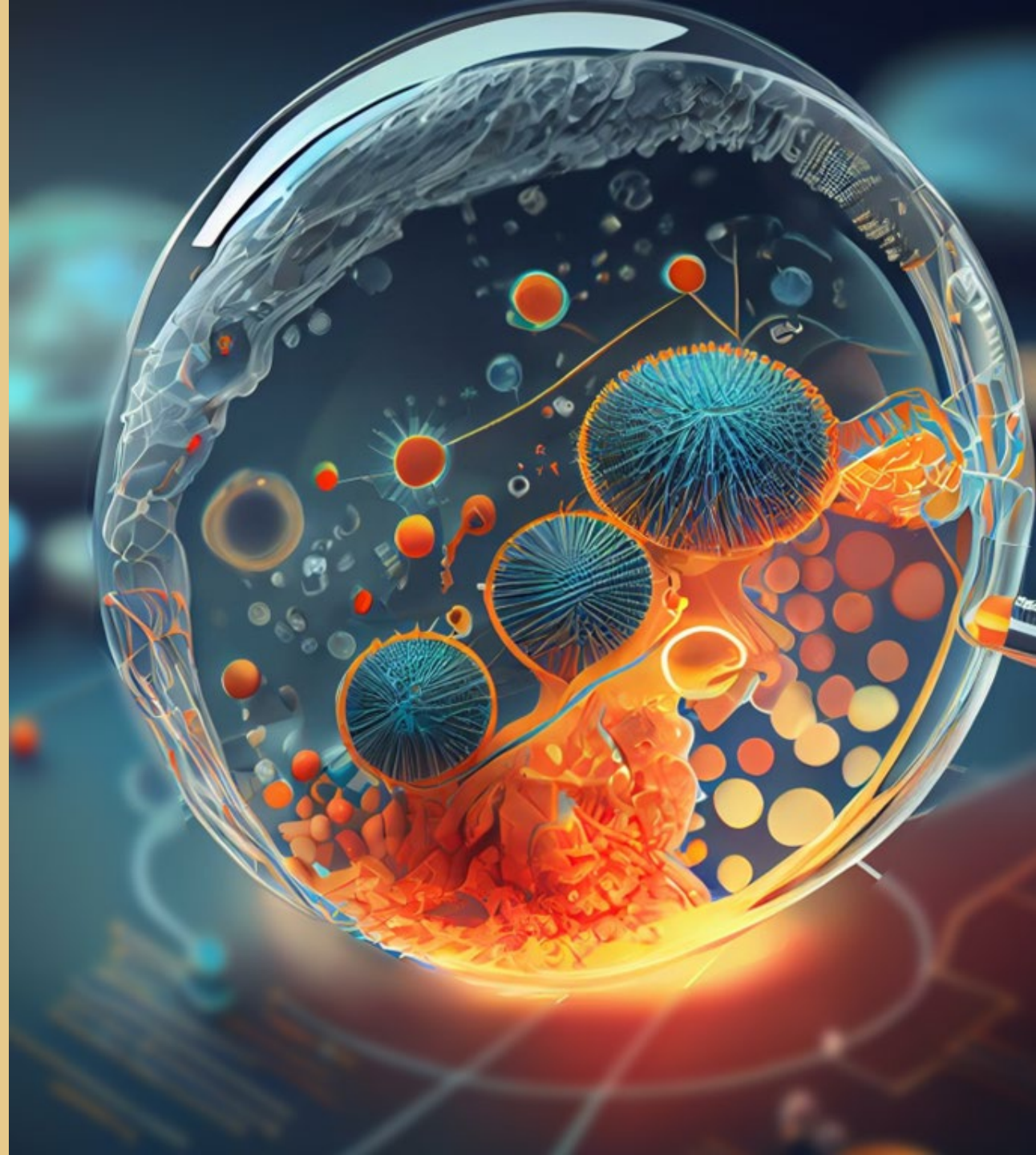


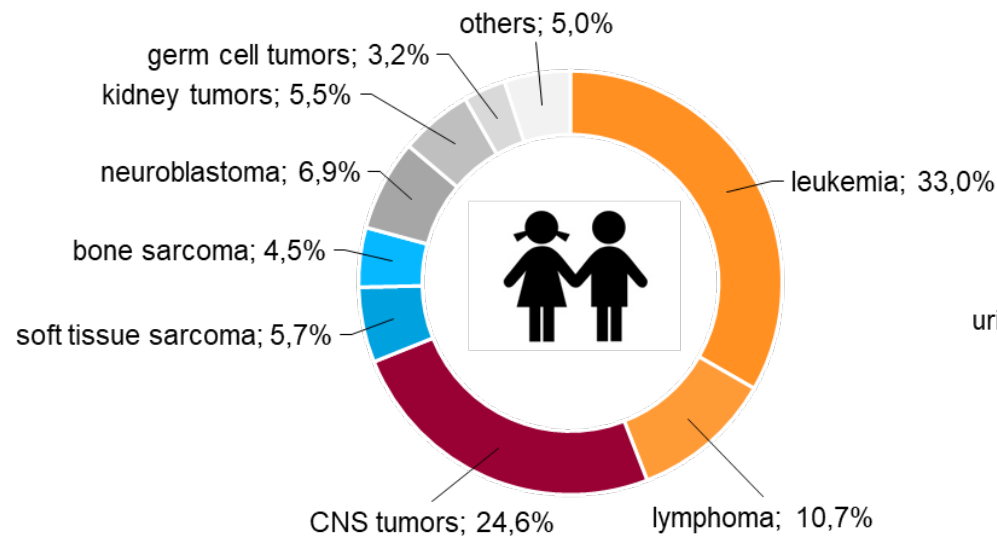
 eha **Sf(PM)**

# The pediatric drug sensitivity profiling

Sept 25th, 2024; Prof. Dr. Ina Oehme, Hopp Children's  
Cancer Center, Heidelberg, Germany

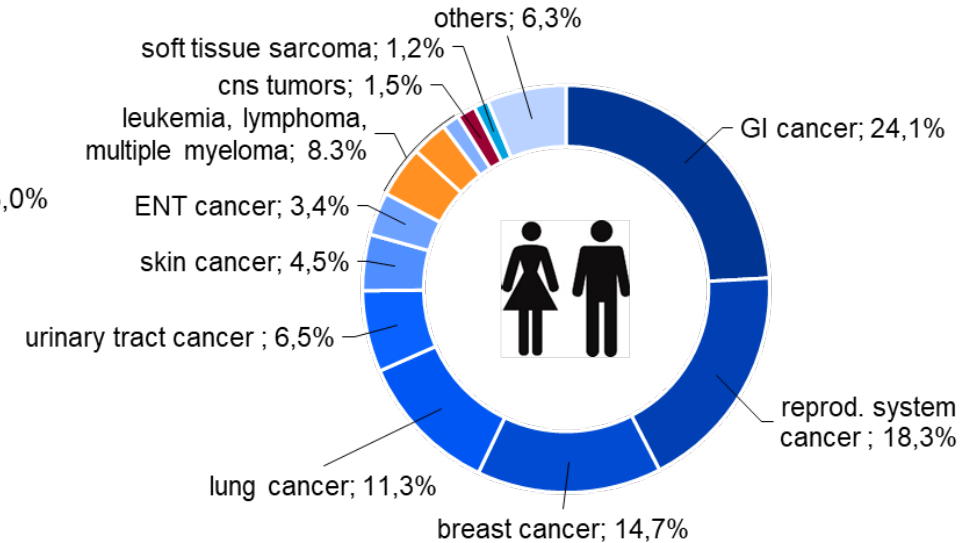


# Pediatric



~1%

# Oncology



~99%

- Cancer diagnoses in children are completely different from adults (children are not small adults)
- Cancer in children is very rare (2000 cases per year in Germany)
- European and global collaboration required at all levels (PMC, Curie, ZERO, ...)

# Pediatric

# Oncology

- High cure rates (80%) for children with new cancer diagnoses achieved



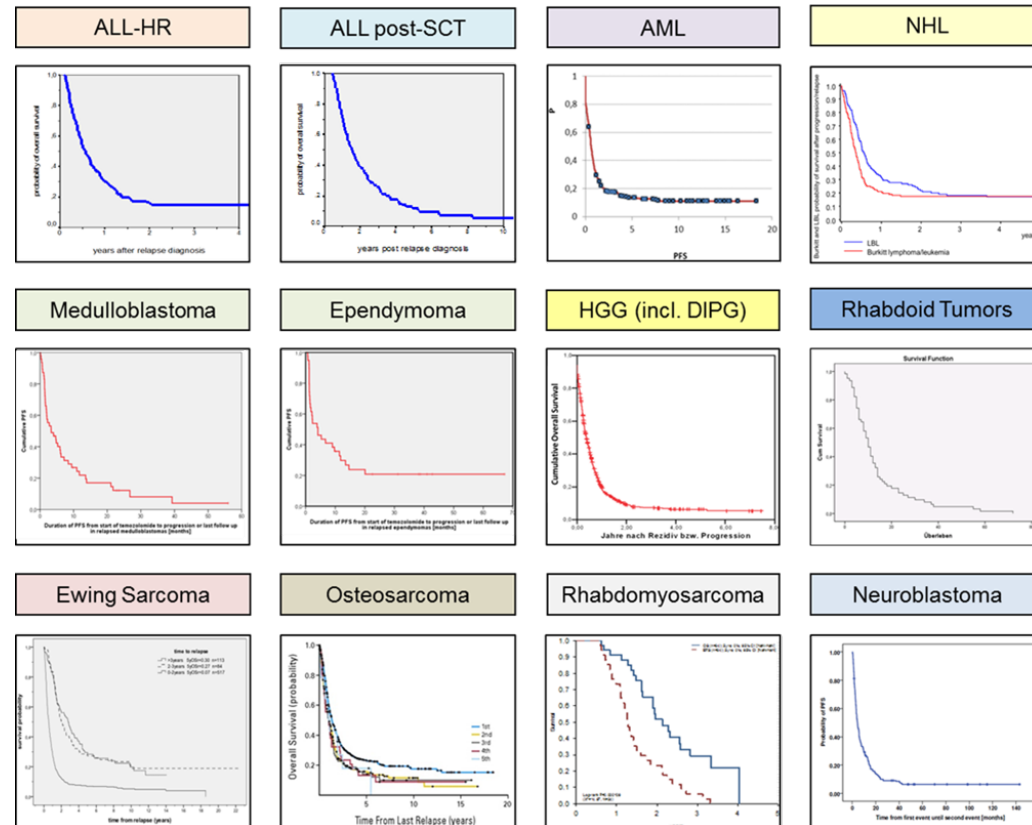
# Pediatric

# Oncology



- High cure rates (80%) for children with new cancer diagnoses achieved
- almost all children die if tumor comes back (solid tumors, high grade brain tumors)

INFORM cohorts - Survival at relapse



# Pediatric Precision Oncology - INFORM

- High cure rates (80%) for children with new cancer diagnoses achieved
- almost all children die if tumor comes back (solid tumors, high grade brain tumors)



13 countries, >100 centers,  
>2500 patients enrolled



➔ IDENTIFICATION OF MOLECULAR TARGETS

## Since Feb 2023:

some of the German health insurance companies cover the costs of INFORM services

# INFORM Molecular Targets Study Results

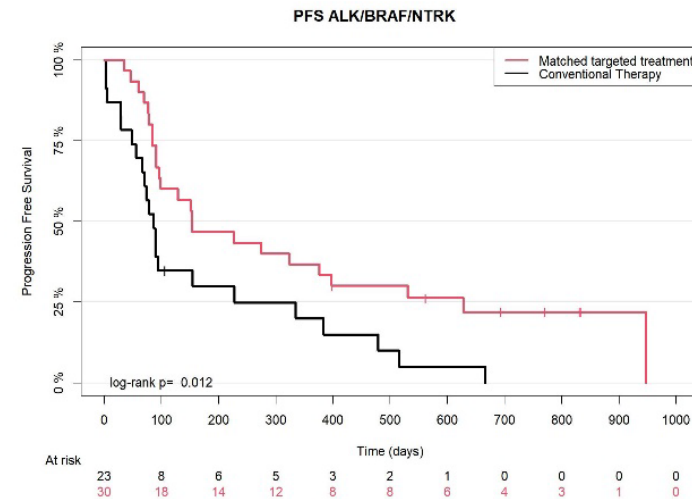


● PFS doubling in patients with „high priority“ target and matched therapy  
→ precision oncology shows the potential to extend survival in children

● **“high priority” targets (8%):**

- ALK and BRAF mutations
- *MET* and *NTRK* fusion

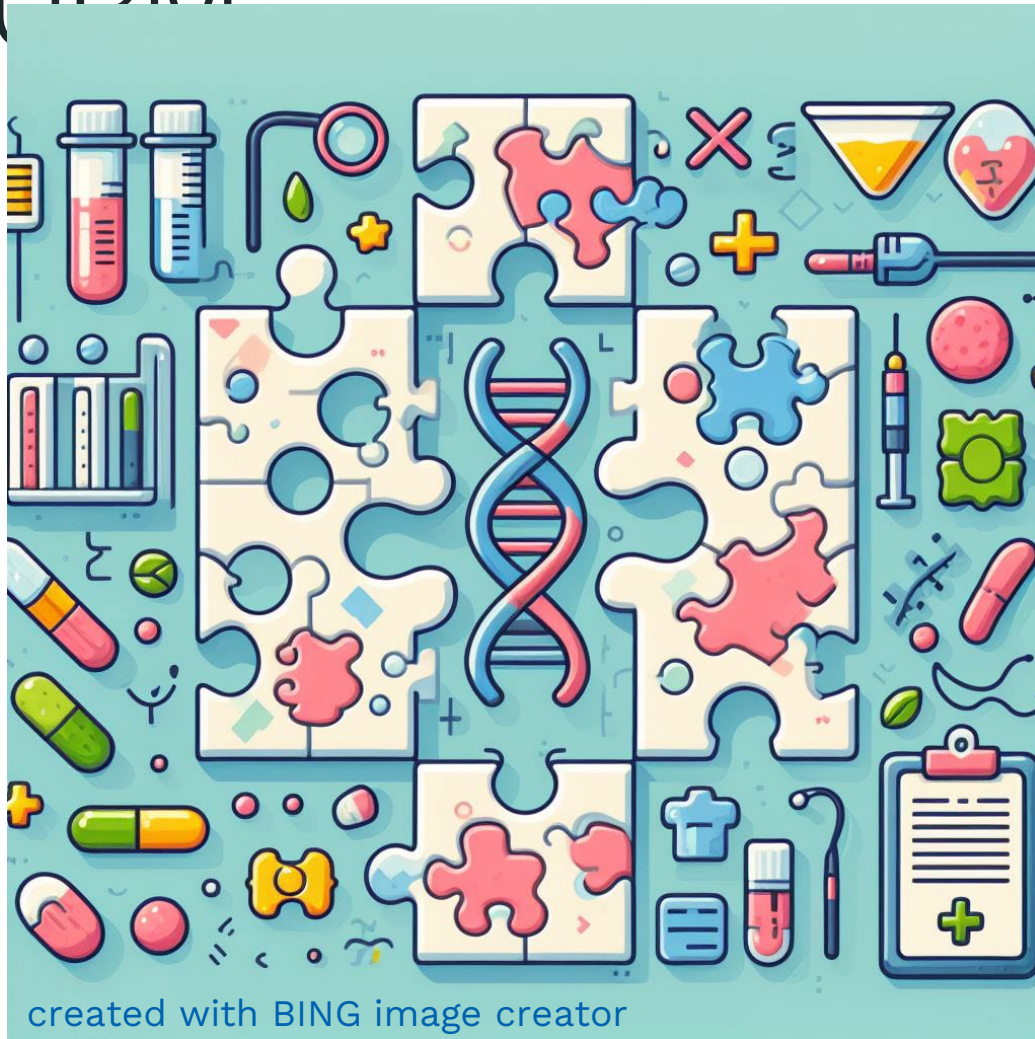
● other targets: no significant differences



Van Tilburg, Pfaff, Pajtler et al., *Cancer Discovery* 2021  
Heipertz, van Tilburg et al. *JCO Prec Oncol* 2023

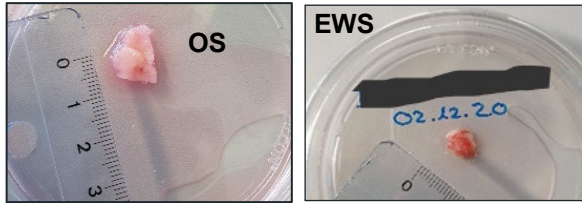
➔ **FURTHER LAYERS OF E.G., FUNCTIONAL DATA SHOULD BE ADDED**

# Functional Precision Medicine within INFORM

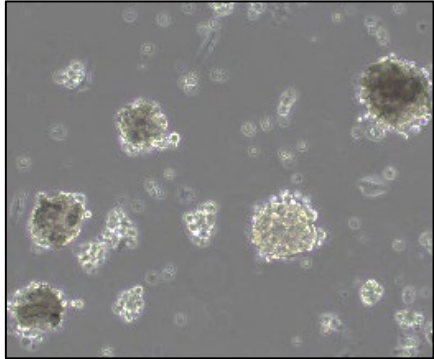


establishment of a cohort-based  
predictive drug response classification  
pipeline  
for fresh-tissue organoid-like cultures  
obtained through INFORM

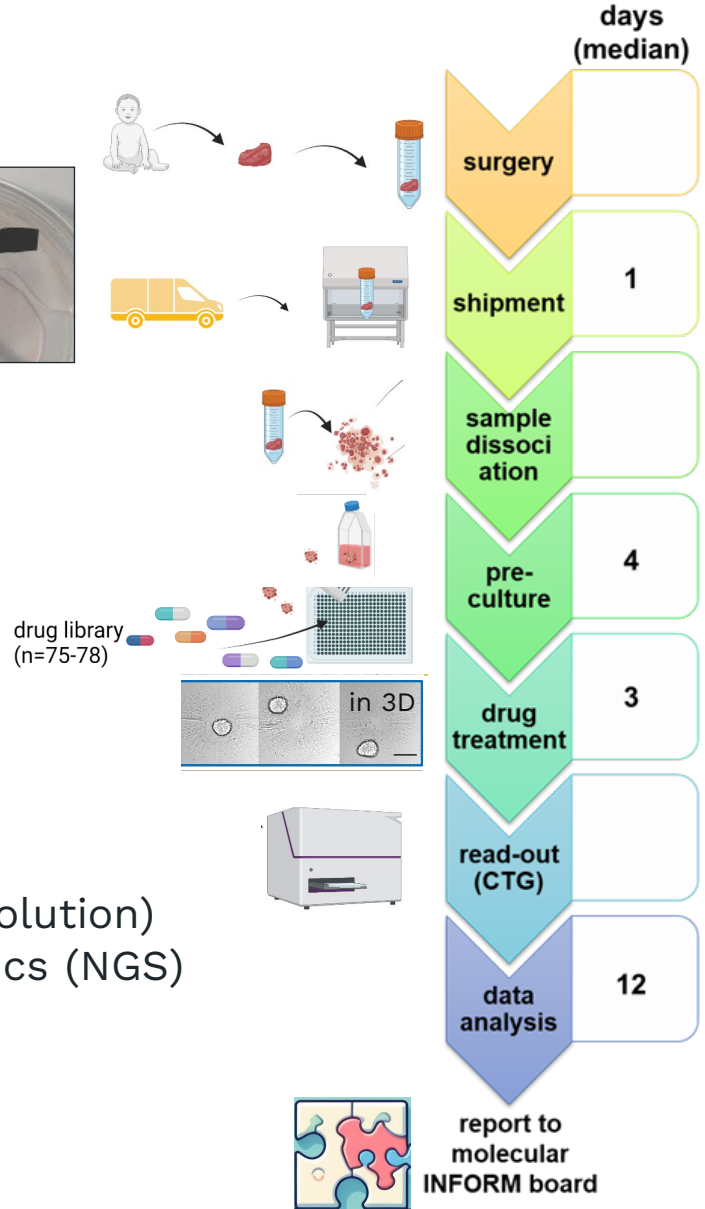
# Workflow



patient-derived 3D multicellular  
fresh tissue culture (FTC)  
in serum-free / stem cell medium

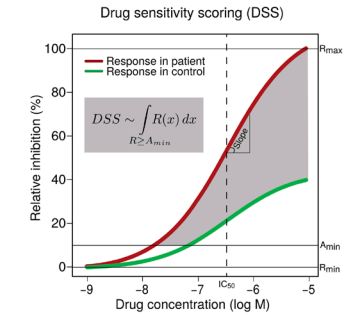
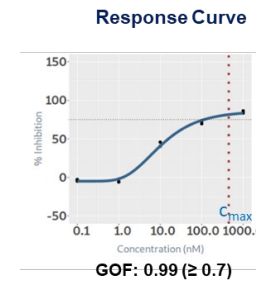
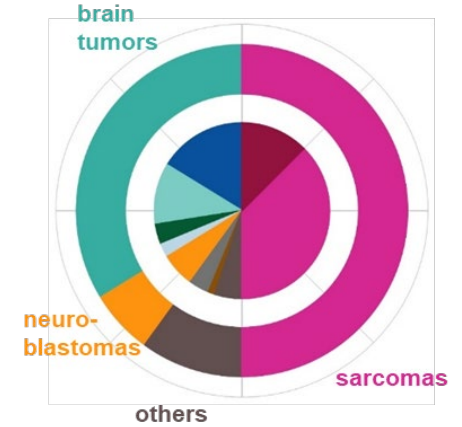


→ multicellular (RNAseq deconvolution)  
→ stable molecular characteristics (NGS)

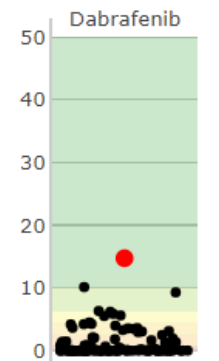


> 80 samples / year

~ 20 d



Yadav et al. *Sci Rep* (2014).





predictive



drug A

# DSP as predictive biomarker for response



1) DSP of cell lines (positive models) identifies expected drugs

$BRAF^{V600E}$ : 2/2 BRAFi (dabrafenib, vemurafenib); 3/3 MEKi (cobimetinib, selumetinib, trametinib)

$MET_{fusion}$ : 4/4 METi (cabozantinib, foretinib, merestinib, crizotinib)

$ALK_{amp}$ : 5/5 ALKi (alectinib, ceritinib, entrectinib, lorlatinib, crizotinib)

$ALK_{fusion}$ : 5/5 ALKi (alectinib, ceritinib, entrectinib, lorlatinib, crizotinib)

BCR-ABL: 5/5 ABLi (dasatinib, imatinib, nilotinib, ponatinib, vandetanib)

$NTRK_{fusion}$ : 3/3 NTRKi (larotrectinib, selitrectinib, entrectinib)

$PIK3CA_{mut}$ : 1/1 PI3Ki (alpelisib)

etc.

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**Immune Profiling**

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Ministerium für Ländlichen Raum und Verbraucherschutz Baden-Württemberg



DKTK German Cancer Consortium



Graphics  
 BioRender  
 Bing Image Creator



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