



Lungentumorboard

Freitag, 22.04.2022, 17:00 bis 17:45

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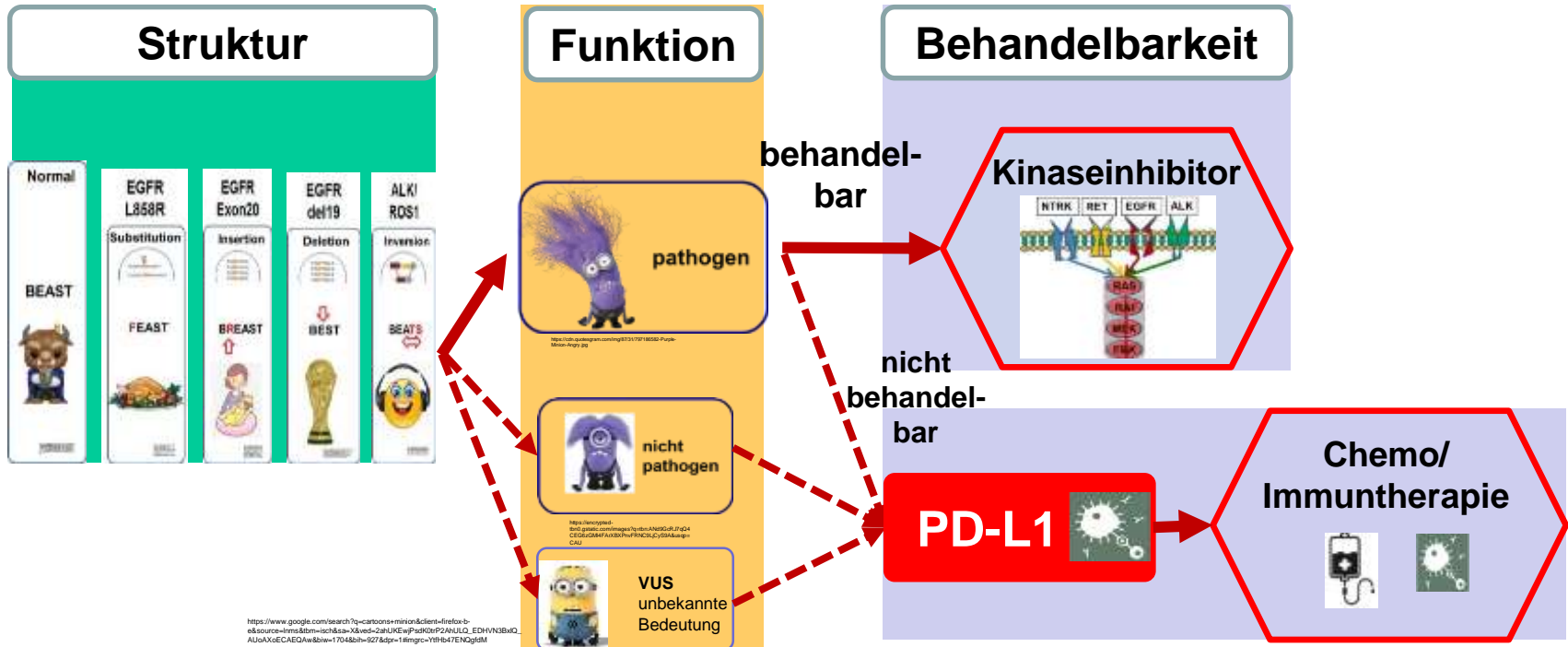
Pneumologie, Hannover
Pathologie, Hannover
Radiologie, Göttingen
Strahlentherapie, Göttingen
Onkologie, Göttingen

Fall 1

Der klinische Fall wird in der öffentlich zugänglichen Fassung ausgeblendet.

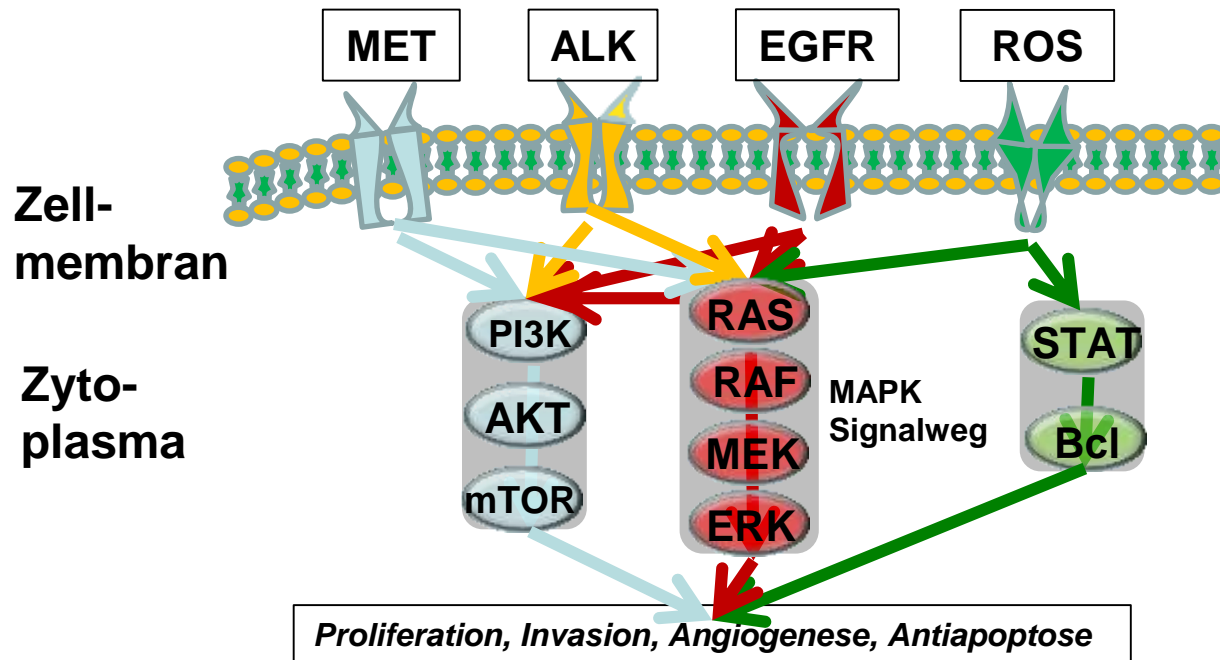
Fall 1

Genetische Alteration



https://www.google.com/search?q=cartoons+minion&client=firefox-b&source=msn&sm=isch&sa=X&ved=2ahUKEwPz0R0P2ANULQ_EdHYN3BwQ_AJl0AxeCAEQAw&biw=1704&bih=577&pg=1#img=1YF647ENq8tM

Fall 1



Fall 1

EGFR

- Gefitinib
- Erlotinib
- Afatinib
- Osimertinib
- Dacomitinib

ALK

- Crizotinib
- Alectinib
- Brigatinib
- Lorlatinib
- Ceritinib

BRAF

- Dabrafenib + Trametinib

ROS1

- Crizotinib
- Entrectinib

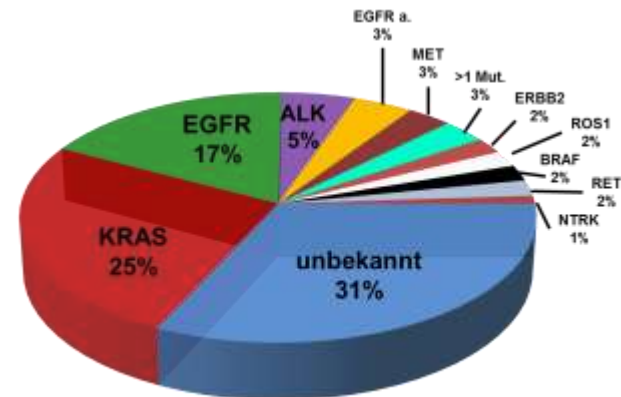
KRAS

- Sotorasib



Big Five

https://www.africa-royal-tours.de/media/_processed_/b/3/csm_Namibia-Reise-Big-Five-Collage_e21b3d6525.jpg



RET

- Selpercatinib
- Pralsetinib

NTRK

- Larotrectinib
- Entrectinib

MET

- Tepotinib

Fall 1

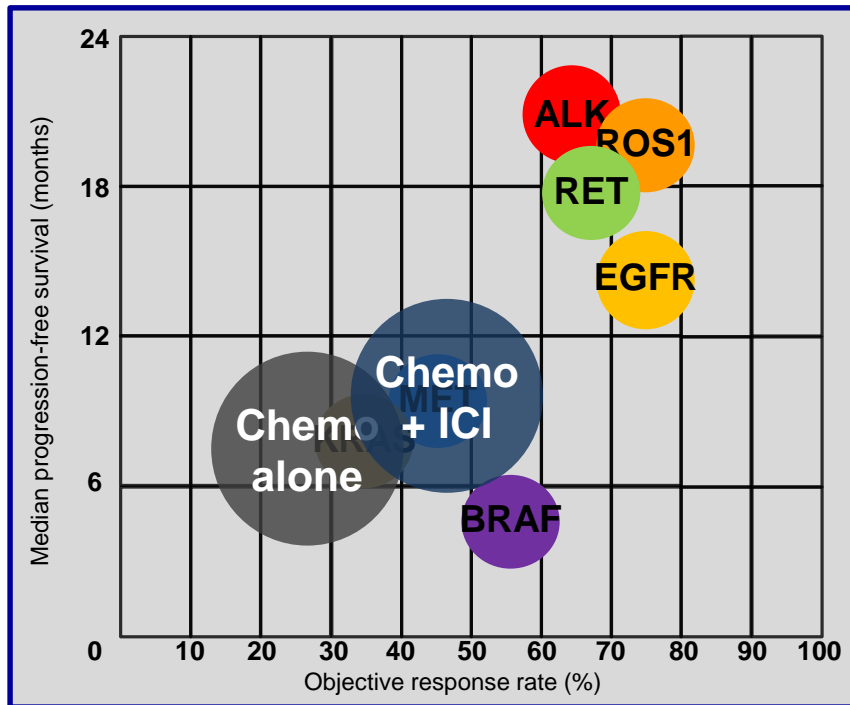
The Clinical Knowledgebase (CKB)

Powered by The Jackson Laboratory

BRAF D594N	gallbladder cancer	predicted - sensitive	<ul style="list-style-type: none"> MEK inhibitor (Pan) MEK1 inhibitor MEK2 inhibitor 	Bisimertinib + Encorafenib	Case Reports/Case Series	Actionable	In a Phase II trial (BEAVER), Mektovi (bisimertinib) and Braflovi (encorafenib) combination therapy resulted in stable disease in a patient with gallbladder cancer harboring BRAF D594N (<i>J Clin Oncol</i> 39, no. 15_suppl, abstr e15038; NCT03839342).
BRAF D594N	female reproductive organ cancer	no benefit	<ul style="list-style-type: none"> MEK inhibitor (Pan) MEK1 inhibitor MEK2 inhibitor 	Trametinib	Case Reports/Case Series	Actionable	In a Phase II trial (NCI-MATCH), Mekinist (trametinib) treatment did not demonstrate clinical activity in patients with advanced solid tumors or lymphoma harboring BRAF fusion or non-V600 mutations, resulted in stable disease in a patient with gynecological cancer harboring BRAF D594N (PMID: 31924734; NCT02465060).
BRAF D594N	lung non-small cell carcinoma	predicted - sensitive		EMC-4150	Preclinical - Pdx	Actionable	In a preclinical study, RMC-4150 treatment resulted in decreased Erk phosphorylation and dose-dependent tumor growth inhibition in patient-derived xenograft (PDX) models of non-small cell lung cancer harboring BRAF D594N (PMID: 30104724).
BRAF D594N	Advanced Solid Tumor	predicted - resistant		Vemurafenib	Preclinical - Cell culture	Actionable	In a preclinical study, Zelboxaf (vemurafenib) did not reduce activation of Mek in transformed cells expressing BRAF D594N in culture (PMID: 24783719).

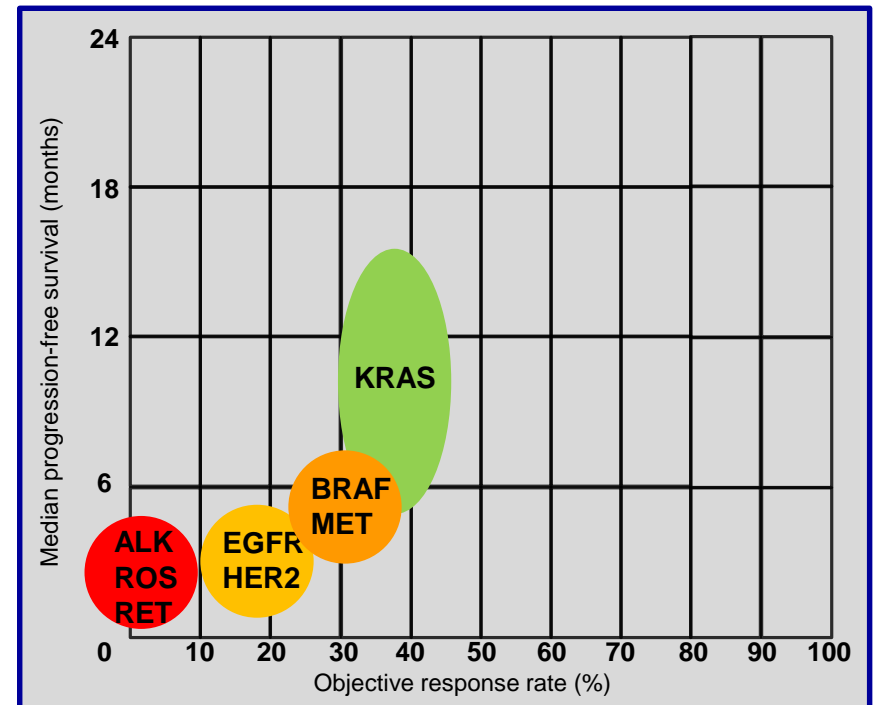
Fall 1

Kinaseinhibitoren



mod. nach Nokin et al. Trends Cancer 2020 10.1016/j.trecan.2020.11.005

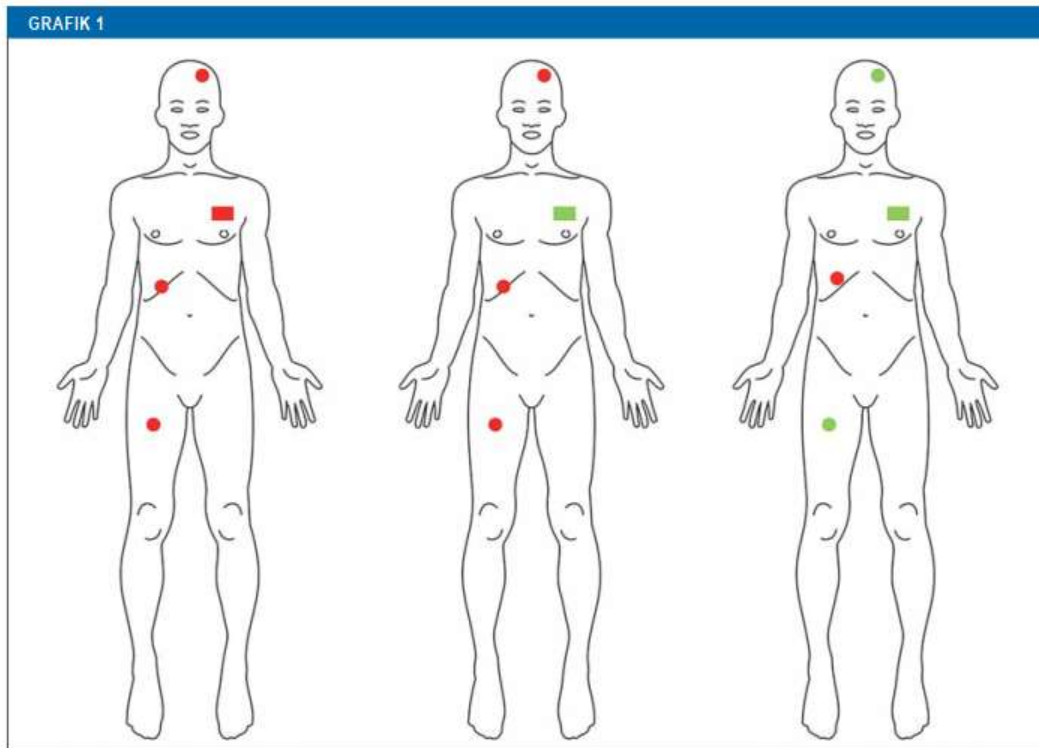
Monoimmuntherapie



mod. nach Mazieres et al. Ann Oncol 2019 30:1321; Dantoing et al. Int J Mol Sci 2021 22:6288; Seegobin et al. Front Oncol 2021 11:750657

Metastasierung

synchron, metachron (OMD)
Oligoprogression (OPD)



Schematische Darstellung unterschiedlicher Metastasierungskonzepte

Links: synchrone Oligometastasierung: gleichzeitiges Auftreten von Primärtumor (Rechteck) und Metastasen (Kreis).

Mitte: metachrone Oligometastasierung: Bei einem kontrollierten Primärtumor (grünes Rechteck) treten nachfolgend Metastasen (Kreis) auf.

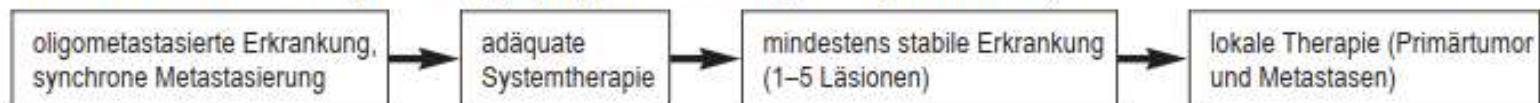
Rechts: Oligoprogression: Eine systemische Therapie kontrolliert Primärtumor (grünes Rechteck) und Metastasen (grüner Kreis).

Einzelne Metastasen sprechen nicht an (roter Kreis).

Optionen bei OMD und OPD

GRAFIK 2

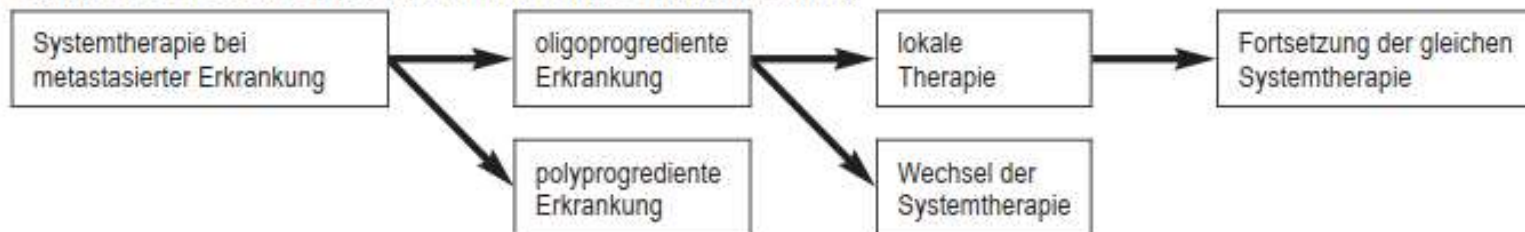
konsolidierende Lokalthherapie analog (14, 16) (nichtkleinzelliges Lungenkarzinom)



Lokalthherapie bei metachroner Oligometastasierung analog (9) (verschiedene Histologien)



Oligoprogression analog (e12) (nichtkleinzelliges Lungenkarzinom)



Darstellung möglicher Therapiealgorithmen bei Oligometastasierung und Oligoprogression.

TAPISTRY

BRAF Klasse II / III Mutationen

Biomarker Definitions - Protocol Version 2

TAPISTRY

Cohort I
Belvarafenib

Gene **FUSION** positivity: 3' *BRAF* fusion with a protein coding 5' gene fusion partner, which are predicted to be in frame with an intact kinase domain

OR

Table 1 List of Eligible BRAF Class II Mutations

Category	Eligible Mutations		
In-frame deletions	N486_P490del	T488_Q493delinsK	V600_K601delinsE
	N486_A489delinsK	A489_Q493del	V600_R603del
	T488_P492del	P490_Q494del	K601_W604del
Single-nucleotide variants	T241M/R	G464 V/E/R/A	A598V
	P367L/S	G469 A/V/R/S	T599 I/K/R
	E451Q	L485W/F	K601X ^a
	R462I	E586K	A728V
	I463S	L597 Q/R/S/V	

BRAF
D594N-Mutation

Cohort J
Belvarafenib

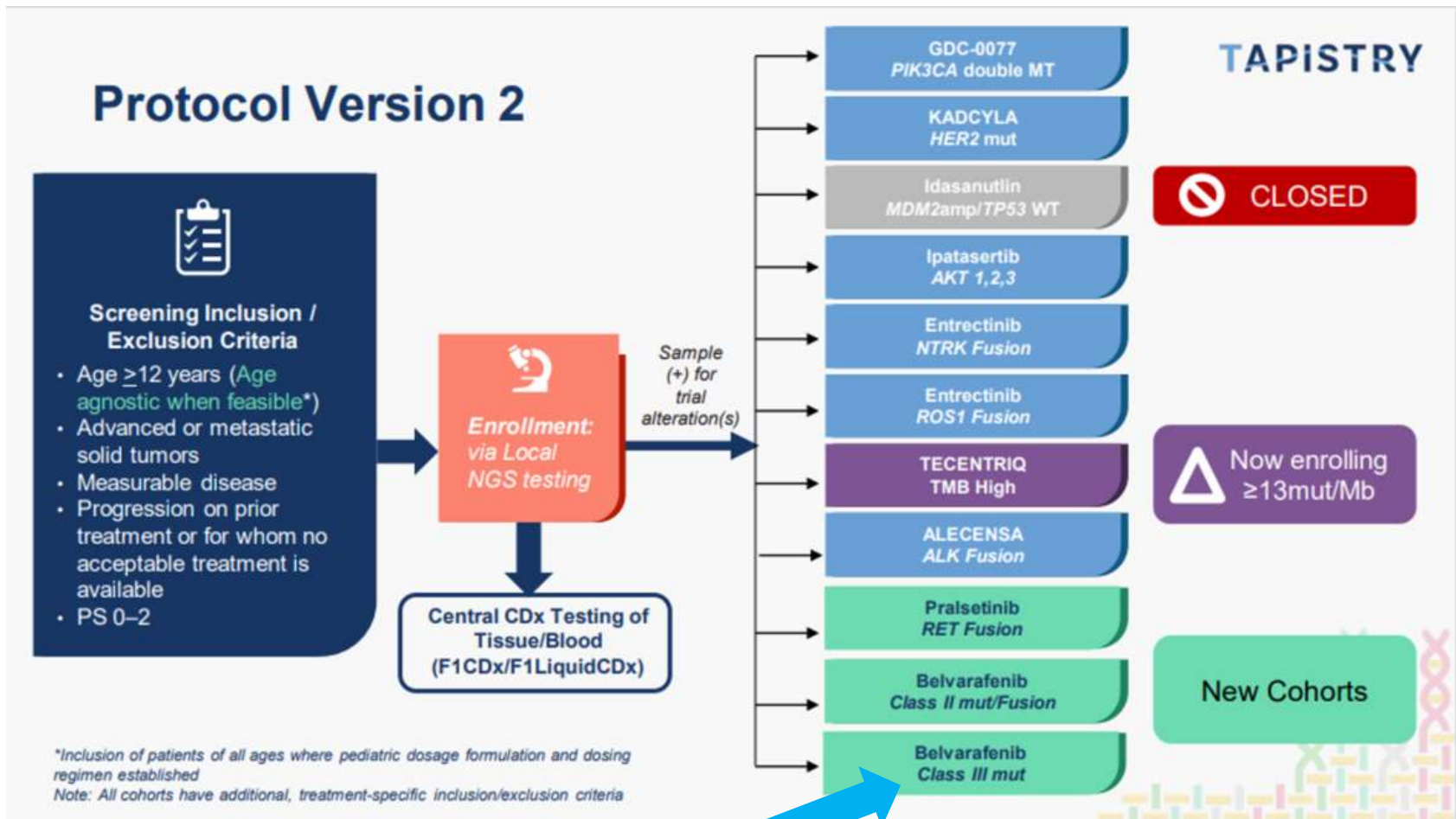
Table 1 List of Eligible BRAF Class III Mutations

D287H/Y	G469E	N581X ^a	G596X ^a
V459L	V471F	L584F	
G466X ^a	K483M/E	D594X ^a	
S467A/E/L	E501X ^a	F595L	

^a "X" denotes "any other amino acid."

TAPISTRY

Basket-Studie

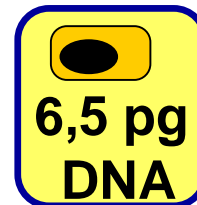
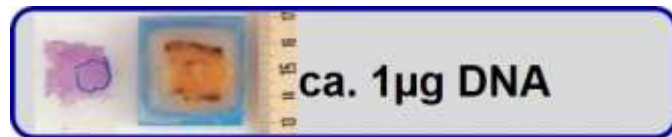


Fall 2


Der klinische Fall wird in der öffentlich zugänglichen Fassung ausgeblendet.

Fall 2

Sequenzierung als Biomarker



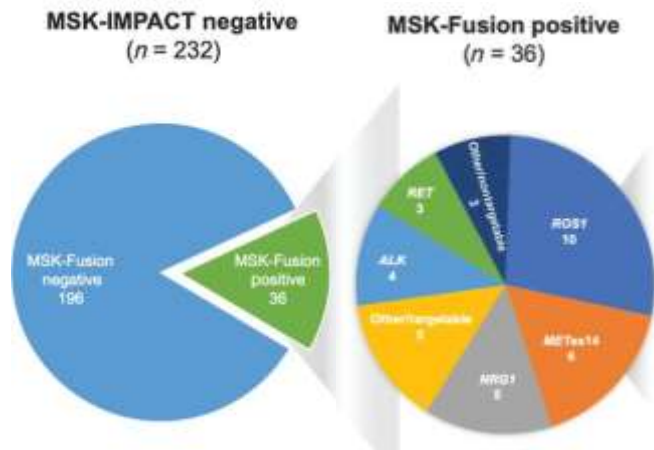
1 pg = 0,000 000 000 001 g

5 ng DNA  **Einzelgen
Mutation
Sanger**
Sensitivität 25%

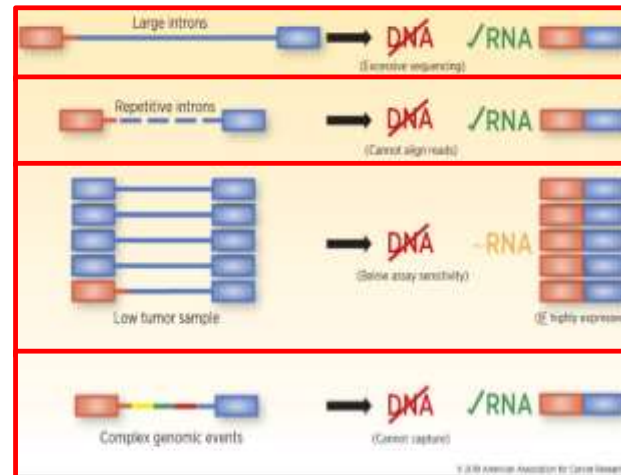
10-50
ng DNA  **Multigen
Mutation
NGS**
Sensitivität 1%

Fall 2

DNA vs. RNA




Rearrangement	Matched therapy	Best response*
ERV4-ALK	Alectinib	SD
CD74-ROS1	Crizotinib	SD
SQ5/MS-MIAC3	Larotrectinib	PR**
STRV-NTRK2	Larotrectinib	SD
CD74-ROS1	Crizotinib	PR**
CD74-NRG1	Alectinib	SD
MET exon14 skipping	Crizotinib	SD
SLC34A2-ROS1	Crizotinib	PD
SLC34A2-ROS1	Crizotinib	SD
SLC4-MSI2	Atrasinib	PD



Davies, Aisner Clin Cancer Res 2019 25:4586
Benayed et al. Clin Cancer Res 2019 25:4712

Fall 2

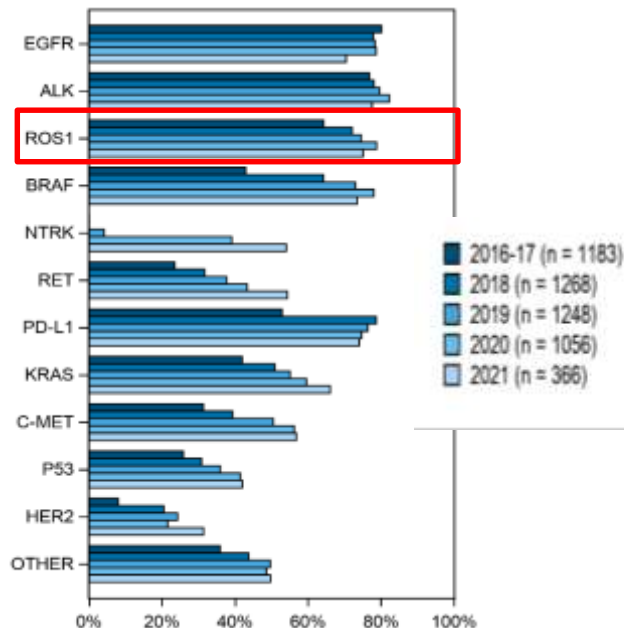
Nachweis von Translokationen

	Sensitivität	Spezifität	Bruchpunkt	Dauer
 IHC	✓	⊘ ✓	⊘	1-2d
 FISH	✓	✓	⊘	2d
 DNA NGS	✓	✓ ✓	✓	7-10d
 RNA NGS	✓ ✓	✓ ✓	✓	7-10d

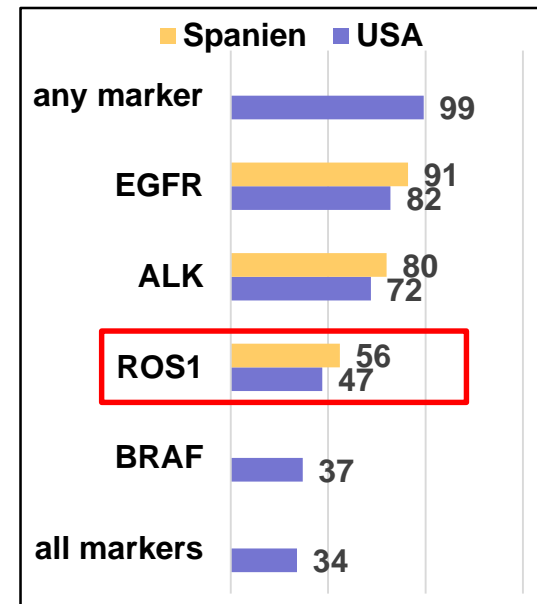
Fall 2

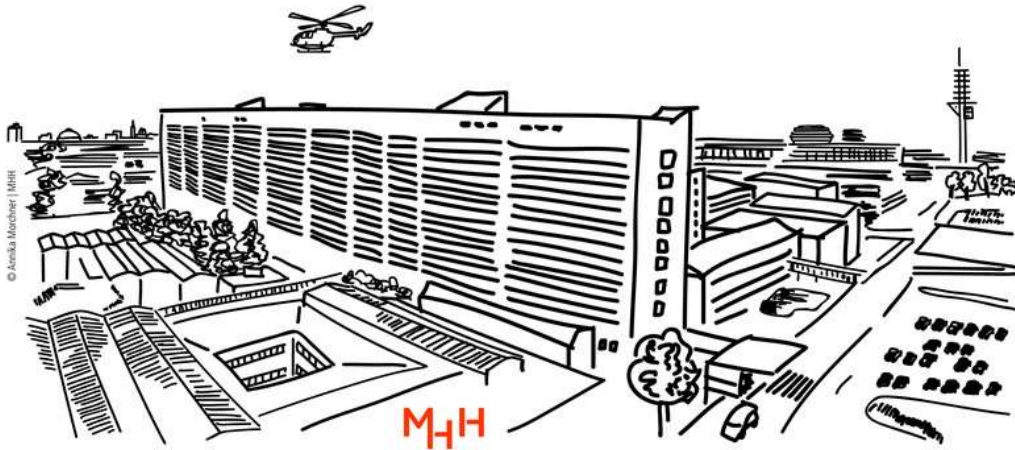
Teststraten vor Ersttherapie

Daten des CRISP Registers



Literaturdaten





VIELEN DANK FÜR IHRE AUFMERKSAMKEIT!