HIRSLANDEN
KLINIK LINDE
CLINIQUE DES TILLEULS

LINDE ACADEMY
ACADEMY DES TILLEULS

2. SEPTEMBER 2021

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LUNGENKREBS: THERAPEUTISCHE REVOLUTION DURCH DRIVERMUTATIONS

PD DR. MED. MARCO SIANO,
FACHARZT FÜR MEDIZINISCHE ONKOLOGIE UND FÜR ALLGEMEINE INNERE MEDIZIN

AGENDA

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- Hallmarks of Cancer : The next generation [1]
- Was sind ‚Driver'mutationen ?
- Oncogenesis
- Implikationen für den klinischen Alltag

1. Hanahan D, Weinberg RA. Cell 2011

HALLMARKS OF CANCER
THE NEXT GENERATION

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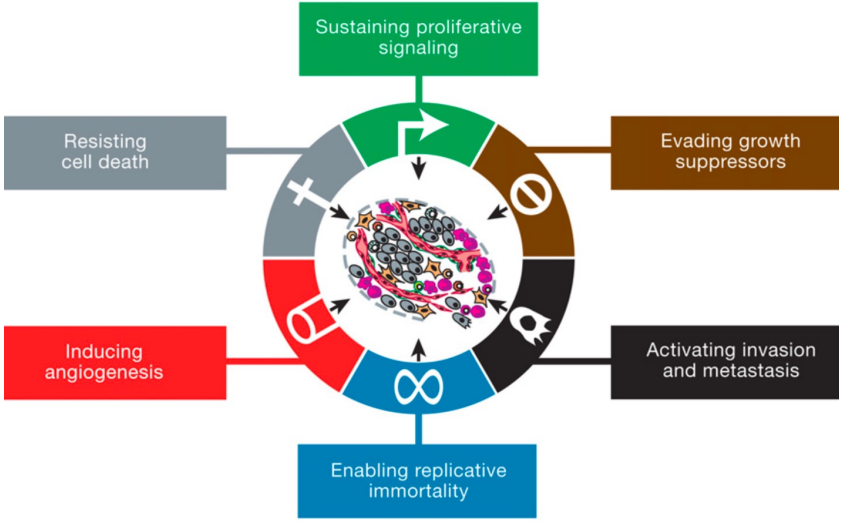

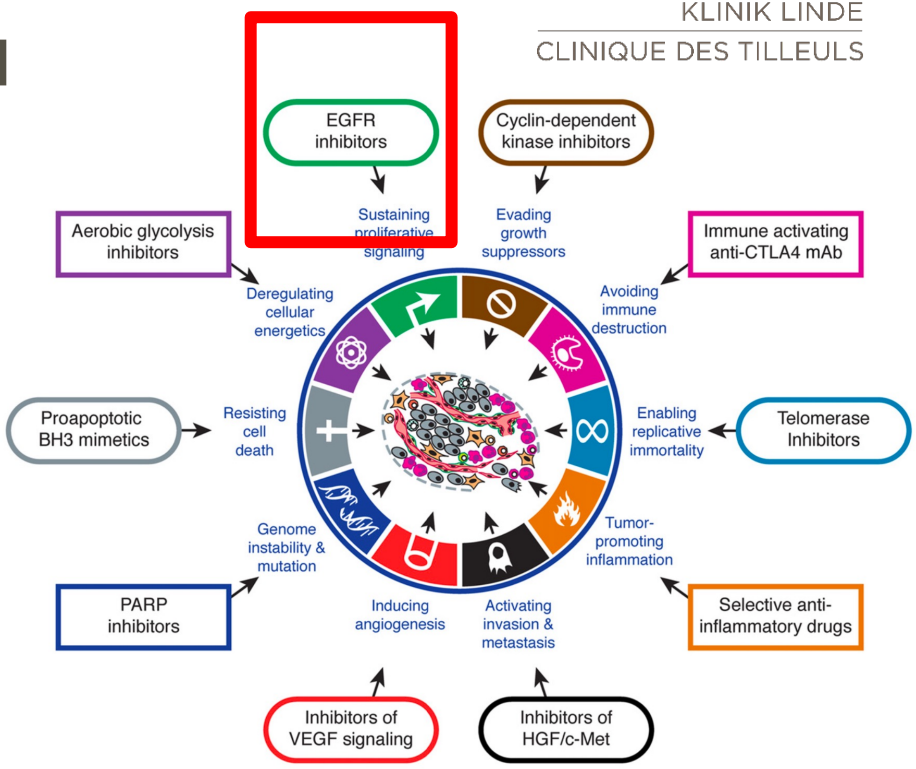

1. Hanahan D, Weinberg RA. Cell 2000 & 2011

TREIBERMUTATIONEN ?

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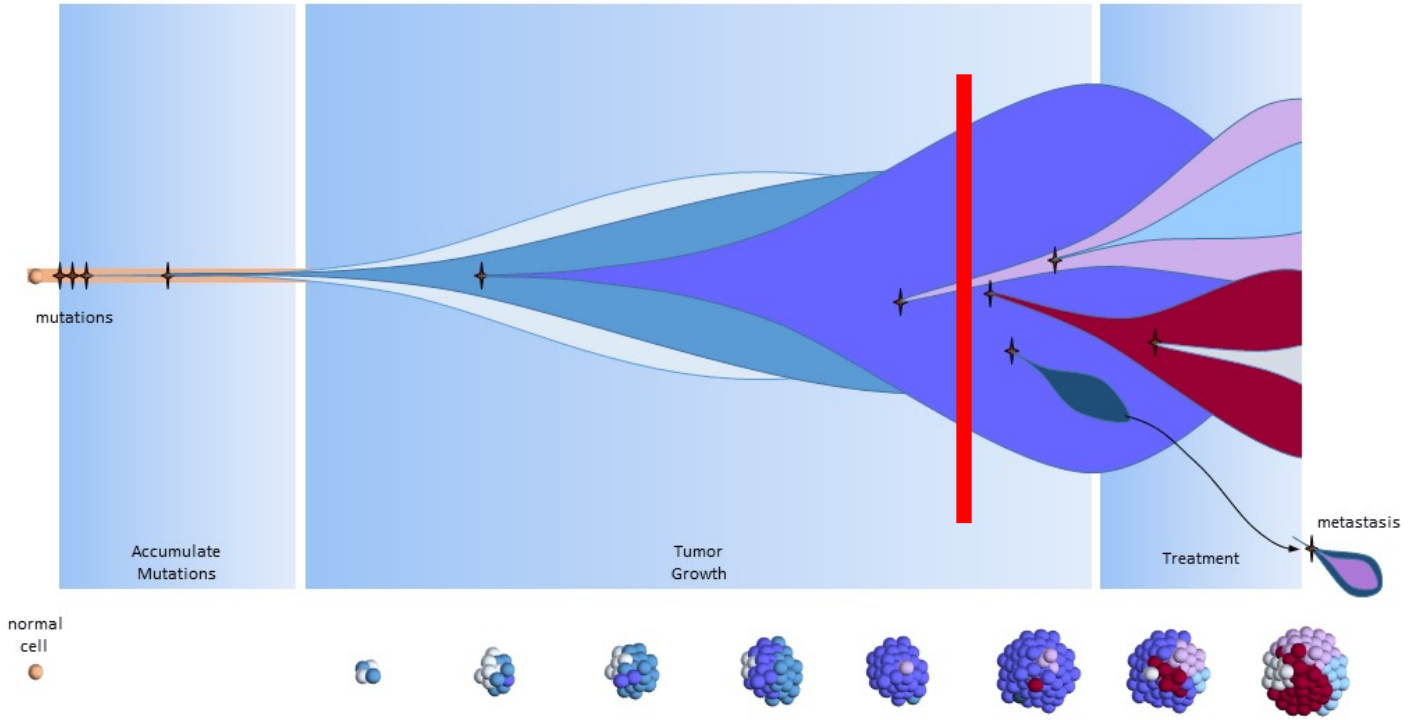
- Treibermutationen führen zu einem Selektionsvorteil Ihrer Trägerzellen und werden somit prominent in der Tumorentwicklung.

- Per Definition gehören sie zu den Krebs-definierenden Genen (Tumorsuppressor-Gene, Oncogene (TP53, KRAS, APC etc.))

- ‘Passagiermutationen’ führen nicht zu einem Selektionsvorteil

ONKOGENESE / AKKUMULATION



AKKUMULATION VON MUTATIONEN
TUMOR-MUTATION-BURDEN

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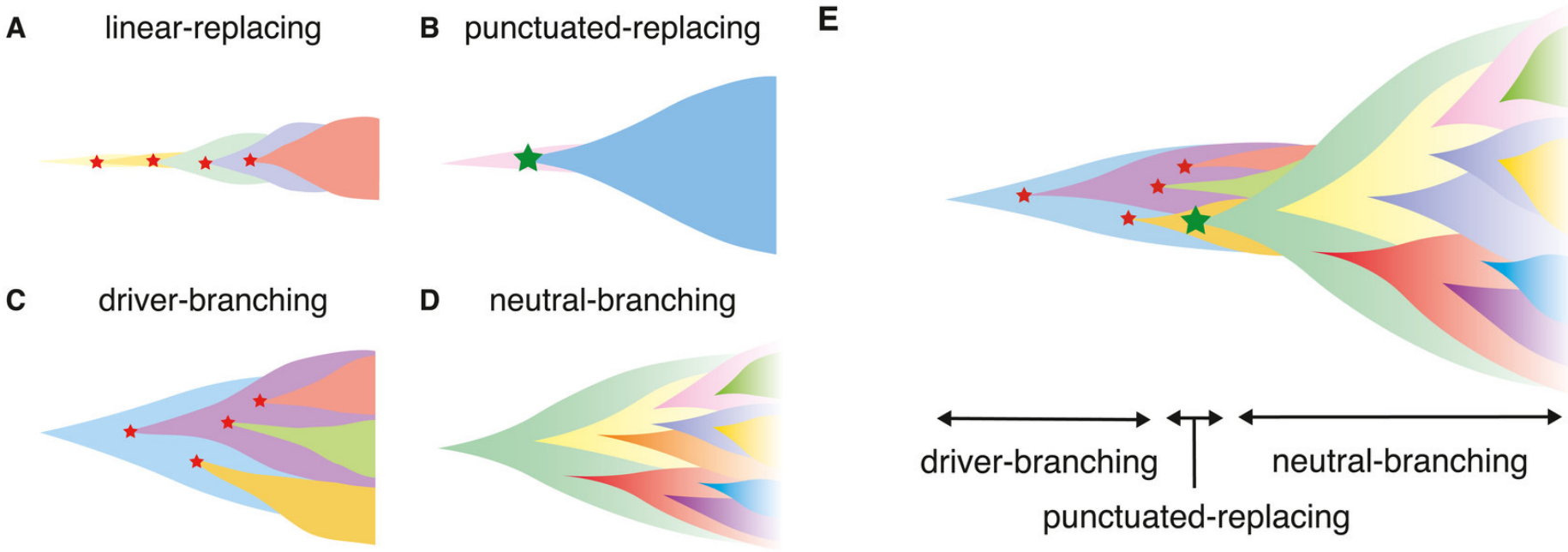

EIN GEGNER ODER MEHRERE ?

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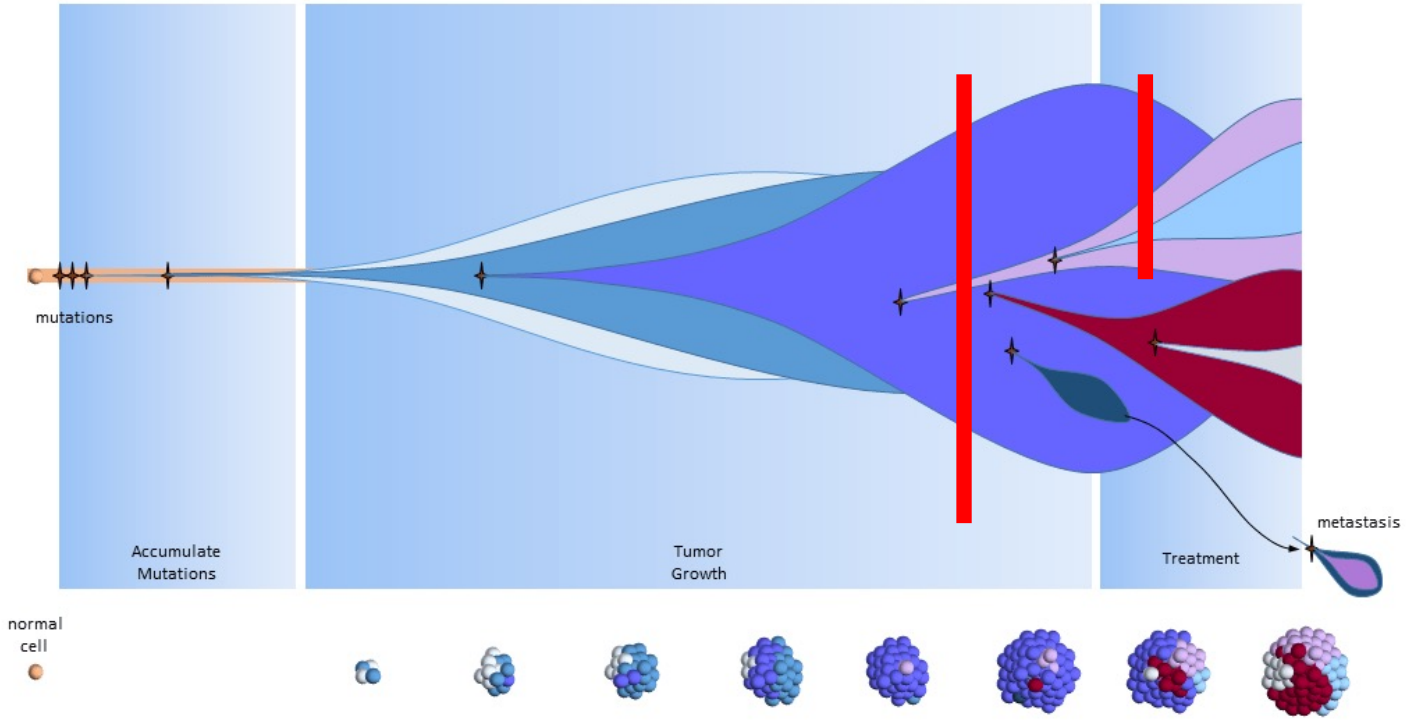

1. Gerlinger M. NEJM. 2012

PAST - PRESENT

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- NSCLC vs. SCLC (nicht-kleinzelliges vs. kleinzelliges)
- NSCLC : SCC & ADC (Plattenepithel vs. Adenokarzinom)
- Platin-Kombinationstherapie Erstlinientherapie
- Zweitlinien-Monotherapie
- anti-EGFR Tyrosin-Kinase-Inhibitoren

MUTATIONEN – NSCLC ?

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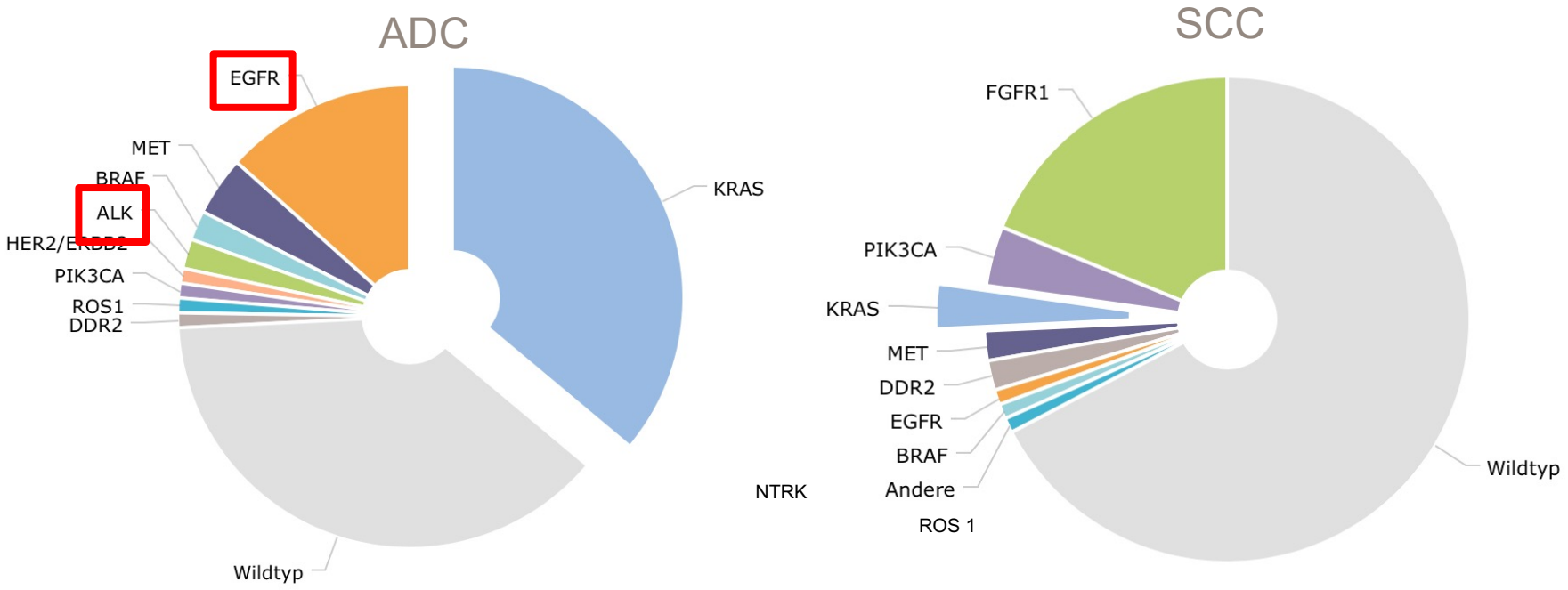

Ha SY et al. Oncotarget. 2015

EGFR MUTATIONEN – NOT SO EASY

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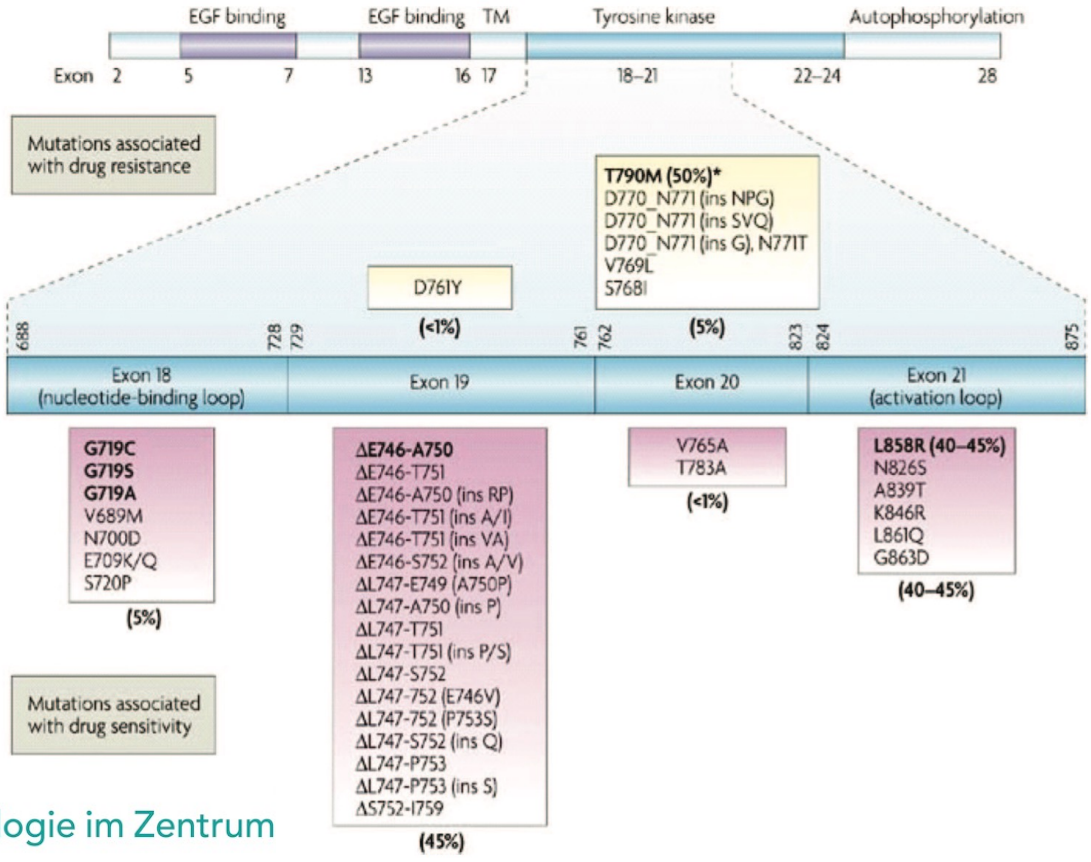
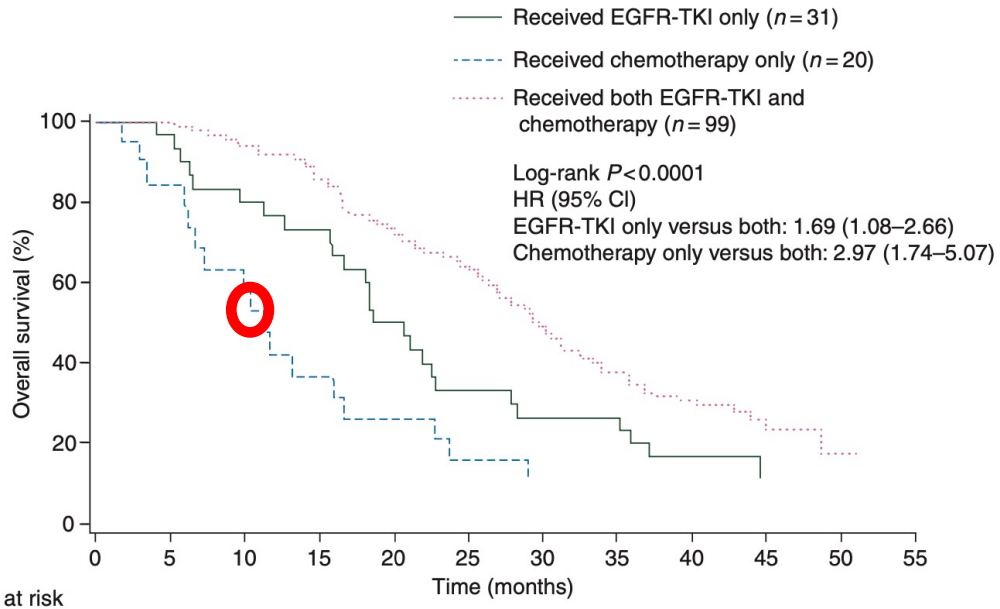


Pirker R et al. JTO 2010

EGFR TYROSIN-KINASE-INHIBITOR



Number at risk												
EGFR-TKI	31	29	24	22	15	10	8	8	5	2	0	0
Chemotherapy	20	16	11	7	5	3	2	2	2	2	0	0
EGFR-TKI and chemotherapy	99	99	93	85	73	64	48	37	29	11	2	0

Cave
Cross-over

Rosell R et al. Lancet Oncol 2012; Zhou C et al. Lancet Oncol 2013

EGFR TYROSIN-KINASE-INHIBITOR

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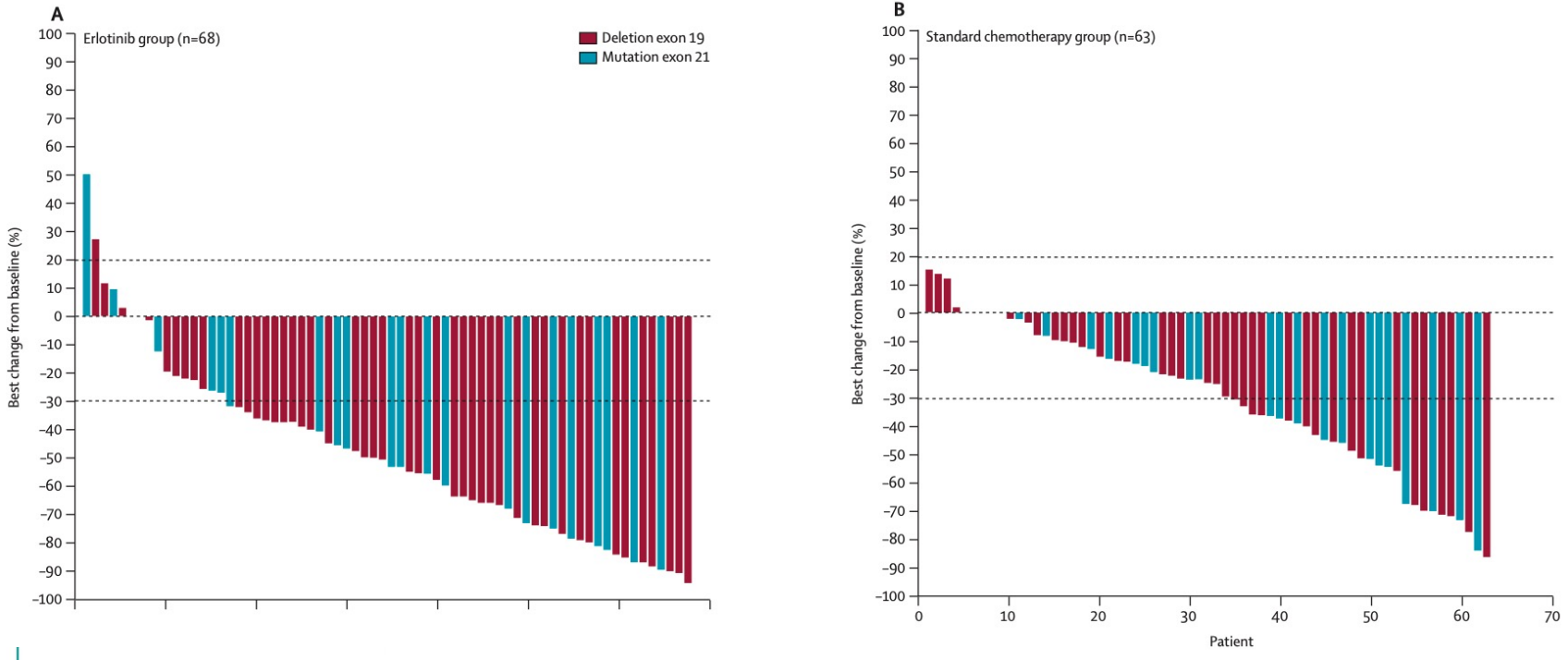

WAS PASSIERT UNTER EGFR-TKI

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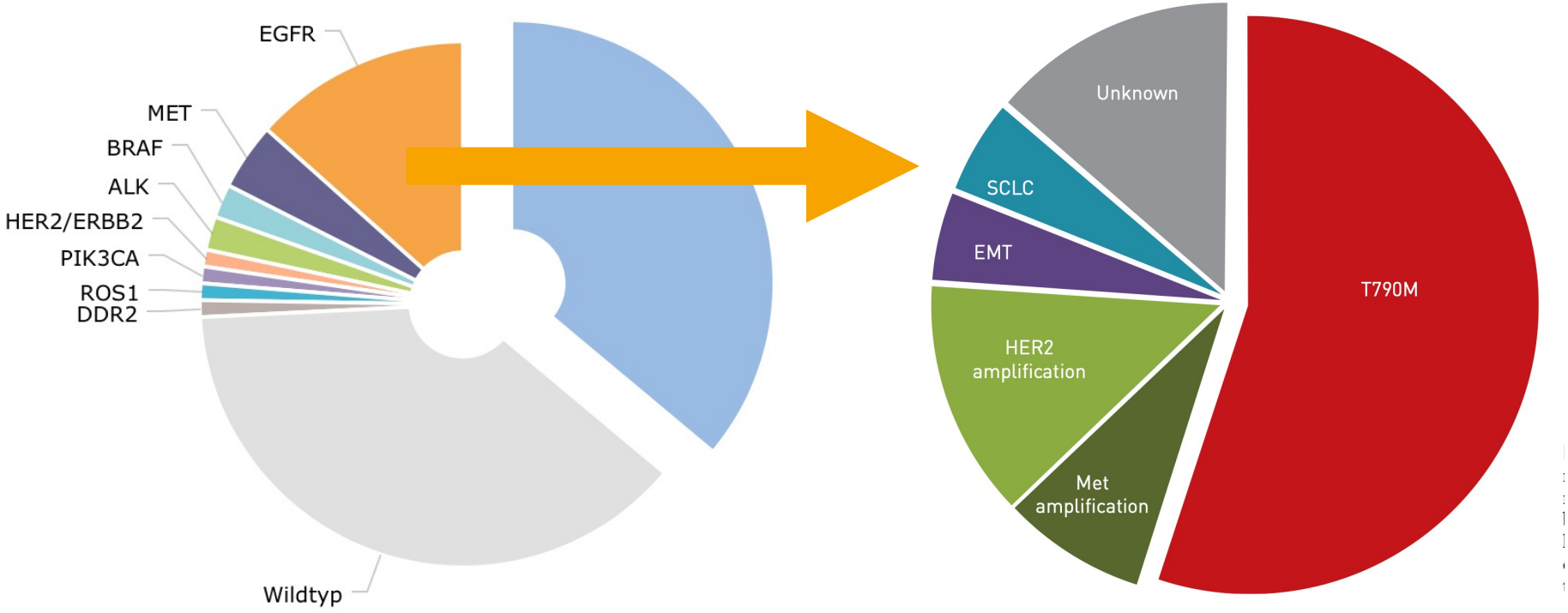

Cortot AB et al. Eur Respir Rev 2014

OSIMERTINIB FIRST-LINE

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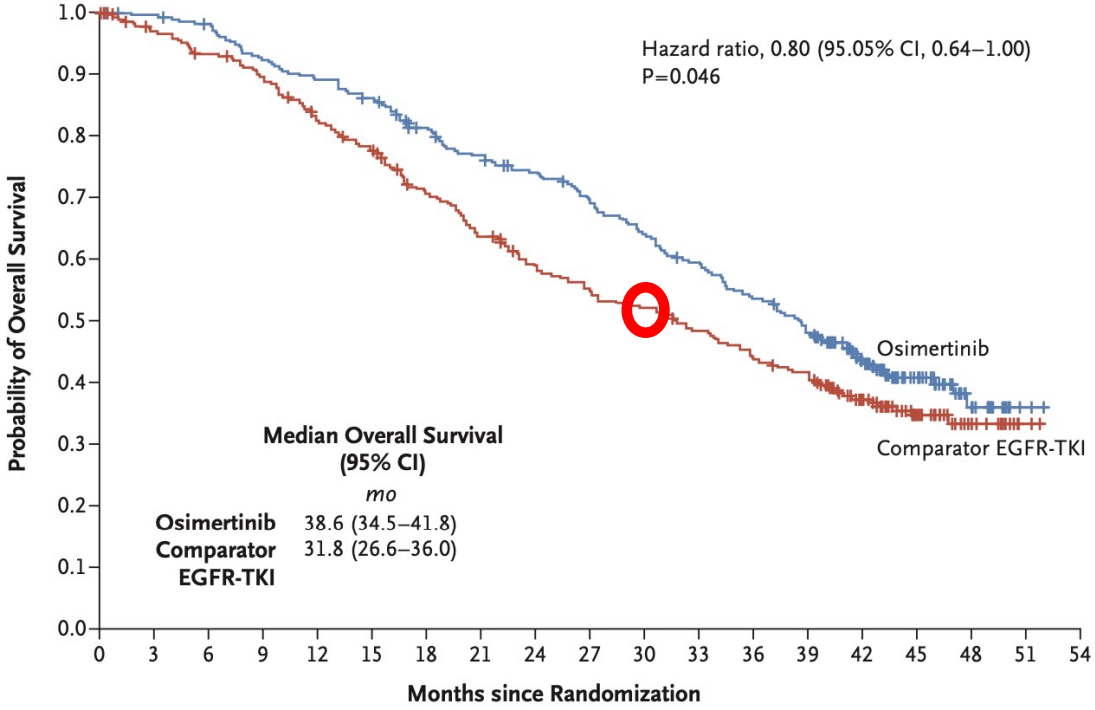

No. at Risk

Osimertinib	279	276	270	254	245	236	217	204	193	180	166	153	138	123	86	50	17	2	0
Comparator EGFR-TKI	277	263	252	239	219	205	182	165	148	138	131	121	110	101	72	40	17	2	0

Ramalingam SS et al. NEJM 2014

OSIMERTINIB FIRST-LINE (2ND)

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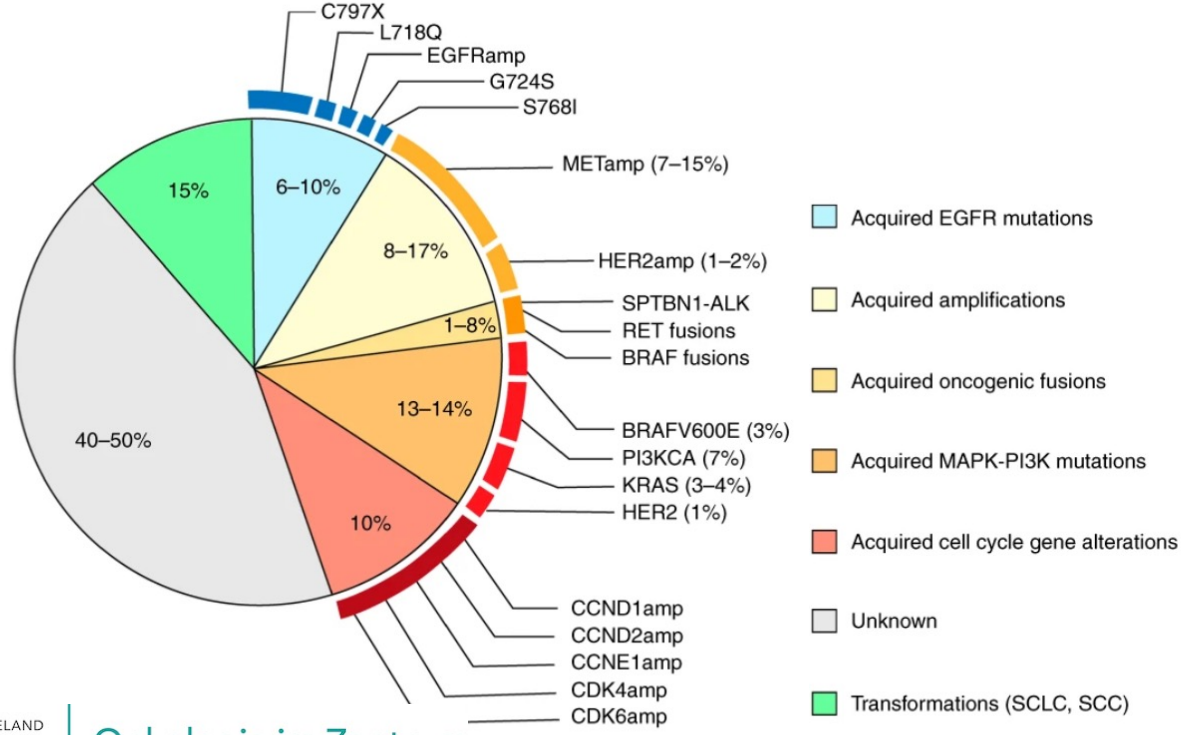
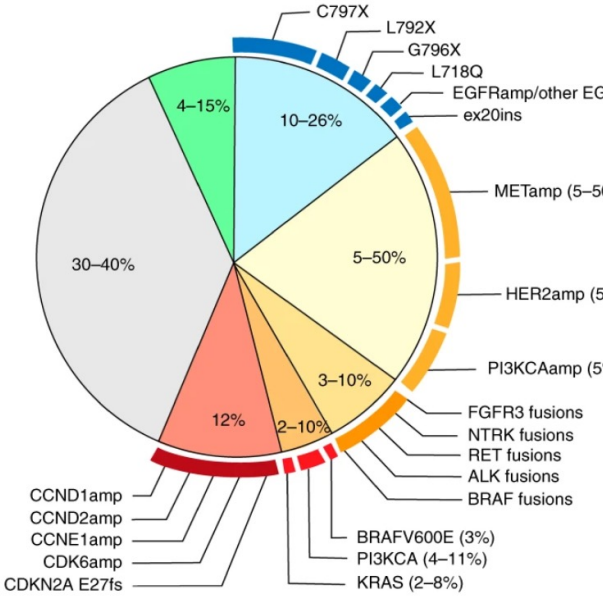
Re-Biopsy or Liquid biopsy

Resistance mechanisms to first-line osimertinib



Resistance mechanisms to second-line osimer



* Other EGFR tertiary mutations include G719X, G724S AND S768I
▲Mutations have also been reported

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LINDE TILLEULS ACADEMY

ALK-TKI'S

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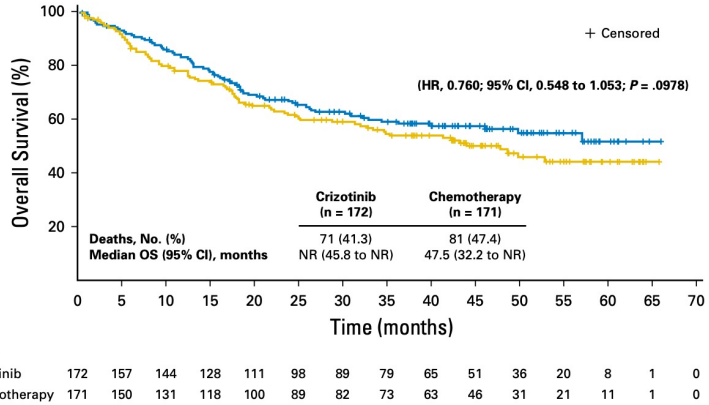
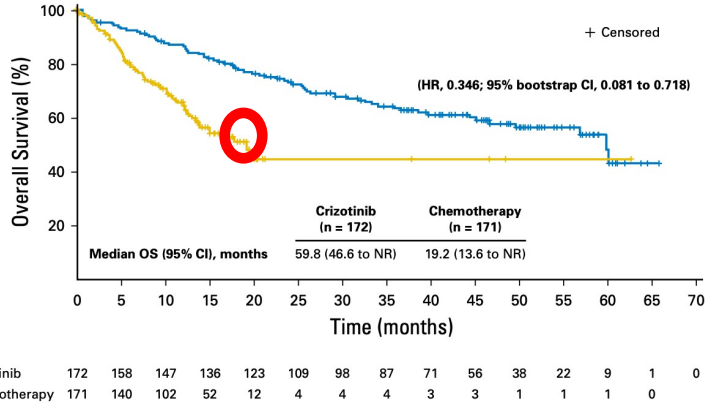
A



No. at risk:

Crizotinib	172	157	144	128	111	98	89	79	65	51	36	20	8	1	0
Chemotherapy	171	150	131	118	100	89	82	73	63	46	31	21	11	1	0

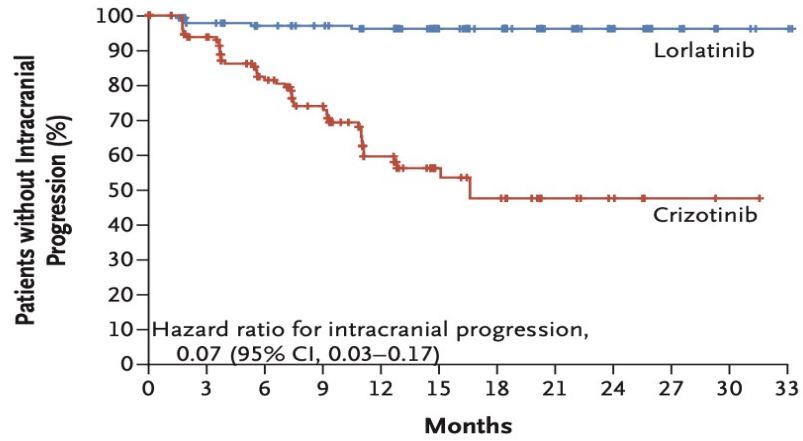
B



No. at risk:

Crizotinib	172	158	147	136	123	109	98	87	71	56	38	22	9	1	0
Chemotherapy	171	140	102	52	12	4	4	4	3	3	1	1	1	0	

B Survival without CNS Progression



No. at Risk

Lorlatinib	149	131	122	117	110	78	65	39	25	12	4	2
Crizotinib	147	115	84	65	38	21	16	8	5	2	1	0

Solomon BJ et al. JCO 2018
Shaw AT et al. NEJM 2020

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ALK-TKI'S

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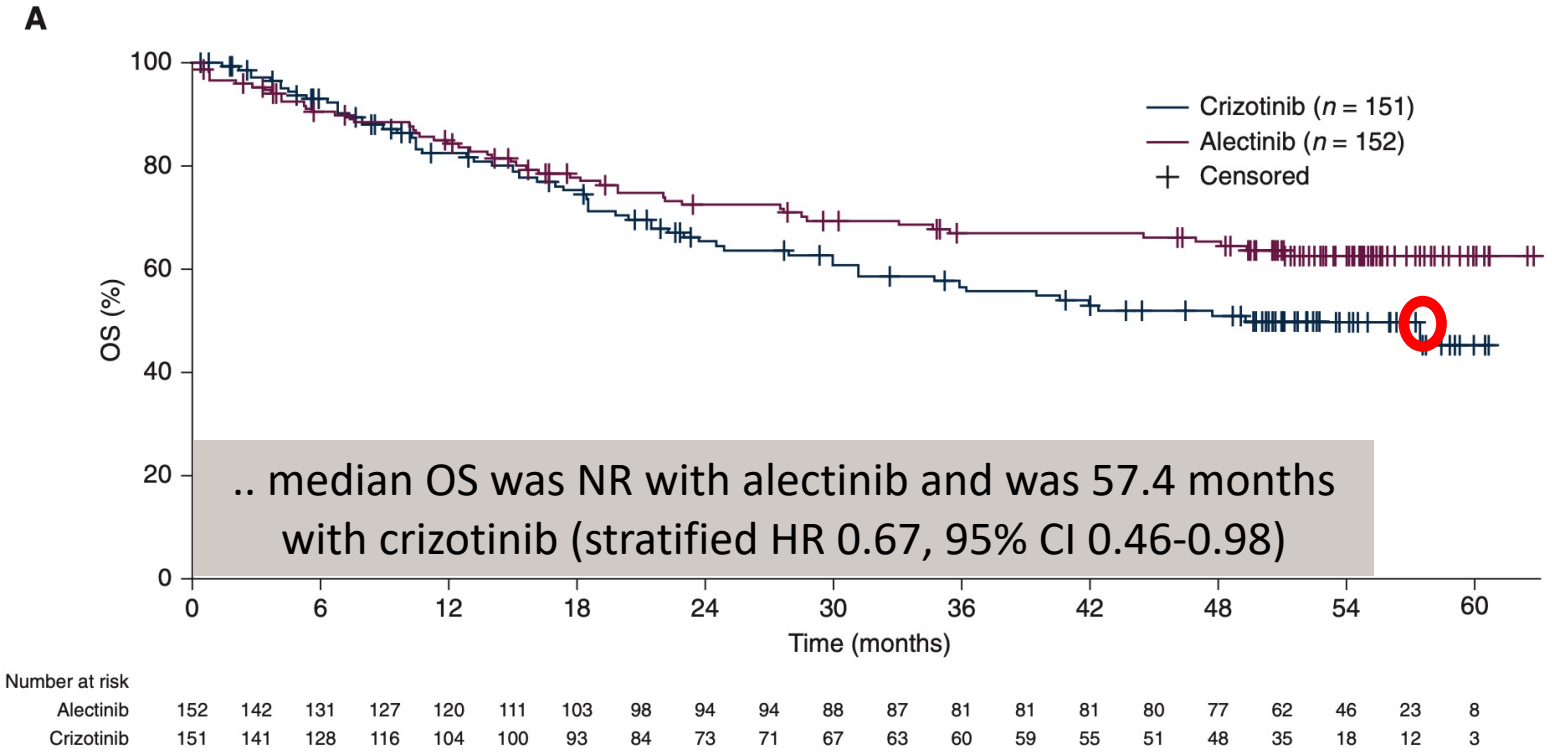

Mok T et al. Ann Oncol 2020

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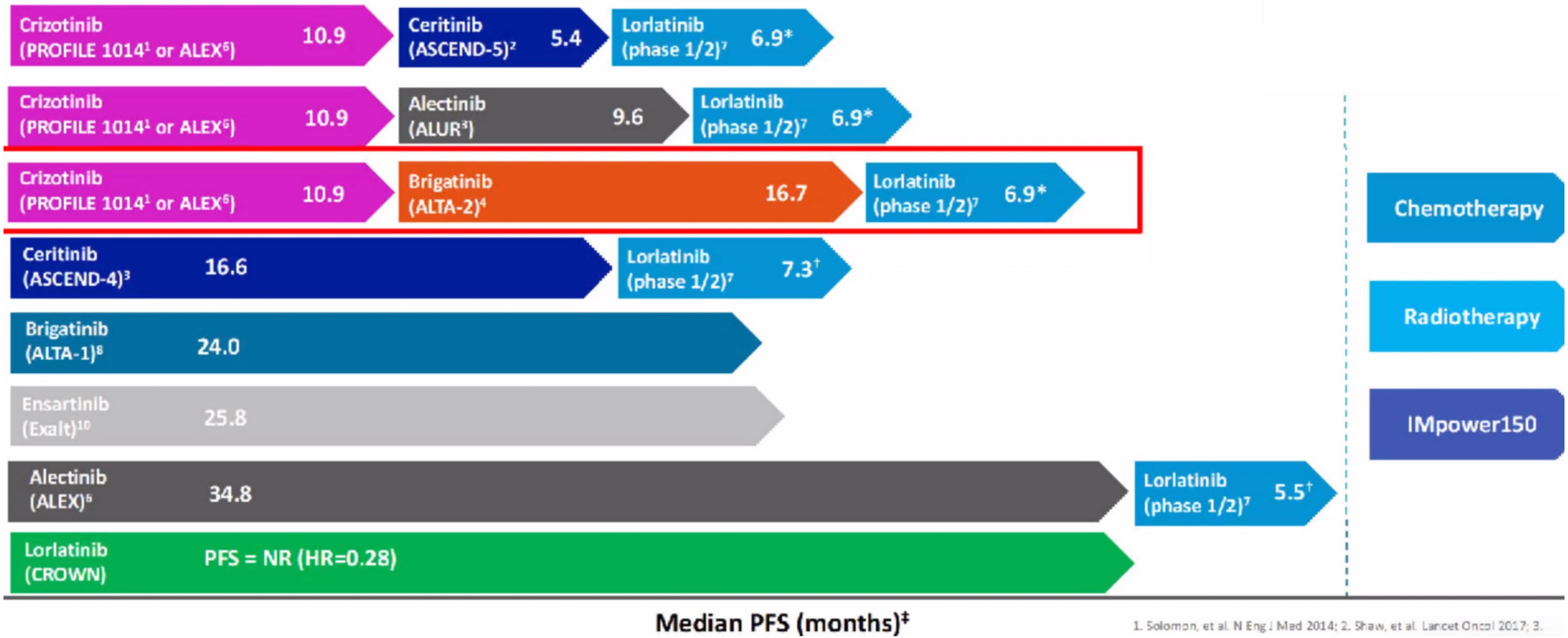

1. Solomon, et al. N Eng J Med 2014; 2. Shaw, et al. Lancet Oncol 2017; 3.

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METASTASIERT

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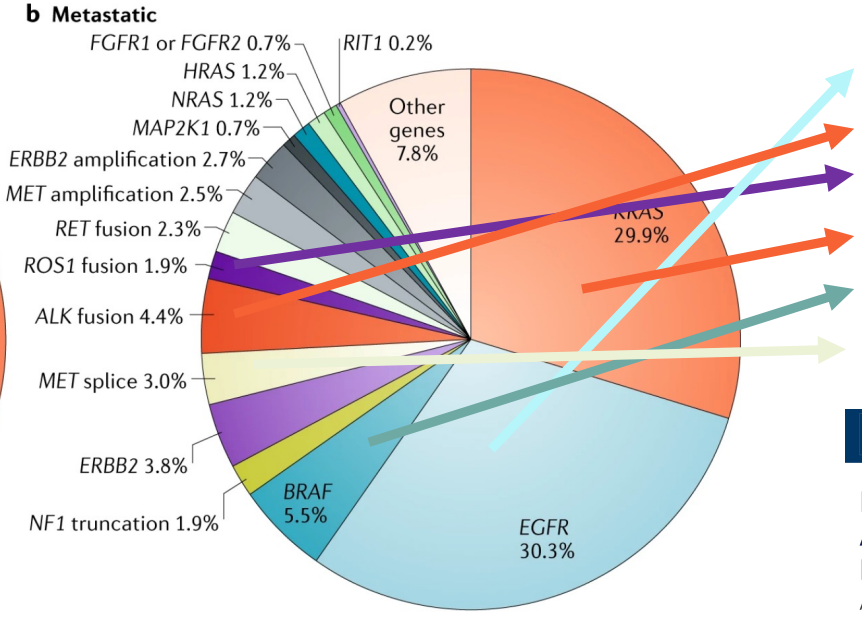

Data from MSK-IMPACT (Jordan et al.[59]) and FoundationOne (Frampton et al.[15]) panels (n = 5262)

- Osimertinib / Erlotinib/Gefitinib/Afatinib..
- Alectinib/Lorlatinib/Brigatinib.. Crizotinib
- Crizotinib / Lorlatinib / Entrectinib
- Adagrasib / Sotarasib (G12C)
- Dabrafenib / Trametinib (Vemurafenib..)
- Capmatinib

Targeted Oncology

Neratinib Is Effective Against EGFR Exon 18 Mutations in NSCLC

April 6, 2021
Targeted Oncology Staff
Targeted Therapies in Oncology, April 1, 2021, Volume 10, Issue 5
Pages: 39

Oncology ... on Twitter! @Target

FDA Approves Amivantamab for Frontline EGFR Exon 20-Positive NSCLC

May 21, 2021
Nichole Tucker

The FDA has granted approval to amivantamab-vmjw for the frontline treatment of adult patients with non-small cell lung cancer whose tumors have EGFR exon 20 insertion mutations.

The FDA has granted approval to amivantamab-vmjw (Rybrevant) for the frontline treatment of adult patients with non-small cell lung cancer (NSCLC) whose tumors have *EGFR* exon 20

FDA

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LINDE TILLEULS ACADEMY

METASTASIERT

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• Osimertinib / Erlotinib/Gefitinib/Afatinib	EGFR
• Crizotinib / Alectinib/Lorlatinib/Cediranib	ALK
• Crizotinib / Ceritinib / Lorlatinib	ROS1
• Sotarasib / Adagrasib	KRAS G12C
• Selpercatinib	RET
• Larotrectinib / Entrectinib	NTRK
• **Dabrafenib / Trametinib (Vemurafenib..)**	**BRAF V600**
• **Capmatinib**	**MET**

ZUSAMMENGEFASST

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- Treibermutationen haben Fortschritt gebracht mit durativen Ansprechen (8-10m -> über 60m Gesamtüberleben)
- Initiale Panel-Diagnostik in Abhängigkeit der Verfügbarkeit und Zulassung der TKI’s (Gewebe !)
- Re-Biopsien um möglichst das Target nicht zu verpassen (SCLC!)
- Spezialisierung nimmt zu !

THE END

FRAGEN?

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www. SEELAND CANCER CENTER .ch