Med Uni Graz *Pioneering Minds*

ONKOLOGIE 2.0 IN DER INNERE MEDIZIN

neue Substanzen & Nebenwirkungsmanagement

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LKH-Univ. Klinikum Graz
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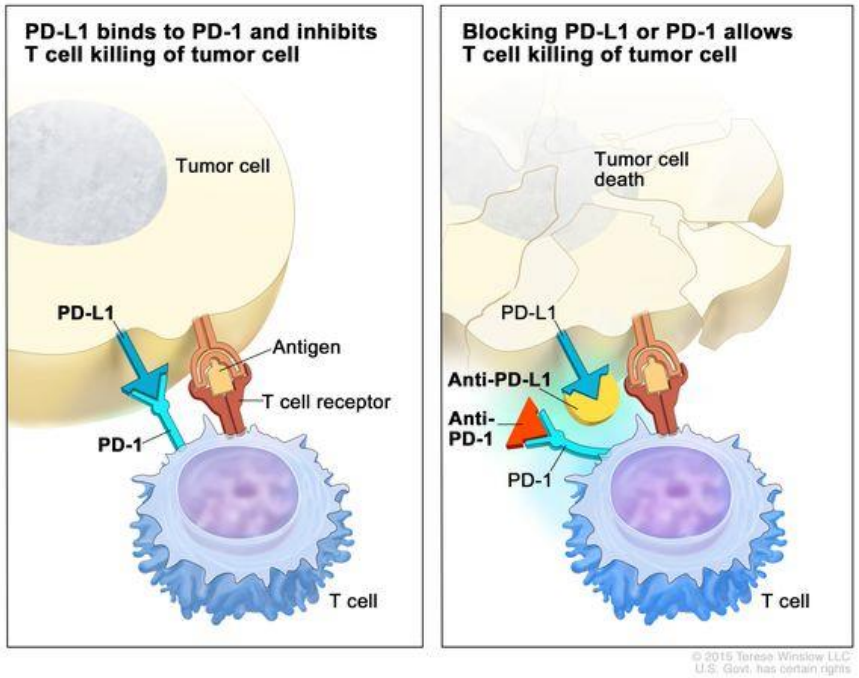
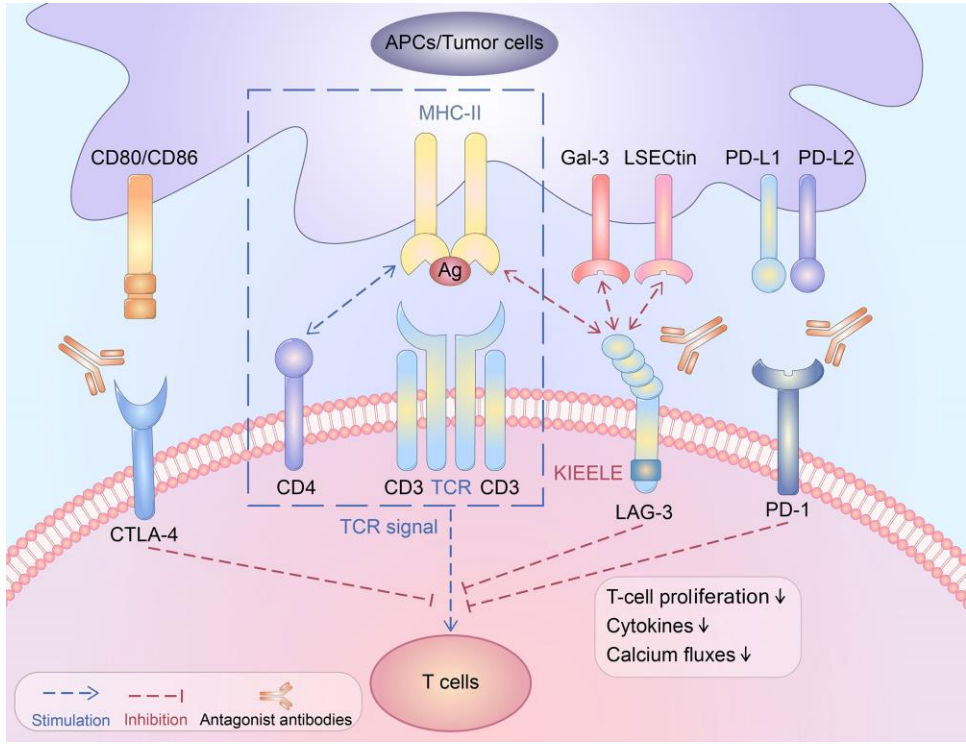


Atezolizumab	PD-L1
Avelumab	PD-L1
Cemiplimab	PD-1
Dostarlimab	PD-1
Durvalumab	PD-L1
Nivolumab	PD-1
Pembrolizumab	PD-1
Spartalizumab	PD-1
Tislelizumab	PD-1



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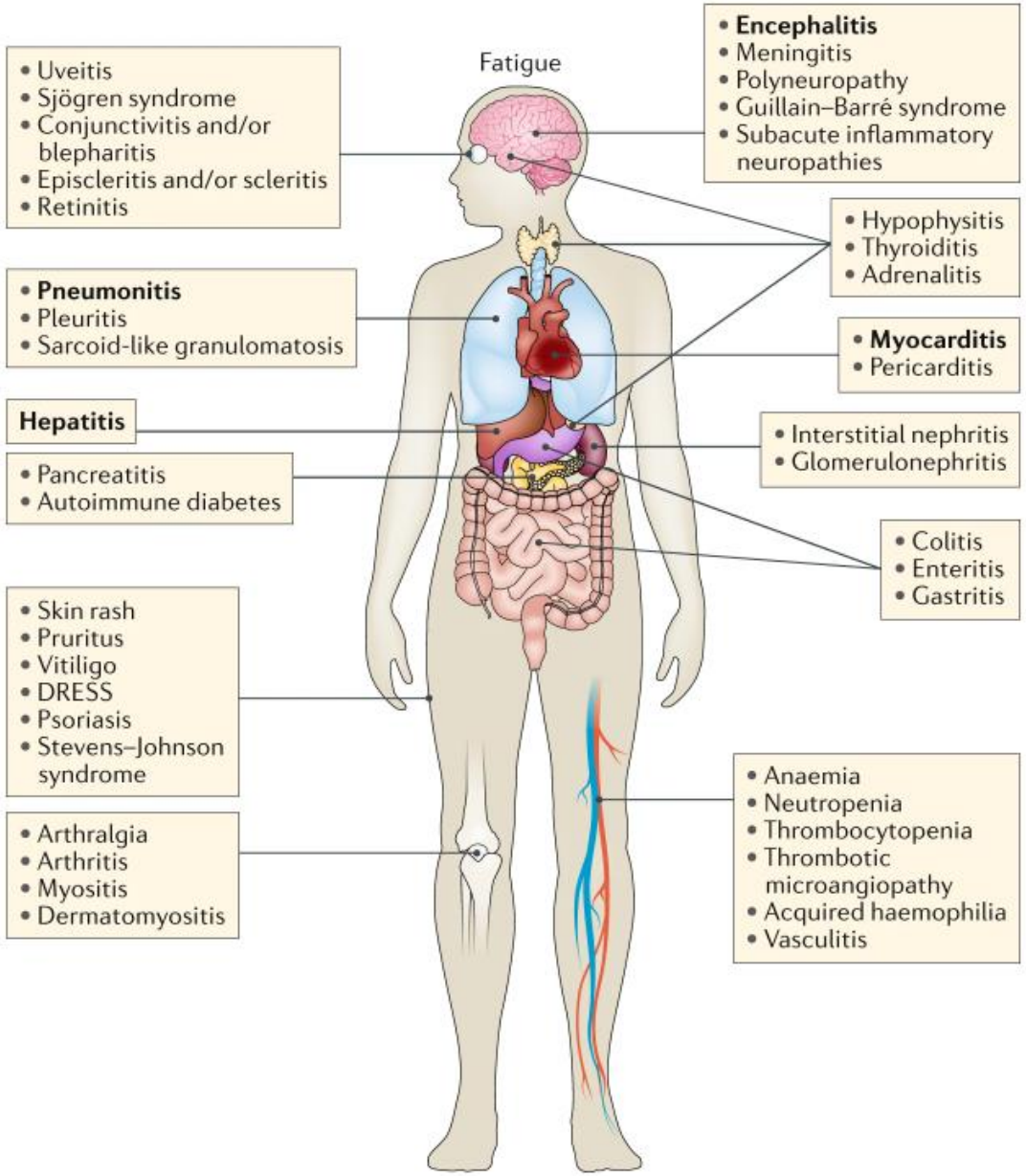
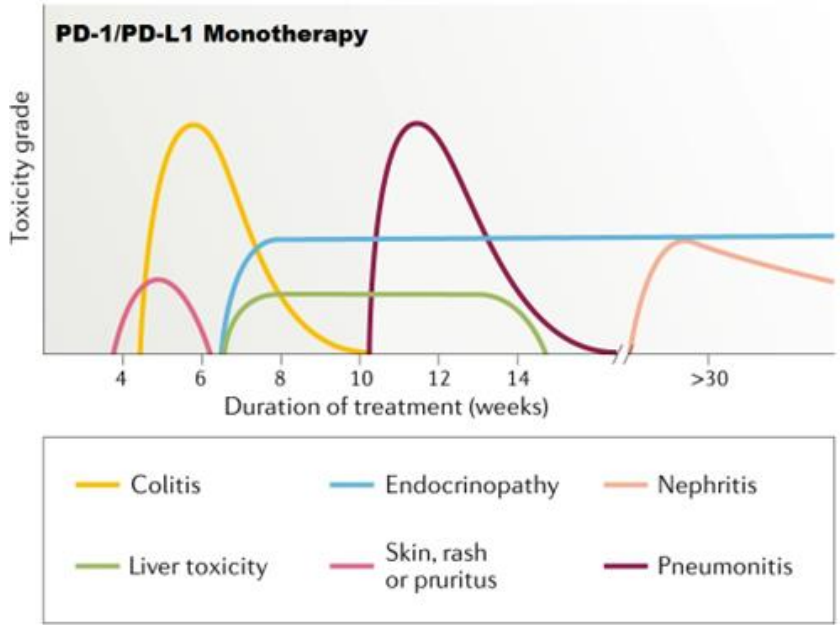
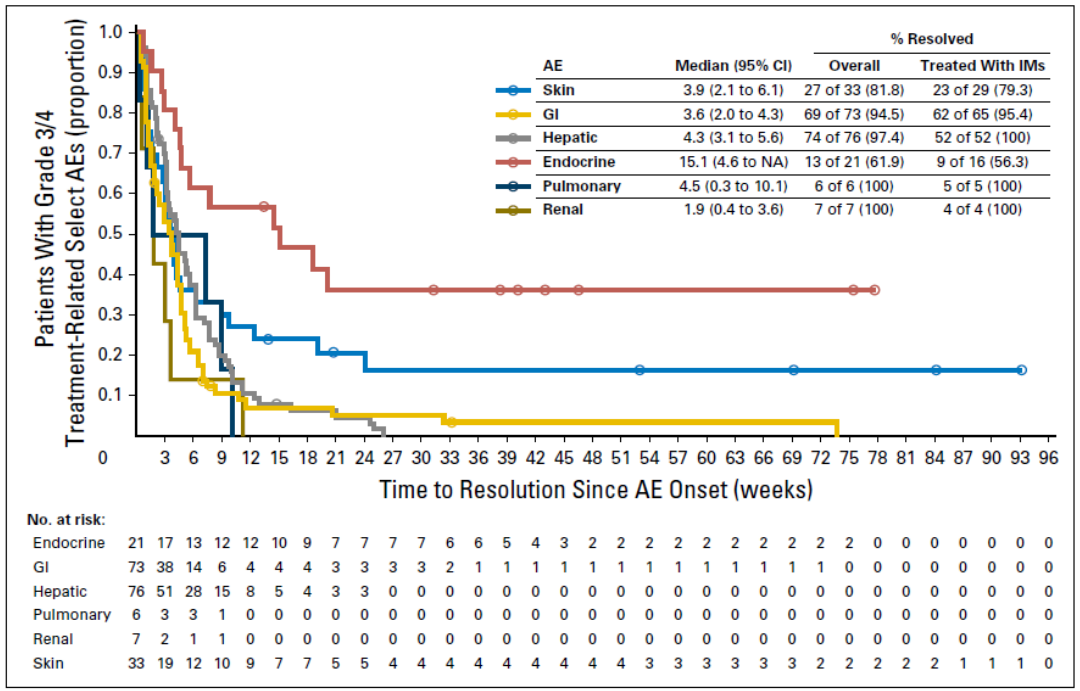






Sznol M et al., J Clin Oncol 2017; 35(34):3815–22

Checkpointinhibitoren

YERVOY is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody indicated for:

Melanoma

- Treatment of unresectable or metastatic melanoma in adults and pediatric patients 12 years and older. (1.1)
- Adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy. (1.2)

Renal Cell Carcinoma (RCC)

- Treatment of patients with intermediate or poor risk, previously untreated advanced renal cell carcinoma, in combination with nivolumab. (1.3)

Colorectal Cancer

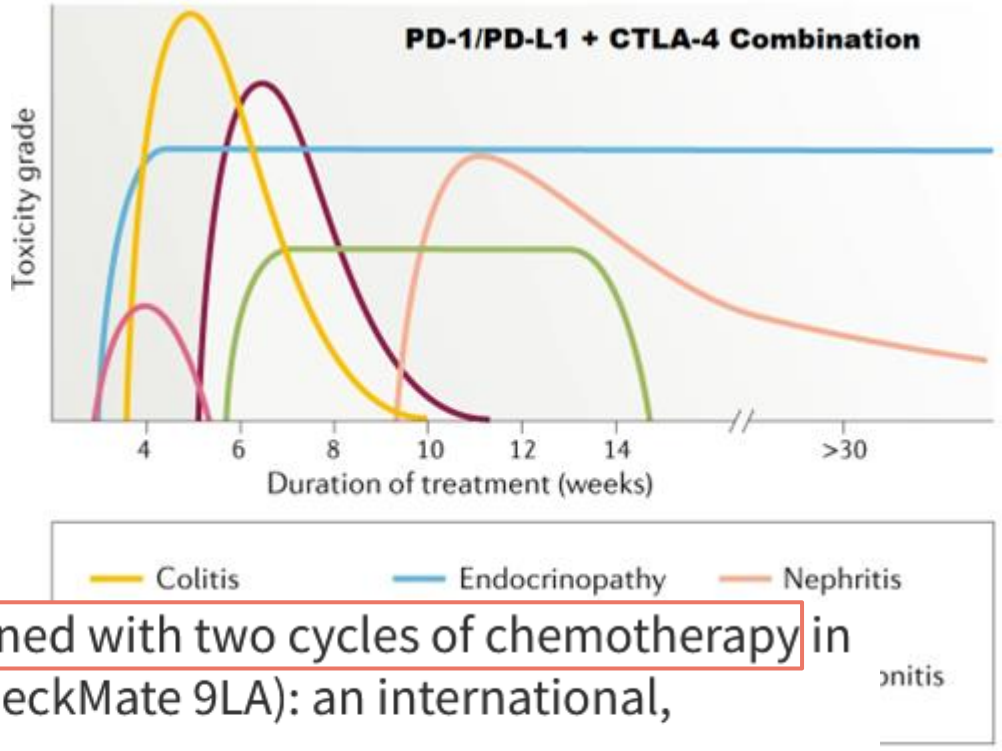
- Treatment of adult and pediatric patients 12 years and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan, in combination with nivolumab. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. (1.4)

Hepatocellular Carcinoma

- Treatment of patients with hepatocellular carcinoma who have been previously treated with sorafenib, in combination with nivolumab. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. (1.5)

Non-Small Cell Lung Cancer (NSCLC)

- Treatment of adult patients with metastatic non-small cell lung cancer expressing PD-L1 (≥1%) as determined by an FDA-approved test, with



First-line nivolumab plus ipilimumab combined with two cycles of chemotherapy in patients with non-small-cell lung cancer (CheckMate 9LA): an international, randomised, open-label, phase 3 trial

Prof Luis Paz-Ares, MD [a] · Tudor-Eliade Ciuleanu, MD [b] · Manuel Cobo, MD [c] · Michael Schenker, MD [d] · Bogdan Zurawski, MD [e] · Juliana Menezes, MD [f] · et al. Show more

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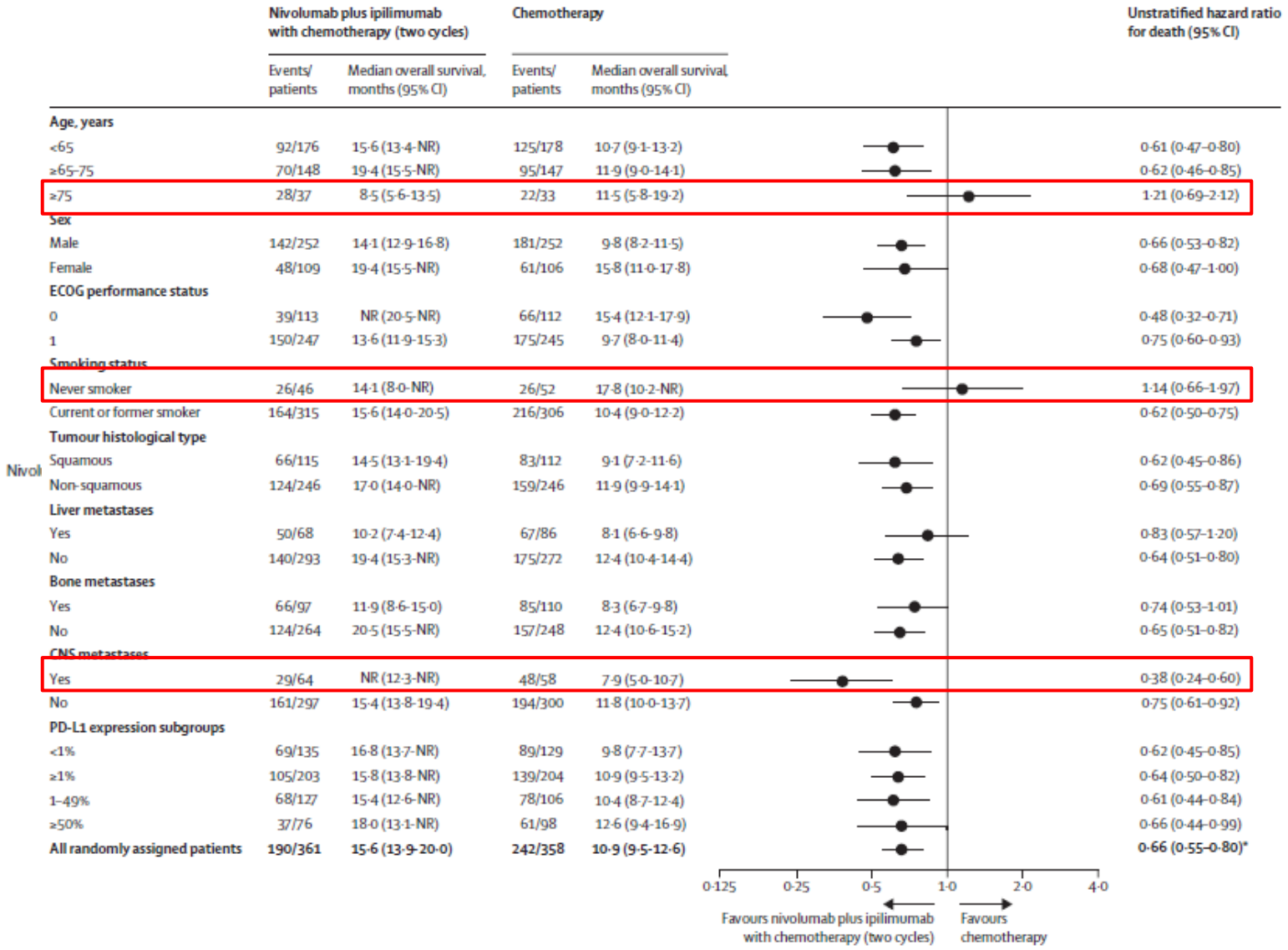

	Nivolumab plus ipilimumab with chemotherapy (two cycles)		Chemotherapy		Unstratified hazard ratio for death (95% CI)
	Events/ patients	Median overall survival, months (95% CI)	Events/ patients	Median overall survival, months (95% CI)	
Age, years					
<65	92/176	15·6 (13·4-NR)	125/178	10·7 (9·1-13·2)	0·61 (0·47–0·80)
≥65–75	70/148	19·4 (15·5-NR)	95/147	11·9 (9·0-14·1)	0·62 (0·46–0·85)
≥75	28/37	8·5 (5·6-13·5)	22/33	11·5 (5·8-19·2)	1·21 (0·69–2·12)
Sex					
Male	142/252	14·1 (12·9-16·8)	181/252	9·8 (8·2-11·5)	0·66 (0·53–0·82)
Female	48/109	19·4 (15·5-NR)	61/106	15·8 (11·0-17·8)	0·68 (0·47–1·00)
ECOG performance status					
0	39/113	NR (20·5-NR)	66/112	15·4 (12·1-17·9)	0·48 (0·32–0·71)
1	150/247	13·6 (11·9-15·3)	175/245	9·7 (8·0-11·4)	0·75 (0·60–0·93)
Smoking status					
Never smoker	26/46	14·1 (8·0-NR)	26/52	17·8 (10·2-NR)	1·14 (0·66–1·97)
Current or former smoker	164/315	15·6 (14·0-20·5)	216/306	10·4 (9·0-12·2)	0·62 (0·50–0·75)
Tumour histological type					
Squamous	66/115	14·5 (13·1-19·4)	83/112	9·1 (7·2-11·6)	0·62 (0·45–0·86)
Non-squamous	124/246	17·0 (14·0-NR)	159/246	11·9 (9·9-14·1)	0·69 (0·55–0·87)
Liver metastases					
Yes	50/68	10·2 (7·4-12·4)	67/86	8·1 (6·6-9·8)	0·83 (0·57–1·20)
No	140/293	19·4 (15·3-NR)	175/272	12·4 (10·4-14·4)	0·64 (0·51–0·80)
Bone metastases					
Yes	66/97	11·9 (8·6-15·0)	85/110	8·3 (6·7-9·8)	0·74 (0·53–1·01)
No	124/264	20·5 (15·5-NR)	157/248	12·4 (10·6-15·2)	0·65 (0·51–0·82)
CNS metastases					
Yes	29/64	NR (12·3-NR)	48/58	7·9 (5·0-10·7)	0·38 (0·24–0·60)
No	161/297	15·4 (13·8-19·4)	194/300	11·8 (10·0-13·7)	0·75 (0·61–0·92)
PD-L1 expression subgroups					
<1%	69/135	16·8 (13·7-NR)	89/129	9·8 (7·7-13·7)	0·62 (0·45–0·85)
≥1%	105/203	15·8 (13·8-NR)	139/204	10·9 (9·5-13·2)	0·64 (0·50–0·82)
1–49%	68/127	15·4 (12·6-NR)	78/106	10·4 (8·7-12·4)	0·61 (0·44–0·84)
≥50%	37/76	18·0 (13·1-NR)	61/98	12·6 (9·4-16·9)	0·66 (0·44–0·99)
All randomly assigned patients	**190/361**	**15·6 (13·9-20·0)**	**242/358**	**10·9 (9·5-12·6)**	**0·66 (0·55–0·80)***

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	Nivolumab plus ipilimumab with two cycles of chemotherapy group (n=358)			Chemotherapy group (n=349)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
Any	159 (44%)	124 (35%)	44 (12%)	171 (49%)	111 (32%)	21 (6%)
Nausea	91 (25%)	5 (1%)	0	122 (35%)	3 (1%)	0
Asthenia	72 (20%)	3 (1%)	0	54 (16%)	8 (2%)	0
Pruritus	72 (20%)	3 (1%)	0	6 (2%)	0	0
Anaemia	62 (17%)	20 (6%)	1 (<1%)	82 (24%)	50 (14%)	0
Diarrhoea	60 (17%)	13 (4%)	1 (<1%)	39 (11%)	2 (1%)	0
Rash	61 (17%)	6 (2%)	0	11 (3%)	0	0
Hypothyroidism	56 (16%)	1 (<1%)	0	1 (<1%)	0	0
Fatigue	53 (15%)	8 (2%)	0	36 (10%)	2 (1%)	0
Decreased appetite	55 (15%)	4 (1%)	0	51 (15%)	4 (1%)	0
Vomiting	42 (12%)	6 (2%)	0	47 (14%)	5 (1%)	0
Constipation	32 (9%)	0	0	40 (12%)	0	0
Increased lipase	4 (1%)	17 (5%)	5 (1%)	1 (<1%)	3 (1%)	0
Neutropenia	11 (3%)	14 (4%)	10 (3%)	27 (8%)	26 (7%)	6 (2%)
Increased amylase	11 (3%)	10 (3%)	1 (<1%)	6 (2%)	0	0
Febrile neutropenia	0	9 (2%)	5 (1%)	1 (<1%)	7 (2%)	3 (1%)
Decreased neutrophil count	5 (1%)	6 (2%)	6 (2%)	4 (1%)	5 (1%)	4 (1%)
Thrombocytopenia	7 (2%)	5 (1%)	5 (1%)	25 (7%)	6 (2%)	3 (1%)
Maculo-papular rash	14 (4%)	5 (1%)	0	3 (1%)	1 (<1%)	0
Colitis	6 (2%)	5 (1%)	0	1 (<1%)	0	0
Increased alanine aminotransferase	19 (5%)	5 (1%)	0	12 (3%)	2 (1%)	0
Dehydration	6 (2%)	5 (1%)	0	5 (1%)	2 (1%)	0
Hepatotoxicity	5 (1%)	5 (1%)	0	2 (1%)	0	0
Decreased white blood cell count	7 (2%)	5 (1%)	0	6 (2%)	2 (1%)	0
Decreased platelet count	6 (2%)	2 (1%)	0	11 (3%)	5 (1%)	0
Adrenal insufficency	8 (2%)	4 (1%)	0	0	0	0

Data are n (%). Grade 1–2 treatment-related adverse events with an incidence of at least 10% in either group, and grade 3–4 events with an incidence of at least 1% in either group are shown. All grade 3 and 4 events are listed in the appendix (pp 20–23). Treatment-related adverse events included those reported between the first dose of study drug and 30 days after the last dose of study drug. According to the study sponsor practice, only events that led to death within 24 h were documented as grade 5 and are reported as deaths in the main text Results section. Events leading to death more than 24 h after onset are reported with the worst grade before death.

Table 3: **Treatment-related adverse events in all treated patients**

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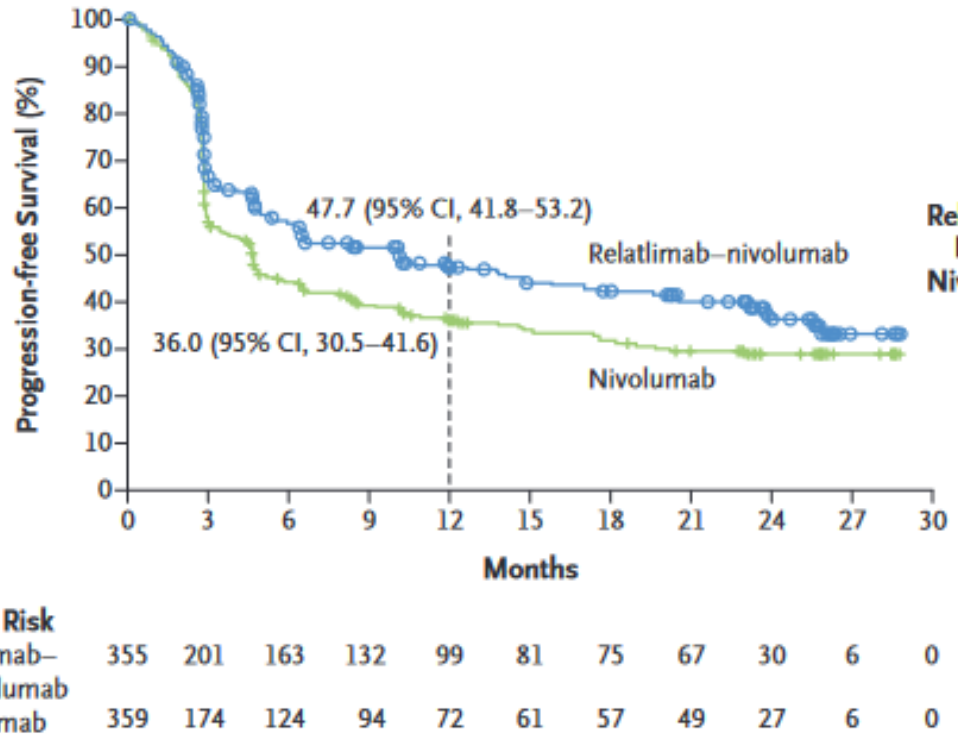
ORIGINAL ARTICLE

Relatlimab and Nivolumab versus Nivolumab in Uni

Hussein A. Tawbi, M
Paolo A. Ascierto, M
Piotr Rutkowski, M.D.,
Juliana Janos
Ana Arance, M.D.,
Mena Abaskharoun, P
Katy L. Simon
F. Stepher



	No. of Patients	Median Progression-free Survival (95% CI)
		mo
Relatlimab–Nivolumab	355	10.12 (6.37–15.74)
Nivolumab	359	4.63 (3.38–5.62)

Hazard ratio for progression or death, 0.75 (95% CI, 0.62–0.92)
P=0.006

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Adverse Event	Relatlimab–Nivolumab (N=355)		Nivolumab (N=359)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
	number of events (percent)			
Any adverse event	345 (97.2)	143 (40.3)	[redacted]	120 (33.4)
Treatment-related adverse event	288 (81.1)	67 (18.9)	251 (69.9)	35 (9.7)
Led to discontinuation of treatment	52 (14.6)	30 (8.5)	24 (6.7)	11 (3.1)
Treatment-related adverse event in ≥10% of patients in the relatlimab–nivolumab group				
Pruritus	83 (23.4)	0	57 (15.9)	2 (0.6)
Fatigue	82 (23.1)	4 (1.1)	46 (12.8)	1 (0.3)
Rash	55 (15.5)	3 (0.8)	43 (12.0)	2 (0.6)
Arthralgia	51 (14.4)	3 (0.8)	26 (7.2)	1 (0.3)
Hypothyroidism	51 (14.4)	0	43 (12.0)	0
Diarrhea	48 (13.5)	[redacted]	33 (9.2)	2 (0.6)
Vitiligo	37 (10.4)	0	35 (9.7)	0
Immune-mediated adverse event*				
Hypothyroidism or thyroiditis	64 (18.0)	[redacted]	50 (13.9)	0
Rash	33 (9.3)	2 (0.6)	24 (6.7)	5 (1.4)
Diarrhea or colitis	24 (6.8)	4 (1.1)	11 (3.1)	5 (1.4)
Hyperthyroidism	22 (6.2)	0	24 (6.7)	0
Hepatitis	20 (5.6)	14 (3.9)	9 (2.5)	4 (1.1)
Adrenal insufficiency	15 (4.2)	5 (1.4)	3 (0.8)	0
Pneumonitis	13 (3.7)	[redacted]	6 (1.7)	2 (0.6)
Hypophysitis	9 (2.5)	1 (0.3)	3 (0.8)	1 (0.3)
Nephritis and renal dysfunction	7 (2.0)	4 (1.1)	5 (1.4)	4 (1.1)
Hypersensitivity	4 (1.1)	0	4 (1.1)	0

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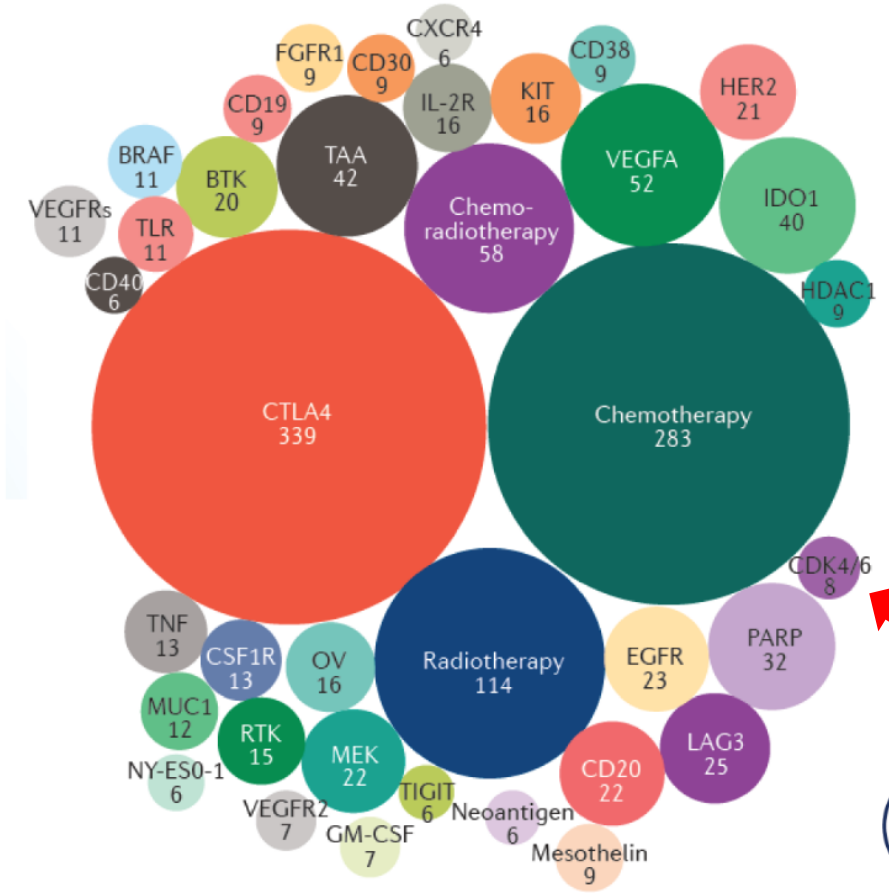
TOP 38 AGENTS IN COMBINATION WITH PD-1/L1 IN CLINICAL TRIALS



CANCER RESEARCH INSTITUTE

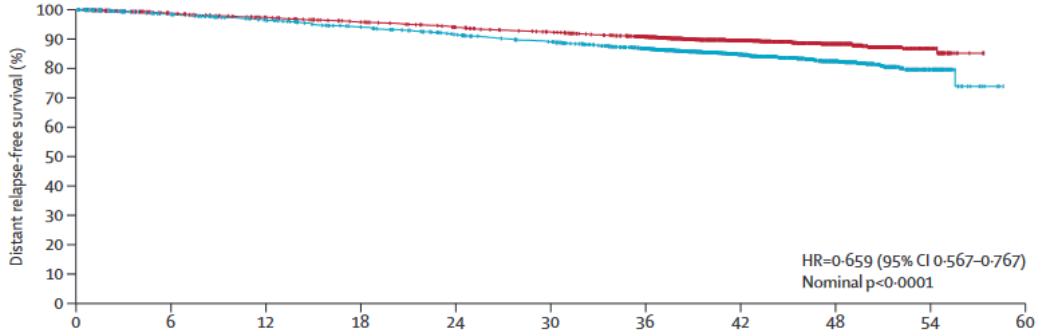
The Anna-Maria Kellen Clinical Accelerator

CDK 4/6i

Abemaciclib plus endocrine therapy for hormone receptor-positive, HER2-negative, node-positive, high-risk early breast cancer (monarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial

*Stephen R D Johnston, Masakazu Toi, Joyce O'Shaughnessy, Priya Rastogi, Mario Campone, Patrick Neven, Chiun-Sheng Huang, Jens Huober, Georgina Garnica Jaliffe, Irfan Cicin, Sara M Tolaney, Matthew P Goetz, Hope S Rugo, Elzbieta Senkus, Laura Testa, Lucia Del Mastro, Chikako Shimizu, Ran Wei, Ashwin Shahir, Maria Munoz, Belen San Antonio, Valérie André, Nadia Harbeck, Miguel Martin, on behalf of the monarchE Committee Members**

Distant relapse-free survival



Number at risk (number censored)											
Abemaciclib plus endocrine therapy	2808 (0)	2629 (147)	2567 (174)	2500 (196)	2434 (217)	2374 (236)	2244 (326)	1251 (1293)	535 (2001)	81 (2447)	0 (2527)
Endocrine therapy alone	2829 (0)	2659 (127)	2589 (148)	2499 (172)	2410 (194)	2327 (213)	2151 (334)	1231 (1210)	526 (1895)	85 (2324)	0 (2408)

Gängige Präparate

Abemaciclib (Verzenios®)
Ribociclib (Kisqali®)
Palbociclib (Ibrance®)

	Abemaciclib (*Verzenios*)	**Ribociclib** (*Kisqali*)	**Palbociclib** (*Ibrance*)
Dosierungsschema	Kontinuierlich, täglich	Diskontinuierlich, 21 Tage + 7 Tage Pause	Diskontinuierlich, 21 Tage + 7 Tage Pause
Reguläre Dosis	150 mg 1-0-1	600 mg / Tag	125 mg / Tag
1te Dosisreduktion	100 mg 1-0-1	400 mg / Tag	100 mg / Tag
2te Dosisreduktion	50 mg 1-0-1	200 mg / Tag	75 mg / Tag

CDK 4/6i

	Abemaciclib plus endocrine therapy (n=2791)			
	Grade 1–2	Grade 3	Grade 4	Grade 5
Any	1353 (48·5%)	1289 (46·2%)	88 (3·2%)	16 (0·6%)
Diarrhoea	2114 (75·7%)	218 (7·8%)	0	1 (<0·1%)
Fatigue	1060 (38·0%)	80 (2·9%)	0	0
Abdominal pain	957 (34·3%)	39 (1·4%)	0	0
Nausea	811 (29·1%)	14 (0·5%)	0	0
Leukopenia	734 (26·3%)	314 (11·3%)	4 (0·1%)	0
Neutropenia	733 (26·3%)	529 (19·0%)	19 (0·7%)	0
Arthralgia	731 (26·2%)	9 (0·3%)	0	0
Anaemia	626 (22·4%)	57 (2·0%)	1 (<0·1%)	0
Headache	545 (19·5%)	8 (0·3%)	0	0
Vomiting	476 (17·1%)	15 (0·5%)	0	0
Hot flush	427 (15·3%)	4 (0·1%)	0	0
Cough	390 (14·0%)	1 (<0·1%)	0	0
Lymphoedema	346 (12·4%)	5 (0·2%)	0	0
Thrombocytopenia	337 (12·1%)	28 (1·0%)	8 (0·3%)	0
Constipation	334 (12·0%)	2 (0·1%)	0	0
Urinary tract infection	321 (11·5%)	16 (0·6%)	0	0
Alopecia	318 (11·4%)	0	0	0
Decreased appetite	315 (11·3%)	16 (0·6%)	0	0
Blood creatinine increased	308 (11·0%)	3 (0·1%)	0	0
Rash	305 (10·9%)	11 (0·4%)	0	0
Dizziness	301 (10·8%)	4 (0·1%)	0	0
Upper respiratory tract infection	296 (10·6%)	6 (0·2%)	0	0
Pain in extremity	284 (10·2%)	3 (0·1%)	0	0
Aspartate aminotransferase increased	283 (10·1%)	50 (1·8%)	3 (0·1%)	0
Pyrexia	279 (10·0%)	2 (0·1%)	0	0
Alanine aminotransferase increased	274 (9·8%)	72 (2·6%)	5 (0·2%)	0
Lymphopenia	246 (8·8%)	148 (5·3%)	3 (0·1%)	0
Hypertension	106 (3·8%)	30 (1·1%)		0
Hypokalaemia	90 (3·2%)	28 (1·0%)	4 (0·1%)	0

VERZENIO® is a kinase inhibitor indicated:

- in combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence and a Ki-67 score ≥20% as determined by an FDA approved test. (1.1, 2.1, 14.1)
- in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer. (1.2)
- in combination with fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy. (1.2)
- as monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting. (1.2)

Clinicaltrials.gov

Search Results

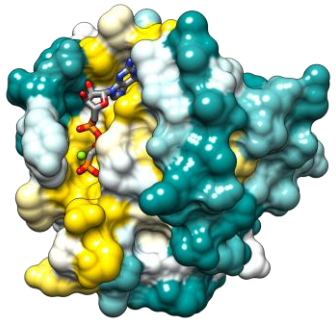
Viewing 1-10 out of 155 studies

Showing results for: **abemaciclib**

Med Uni Graz

KRAS

KRAS is the most frequently mutated isoform of RAS mutations (86%), and is mutated in 90% of pancreatic cancers, 40% of colorectal cancers, and 30% of lung cancers. Cancers with these mutations are associated with poor treatment responses and a poor prognosis[a]



KRAS: 189 AA
BRAF: 766 AA
TP53: 1972 AA
PTEN: 403 AA
EGFR: 1210 AA

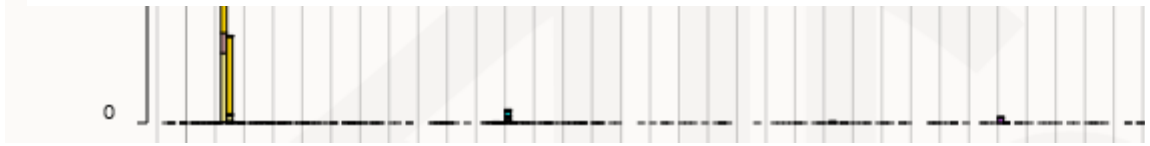
Med Uni Graz

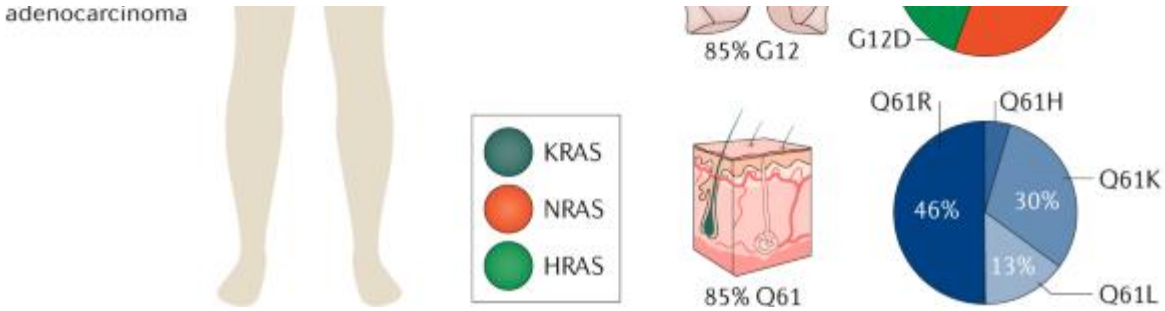
Review Article | Published: 17 October 2014

Drugging the undruggable RAS: Mission Possible?

Adrienne D. Cox, Stephen W. Fesik, Alec C. Kimmelman, Ji Luo & Channing J. Der

Nature Reviews Drug Discovery 13, 828–851 (2014) | Cite this article



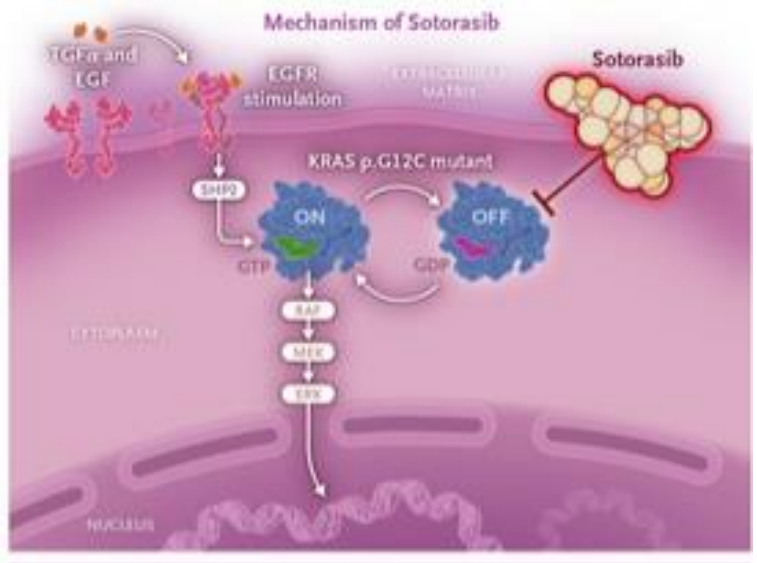


10.1016/j.lungcan.2024.107886
10.1016/S1470-2045(21)00091-7
10.1038/s41573-020-0089-1

https://cancer.sanger.ac.uk/cosmic/gene/analysis?ln=KRAS

KRAS

	Any Grade	Grade 1 or 2	Grade 3	Grade 4	Fatal
	number of patients (percent)				
Adverse event	125 (99.2)	48 (38.1)	53 (42.1)	4 (3.2)	20 (15.9)
Treatment-related adverse event	88 (69.8)	62 (49.2)	25 (19.8)	1 (0.8)	0
Treatment-related adverse event leading to dose modification	28 (22.2)	8 (6.3)	20 (15.9)	0	0
Treatment-related adverse event leading to discontinuation of therapy	9 (7.1)	4 (3.2)	4 (3.2)	1 (0.8)	0
Treatment-related adverse event of any grade occurring in >5% of the patients or that was grade ≥3					
Diarrhea	40 (31.7)	35 (27.8)	5 (4.0)	0	0
Nausea	24 (19.0)	24 (19.0)	0	0	0
Alanine aminotransferase increase	19 (15.1)	11 (8.7)	8 (6.3)	0	0
Aspartate aminotransferase increase	19 (15.1)	12 (9.5)	7 (5.6)	0	0
Fatigue	14 (11.1)	14 (11.1)	0	0	0
Vomiting	10 (7.9)	10 (7.9)	0	0	0
Blood alkaline phosphatase increase	9 (7.1)	8 (6.3)	1 (0.8)	0	0
Maculopapular rash	7 (5.6)	7 (5.6)	0	0	0
Hypokalemia	5 (4.0)	4 (3.2)	1 (0.8)	0	0
Drug-induced liver injury	3 (2.4)	1 (0.8)	2 (1.6)	0	0
γ-Glutamyltransferase increase	3 (2.4)	0	3 (2.4)	0	0
Lymphocyte count decrease	3 (2.4)	2 (1.6)	1 (0.8)	0	0
Dyspnea	2 (1.6)	1 (0.8)	0	1 (0.8)	0
Pneumonitis	2 (1.6)	0	1 (0.8)	1 (0.8)	0
Abnormal hepatic function	2 (1.6)	1 (0.8)	1 (0.8)	0	0
Lymphopenia	1 (0.8)	0	1 (0.8)	0	0
Neutropenia	1 (0.8)	0	1 (0.8)	0	0
Hepatotoxic event	1 (0.8)	0	1 (0.8)	0	0
Drug hypersensitivity	1 (0.8)	0	1 (0.8)	0	0
Cellulitis	1 (0.8)	0	1 (0.8)	0	0
Lipase increased	1 (0.8)	0	1 (0.8)	0	0
Increase in liver-function level†	1 (0.8)	0	1 (0.8)	0	0
Neutrophil count decrease	1 (0.8)	0	1 (0.8)	0	0
Abnormal aminotransferase level‡	1 (0.8)	0	1 (0.8)	0	0



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10.1016/j.lungcan.2024.107886
10.1056/NEJMoa2103695

KRAS

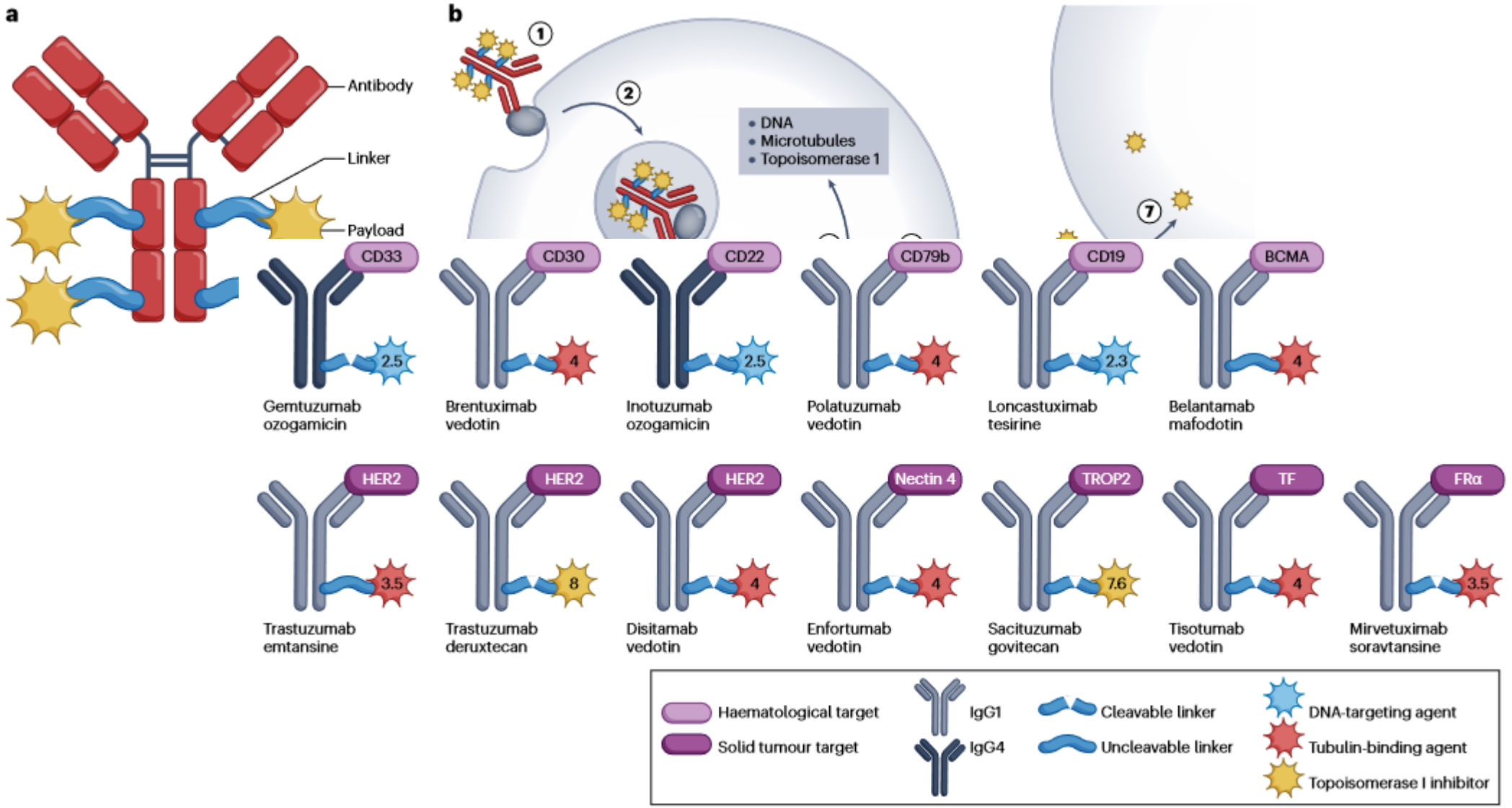
Med Uni Graz

Meeting Abstract: 2024 ASCO Annual Meeting I
FREE ACCESS | Lung Cancer—Non–Small Cell Metastatic | May 29, 2024

Sotorasib versus pembrolizumab in combination with platinum doublet chemotherapy as first-line treatment for metastatic or locally advanced, PD-L1 negative, *KRAS* G12C-mutated NSCLC (CodeBreaK 202).

Authors: Fabrice Barlesi, Enriqueta Felip, Sanjay Popat, Benjamin J. Solomon, Juergen Wolf, Bob T. Li, Yi-Long Wu, ... SHOW ALL ..., and Hossein

ADC - Antibody-drug conjugates



10.1038/s41573-023-00709-2

ADC

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 7, 2022 VOL. 387 NO. 1

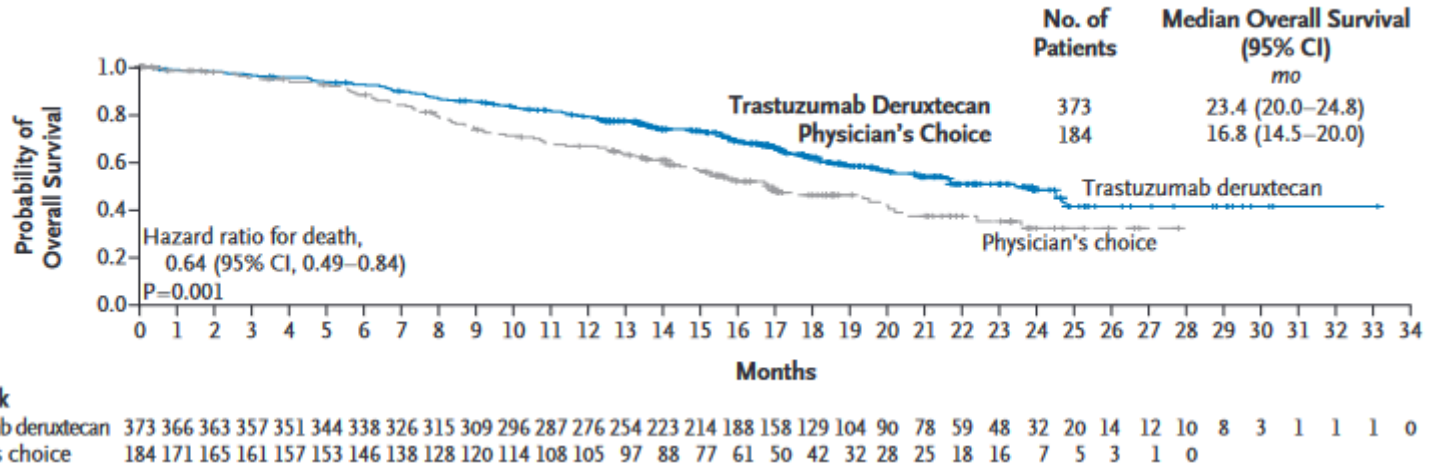
Med Uni Graz

Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer

S. Modi, W. Jacot, T. Yamashita, J. Sohn, M. Vidal, E. Tokunaga, J. Tsurutani, N.T. Ueno, A. Prat, Y.S. Chae, K.S. Lee, N. Niikura, Y.H. Park, B. Xu, X. Wang, M. Gil-Gil, W. Li, J.-Y. Pierga, S.-A. Im, H.C.F. Moore, H.S. Rugo, R. Yerushalmi, F. Zagouri, A. Gombos, S.-B. Kim, Q. Liu, T. Luo, C. Saura, P. Schmid, T. Sun, D. Gambhire, L. Yung, Y. Wang, J. Singh, P. Vitazka, G. Meinhardt, N. Harbeck, and D.A. Cameron, for the DESTINY-Breast04 Trial Investigators*

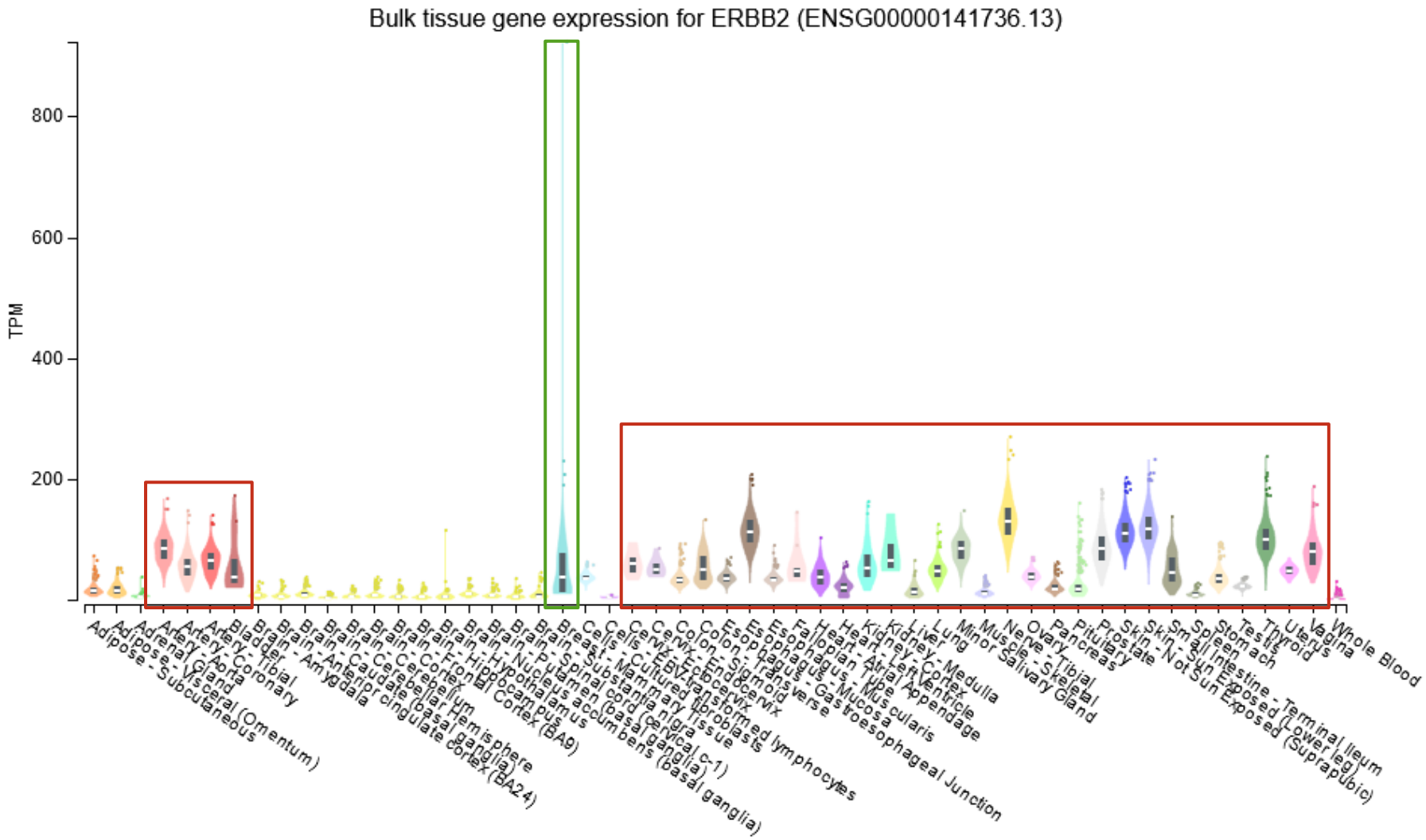
Lines of therapy for metastatic disease	
Median no. of lines (range)	3 (1–9)
No. of lines — no. of patients (%)	
1	23 (6.9)
2	85 (25.7)
≥3	223 (67.4)

D Overall Survival among All Patients



ADC

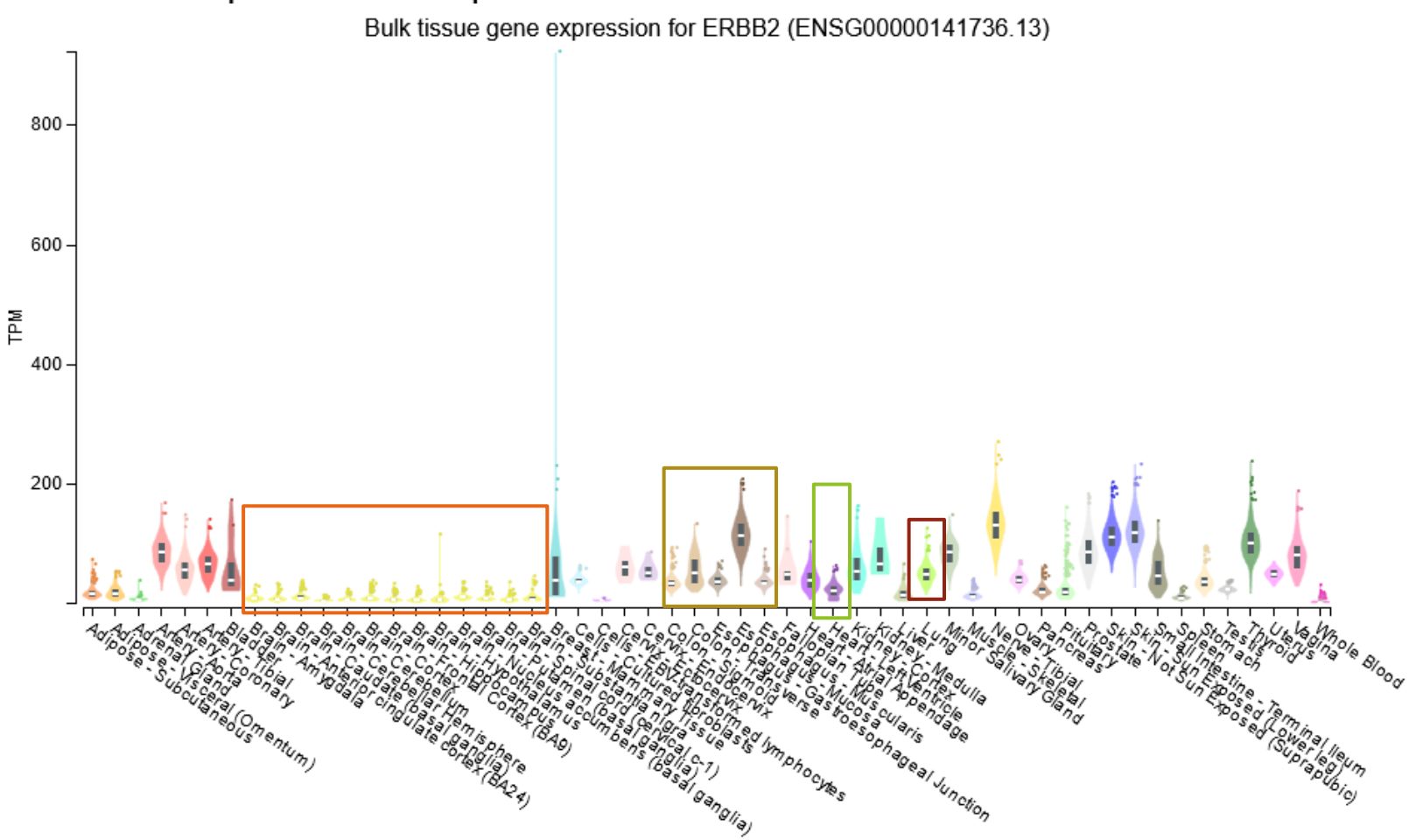
Spezifität?



HER2/neu Expression -> guter Marker für die Wirksamkeit der Therapie

ADC

System organ class	*Very Common*	*Common*	*Uncommon*	*Rare*
Infections and infestations	Nasopharyngitis	Paronychia Upper respiratory tract infection		
Blood and lymphatic system disorders	Febrile neutropenia* Neutropenia Leucopenia Anaemia			
Immune system disorders	Infusion reaction°°, *	Hypersensitivity°, * Drug hypersensitivity°, *		
Metabolism and nutrition disorders	Decreased appetite			
Psychiatric disorders	Insomnia			
Nervous system disorders	Neuropathy peripheral Headache Dysgeusia Peripheral sensory neuropathy Dizziness Paraesthesia			
Eye disorders	Lacrimation increased			
Cardiac disorders		Left ventricular dysfunction **		
Vascular disorders	Hot flush			
Respiratory, thoracic and mediastinal disorders	Cough Epistaxis Dyspnoea			
Gastrointestinal disorders	Diarrhoea Vomiting Stomatitis Nausea Constipation Dyspepsia Abdominal pain			



ADC

Table 3. Most Common Drug-Related Advers

Event
Blood and lymphatic system disorders
Neutropenia†
Anemia‡
Thrombocytopenia§
Leukopenia¶
Gastrointestinal disorders
Nausea
Vomiting
Diarrhea
Constipation
Investigations: increased aminotransferase l
General disorders: fatigue**
Metabolism and nutrition disorders: decreas appetite
Skin and subcutaneous tissue disorders: alo

Company, Partner	Drug code (INN)	Target	Isotype	Linker	Average DAR	Payload	Clinical status	Indications[c]
Eisai, Bristol Myers Squibb	MORAb-202 (farletuzumab ecteribulin)	FRα	IgG1	Valine–citrulline (cleavable)	4 (Cys)	Eribulin	Phase II	NSCLC, ovarian cancer
Hangzhou DAC Biotechnology	DX126-262, DAC-001	HER2	Unknown	Undisclosed	3.5–3.8 (Cys)	Tubulysin B analogue Tub114	Phase II	HER2+ BC
Shanghai Miracogen	MRG002	HER2	IgG1	Valine–citrulline (cleavable)	3.6 (Cys)	MMAE	Phase II	BC, NSCLC, urothelium cancer, BT cancer, GC
Shanghai Miracogen	MRG003	EGFR	IgG1	Valine–citrulline (cleavable)	(Cys)	MMAE	Phase II	GC/GOJ, NPC, BT cancer, NSCLC, HNSCC
BioAlta, Himalaya Therapeutics	BA3021 (ozuriftamab vedotin)	ROR2	IgG1κ	Valine–citrulline (cleavable)	4 (Cys)	MMAE	Phase II	HNSCC, NSCLC, ovarian cancer
BioAlta, Himalaya Therapeutics	BA3011 (mecbotamab vedotin)	AXL receptor tyrosine kinase	IgG1κ	Valine–citrulline (cleavable)	4 (Cys)	MMAE	Phase II	Ovarian cancer, NSCLC
Seagen, Merck Sharp & Dohme	SGN-LIV1A (ladiratuzumab vedotin)	LIV-1 (SLC39A6)	IgG1κ	Valine–citrulline (cleavable)	4 (Cys)	MMAE	Phase II	Lung cancer, solid tumours
Daiichi Sankyo	DS-7300a (ifinatamab deruxtecan)	B7-H3	IgG1κ	Glycine–glycine–phenylalanine–glycine (cleavable)	4 (Cys)	DXD	Phase II	SCLC
CytomX Therapeutics	CX-2009 (Praluzatamab ravtansine)	ALCAM	IgG1κ	SPDB (cleavable)	3.5 (Lys)	DM4	Phase II	BC
ImmunoGen	IMGN632 (pivekimab sunirine)	CD123	IgG1κ	Alanine–alanine (cleavable)	2 (engineered Cys 446)	DGN549 IGN, site-specific	Phase II (pivotal)	Blastic plasmacytoid dendritic cell neoplasm
ADC Therapeutics Sarl	ADCT-301 (camidanlumab tesirine)	CD25	IgG1κ	Valine–alanine (cleavable)	2.3 (Cys)	PBD SG3199	Phase II (pivotal)	HL, AML/ MDS/ MPN
Macrogenics	MGC018 (vobramitamab duocarmazine)	B7-H3	IgG1κ	Valine–citrulline (cleavable)	2.7	Duocarmycin	Phase II/III	Prostate cancer
Merck Sharp & Dohme	MK-2140 (zilovertamab vedotin)	ROR1	IgG1κ	Valine–citrulline (cleavable)	4 (Cys)	MMAE	Phase II/III	DLBCL
Kelun-Biotech, MSD	SKB264	TROP2		Stable linker	7.4 (Cys)	Belotecan	Phase III pending	TNBC
Daiichi Sankyo, AstraZeneca	DS-1062 (datopotamab deruxtecan)	TROP2	IgG1κ	Glycine–glycine–phenylalanine–glycine (cleavable)	4 (Cys)	DXD	Phase III	BC
Sanofi, Innovent	SAR408701 (tusamitamab ravtansine)	CEACAM5	IgG1κ	SPDB (cleavable)	3.8 (Lys)	DM4	Phase III	NSCLC
Daiichi Sankyo	U3-1402 (patritumab deruxtecan)	HER3	IgG1κ	Glycine–glycine–phenylalanine–glycine (cleavable)	8 (Cys)	DXD	Phase III	NSCLC
AbbVie	ABBV-399 (telisotuzumab vedotin)	MET	IgG1κ	Valine–citrulline (cleavable)	3.1 (Cys)	MMAE	Phase III	NSLC
Ambrx, NovoCodex	ARX788	HER2	IgG1	Oxime (non-cleavable)	1.8; site-specific	Amberstatin 269	Phase III	HER2+ BC
Jiangsu HengRui Medicine	SHR-A1811 (trastuzumab rezetecan)	HER2	IgG1κ	Undisclosed	5.3–6.4 (Cys)	Rezetecan	Phase III	HER2+ BC
Mersana Therapeutics	XMT-1536 (upifitamab rilsodotin)	NaPi2b	IgG1κ	Dolaflexin polymer scaffold	10–15 (Cys)	Auristatin F-hydroxypropylamide	Phase III	Ovarian cancer

Anzuwendende Dosis
4,4 mg/kg
3,2 mg/kg
Behandlungsabbruch

Bedarf für eine weitere Dosisreduktion

10.1038/s41573-023-00709-2

Bispecific antibodies

ORIGINAL ARTICLE

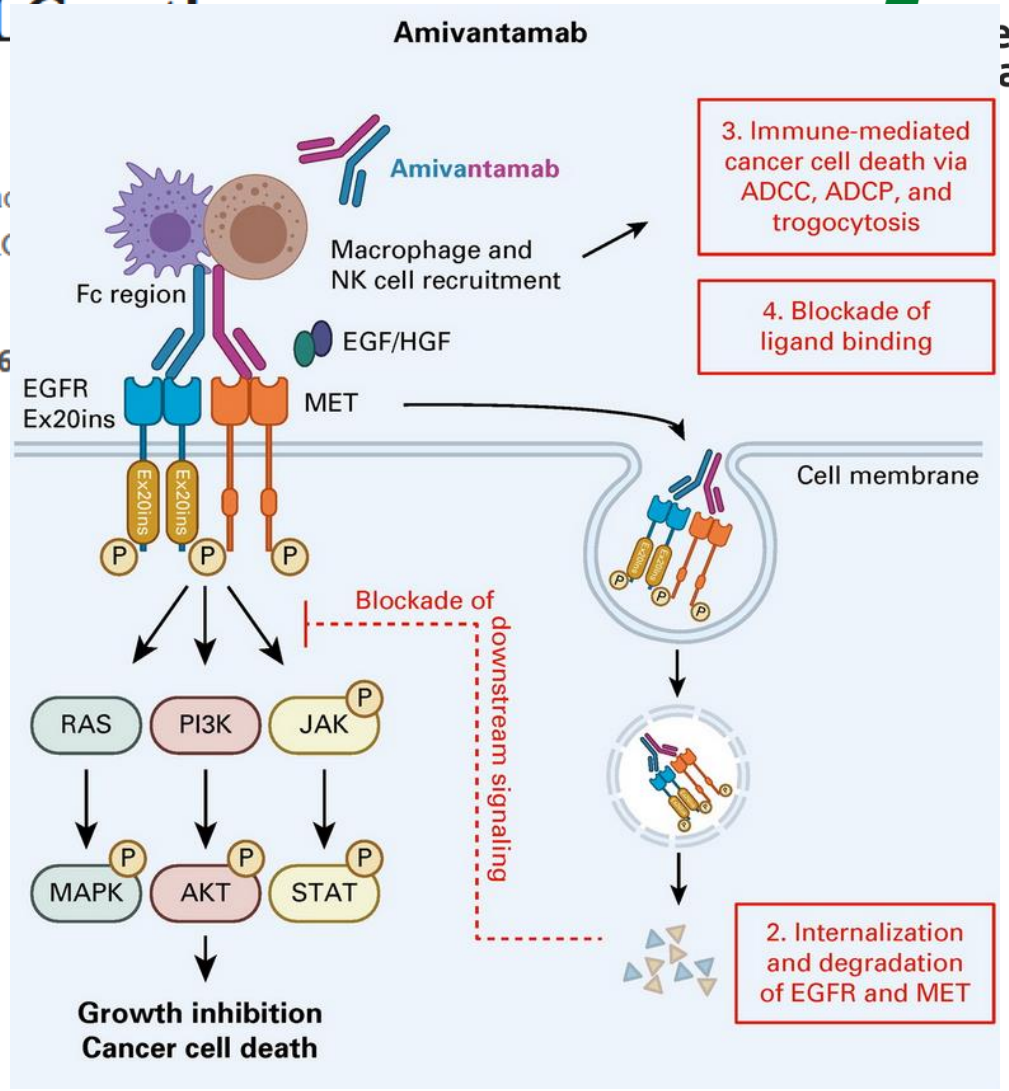
Amivantamab plus Chemotherapy in NSCL[illegible] EGFR Exon 20 Insertions

Authors: Caicun Zhou, M.D., Ph.D., Ke-Jing Tang, M.D., Ph.D., Byoung Chul Cho, M.D., Ph.D., Bac[illegible] Paz-Ares, M.D., Ph.D., Susanna Cheng, M.D., Satoru Kitazono, M.D., Ph.D., +21, for the PAPILL[illegible] Investigators* Author Info & Affiliations

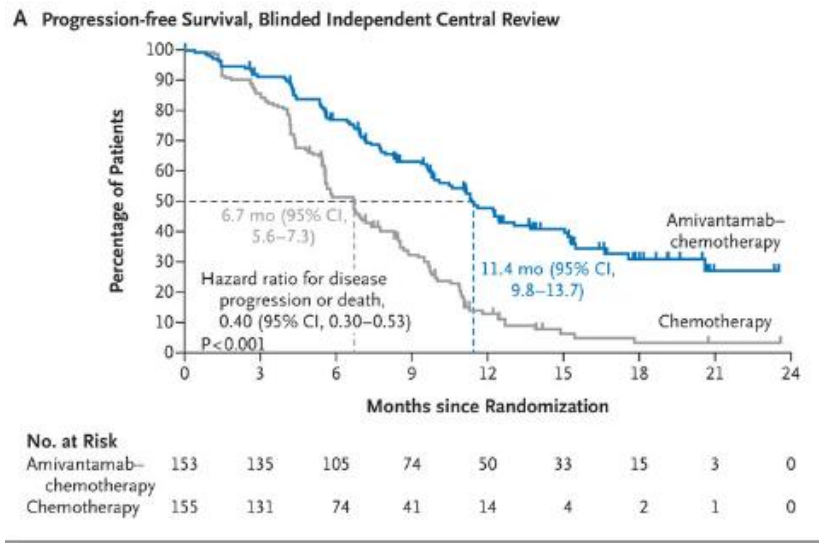
Published October 21, 2023 | **N Engl J Med 2023;389:2039-2051** | **DOI: 10.1056/NEJMoa2306**

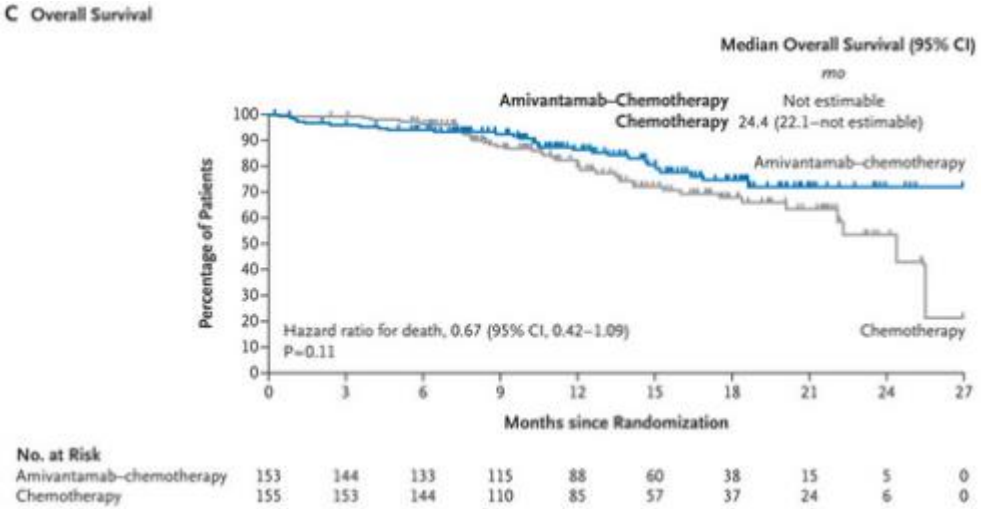
VOL. 389 NO. 22

Amivantamab is an EGFR mesenchymal–epithelial transition factor (MET) bispecific antibody with immune cell–directing activity



Bispecific antibodies





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Bispecific antibodies

Table 3. (Continued.)

Adverse Events	Amivantamab–Chemotherapy (N=151)		Chemotherapy (N=155)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
	number of patients (percent)			
Adverse events reported in ≥15% of patients in either group§				
Neutropenia	89 (59)	50 (33)	70 (45)	35 (23)
Paronychia	85 (56)	10 (7)	0	0
Rash	81 (54)	17 (11)	12 (8)	0
Anemia	76 (50)	16 (11)	85 (55)	19 (12)
Infusion-related reaction	63 (42)	2 (1)	2 (1)	0
Hypoalbuminemia	62 (41)	6 (4)	15 (10)	0
Constipation	60 (40)	0	47 (30)	1 (1)
Leukopenia	57 (38)	17 (11)	50 (32)	5 (3)
Nausea	55 (36)	1 (1)	65 (42)	0
Thrombocytopenia	55 (36)	15 (10)	46 (30)	16 (10)
Decreased appetite	54 (36)	4 (3)	43 (28)	2 (1)
Increased alanine aminotransferase	50 (33)	6 (4)	56 (36)	2 (1)
Increased aspartate aminotransferase	47 (31)	1 (1)	51 (33)	1 (1)
Dermatitis acneiform	47 (31)	6 (4)	5 (3)	0
Peripheral edema	45 (30)	2 (1)	16 (10)	0
Stomatitis	38 (25)	2 (1)	9 (6)	0
Covid-19	36 (24)	3 (2)	21 (14)	1 (1)
Diarrhea	31 (21)	5 (3)	20 (13)	2 (1)
Hypokalemia	32 (21)	13 (9)	13 (8)	2 (1)
Vomiting	32 (21)	5 (3)	29 (19)	1 (1)
Asthenia	30 (20)	8 (5)	29 (19)	4 (3)
Pyrexia	24 (16)	0	9 (6)	0
Fatigue	23 (15)	1 (1)	32 (21)	2 (1)
Increased γ-glutamyltransferase	21 (14)	4 (3)	26 (17)	6 (4)
Cough	21 (14)	0	24 (15)	0

Ausblick: mRNA Vaccination

Med Uni Graz

Article | Published: 29 July 2020

An RNA vaccine drives immunity in checkpoint-inhibitor-treated melanoma

Ugur Sahin, Petra Oehm, [...] Özlem Türeci

Nature **585**, 107–112(2020) | Cite this article

15k Accesses | **26** Citations | **182** Altmetric | Metrics

Multicentre, open-label, dose-escalation Phase I trial

Sie entwickelten den Corona-Impfstoff

26.02.2021, 16:00 Uhr

Biontech-Gründer Türeci und Sahin erhalten Bundesverdienstkreuz

Das Forscher-Ehepaar Özlem Türeci und Ugur Sahin soll die Auszeichnung am 19. März im Schloss Bellevue von Bundespräsident Frank-Walter Steinmeier erhalten.

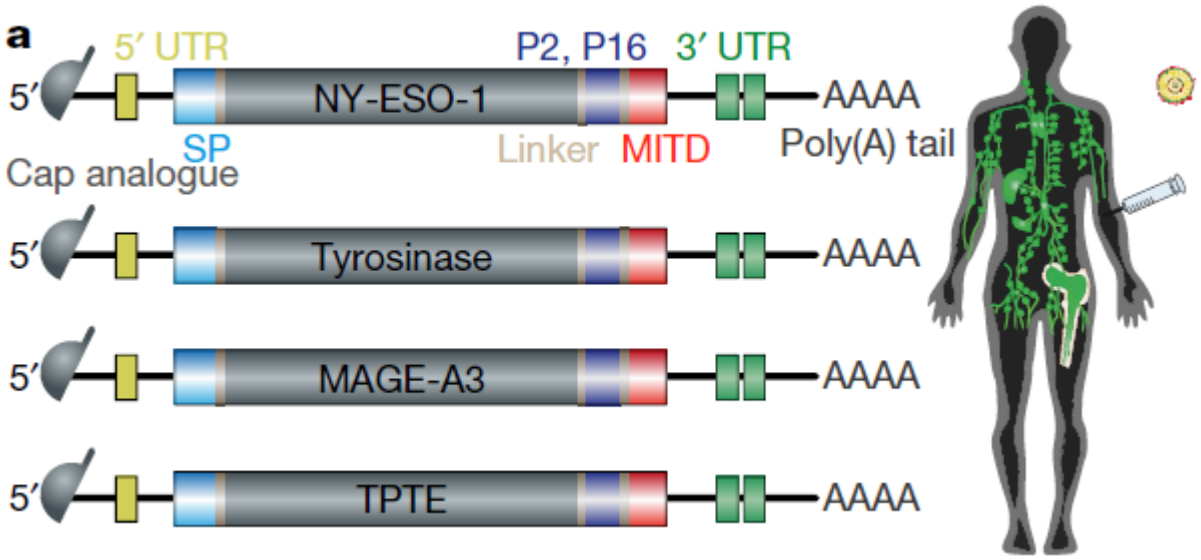
14

Ugur Sahin (l.) und Özlem Türeci sind die Gründer des Impfstoff-Herstellers Biontech. Sie erhalten am 19. März das… FOTO: IMAGO/SÄMMER

BNT111

Ausblick: mRNA Vaccination

TAA RNA Design



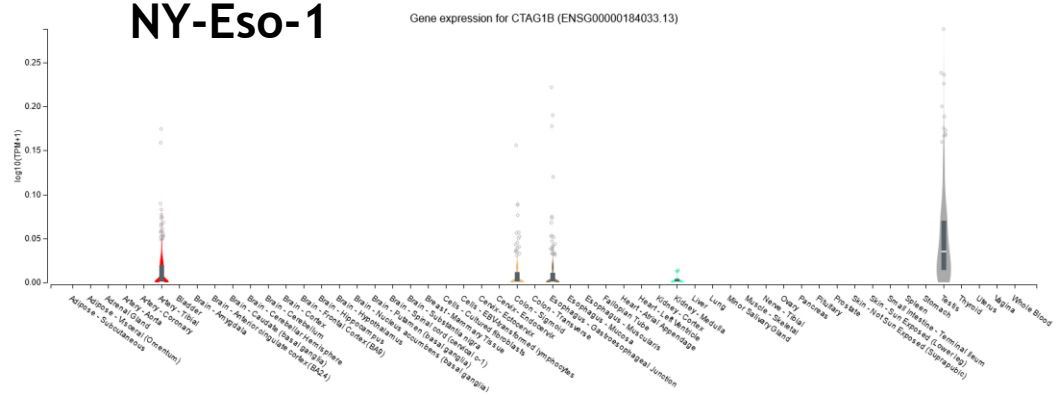
SP = signal peptide
P2,P16 = tetanus toxoid $CD4^+$ epitopes P2 und P16
MITD = MHC class I trafficking domain

HGNC approved name/symbol
NY-ESO-1 = cancer/testis antigen 1B (CTAG1B)
MAGE-A3 = MAGE (melanoma-associated antigen) family member A3 (MAGEA3)
TPTE = transmembrane phosphatase with tensin homology (TPTE)

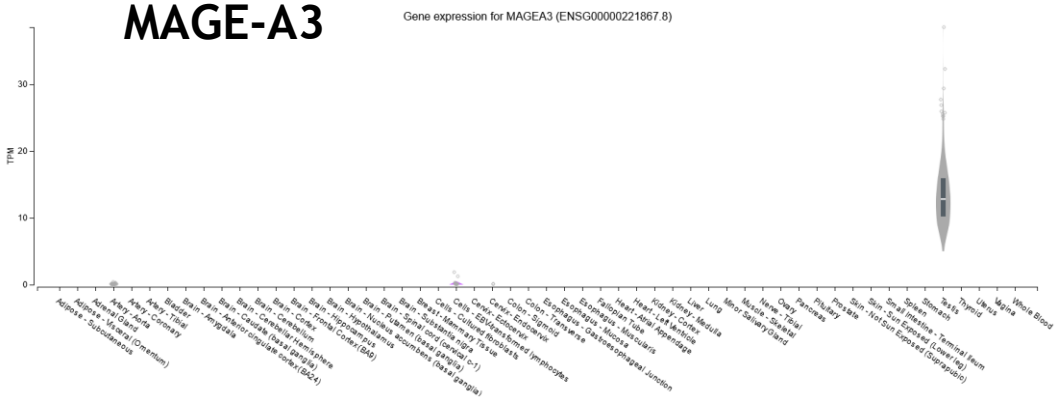
Ausblick: mRNA Vaccination

Tissue gene expression

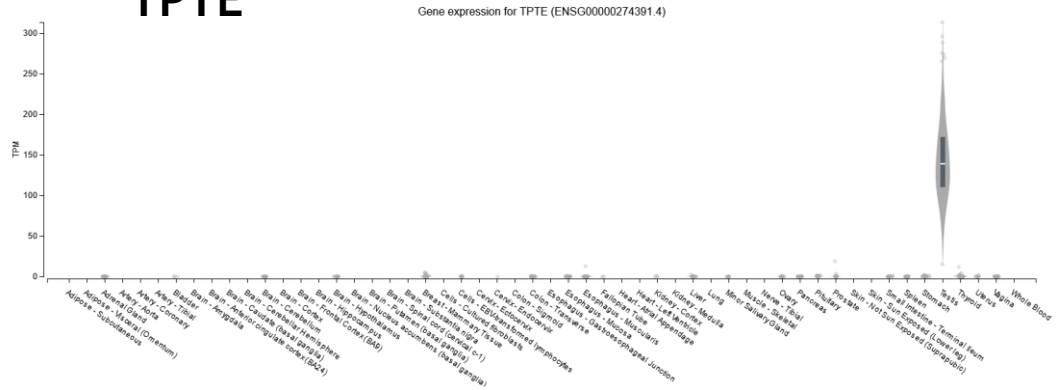
NY-Eso-1



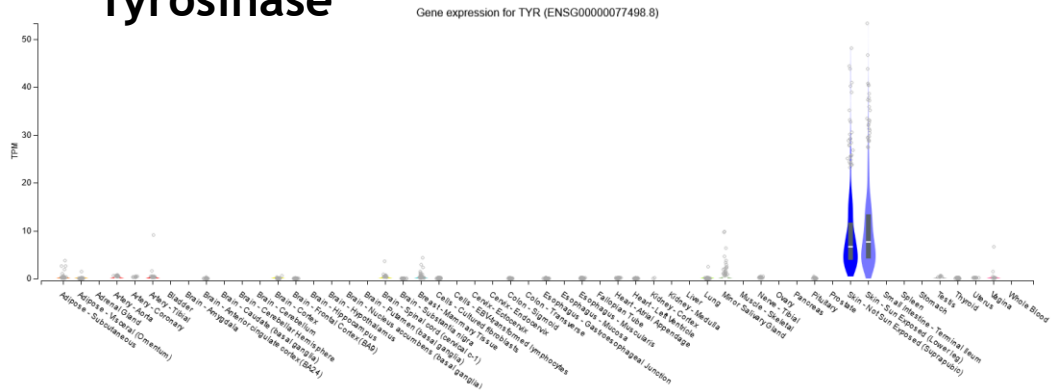
MAGE-A3



TPTE



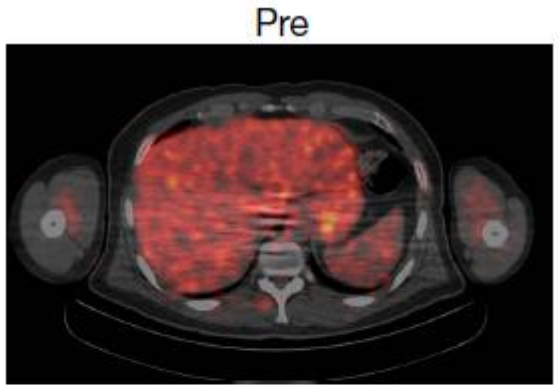
Tyrosinase



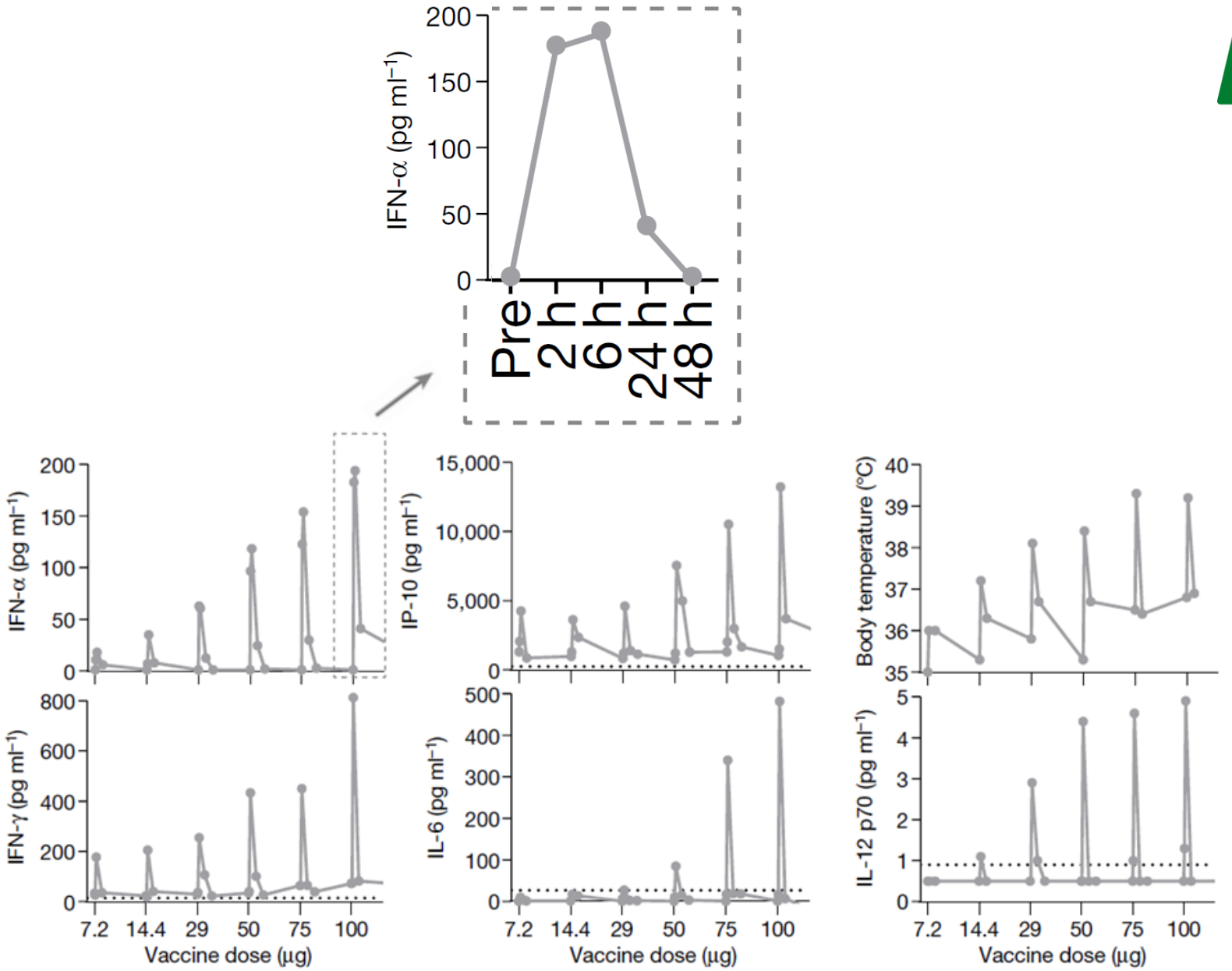
Source: https://gtexportal.org

Ausblick: mRNA Vaccination

Post-Injection reaction?



FDG-PET-CT



Ausblick: mRNA Vaccination

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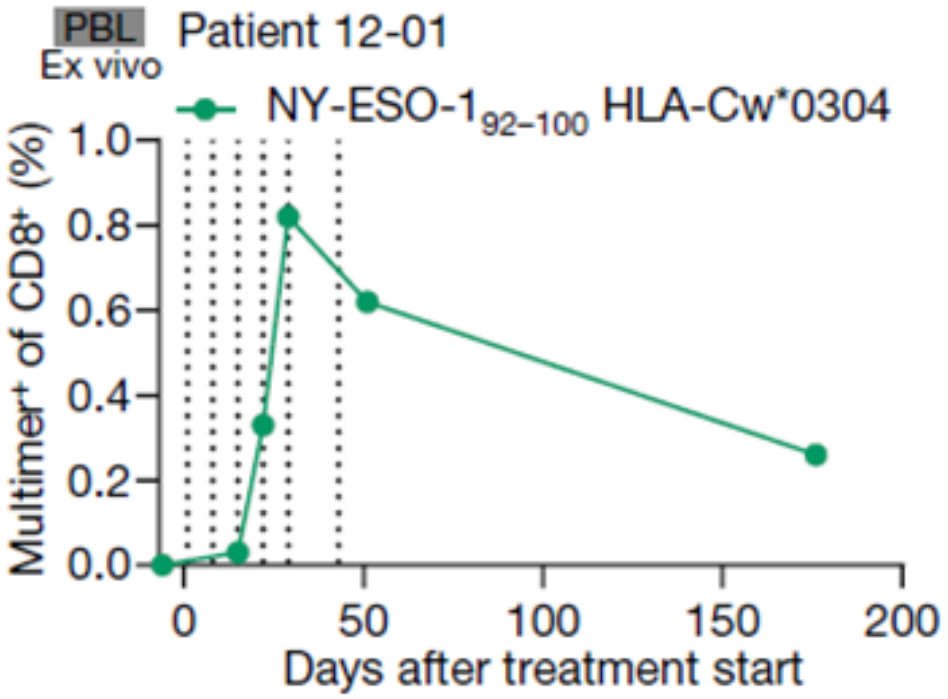
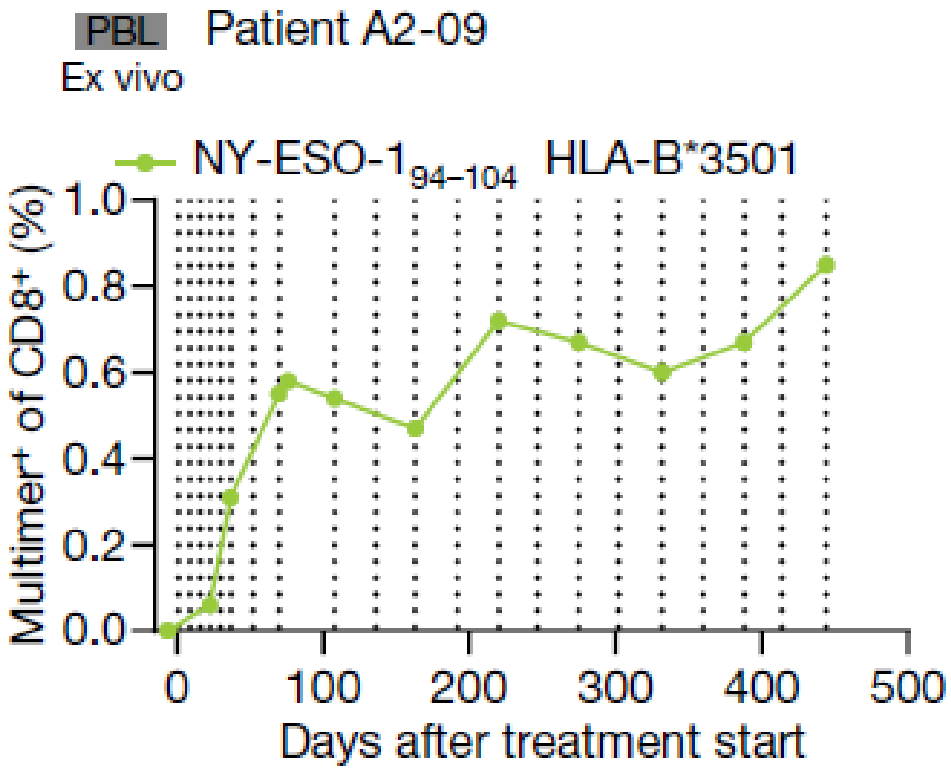
Durability

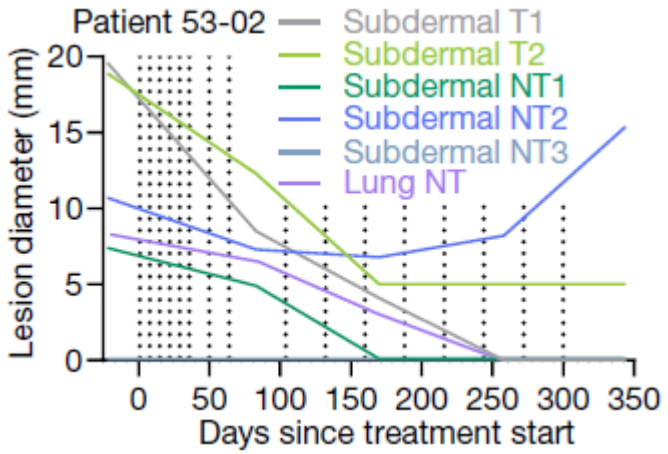


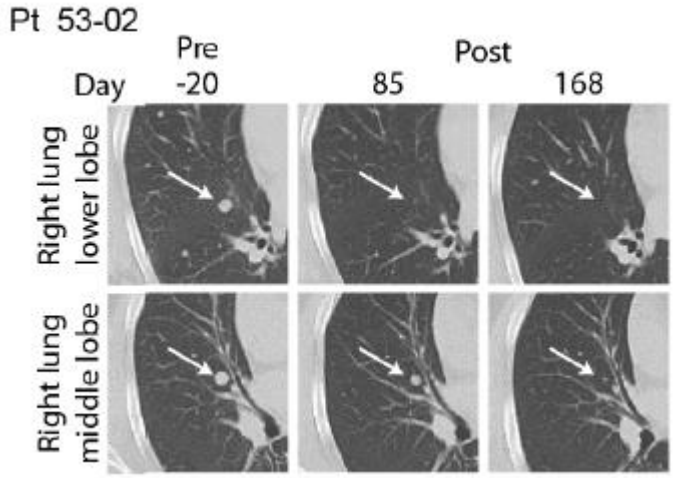
Maintenance vaccination

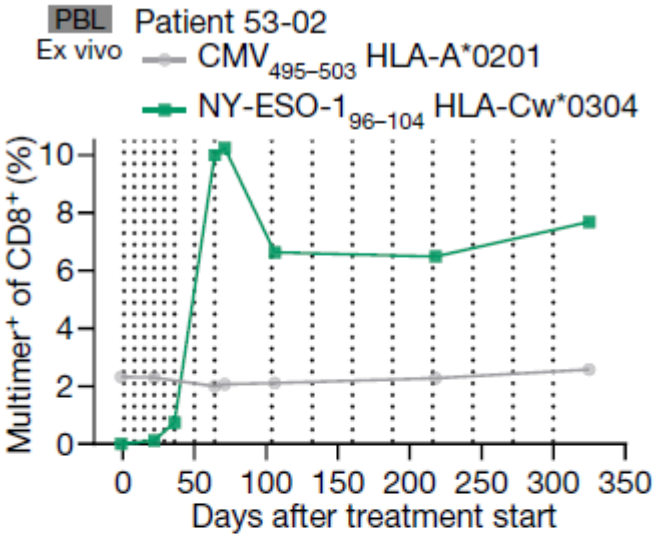


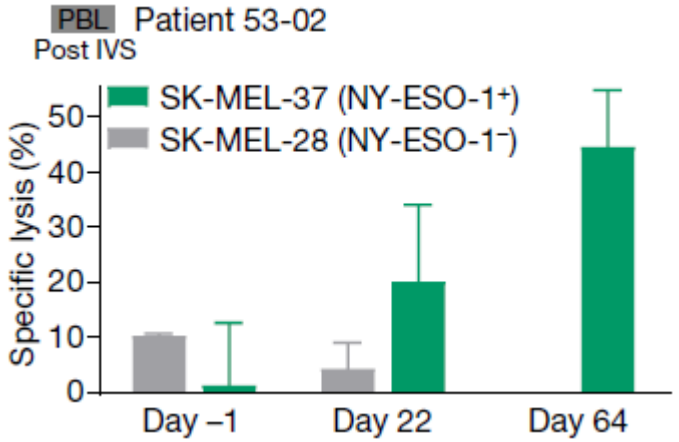
Ausblick: mRNA Vaccination

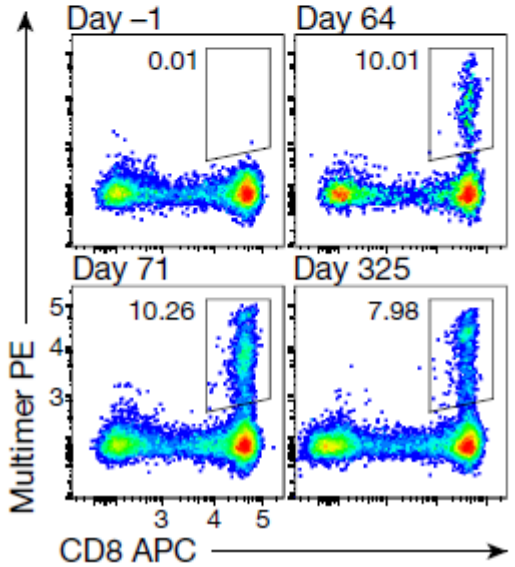
Pt 53-02











Ausblick: mRNA Vaccination

AEs

Extended Data Table 4 | Related adverse events that emerge after treatment in more than 5% of patients

MedDRA preferred term	Grade 1		Grade 2		Grade 3		Grade 4		Grade 5		Total (N=89)	
Pyrexia	36	40%	33	37%	4	4%	.	.	.	.	73	82%
Chills	37	42%	25	28%	1	1%	.	.	.	.	63	71%
Headache	27	30%	6	7%	.	.	.	.	.	.	33	37%
Fatigue	18	20%	3	3%	.	.	.	.	.	.	21	24%
Nausea	11	12%	9	10%	.	.	.	.	.	.	20	22%
Tachycardia	16	18%	3	3%	.	.	.	.	.	.	19	21%
Feeling cold	15	17%	1	1%	.	.	.	.	.	.	16	18%
Arthralgia	11	12%	2	2%	.	.	.	.	.	.	13	15%
Pain in extremity	11	12%	2	2%	.	.	.	.	.	.	13	15%
Vomiting	6	7%	6	7%	.	.	.	.	.	.	12	13%
Lymphocyte count decreased	1	1%	3	3%	6	7%	1	1%	.	.	11	12%
Interferon gamma level increased	8	9%	2	2%	.	.	.	.	.	.	10	11%
Lymphopenia	.	.	4	4%	5	6%	.	.	.	.	9	10%
Cytokine abnormal	7	8%	2	2%	.	.	.	.	.	.	9	10%
Interleukin level increased	8	9%	.	.	.	.	.	.	.	.	8	9%
Hypertension	1	1%	2	2%	4	4%	.	.	.	.	7	8%
Dizziness	4	4%	1	1%	1	1%	.	.	.	.	6	7%
Diarrhoea	5	6%	1	1%	.	.	.	.	.	.	6	7%
Alpha tumour necrosis factor increased	6	7%	.	.	.	.	.	.	.	.	6	7%
Body temperature increased	6	7%	.	.	.	.	.	.	.	.	6	7%
Influenza like illness	4	4%	1	1%	.	.	.	.	.	.	5	6%
White blood cell count decreased	4	4%	1	1%	.	.	.	.	.	.	5	6%
Not coded	1	1%	3	3%	1	1%	.	.	.	.	5	6%

MedDRA, Medical Dictionary for Regulatory Activities. Worst intensities are shown.

Med Uni Graz

Ausblick: mRNA Vaccination

Med Uni Graz

Article | Open access | Published: 10 May 2023

Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer

Luis A. Rojas, Zachary Sethna, Kevin C. Soares, Cristina Olcese, Nan Pang, Erin Patterson, Jayon Lihm, Nicholas Ceglia, Pablo Guasp, Alexander Chu, Rebecca Yu, Adrienne Kaya Chandra, Theresa Waters, Jennifer Ruan, Masataka Amisaki, Abderezak Zebboudj, Zagaa Odgerel, George Payne, Evelyna Derhovanessian, Felicitas Müller, Ina Rhee, Mahesh Yadav, Anton Dobrin, Michel Sadelain, ... Vinod P. Balachandran + Show authors

Nature **618**, 144–150 (2023) | Cite this article

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