Lungenkarzinom: frühe Stadien (Histologien und Therapie)

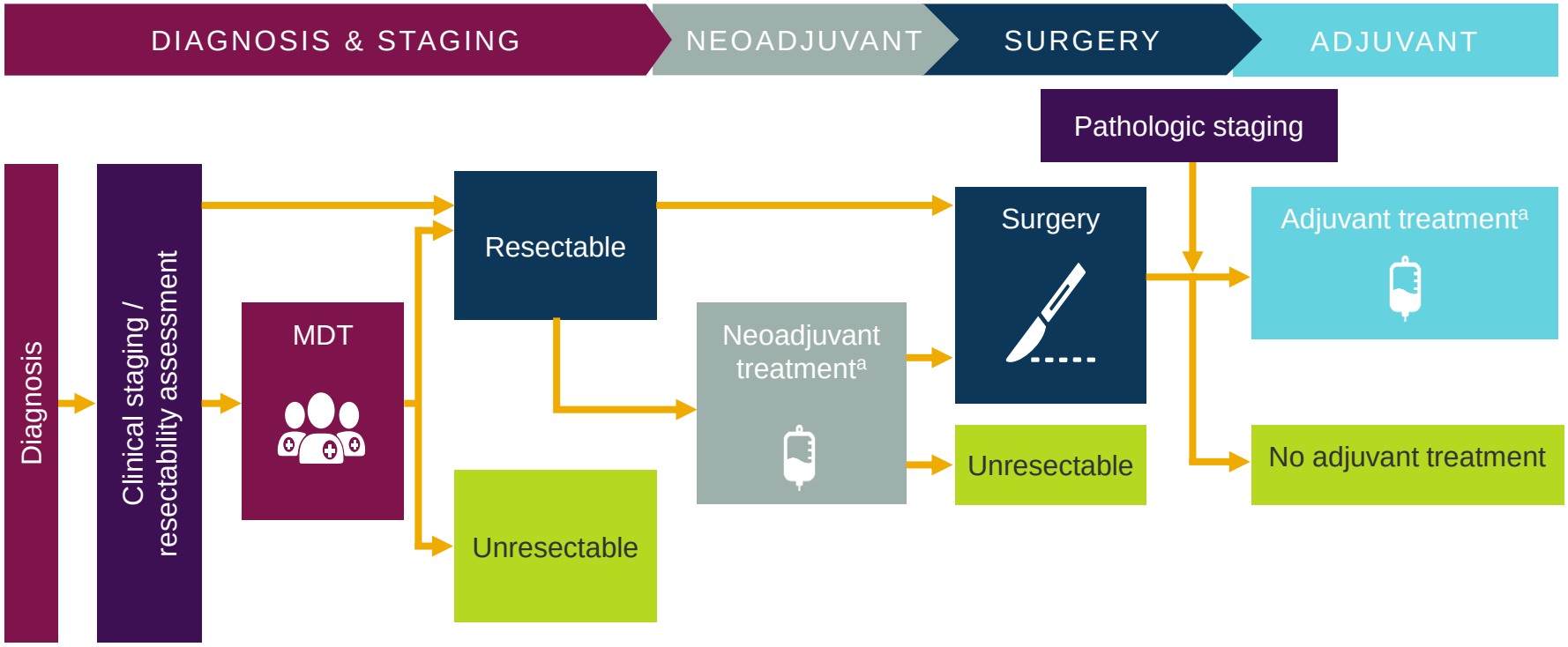
Auswertungen aus dem Klinischen Krebsregister für Brandenburg und Berlin

26.1.2022

C. Grohé

Standard of care treatment for resectable NSCLC is surgery with curative intent with or without additional therapy

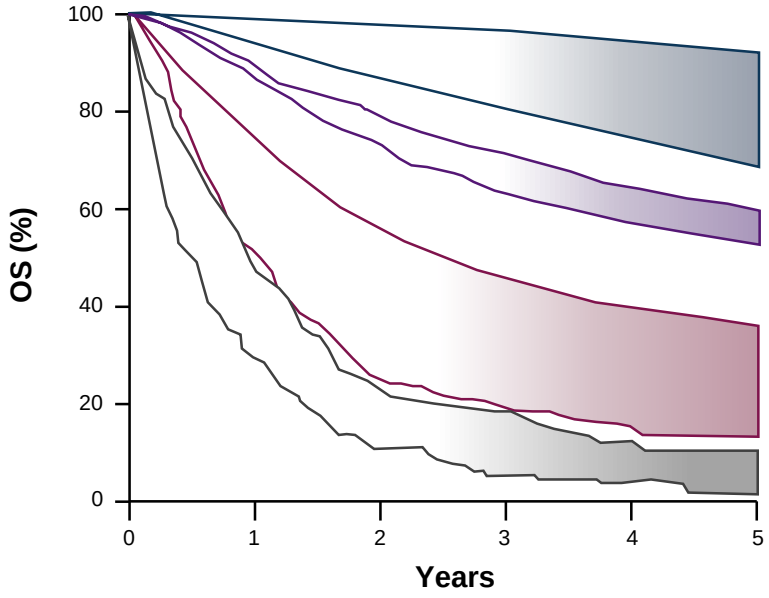
- The decision of whether patients receive neoadjuvant or adjuvant therapy as well as surgery depends on the stage of disease and degree of lymph node involvement

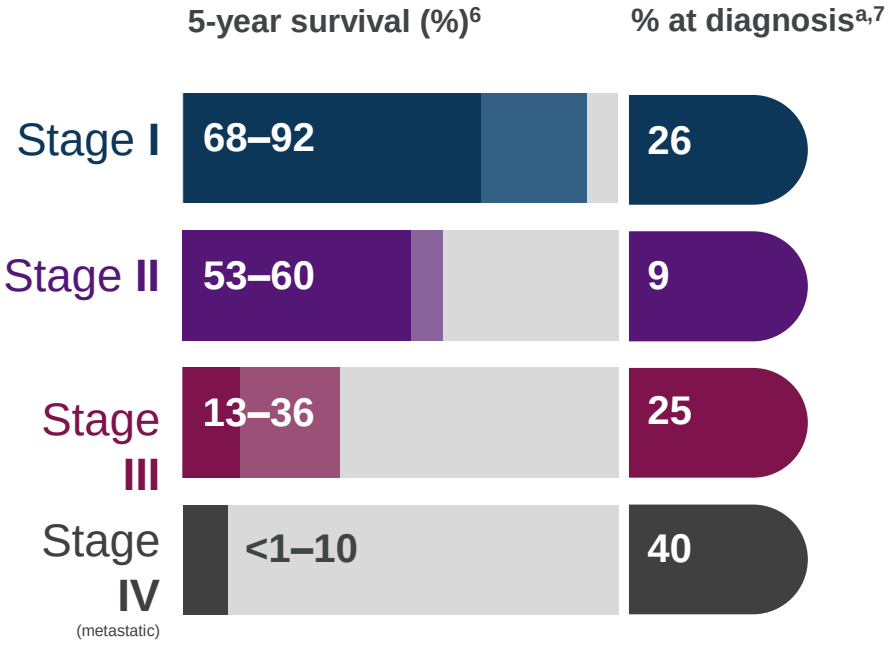


There is a strong correlation between NSCLC stage and prognosis, with considerable differences in 5-Year OS

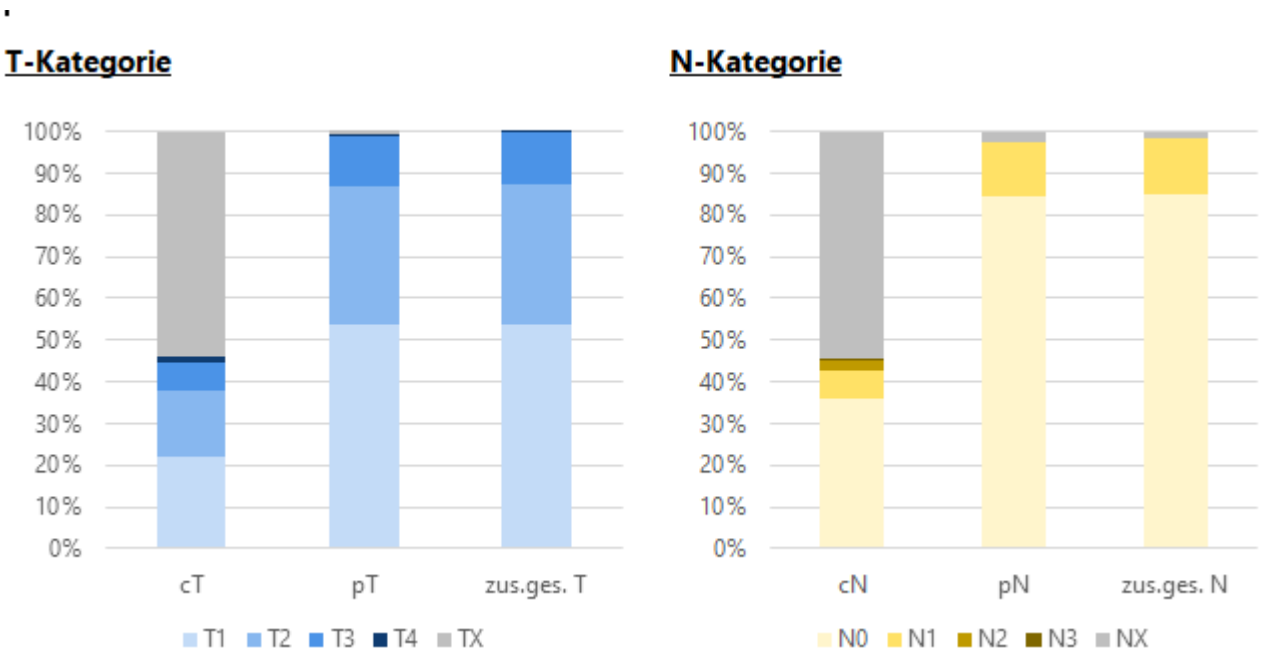
- Adjuvant cisplatin-based chemotherapy is recommended for patients with resected stage II–IIIA NSCLC and select patients with stage IB disease[1–4]
- Despite complete surgical resection and adjuvant chemotherapy, disease recurrence and death remains high across disease stages I–III[5]

5-year NSCLC survival rates by stage at diagnosis[6]



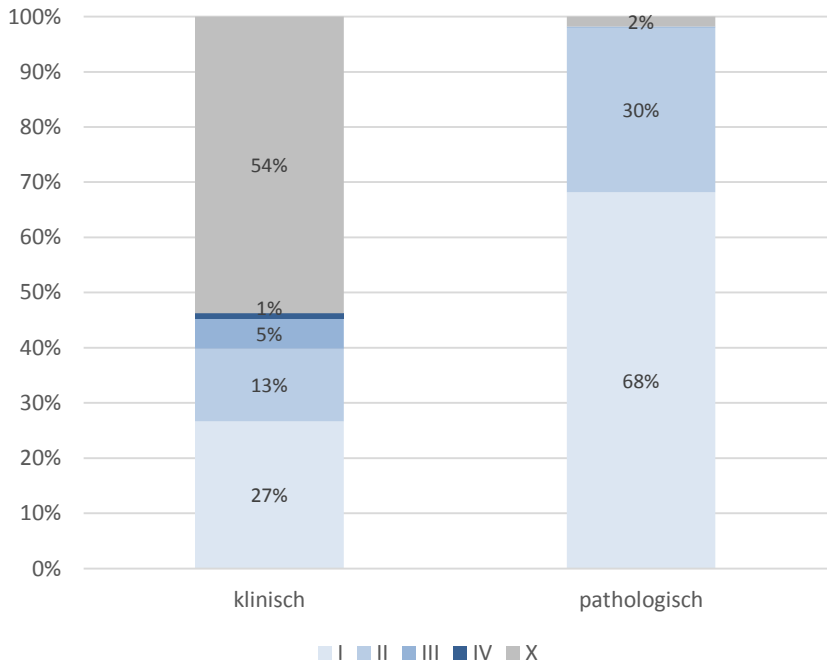


TNK Klassifikation

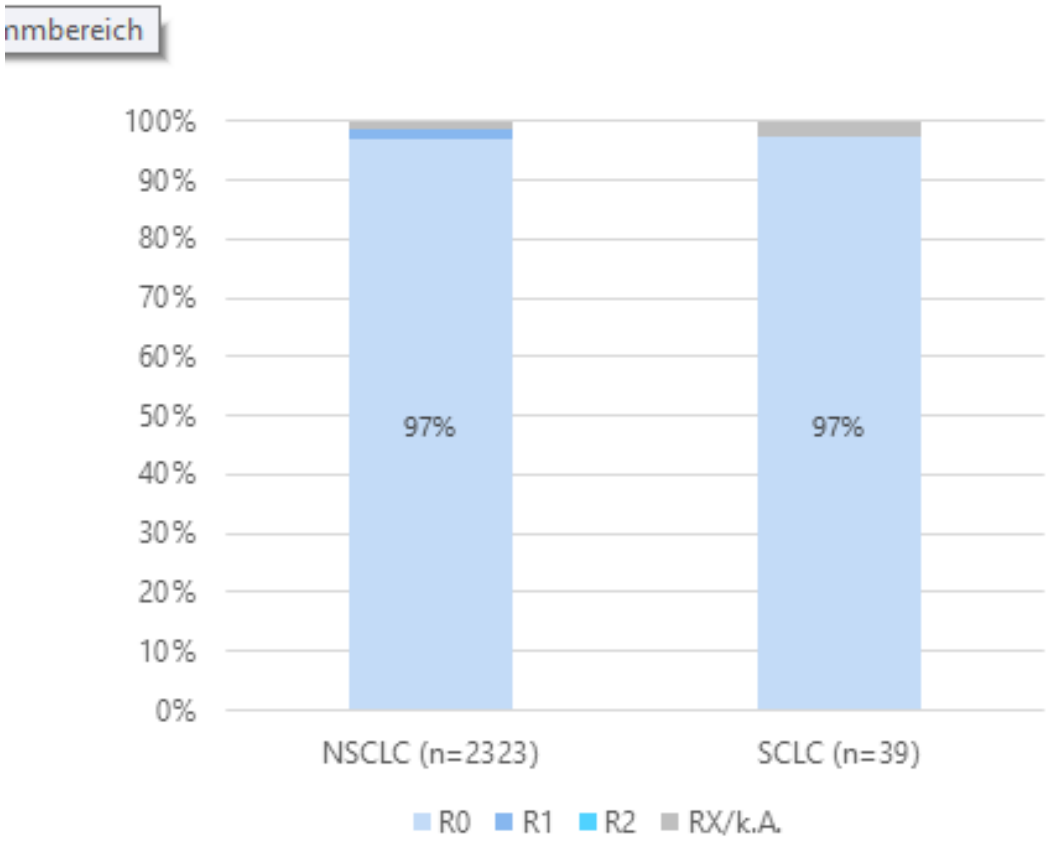


Klinische, pathologische und zusammengesetzte T- und N-Kategorie bei operierten Patienten mit Lungenkarzinom im zusammengesetzten UICC-Stadium I und II, Bundesland der Tumorresektion Brandenburg oder Berlin, Diagnosejahre 2016-2019 (n=2555)

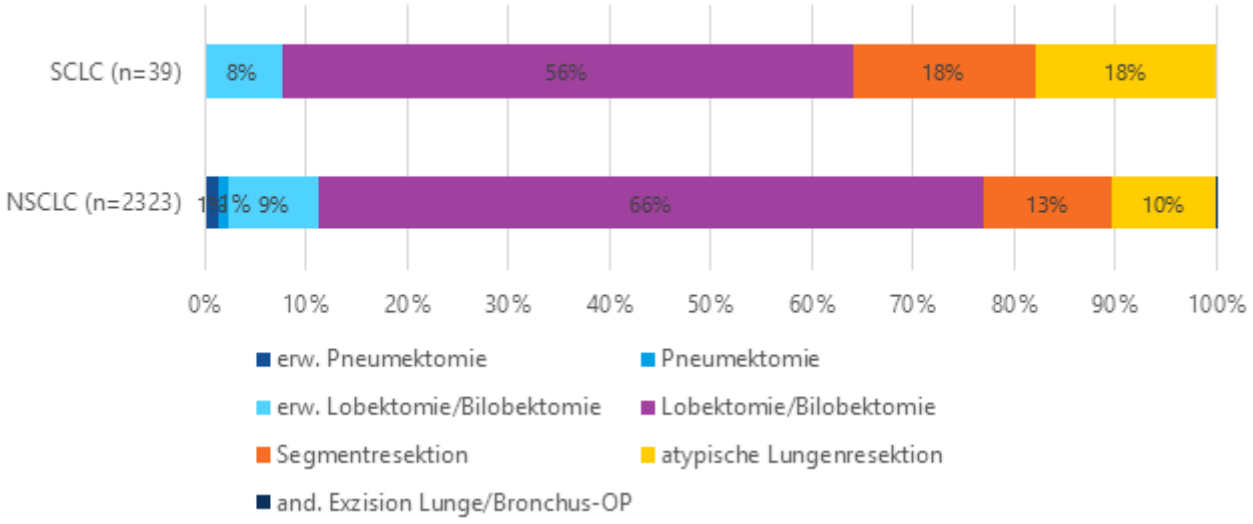
cTNM vs. pTNM bei Operierten



Lokale R-Klassifikation



Art der Tumorresektion



Art der umfangreichsten tumorresezierenden Operation bei Patienten mit Lungenkarzinom im Stadium I und II, separiert nach NSCLC/SCLC, Bundesland der Tumorresektion Brandenburg oder Berlin, Diagnosejahre 2016-2019 (n=2362)
Gruppe der anderen Karzinome hier nicht mit gezeigt, daher etwas geringere Fallzahl als für übrige Abbildungen

International Tailored Chemotherapy Adjuvant (ITACA) Phase III study of Pharmacogenomic-Driven versus Standard Adjuvant Chemotherapy in completely Resected Stage II-IIIA Non-Small Cell Lung Cancer

Silvia Novello

(**on behalf of the ITACA investigators**)

University of Turin,

Department of Oncology

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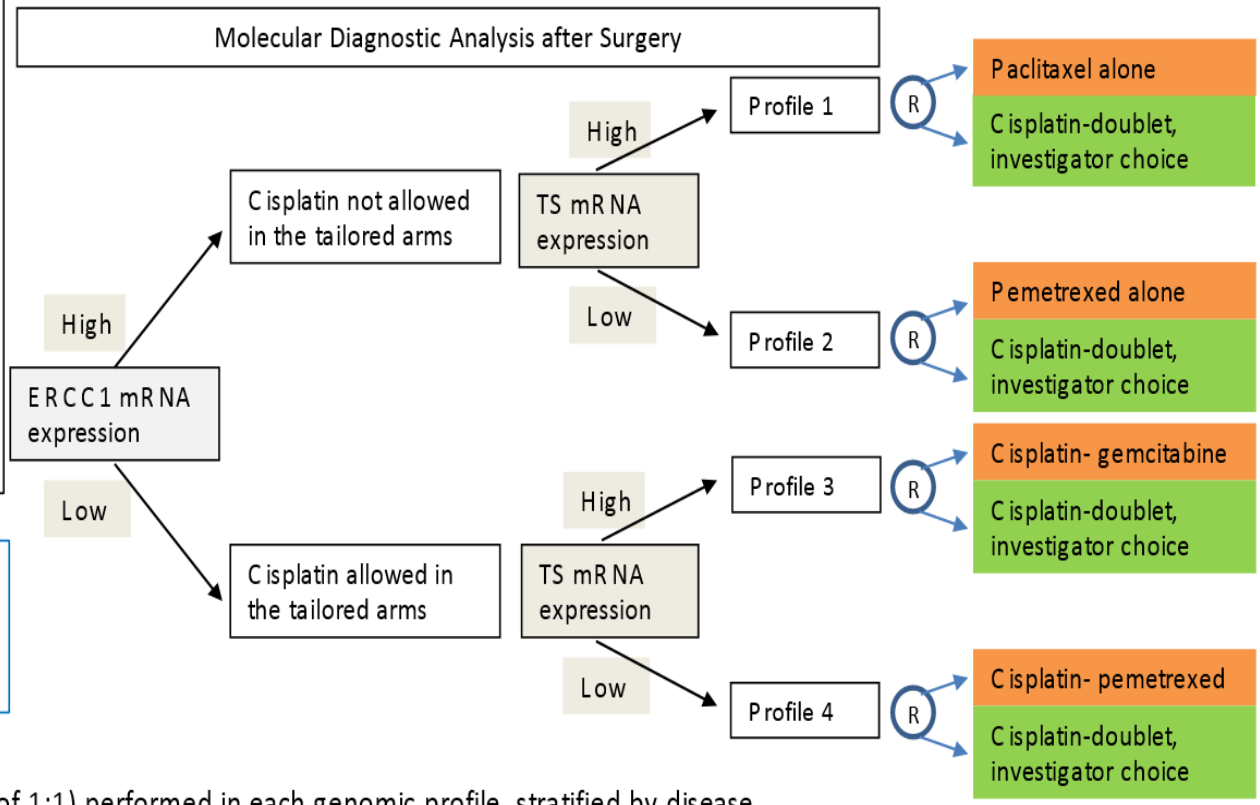
Design of the study

- Completely resected NSCLC R0 stage II-IIIA, Complete mediastinal LN resection or sampling
- ECOG PS 0-1
- Interval of 45-60 days between surgery and start of chemotherapy
- Adequate organ functions
- No prior malignancies except for treated basal cell or squamous cell skin cancer, in situ cervical cancer, or other cancers from which the patient has been disease-free for at least five years prior to enrolment

- 8Aug 2008: first pt randomized; 29Aug 2014 last pt randomized
- Dec 2010: Study Amendment for Staging (21% pts randomized)



- Randomization (allocation ratio of 1:1) performed in each genomic profile, stratified by disease stage (stage II *v* IIIA) and smoking status (never/former versus current)

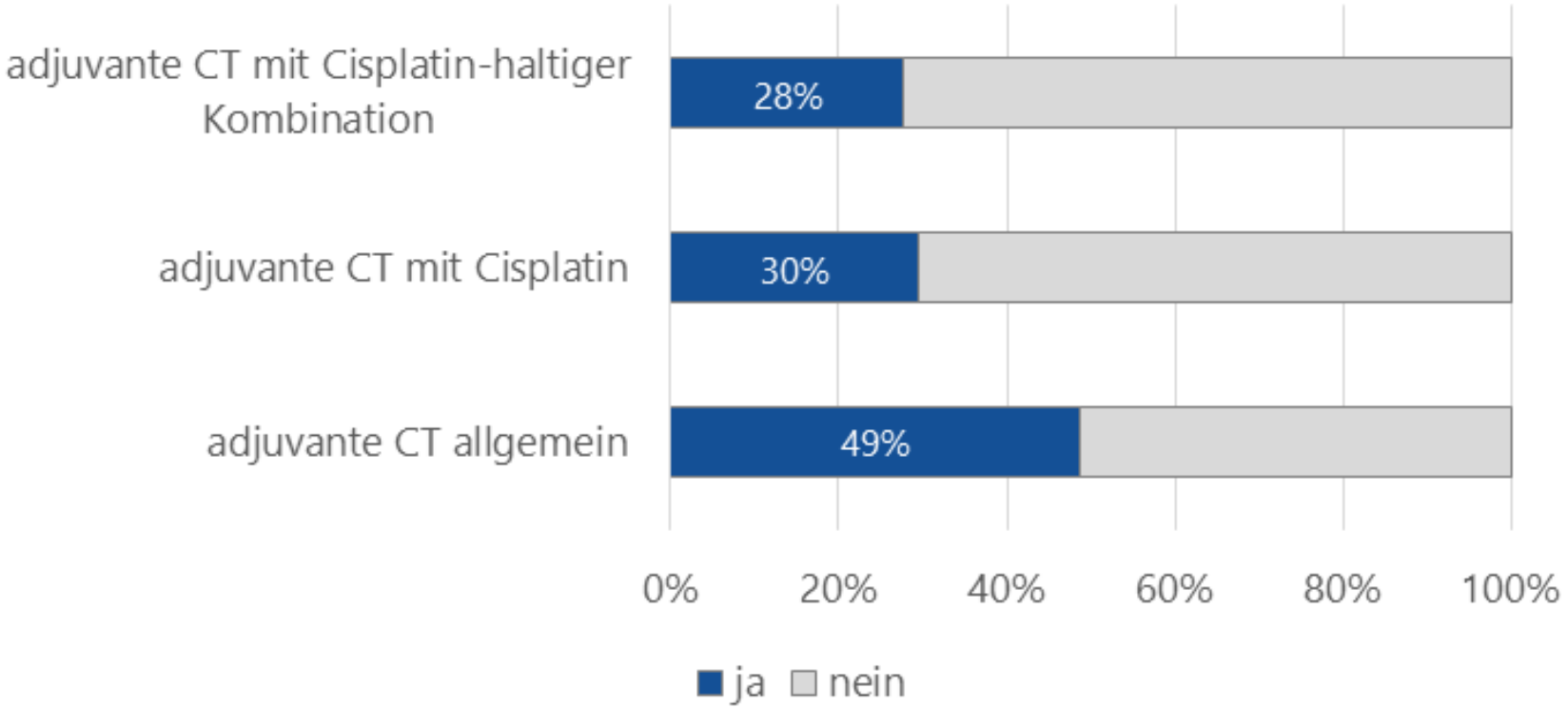
Adjuvante Therapie und Stadien

Stellung der Chemotherapie zur OP	Stadium I	Stadium II	Gesamt
keine Chemotherapie dokumentiert	2140	721	2861
	94,1%	60,4%	82,5%
Chemotherapie ohne primäre Tumorresektion	58	124	182
	2,5%	10,4%	5,2%
neoadjuvante Chemotherapie mit nachfolgender Tumorresektion	6	23	29
	0,3%	1,9%	0,8%
postoperative Chemotherapie nach Tumorresektion	71	326	397
	3,1%	27,3%	11,4%
Gesamt	2275	1194	3469
	100,0%	100,0%	100,0%

Adjuvante Therapie und Histologie

Stellung der Chemotherapie zur OP	NSCLC	SCLC	Andere	k.A.	Gesamt
keine Chemotherapie dokumentiert	2580	35	241	5	2861
	83,0%	33,7%	96,4%	100,0%	82,5%
Chemotherapie ohne primäre Tumorresektion	130	50	2	0	182
	4,2%	48,1%	0,8%	0,0%	5,2%
neoadjuvante Chemotherapie mit nachfolgender Tumorresektion	22	6	1	0	29
	0,7%	5,8%	0,4%	0,0%	0,8%
postoperative Chemotherapie nach Tumorresektion	378	13	6	0	397
	12,2%	12,5%	2,4%	0,0%	11,4%
Gesamt	3110	104	250	5	3469
	100,0%	100,0%	100,0%	100,0%	100,0%

Häufigkeit adjuvanter Therapie Stadium II



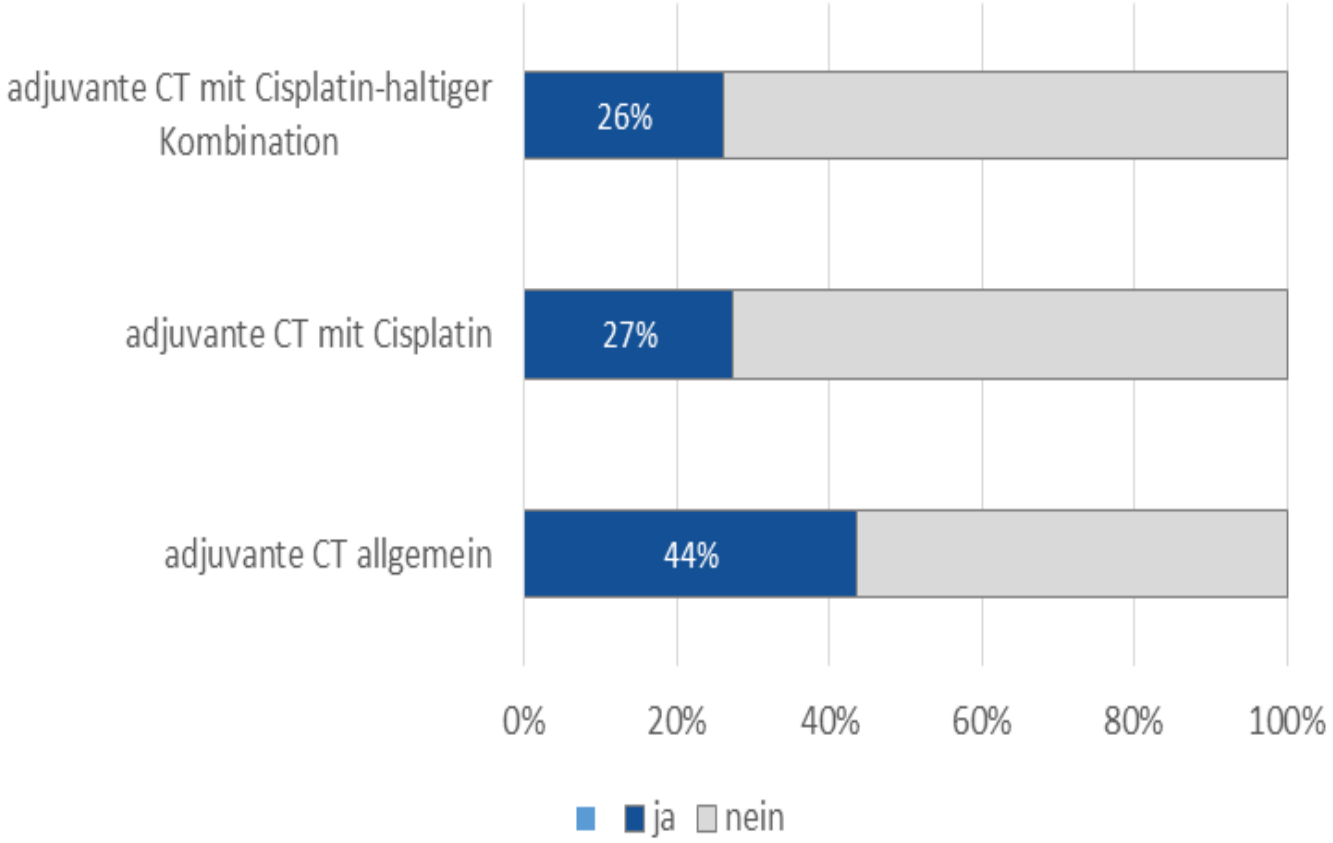
Adjuvante Chemotherapie (CT) bei Patienten mit NSCLC, Stadium II, ECOG 0/1, nach systematischer Lymphknotendissektion und lokaler R0-Resektion, Behandlungsort im Bundesland Brandenburg oder Berlin, Diagnosejahre 2016-2019 (n=352)

Systemtherapie in der Adjuvans Stadium I und II

Stellung der Systemtherapie zur Tumorresektion	Häufigkeit	Prozent
keine Systemtherapie dokumentiert	2811	81%
Systemtherapie ohne primäre Tumorresektion	223	6%
neoadjuvante Systemtherapie mit nachfolgender Tumorresektion	32	1%
postoperative Systemtherapie nach Tumorresektion	403	12%
Gesamt	3469	100%

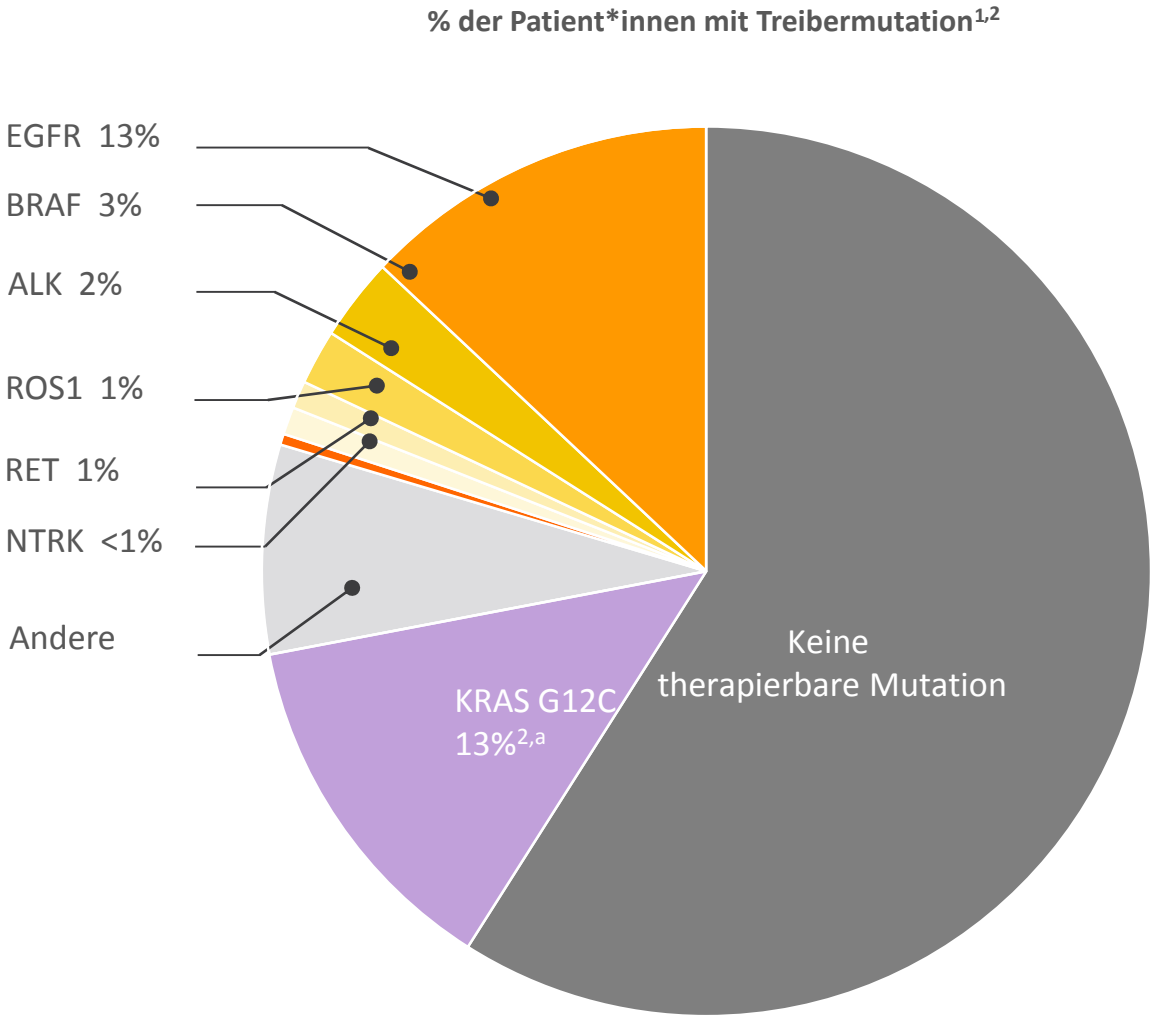
Stellung der Systemtherapie zur Tumorresektion bei Patienten mit Lungenkarzinom im Stadium I und II, Behandlungsort im Bundesland Brandenburg oder Berlin, Diagnosejahre 2016-2019 (n=3469)

Adjuvante Therapie Stadium III



Adjuvante Chemotherapie (CT) bei Patienten mit NSCLC, Stadium II, nach systematischer Lymphknotendissektion, Behandlungsort im Bundesland Brandenburg oder Berlin, Diagnosejahre 2016-2019 (n=691)

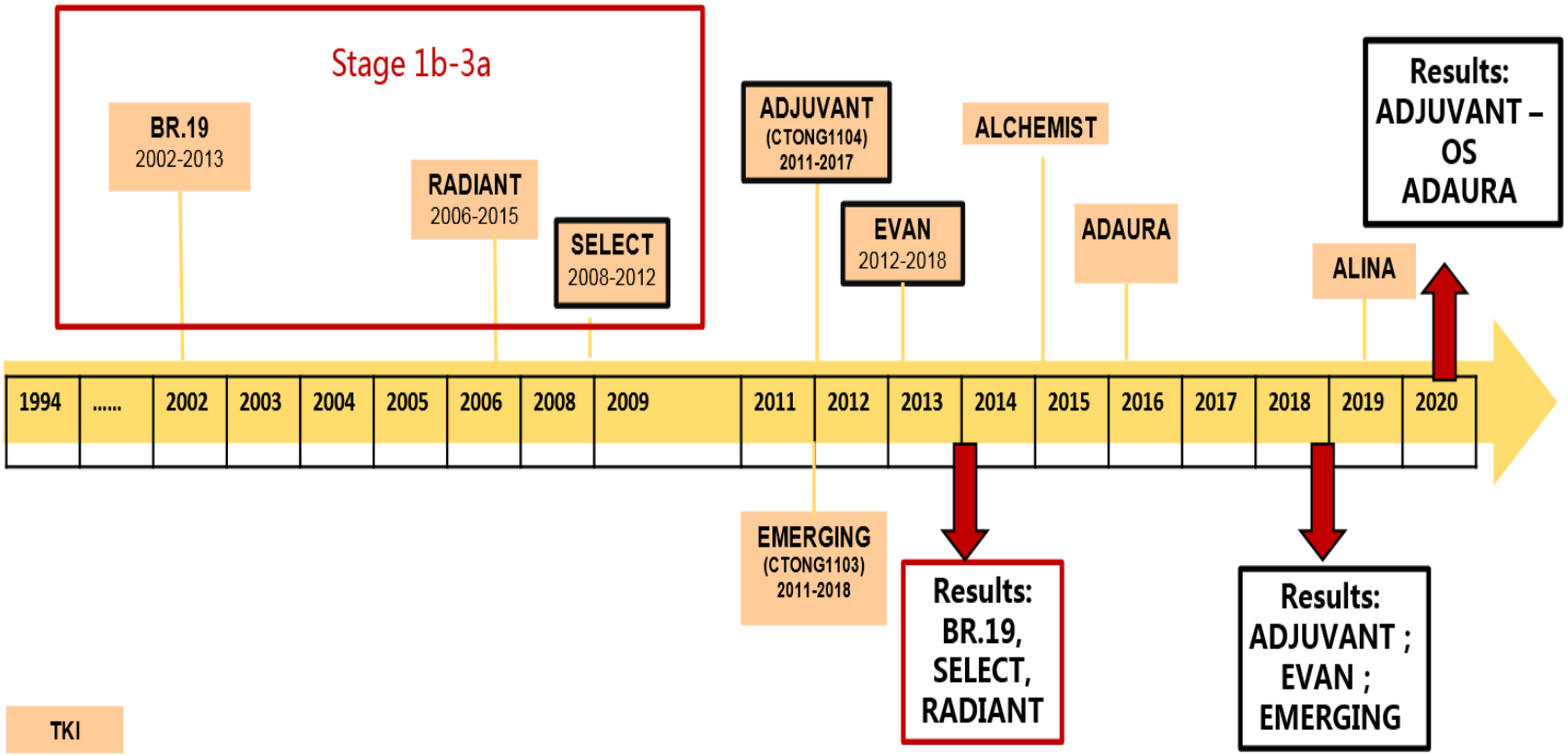
Häufigkeit verschiedener Mutationen bei NSCLC-Patient*innen mit nicht-plattenepithelialer Histologie



a Die Angaben beziehen sich auf das Adenokarzinom.

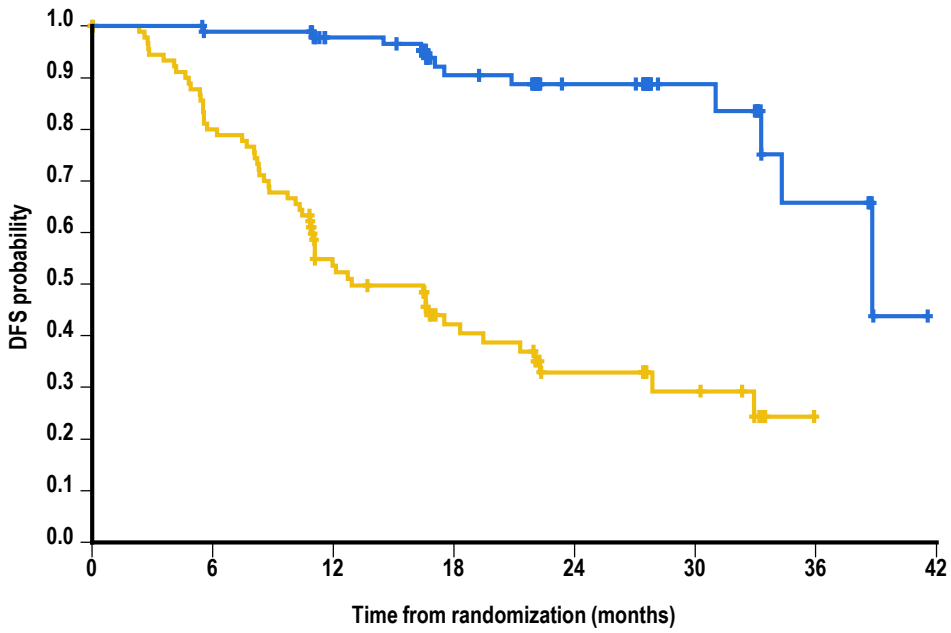
1 Modifiziert nach Netzwerk Genomische Medizin (NGM) Lungenkrebs der Kölner Lungenkrebsgruppe (LCGC); http://lungcancergroup.de/molekularpathologie/treibermutationen; Zugriff: 02.12.2021.| 2 Biernacka A, et al. Cancer Genet.2016;209:195–8.

Targeted therapy in early stage NSCLC

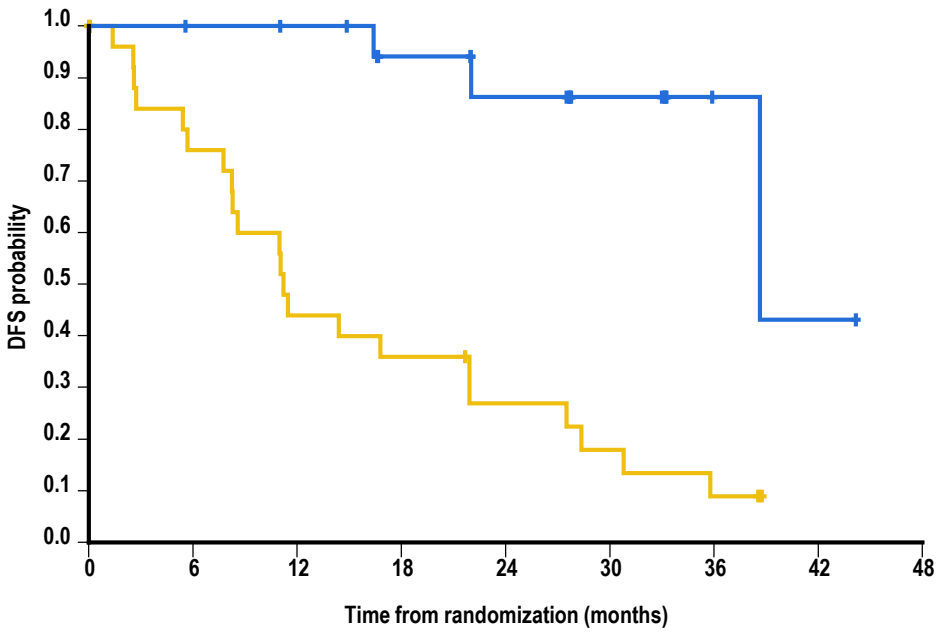


DFS in patients with and without adjuvant chemotherapy (stage IIIA)

With adjuvant chemotherapy



Without adjuvant chemotherapy



No. at risk								
Osimertinib	94	90	80	54	39	17	7	0
Placebo	92	72	42	24	14	8	0	

No. at risk									
Osimertinib	21	19	18	14	11	7	2	1	0
Placebo	27	19	11	9	6	4	2	0	

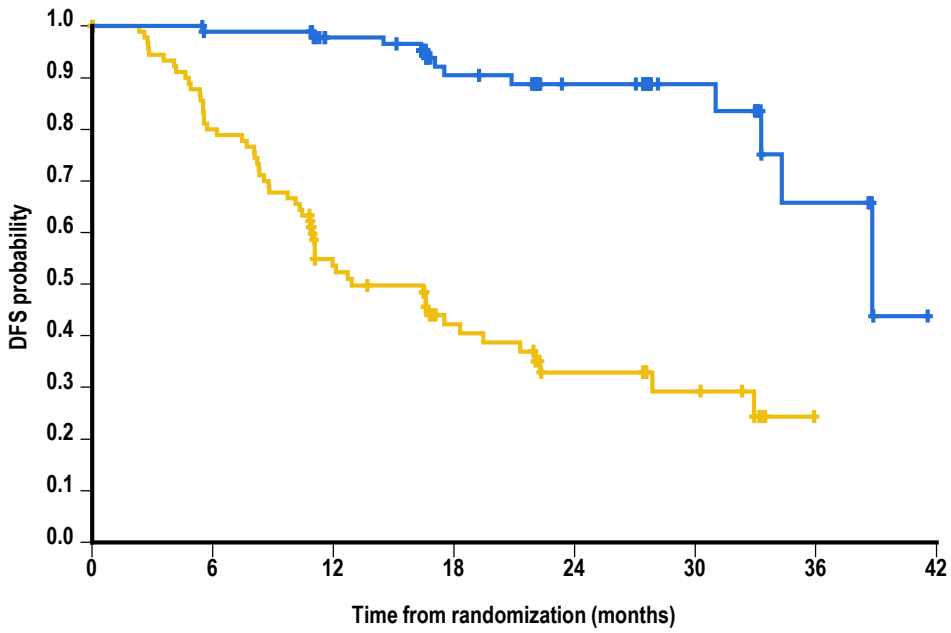
Median DFS, months (95% CI)		HR (95% CI)
Osimertinib	38.8 (34.3, NC)	**0.13 (0.06, 0.23)**
Placebo	12.9 (10.9, 19.4)	
Maturity 37%: osimertinib 13%, placebo 61%		

Median DFS, months (95% CI)		HR (95% CI)
Osimertinib	38.6 (38.6, NC)	**0.10 (0.02, 0.29)**
Placebo	11.2 (8.2, 21.9)	
Maturity 52%: osimertinib 14%, placebo 81%		

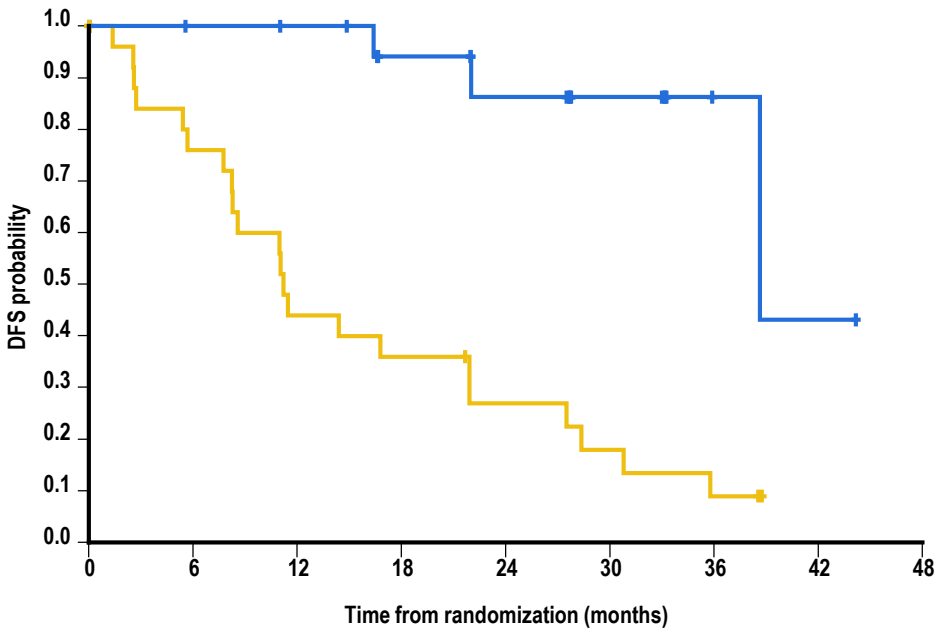
ADAURA data cut-off: January 17, 2020.
Tick marks indicate censored data.

DFS in patients with and without adjuvant chemotherapy (stage IIIA)

With adjuvant chemotherapy



Without adjuvant chemotherapy



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ADAURA data cut-off: January 17, 2020.
Tick marks indicate censored data.

2021 ASCO ANNUAL MEETING

IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs Best Supportive Care After Adjuvant Chemotherapy in Resected Stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC)

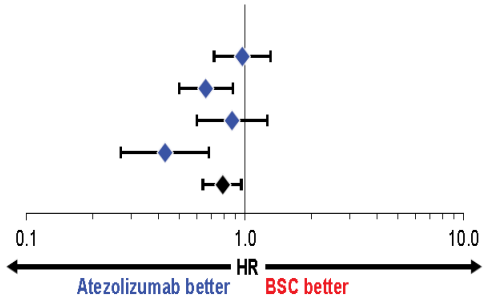
Heather A. Wakelee,[1] Nasser Altorki,[2] Caicun Zhou,[3] Tibor Csőszi,[4] Ihor O. Vynnychenko,[5] Oleksandr Goloborodko,[6] Alexander Luft,[7] Andrey Akopov,[8] Alex Martinez-Marti,[9] Hirotsugu Kenmotsu,[10] Yuh-Min Chen,[11] Antonio Chella,[12] Shunichi Sugawara,[13] Fan Wu,[14] Jing Yi,[15] Yu Deng,[15] Mark McCleland,[15] Elizabeth Bennett,[15] Barbara J. Gitlitz,[15] Enriqueta Felip[16]

[1]Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA, USA; [2]New York-Presbyterian Hospital, Weill Cornell Medicine, New York, NY, USA; [3]Tongji University Affiliated Shanghai Pulmonary Hospital, Shanghai, China; [4]Jasz-Nagykun-Szolnok Megyei Hetenyi Geza Korhaz-Rendelointezet, Szolnok, Hungary; [5]Sumy State University, Regional Municipal Institution Sumy Regional Clinical Oncology Dispensary, Sumy, Ukraine; [6]MI Zaporizhzhia Regional Clinical Oncological Dispensary Zaporizhzhia SMU Ch of Oncology, Zaporizhzhya, Ukraine; [7]Leningrad Regional Clinical Hospital, St. Petersburg, Russia; [8]Pavlov State Med Univ, St. Petersburg, Russia; [9]Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain; [10]Shizuoka Cancer Center, Shizuoka, Japan; [11]Taipei Veterans General Hospital and National Yang Ming Chiao Tung University, Taipei, Taiwan; [12]Azienda Ospedaliero Universitaria Pisana, Pisa, Italy; [13]Sendai Kousei Hospital, Miyagi, Japan; [14]Roche (China) Holding Ltd, Shanghai, China; [15]Genentech, Inc., South San Francisco, CA, USA; [16]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

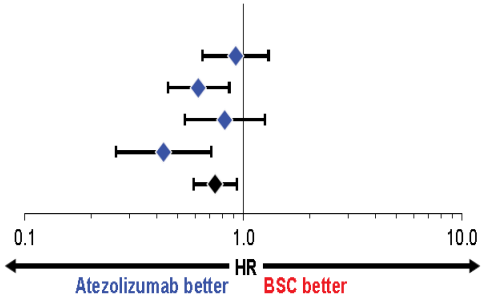
DFS by PD-L1 status[a]

All-randomised stage II-IIIA population (with and without known EGFR/ALK+ disease

Subgroup *(including EGFR/ALK+)*	n	HR (95% CI)[b,c]
PD-L1 status by SP263		
TC <1%	383	0.97 (0.72, 1.31)
TC ≥1%	476	0.66 (0.50, 0.88)
TC 1-49%	247	0.87 (0.60, 1.26)
TC ≥50%	229	0.43 (0.27, 0.68)
All patients[d]	882	0.79 (0.64, 0.96)



Subgroup *(excluding EGFR/ALK+)*[e]	n	HR (95% CI)[f,g]
PD-L1 status by SP263		
TC <1%	312	0.92 (0.65, 1.30)
TC ≥1%	410	0.62 (0.45, 0.86)
TC 1-49%	201	0.82 (0.54, 1.25)
TC ≥50%	209	0.43 (0.26, 0.71)
All patients[h]	743	0.74 (0.59, 0.93)

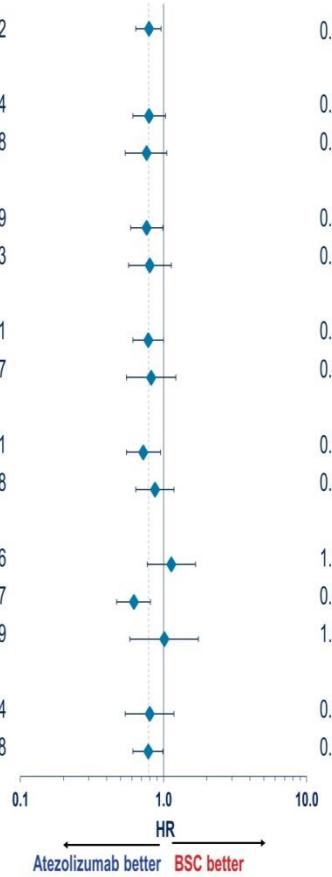


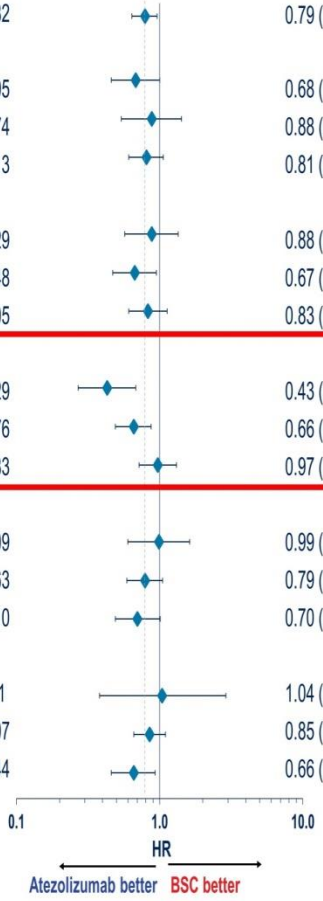
Clinical cutoff: 21 January 2021. [a] Per SP263 assay.
[b] Stratified for all patients and PD-L1 TC ≥1%; unstratified for all other subgroups. [c] DFS analyses in the PD-L1 TC <1% and TC 1-49% subgroups were exploratory. [d] 23 patients had unknown PD-L1 status as assessed by SP263. [e] Excluding patients with known *EGFR/ALK+* NSCLC. [f] Unstratified for all

Felip et al. IMpower010 Relapse Patterns.

IMpower010: DFS in key subgroups of the all-randomized stage II-IIIA population

Subgroup	N	HR (95% CI)[a]
All patients	882	0.79 (0.64, 0.96)
Age		
<65 y	544	0.79 (0.61, 1.03)
≥65 y	338	0.76 (0.54, 1.05)
Sex		
Male	589	0.76 (0.59, 0.99)
Female	293	0.80 (0.57, 1.13)
Race		
White	631	0.78 (0.61, 1.00)
Asian	227	0.82 (0.55, 1.22)
ECOG PS		
0	491	0.72 (0.55, 0.95)
1	388	0.87 (0.64, 1.18)
Tobacco use history		
Never	196	1.13 (0.77, 1.67)
Previous	547	0.62 (0.47, 0.81)
Current	139	1.01 (0.58, 1.75)
Histology		
Squamous	294	0.80 (0.54, 1.18)
Non-squamous	588	0.78 (0.61, 0.99)
All patients	882	0.79 (0.64, 0.96)
Stage		
IIA	295	0.68 (0.46, 1.00)
IIB	174	0.88 (0.54, 1.42)
IIIA	413	0.81 (0.61, 1.06)
Regional lymph node stage (pN)		
N0	229	0.88 (0.57, 1.35)
N1	348	0.67 (0.47, 0.95)
N2	305	0.83 (0.61, 1.13)
SP263 PD-L1 status		
TC≥50%	229	0.43 (0.27, 0.68)
TC≥1%	476	0.66 (0.49, 0.87)
TC<1%	383	0.97 (0.72, 1.31)
***EGFR* mutation status**		
Yes	109	0.99 (0.60, 1.62)
No	463	0.79 (0.59, 1.05)
Unknown	310	0.70 (0.49, 1.01)
***ALK* rearrangement status**		
Yes	31	1.04 (0.38, 2.90)
No	507	0.85 (0.66, 1.10)
Unknown	344	0.66 (0.46, 0.93)

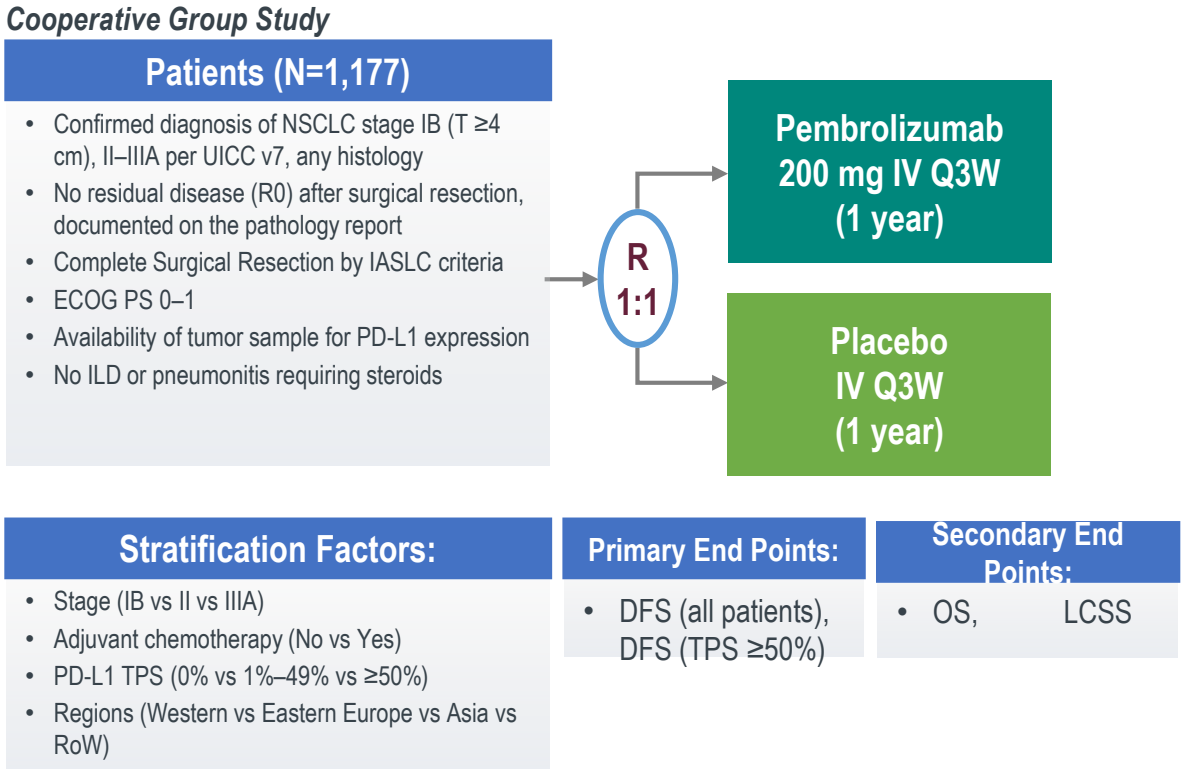




Clinical cutoff: January 21, 2021. [a] Stratified for all patients; unstratified for all other subgroups.

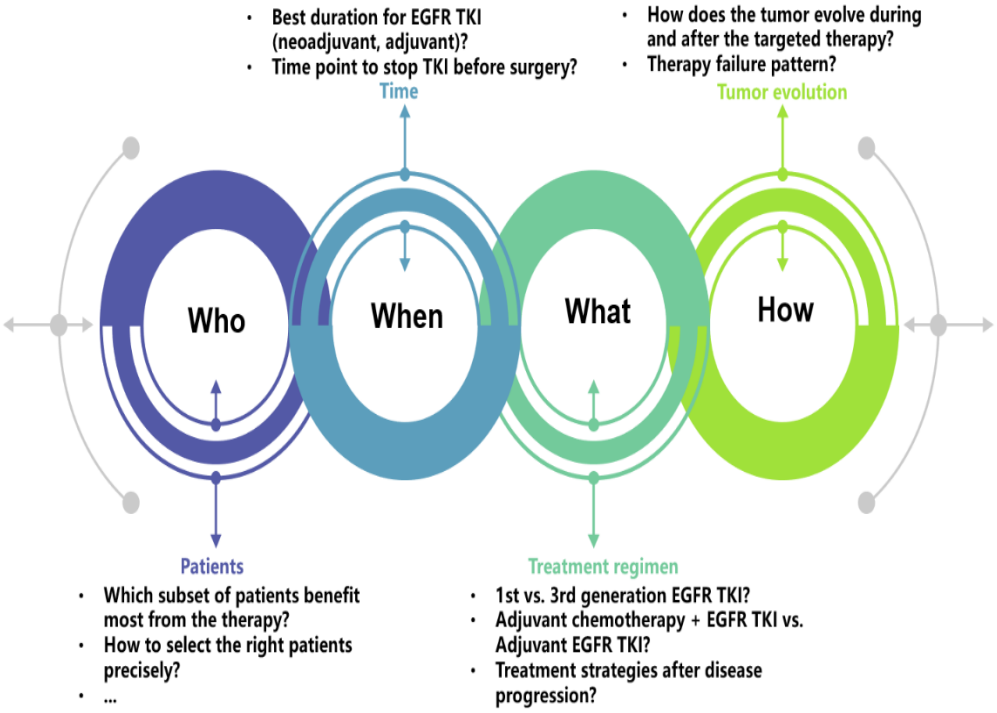
Presented By: Dr. Heather A. Wakelee
IMpower010 Interim Analysis
https://bit.ly/33t6JJP

KEYNOTE-091 (PEARLS): Phase 3 Study of Pembrolizumab vs Placebo for Patients with Early-stage or Locally Advanced NSCLC After Resection and Standard Adjuvant Chemotherapy



1. O'Brien M et al. Presented at ASCO Annual Meeting. June 3–7, 2016; Chicago, IL, USA; Abstract TPS8571. **2.** ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02504372. Accessed December 16, 2020.

Future Considerations



- Best duration for EGFR TKI (neoadjuvant, adjuvant)?
- Time point to stop TKI before surgery?

- How does the tumor evolve during and after the targeted therapy?
- Therapy failure pattern?

- Which subset of patients benefit most from the therapy?
- How to select the right patients precisely?
- ...

- 1st vs. 3rd generation EGFR TKI?
- Adjuvant chemotherapy + EGFR TKI vs. Adjuvant EGFR TKI?
- Treatment strategies after disease progression?