Küçük Hücreli Dışı Akciğer Kanseri Tedavisinde Adjuvan Hedefe Yönelik Tedavi ve İmmunoterapi

Dr. Deniz Tural
Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi
Tıbbi Onkoloji

Ders Planı

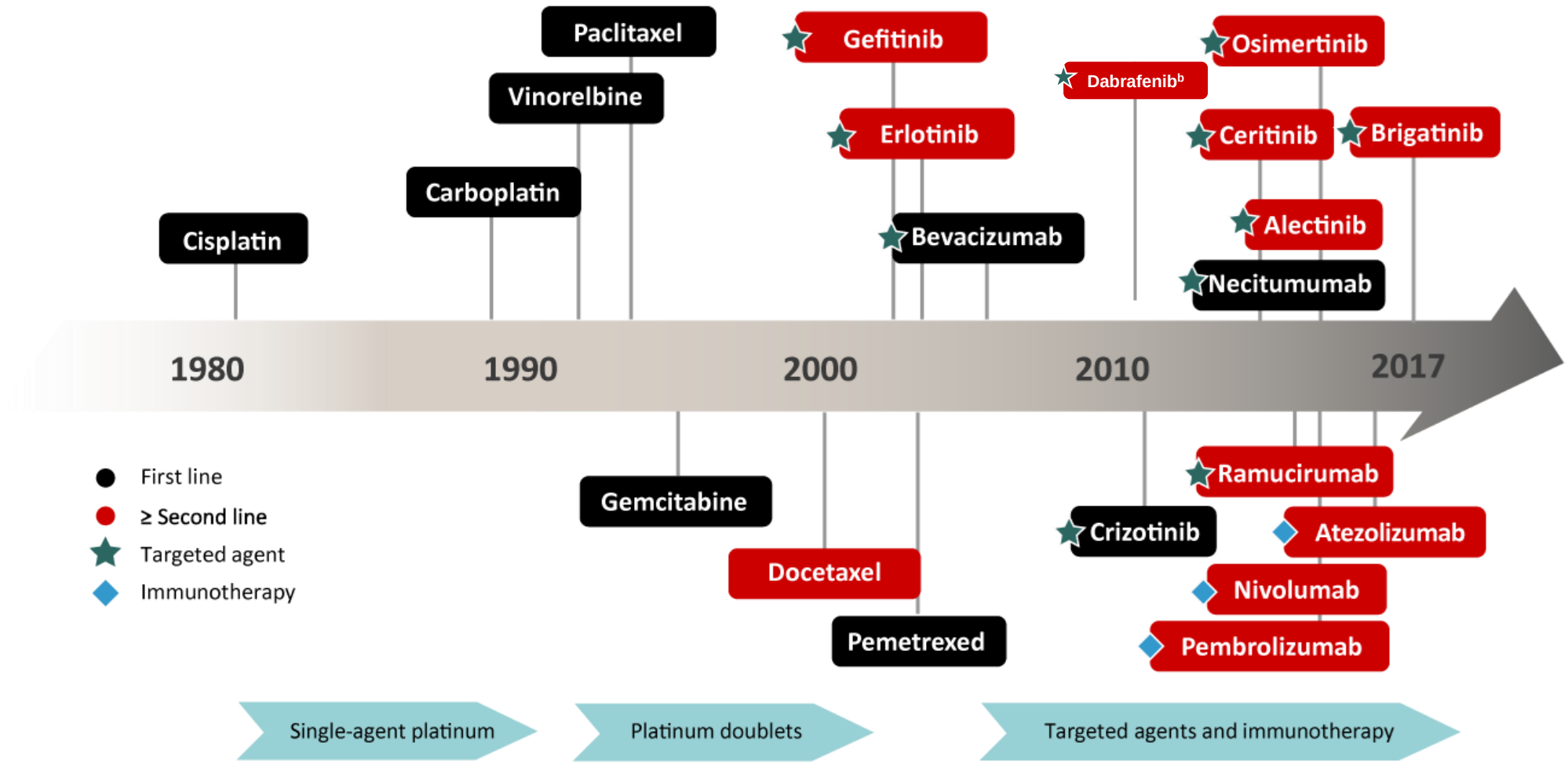
Giriş

Küçük hücreli dışı akciğer kanserinde

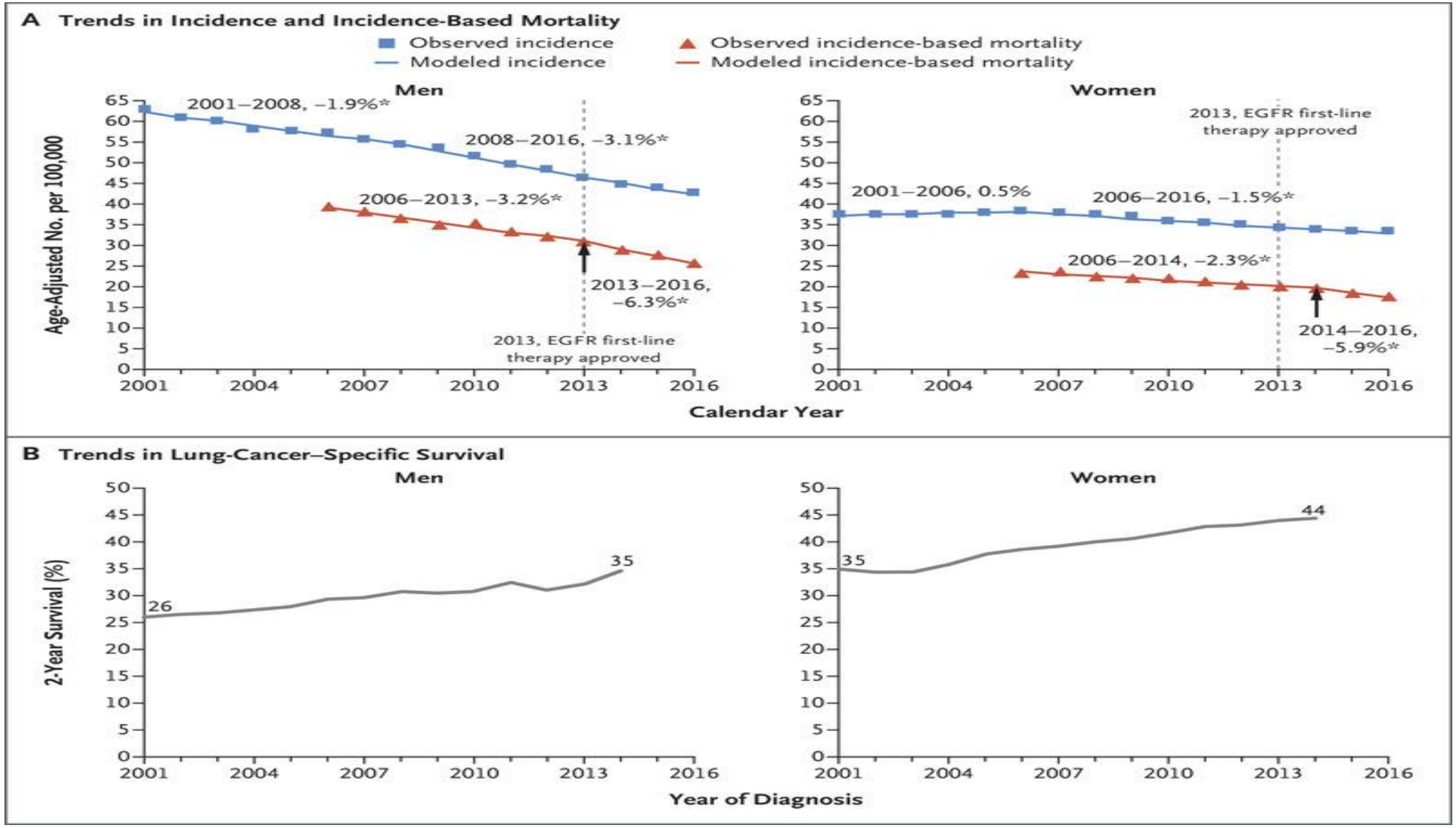
- Adjuvan immünoterapi
- Adjuvan Hedefe Yönelik Tedavi

Sonuç

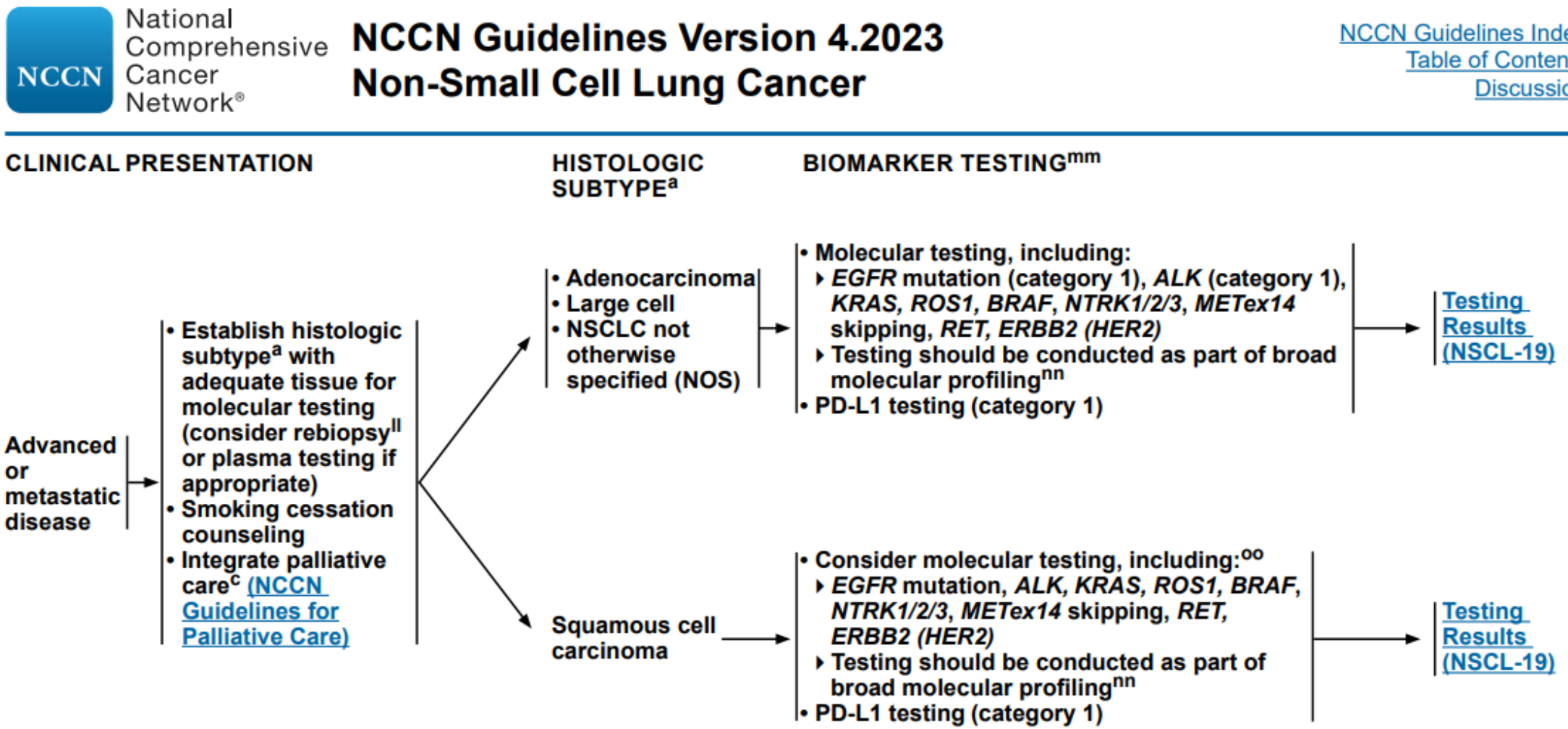
KHDAK'de Sistemik Tedavilerin Tarihsel Yolculuğu



Evre IV Akciğer Kanseri İnsidans ve Mortalite



Histoloji ve Genomik Özeliklere Göre Tedavi



Histoloji ve Genomik Özeliklere Göre Tedavi

National Comprehensive Cancer Network®

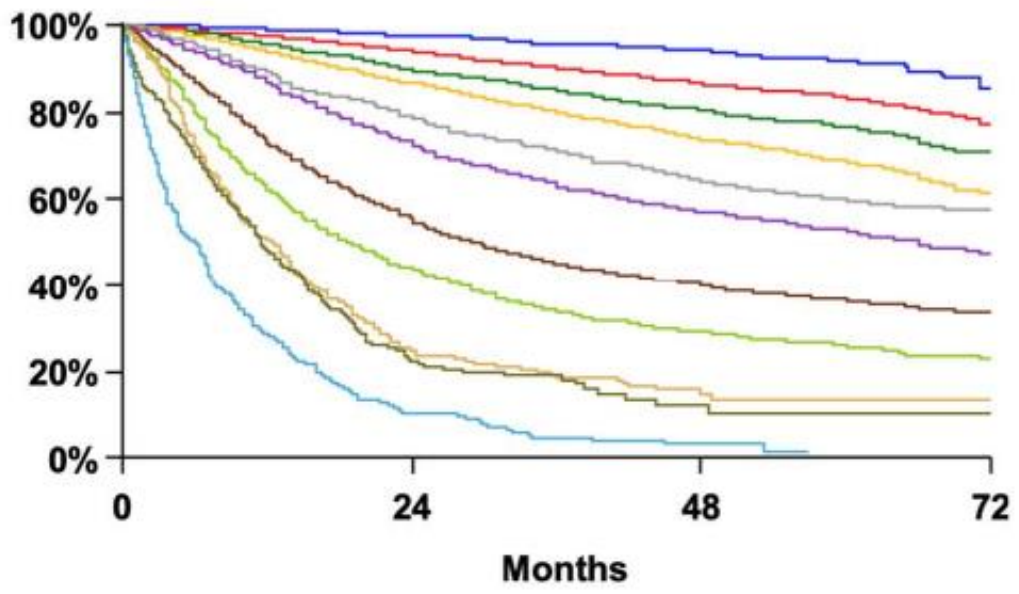
NCCN Guidelines Version 4.2023
Non-Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion

TESTING RESULTS[ll,mm]

EGFR **exon 19 deletion or exon 21 L858R mutation positive**	**NSCL-20**
EGFR **S768I, L861Q, and/or G719X mutation positive**	**NSCL-23**
EGFR **exon 20 insertion mutation positive**	**NSCL-24**
KRAS **G12C mutation positive**	**NSCL-25**
ALK **rearrangement positive**	**NSCL-26**
ROS1 **rearrangement positive**	**NSCL-29**
BRAF **V600E mutation positive**	**NSCL-31**
NTRK1/2/3 **gene fusion positive**	**NSCL-32**
METex14 **skipping mutation positive**	**NSCL-33**
RET **rearrangement positive**	**NSCL-34**
ERBB2 (HER2) **mutation positive**	**NSCL-35**
PD-L1 ≥1% and negative for actionable molecular biomarkers above	**NSCL-36**
PD-L1 <1% and negative for actionable molecular biomarkers above	**NSCL-37**

Metastatik Olmayan KHDAK'de Sistemik Tedaviye İhtiyaç Varmı



Stage (8th edition)	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%
IVB	328 / 398	6.0	10%	0%

UCLA Health | David Geffen School of Medicine

The Journal of Thoracic Oncology. Vol. 11 No. 1: 39-51.

Metastatik Olmayan KHDAK'de Sistemik Tedaviye İhtiyaç Varmı

NCCN Guidelines for Adjuvant Therapy

- **Post-resection with Negative Surgical Margins**

Stage	Post-resection Treatment	Category
IA	Observe only	2A
IB	Observe or chemotherapy for high-risk patients	2A
IIA	Observe or chemotherapy for high-risk patients	2A
IIB	Chemotherapy	1

NCCN High Risk Feature Examples

- Poorly differentiated tumors
- Vascular invasion
- Wedge resection
- Tumors >4 cm
- Visceral pleural involvement
- Unknown lymph node status

National Comprehensive Cancer Network. Non-Small Cell Lung Cancer. Version 2.2020

Courtesy of Eric Vallieres, MD

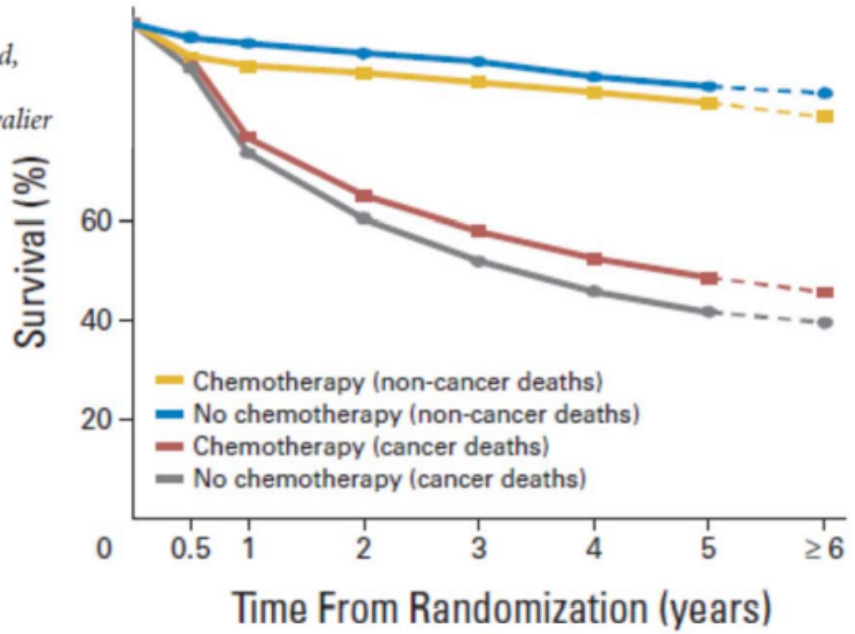
KHDAK'de Sistemik Tedavilerin Tarihsel Yolculuğu

What is the role for adjuvant systemic therapy?
Chemotherapy

Lung Adjuvant Cisplatin Evaluation: A Pooled Analysis by the LACE Collaborative Group

Jean-Pierre Pignon, Hélène Tribodet, Giorgio V. Scagliotti, Jean-Yves Douillard, Frances A. Shepherd, Richard J. Stephens, Ariane Dunant, Valter Torri, Rafael Rosell, Lesley Seymour, Stephen G. Spiro, Estelle Rolland, Roldano Fossati, Delphine Aubert, Keyue Ding, David. Waller, and Thierry Le Chevalier

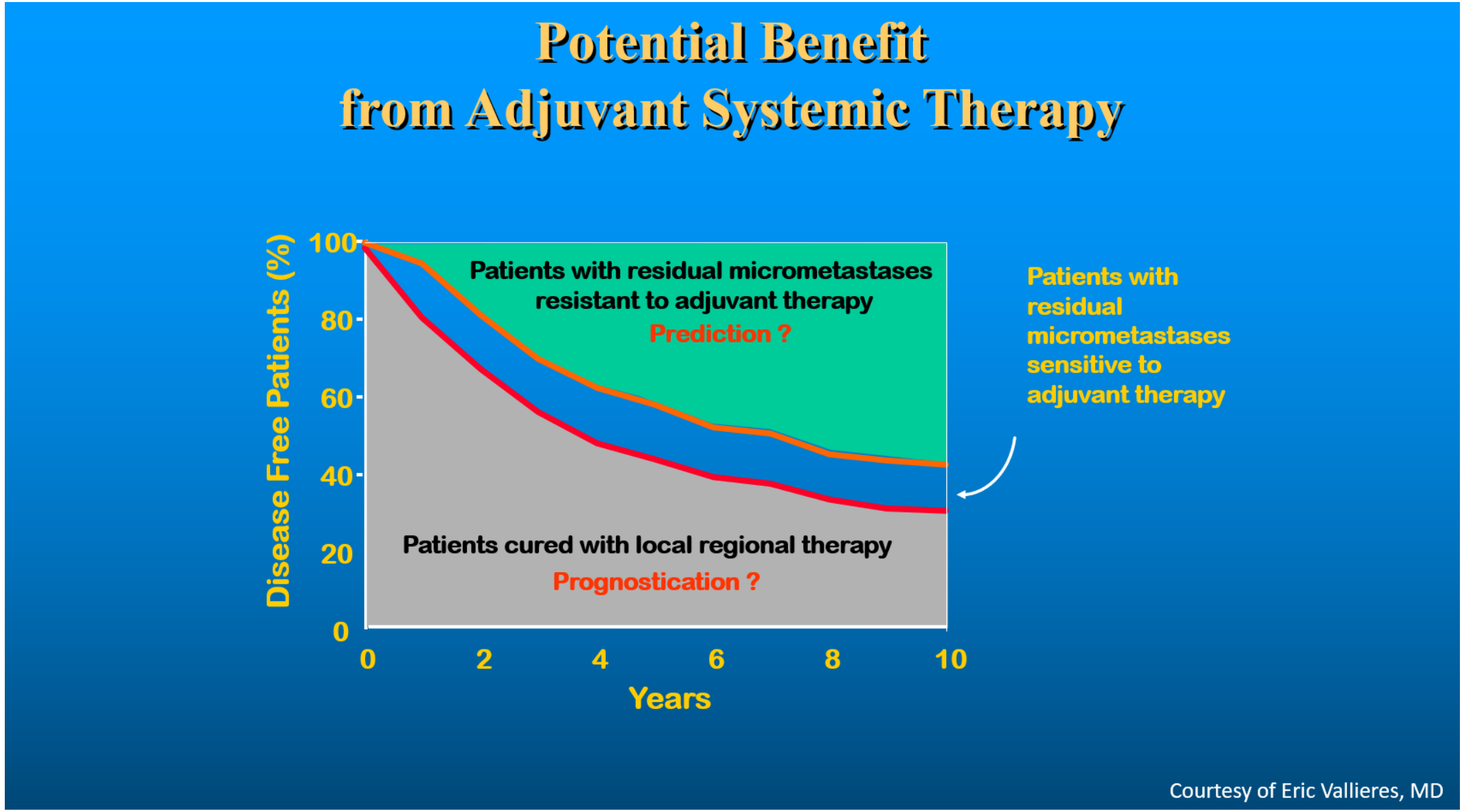
- Platinum based, 4-6 cycles for resected early-stage NSCLC (stage IB-IIIA)
  - DFS HR 0.84 (95% CI 0.78-0.91)
  - OS HR 0.89 (95% CI 0.82-0.96)
  - **4-5% OS improvement at 5 years (1/20)**



UCLA Health | David Geffen School of Medicine

Pignon *J Clin Oncol* 2008

Metastatik Olmayan KHDAK'de Sistemik Tedaviye İhtiyaç Varmı



Devam eden ve sonuçlanan çalışmalar

TABLE. Selected ongoing neoadjuvant and adjuvant clinical trials in earlier-stage NSCLC.

Trial Name	Study ID	Stage/timing	Treatment	Trial Dates*
Immunotherapy				
CheckMate 159	NCT02259621	I-IIIA, neoadjuvant	nivolumab ± ipilimumab	2014-2023
IMpower010	NCT02486718	IB-IIIA, adjuvant	Atezolizumab	2015-2022
KEYNOTE-091	NCT02504372	IB-IIIA	pembrolizumab	2015-2024
ANVIL	NCT02595944	IB-IIIA, adjuvant	nivolumab	2016-2024
LCMC3	NCT02927301	IB-IIIB, both neo/adjuvant	atezolizumab	2017-2025
PRINCEPS	NCT02994576	IB-IIIA, neoadjuvant	atezolizumab	2016-2022
NEOSTAR	NCT03158129	I-IIIA, neoadjuvant	nivolumab ± ipilimumab or chemotherapy	2017-2022
EMPOWER-CSCC-1	NCT03916627	I-IIIA, neoadjuvant	Cemiplimab	2019-2029
LUN0115	NCT04585477	I-III, adjuvant	Durvalumab	2021-2026
AAAT0800	NCT04625699	II-IIIB, adjuvant	durvalumab + tre	
NeoCOAST-2	NCT05061550	II-IIIA, both neo/adjuvant	durvalumab + ole	
Immunotherapy + chemotherapy				
CheckMate 816	NCT02998528	IB-IIIA, neoadjuvant	nivolumab + chemotherapy	2017-2028
KEYNOTE-671	NCT03425643	II-IIIB, both neo/adjuvant	pembrolizumab + chemotherapy	2018-2026
IMpower030	NCT03456063	IB-IIA, neoadjuvant	atezolizumab + platinum chemotherapy	2018-2026
AEGEAN	NCT03800134	II-III, both neo/adjuvant	durvalumab + chemotherapy	2018-2024
IMpower132	NCT04367311	IB-IIIA, adjuvant	atezolizumab + chemotherapy	2020-2024
MERMAID-1	NCT04385368	II-III, adjuvant	durvalumab + chemotherapy	2020-2026
GO42501	NCT04832854	II-IIIB, both neo/adjuvant	tiragolumab + atezolizumab ± chemotherapy	2021-2027
Targeted therapy				
ADAURA	NCT02511106	IB-IIIA, adjuvant	Osimertinib	2015-2023
BO40336	NCT03456076	IB-IIIA, adjuvant	Alectinib ± chemotherapy	2018-2026
NAUTIKA1	NCT04302025	IIA-IIIB, both neo/adjuvant	varied tyrosine kinase inhibitors	2020-2028
NeoADAURA	NCT04351555	II-IIIB, neoadjuvant	osimertinib ± chemotherapy	2020-2029
LIBRETTO-432	NCT04819100	IB-IIIA, adjuvant	Selpercatinib	2021-2032
Geometry-N	NCT04926831	IB-IIIA, both neo/adjuvant	capmatinib	2021-2028
	NCT05118854	IIA-IIIB, neoadjuvant	sotorasib + chemotherapy	2022-2023

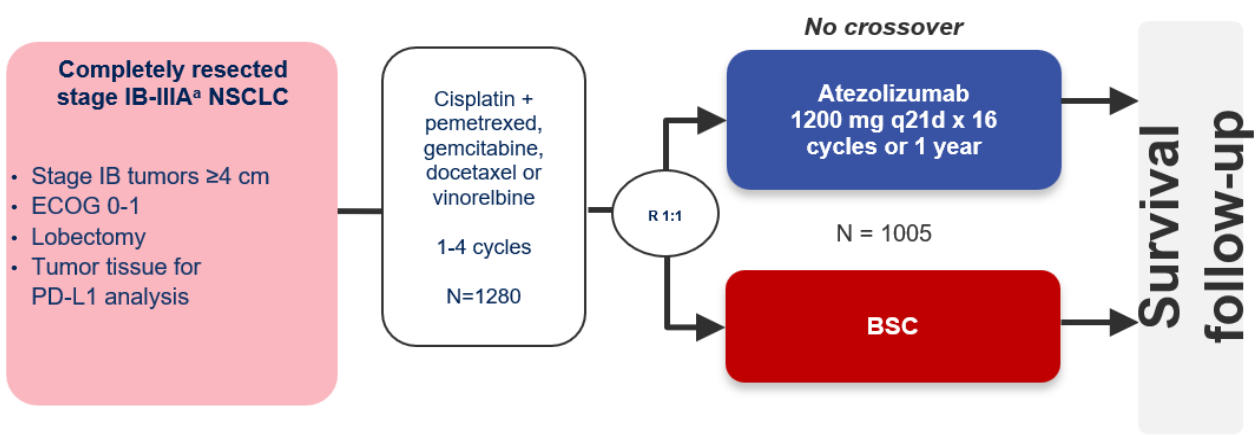
*Study start date and estimated study completion date per clinicaltrials.gov accessed 2022/01/10.

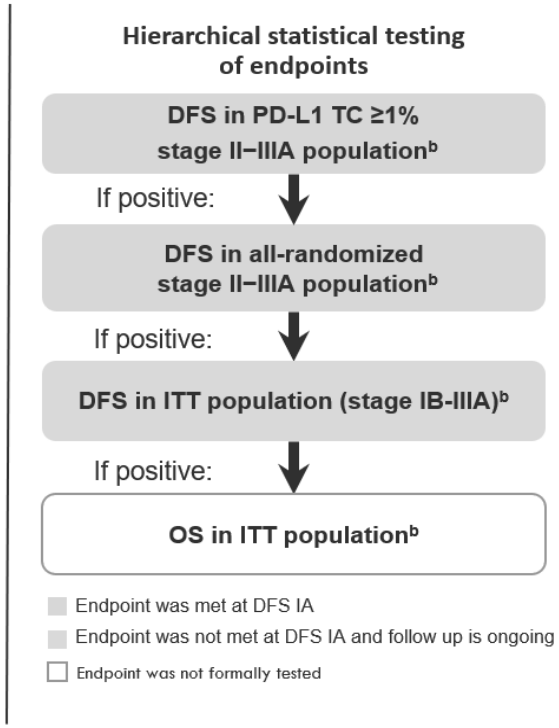
www.onclive.com/view/happy-upheavals-are-unveiled-in-early-stage-lung-cancer
Cummings AL, January 26, 2022

UCLA Health | David Geffen School of Medicine

KHDAK'de Adjuvan İmmünoterapi

IMpower010: Phase III randomised trial of atezolizumab vs BSC in early-stage NSCLC





Stratification factors

- Sex | Stage | Histology | PD-L1 status

Key exploratory endpoints

- OS biomarker analyses

Key secondary endpoints

- OS in ITT | Safety | Exploratory OS biomarker analyses

Clinical cutoff: 18 April 2022. Both arms included observation and regular scans for disease recurrence on the same schedule. ECOG, Eastern Cooperative Oncology Group, q21d, every 21 days.
[a] Per UICC/AJCC staging system, 7th edition. [b] Two-sided α=0.05.

H. Wakelee ASCO 2021, abstr 8500:IMpower010 Interim Analysis; Felip Lancet 2021, Felip IASLC WCLC 2022

KHDAK'de Adjuvan İmmünoterapi

IMpower010: baseline characteristics

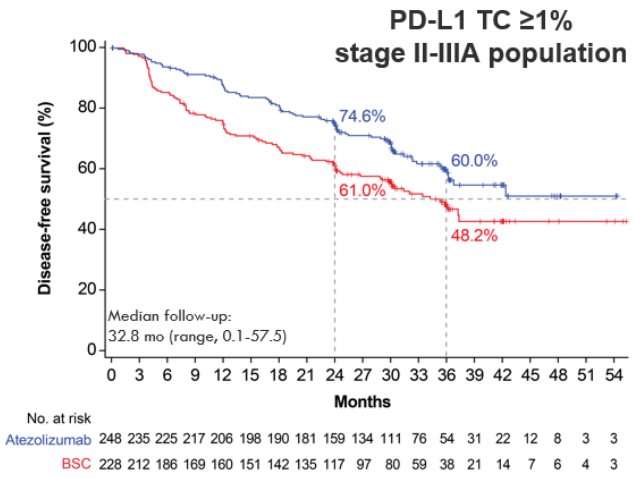
Characteristic	All patients (N=1005)	PD-L1 TC ≥1% (SP263) (stage II-IIIA)		All randomized (stage II-IIIA)		ITT (stage IB-IIIA)	
		Atezo (n=248)	BSC (n=228)	Atezo (n=442)	BSC (n=440)	Atezo (n=507)	BSC (n=498)
Median (range) age,	**62 (26-84)**	61 (34–82)	62 (26–84)	62 (33–82)	62 (26–84)	62 (33–83)	62 (26–84)
Age ≥65 y, n (%)	**382 (38.0)**	92 (37.1)	97 (42.5)	161 (36.4)	177 (40.2)	184 (36.3)	198 (39.8)
Sex, male, n (%)	**672 (66.9)**	171 (69.0)	147 (64.5)	295 (66.7)	294 (66.8)	337 (66.5)	335 (67.3)
Race, n (%)							
White	**738 (73.4)**	162 (65.3)	166 (72.8)	307 (69.5)	324 (73.6)	362 (71.4)	376 (75.5)
Asian	**242 (24.1)**	78 (31.5)	56 (24.6)	121 (27.4)	106 (24.1)	130 (25.6)	112 (22.5)
Other	**25 (2.5)**	8 (3.2)	6 (2.6)	14 (3.2)	10 (2.3)	15 (3.0)	10 (2.0)
Histology, non-SQ	**659 (65.6)**	152 (61.3)	143 (62.7)	292 (66.1)	296 (67.3)	328 (64.7)	331 (66.5)
Stage, n (%)							
IB	**123 (12.2)**	–	–	–	–	65 (12.8)	58 (11.6)
IIA	**295 (29.4)**	85 (34.3)	76 (33.3)	147 (33.3)	148 (33.6)	147 (29.0)	148 (29.7)
IIB	**174 (17.3)**	46 (18.5)	37 (16.2)	90 (20.4)	84 (19.1)	90 (17.8)	84 (16.9)
IIIA	**413 (41.1)**	117 (47.2)	115 (50.4)	205 (46.4)	208 (47.3)	205 (40.4)	208 (41.8)
Tobacco use, n (%)							
Never	**222 (22.1)**	51 (20.6)	41 (18.0)	100 (22.6)	96 (21.8)	114 (22.5)	108 (21.7)
Current/previous	**783 (77.9)**	197 (79.4)	187 (82.0)	342 (77.4)	344 (78.2)	393 (77.5)	390 (78.3)
PD-L1 by SP263, TC≥1%, n (%)[a]	**535 (54.6)**	248 (100)	228 (100)	248 (57.8)	228 (53.0)	283 (57.4)	252 (51.9)

Wakelee ASCO 2021 abstr 8500; Felip Lancet 2021

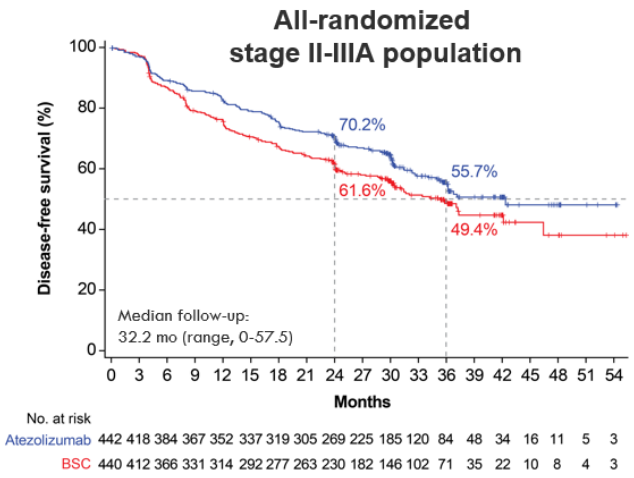
KHDAK'de Adjuvan İmmünoterapi

IMpower010: DFS in the PD-L1 TC ≥1%[a] stage II-IIIA, all-randomized stage II-IIIA and ITT pop (primary endpoint)

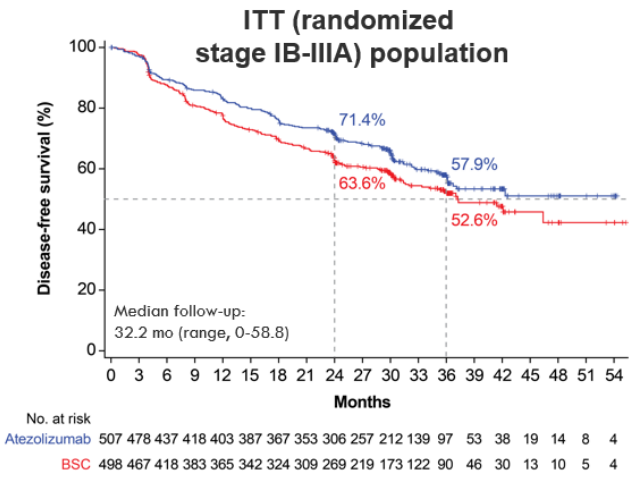
US FDA approval Oct 15, 2021



	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[b]	0.004[c]	



	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[b]	0.02[c]	



	Atezolizumab (n=507)	BSC (n=498)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value[b]	0.04[d]	

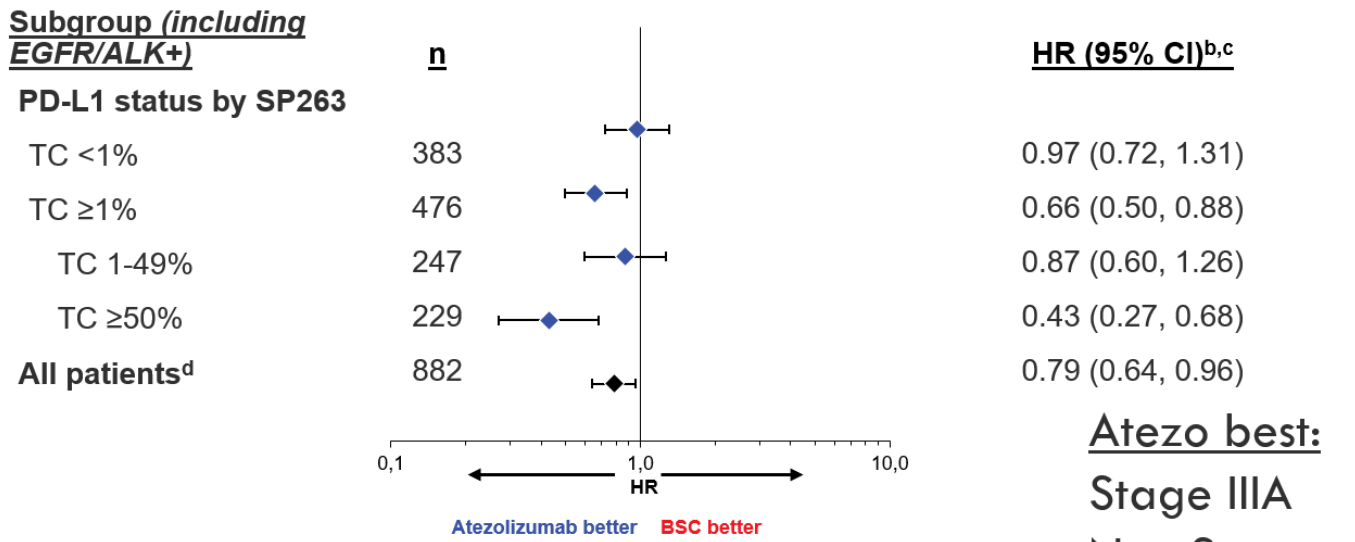
Clinical cutoff: January 21, 2021. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS. [d] The statistical significance boundary for DFS was not crossed.

Wakelee ASCO 2021 abstr 8500; Felip Lancet 2021

KHDAK'de Adjuvan İmmünoterapi

IMpower010 DFS by PD-L1 status[a]

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



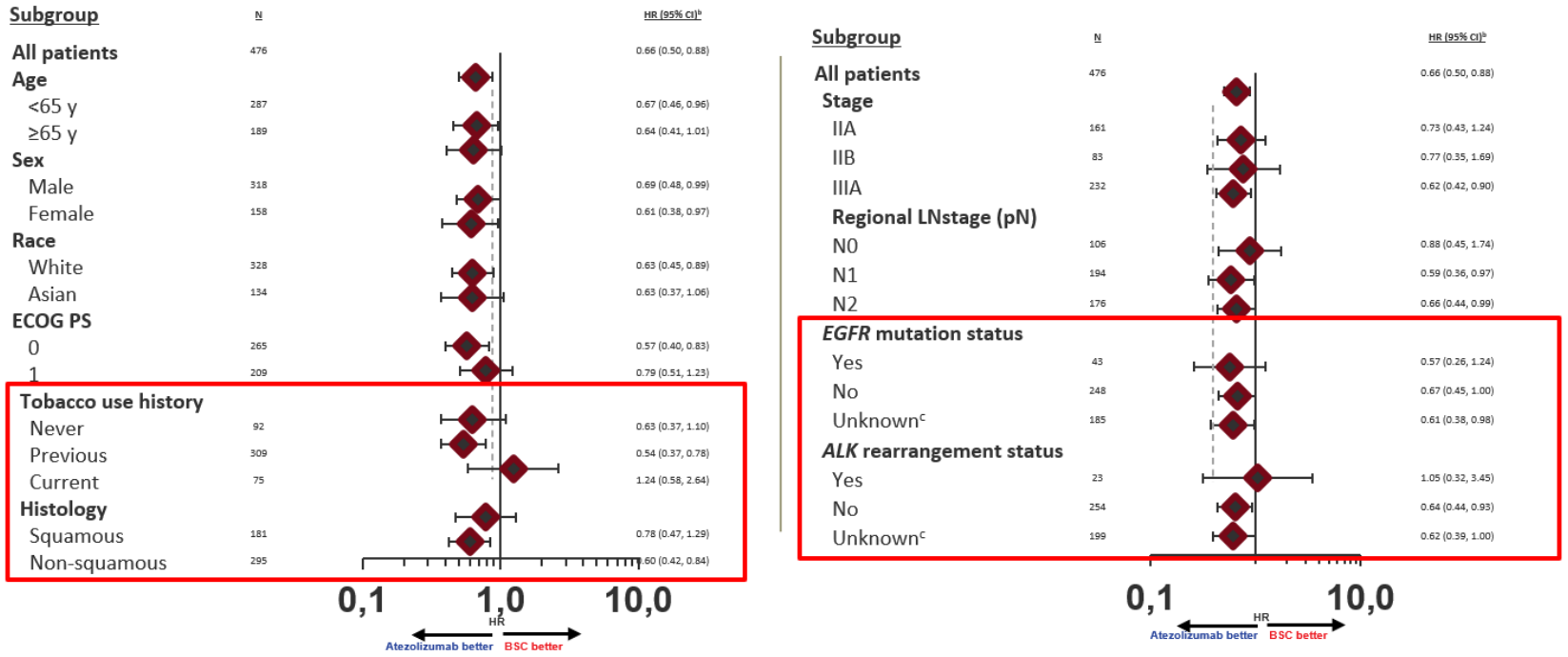
Clinical cutoff: 21 January 2021. [a] Per SP263 assay.
[b] Stratified for all patients and PD-L1 TC ≥1%; unstratified for all other subgroups. [c] DFS analyses in the PD-L1 TC <1% and TC 1-49% subgroups were exploratory. [d] 23 patients had unknown PD-L1 status as assessed by SP263. [e] Excluding patients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

Atezo best:
Stage IIIA
Non-Sq
Never-smoke
PD-L1≥50%

Felip ESMO2021

KHDAK'de Adjuvan İmmünoterapi

IMpower010: DFS in key subgroups of the PD-L1 TC ≥1%[a] stage II-IIIA population



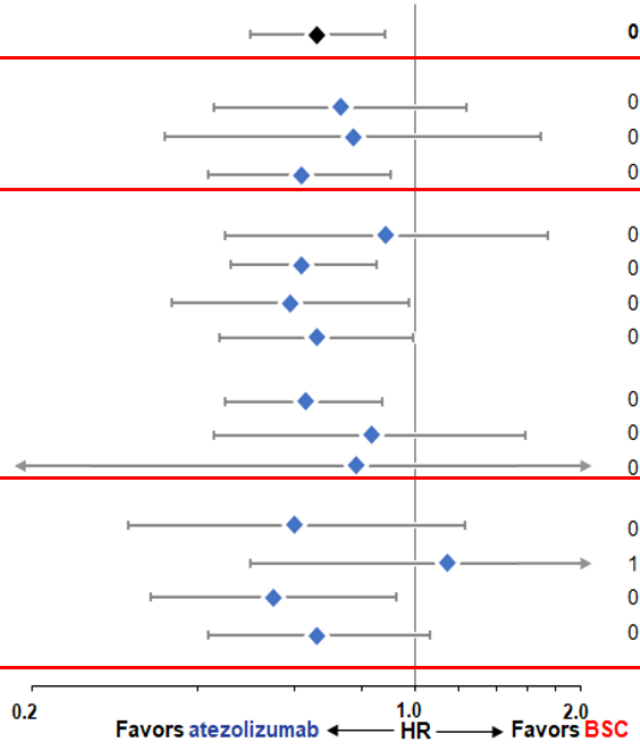
Clinical cutoff: January 21, 2021. [a] Per SP263 assay. [b] Stratified for all patients; unstratified for all other subgroups.
[c] 89.2% and 80.7% of patients in the ITT population with unknown *EGFR* or *ALK* status, respectively, had squamous NSCLC and were not required to undergo local or central testing.

Dr. Heather A. Wakelee ASCO 2021, abstr 8500:IMpower010 Interim Analysis; https://bit.ly/33t6JJ; Felip Lancet 2021

KHDAK'de Adjuvan İmmünoterapi

IMpower010: PD-L1 TC ≥1%[a] stage II-IIIA population: DFS by disease and treatment characteristics

Subgroup	n	HR (95% CI)[b]	Median DFS, mo: Atezolizumab	Median DFS, mo: BSC
All patients	**476**	**0.66 (0.50, 0.88)**	**NE**	**35.3**
Disease stage				
Stage IIA	161	0.73 (0.43, 1.24)	NE	NE
Stage IIB	83	0.77 (0.35, 1.69)	NE	NE
Stage IIIA	232	0.62 (0.42, 0.90)	42.3	26.7
Regional lymph node status (pN)				
N0	106	0.88 (0.45, 1.74)	36.7	NE
N+	370	0.62 (0.46, 0.85)	NE	31.4
N1	194	0.59 (0.36, 0.97)	NE	NE
N2	176	0.66 (0.44, 0.99)	32.3	21.3
Type of surgery[c]				
Lobectomy	359	0.63 (0.45, 0.87)	NE	33.4
Pneumonectomy	85	0.83 (0.43, 1.58)	36.1	NE
Bilobectomy	24	0.78 (0.18, 3.33)	36.7	NE
Chemotherapy regimen				
Cisplatin-docetaxel	71	0.60 (0.30, 1.23)	36.1	18.0
Cisplatin-gemcitabine	75	1.14 (0.50, 2.61)	36.1	NE
Cisplatin-vinorelbine	161	0.55 (0.33, 0.92)	NE	34.2
Cisplatin-pemetrexed	169	0.66 (0.42, 1.06)	NE	31.4



Clinical cutoff: January 21, 2021. [a] Per SP263 assay.
[b] Stratified for all patients; unstratified for all other subgroups.
[c] Subgroups with ≤10 patients are not shown.

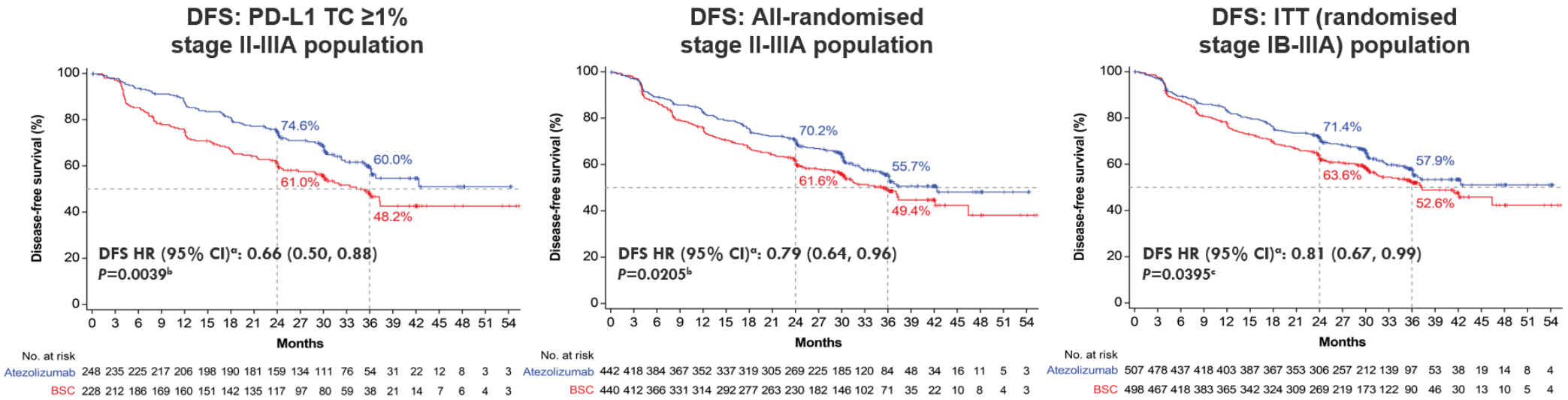
Atezo best:
Stage IIIA
Non-Sq
Prev smoking history
PD-L1≥50%

Altorki WCLC 2021

KHDAK'de Adjuvan İmmünoterapi

Recap of DFS and OS data from the DFS IA[1,2]

(data cutoff: 21 Jan '21, median follow-up: 32 months)



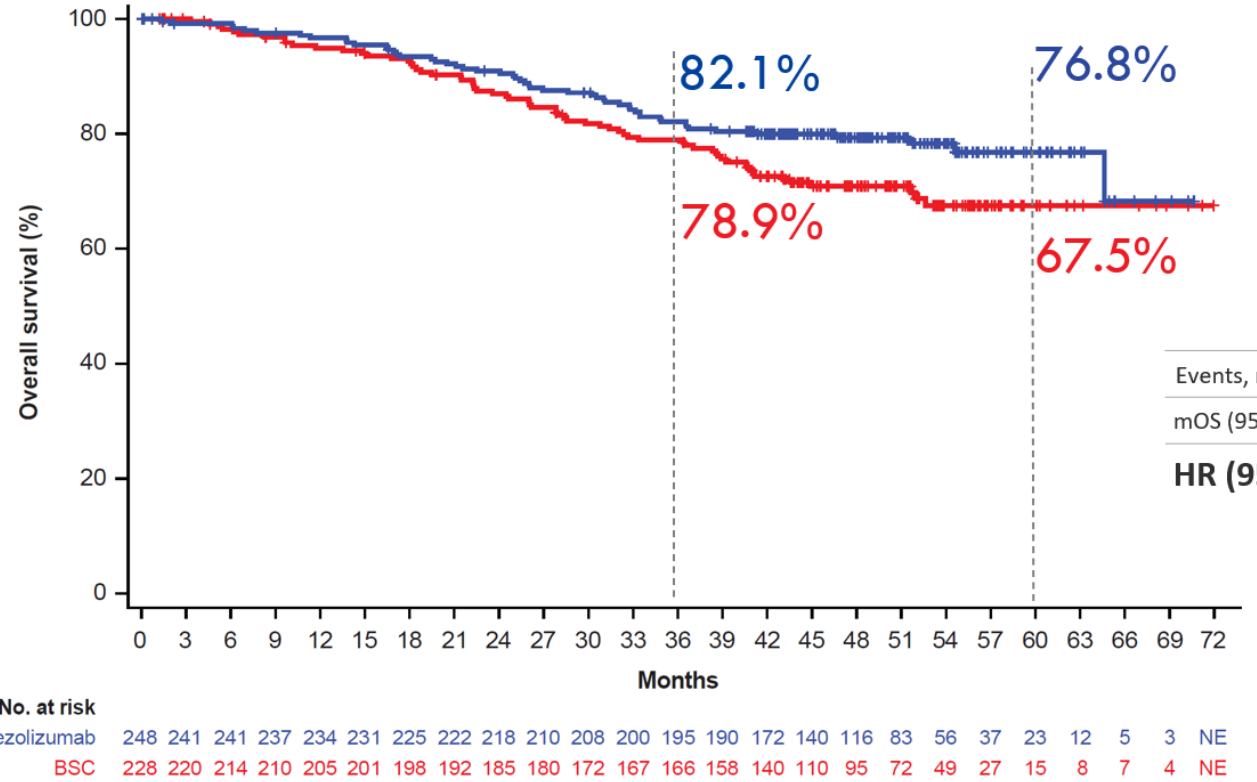
- **OS data** not mature (event to patient ratio in ITT was 19% in atezolizumab arm, 18% in BSC arm)
  - **PD-L1 TC ≥1% stage II-IIIA population: OS HR, 0.77 (95% CI: 0.51, 1.17)[a]**
  - All-randomised stage II-IIIA population: OS HR, 0.99 (95% CI: 0.73, 1.33)[a]
  - ITT (randomised stage IB-IIIA) population: OS HR, 1.07 (95% CI: 0.80, 1.42)[a]

Clinical cutoff: 21 Jan 2021. [a] Stratified. [b] Statistical significance boundary for DFS crossed. [c] Statistical significance boundary for DFS not crossed.

1. Felip, E et al Lancet 2021; 938; 1344-1357; 2. Wakelee. HA et al ASCO 2021; abs #8500., Felip IASLC WCLC 2022 Presidential Plenary

KHDAK'de Adjuvan İmmünoterapi

IMpower010: Results of OS IA(data cut 4/18/22: 46 mo med f/up)
PD-L1 TC ≥1%[a] (stage II-IIIA)

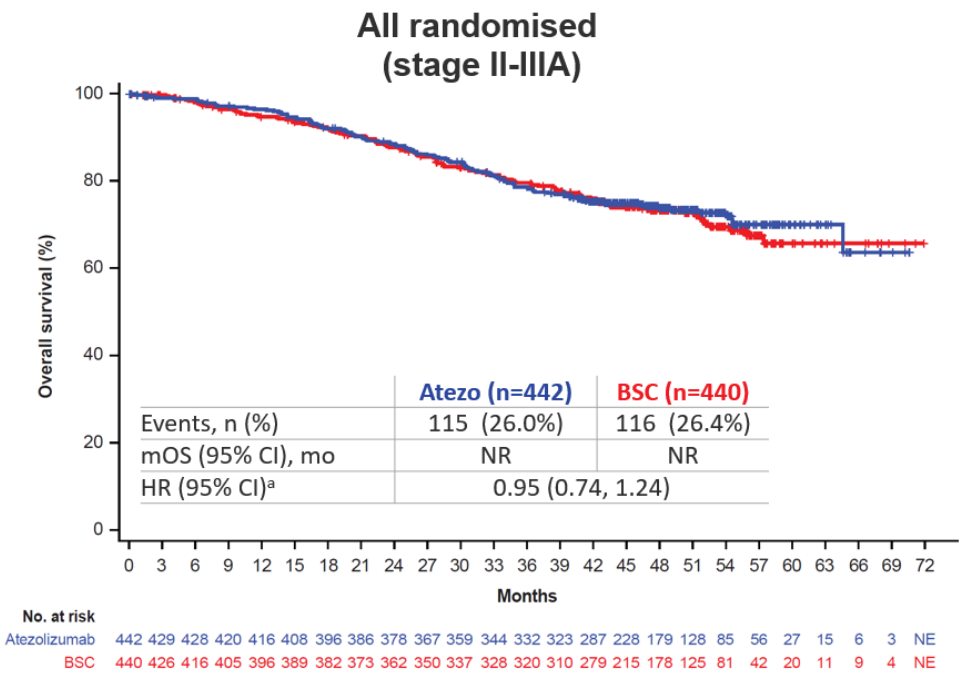


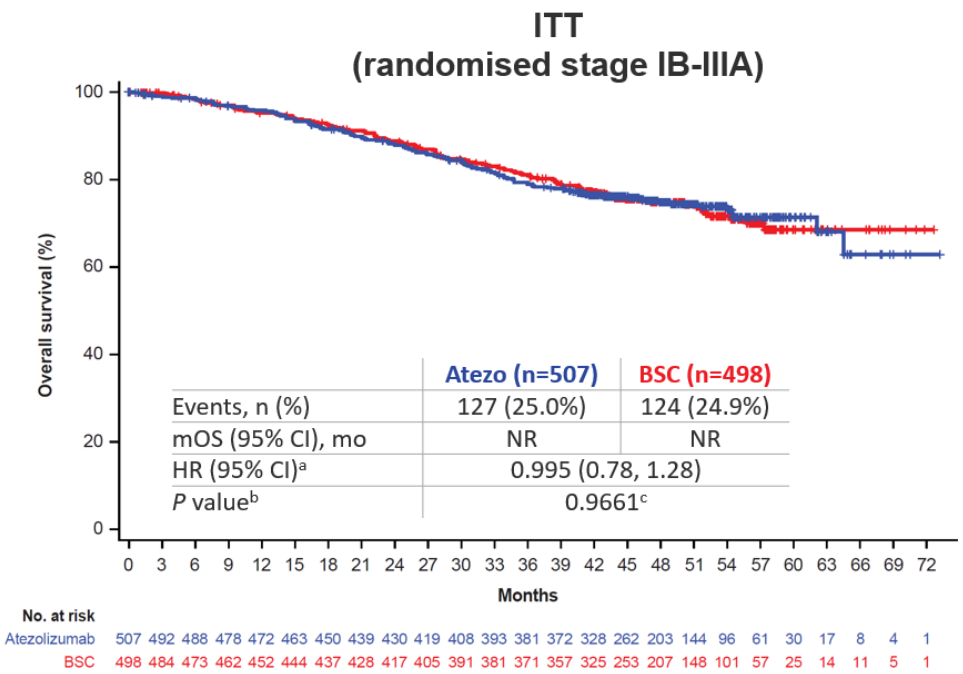
	Atezo (n=248)	BSC (n=228)
Events, n (%)	52 (21.0%)	64 (28.1%)
mOS (95% CI), mo	NR	NR
HR (95% CI)[b]	**0.71 (0.49, 1.03)**	

Felip IASLC WCLC 2022 Presidential Plenary

KHDAK'de Adjuvan İmmünoterapi

IMpower010: Results of OS IA (data cut 4/18/22: 46 mo med f/up)
Other primary populations



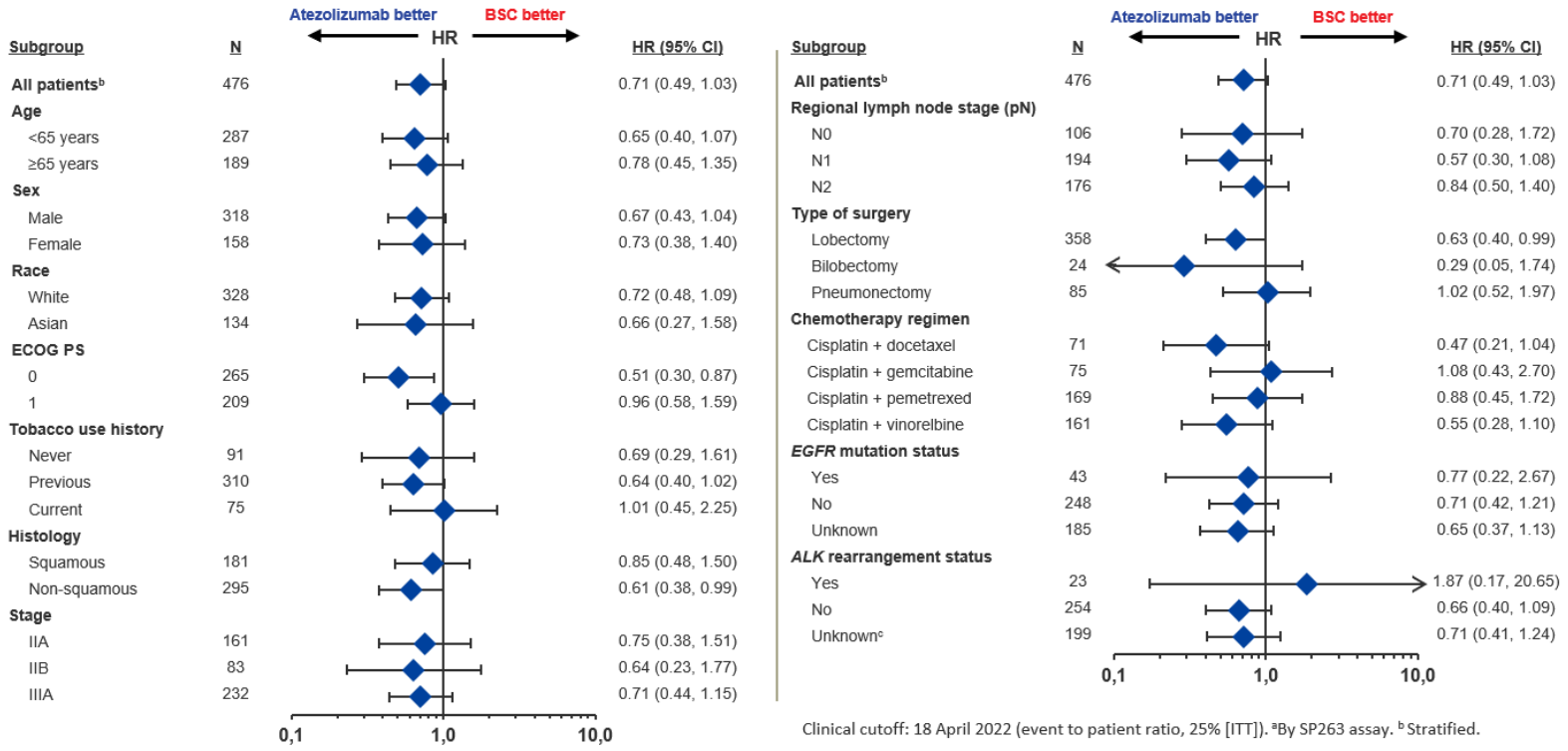


Clinical cutoff: 18 April 2022.[a] Stratified. [b] No formal testing until statistical significance observed for DFS in the ITT population due to the prespecified testing hierarchy.
[c] Descriptive purposes only.

KHDAK'de Adjuvan İmmünoterapi

Subgroup analysis of OS in PD-L1 TC ≥1%[a] (stage II-IIIA)

(data cutoff: 18 Apr '22, median follow-up: 46 months)

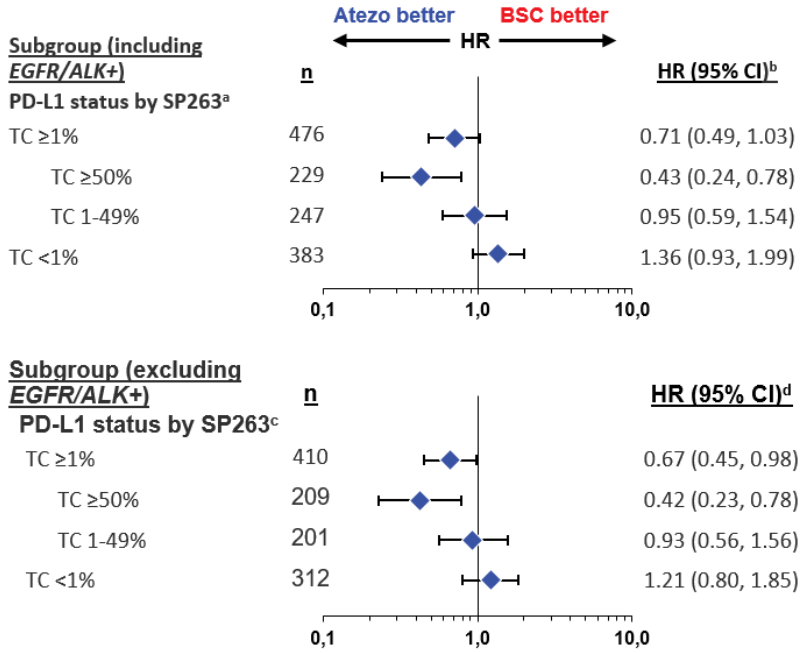


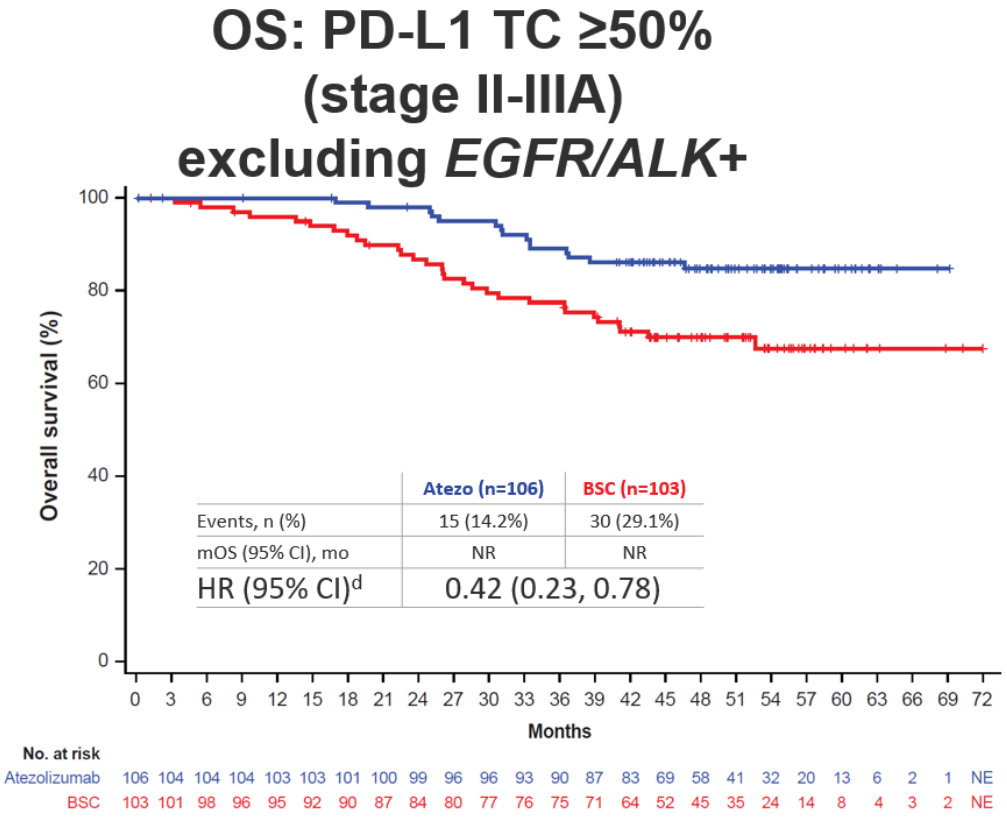
Clinical cutoff: 18 April 2022 (event to patient ratio, 25% [ITT]). [a]By SP263 assay. [b] Stratified.

KHDAK'de Adjuvan İmmünoterapi

OS by Biomarkers (stage II-IIIA)

(data cutoff: 18 Apr '22, 46 mo follow-up)





[a] 23 patients had unknown PD-L1 status. [b] Stratified for PD-L1 TC ≥1%; unstratified for all other subgroups. [c] 21 patients had unknown PD-L1 status. [d] Unstratified.

KHDAK'de Adjuvan İmmünoterapi

Safety summary
(data cutoff: 18 Apr '22)

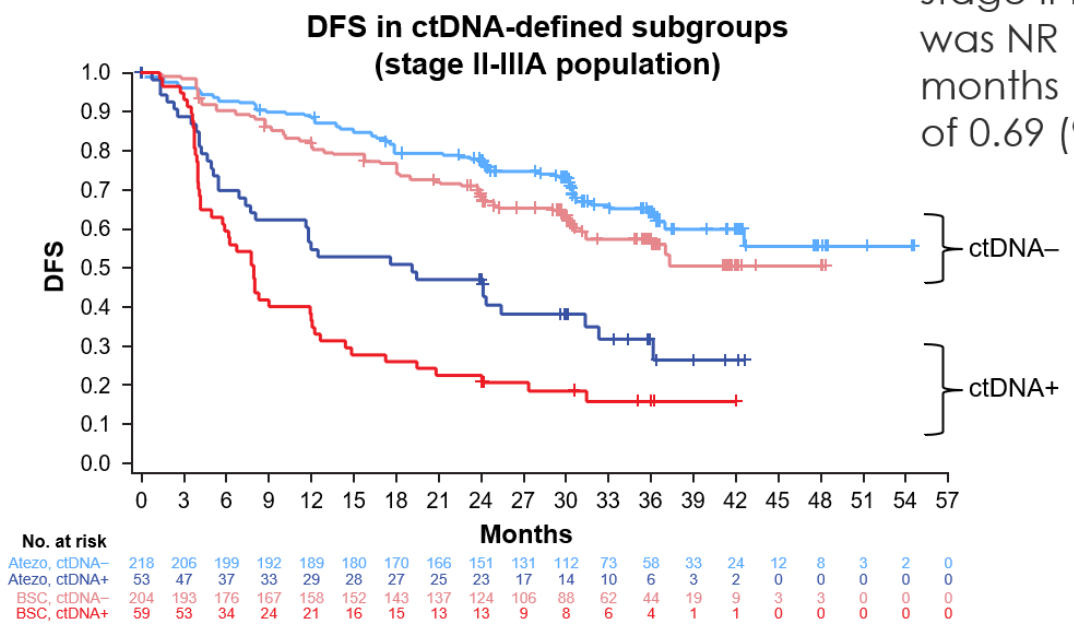
- Overall safety profile was consistent with previous analysis; no new safety signals were seen

	IMpower010 DFS IA (21 Jan '21)	IMpower010 OS IA (18 Apr '22)	
	Atezo (n=495)	Atezo (n=495)	BSC (n=508)
All-grade AE	92.7%	92.5%	70.9%
Treatment-related AE	67.7%	67.9%	0%
Grade 3-4 AE	21.8%	22.0%	11.5%
Treatment-related Grade 3-4 AE	10.7%	10.7%	0%
Serious Adverse Event	17.6%	17.8%	8.5%
Treatment-related SAE	7.5%	7.5%	0%
Grade 5 AE	1.6%	1.8%[a]	0.6%
Treatment-related Grade 5 AE	0.8%	0.8%	0%
AE leading to dose interruption of atezolizumab	28.7%	28.7%	0%
AE leading to any treatment withdrawal	18.2%	18.2%	0%
All-grade Atezo AESI[b]	51.7%	52.1%	9.5%
Grade 3-4 Atezo AESI	7.9%	7.9%	0.6%
All-grade atezo AESI requiring use of corticosteroids	12.1%	12.3%	0.8%

AESI, AE of special interest; SAE, serious AE. [a] No new deaths due to AEs occurred since the DFS IA clinical cutoff date; a previous 'other' death was updated to a Grade 5 AE.
[b] No new AESI medical concepts noted at OS IA vs DFS IA.

KHDAK'de Adjuvan İmmünoterapi

IMpower010 – Exploratory ctDNA results



- In all ctDNA-evaluable stage II-IIIA patients, mDFS was NR (atezo) vs 31.4 months (BSC), with an HR of 0.69 (95% CI: 0.53, 0.89)

ctDNA–	Atezo (n=218)	BSC (n=204)
mDFS, mo	NR	NR
HR (95% CI)	0.72 (0.52, 1.00)	

ctDNA+	Atezo (n=53)	BSC (n=59)
mDFS, mo	19.1	7.9
HR (95% CI)	0.61 (0.39, 0.94)	

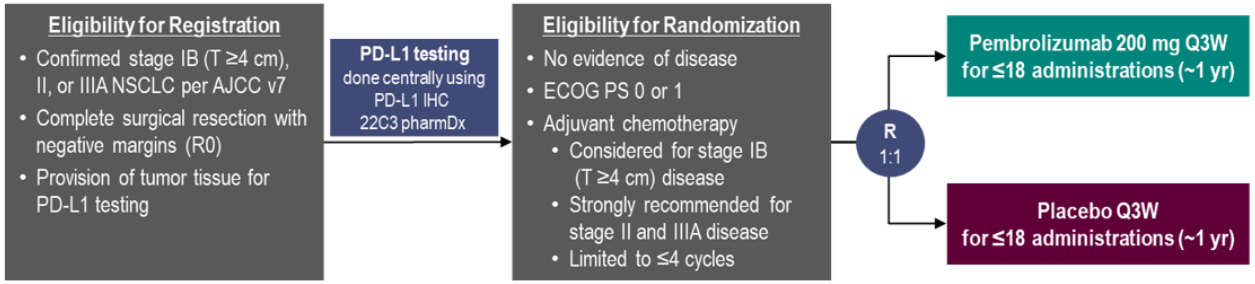
Clinical cutoff: 21 January 2021. Unstratified HRs are shown.

Zhou C et al, ESMO IO 2021

KHDAK'de Adjuvan İmmünoterapi

PEARLS/KEYNOTE-091 Study Design

Global, Randomized, Triple-Blind Phase 3 Study



Dual Primary End Points

- DFS in the overall population
- DFS in the PD-L1 TPS ≥50% population

Secondary End Points

- DFS in the PD-L1 TPS ≥1% population
- OS in the overall, PD-L1 TPS ≥50%, and PD-L1 TPS ≥1% populations
- Lung cancer-specific survival in the overall population
- Safety

Characteristic	Overall		PD-L1 TPS ≥50%	
	Pembro (N = 590)	Placebo (N = 587)	Pembro (N = 168)	Placebo (N = 165)
Age, median (range), y	65.0 (31-87)	65.0 (37-85)	64.5 (38-82)	65.0 (37-85)
Male sex	68.0%	68.7%	72.0%	70.3%
Geographic region				
Asia	18.0%	17.9%	17.3%	17.6%
Eastern Europe	19.7%	19.3%	18.5%	18.2%
Western Europe	51.4%	51.3%	53.6%	53.9%
Rest of world	11.0%	11.6%	10.7%	10.3%
ECOG PS 1	35.6%	41.6%	31.0%	38.8%

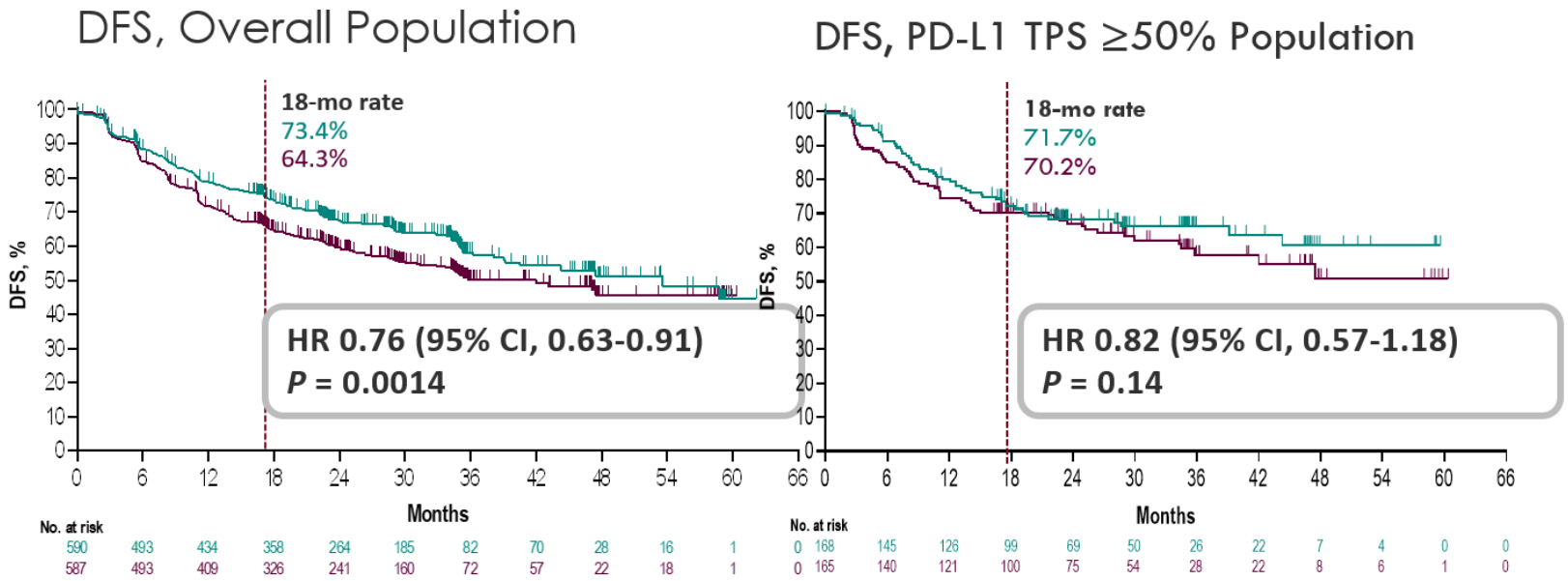
Characteristic	Overall		PD-L1 TPS ≥50%	
	Pembro (N = 590)	Placebo (N = 587)	Pembro (N = 168)	Placebo (N = 165)
Current/former smoker	85.3%	88.8%	91.7%	92.1%
Nonsquamous histology	67.5%	61.8%	61.3%	63.6%
Received adjuvant chemotherapy	85.8%	85.9%	85.1%	85.5%
Pathologic stage[a]				
IB	14.2%	14.5%	12.5%	13.3%
II	55.8%	57.6%	56.5%	56.4%
IIIA	30.0%	27.6%	31.0%	30.3%
EGFR mutation[b]	6.6%	5.8%	3.6%	3.0%
ALK translocation[c]	1.2%	1.2%	1.8%	0.0%

[a]2 (0.3%) participants in the placebo arm had stage IV disease; neither had TPS ≥50%.
[b]*EGFR* mutation status was unknown for 670 (63.5%) in the overall population and 198 (59.5%) in the TPS ≥50% population.
[c]ALK translocation status was unknown for 747 (63.5%) in the overall population and 217 (65.2%) in the TPS ≥50% population.

Paz-Ares ESMO plenary 2022, O'Brien ASCO 2022

KHDAK'de Adjuvan İmmünoterapi

KN-091 DFS curves



	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	35.9%	53.6 (39.2-NR)
Placebo	44.3%	42.0 (31.3-NR)

	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	32.1%	NR (44.3-NR)
Placebo	38.2%	NR (35.8-NR)

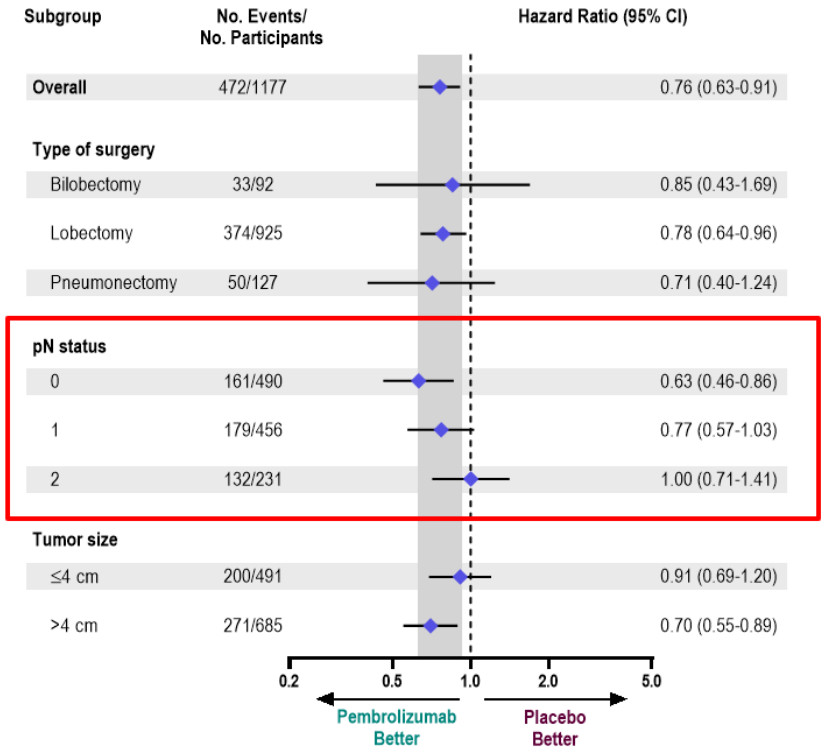
Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: September 20, 2021

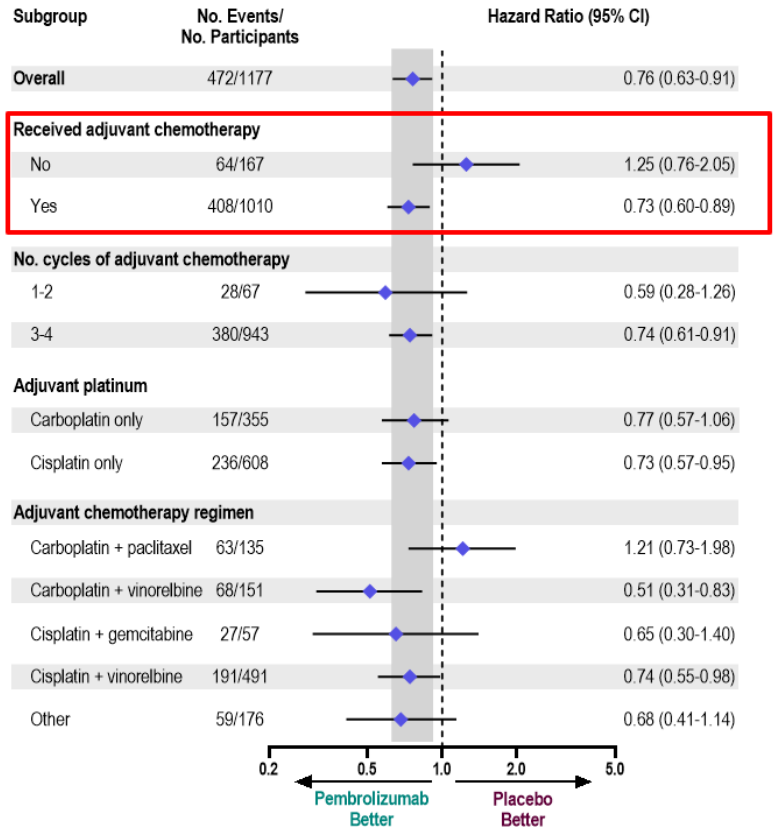
IMpower010 DFS HR: all comer 0.81, PD-L1 ≥50% 0.43

Paz Ares – ESMO Virtual Plenary March 2022

KHDAK'de Adjuvan İmmünoterapi

KN-091 Results: DFS Related to Surgical Resection, Disease Burden, and Use of Adjuvant Chemotherapy

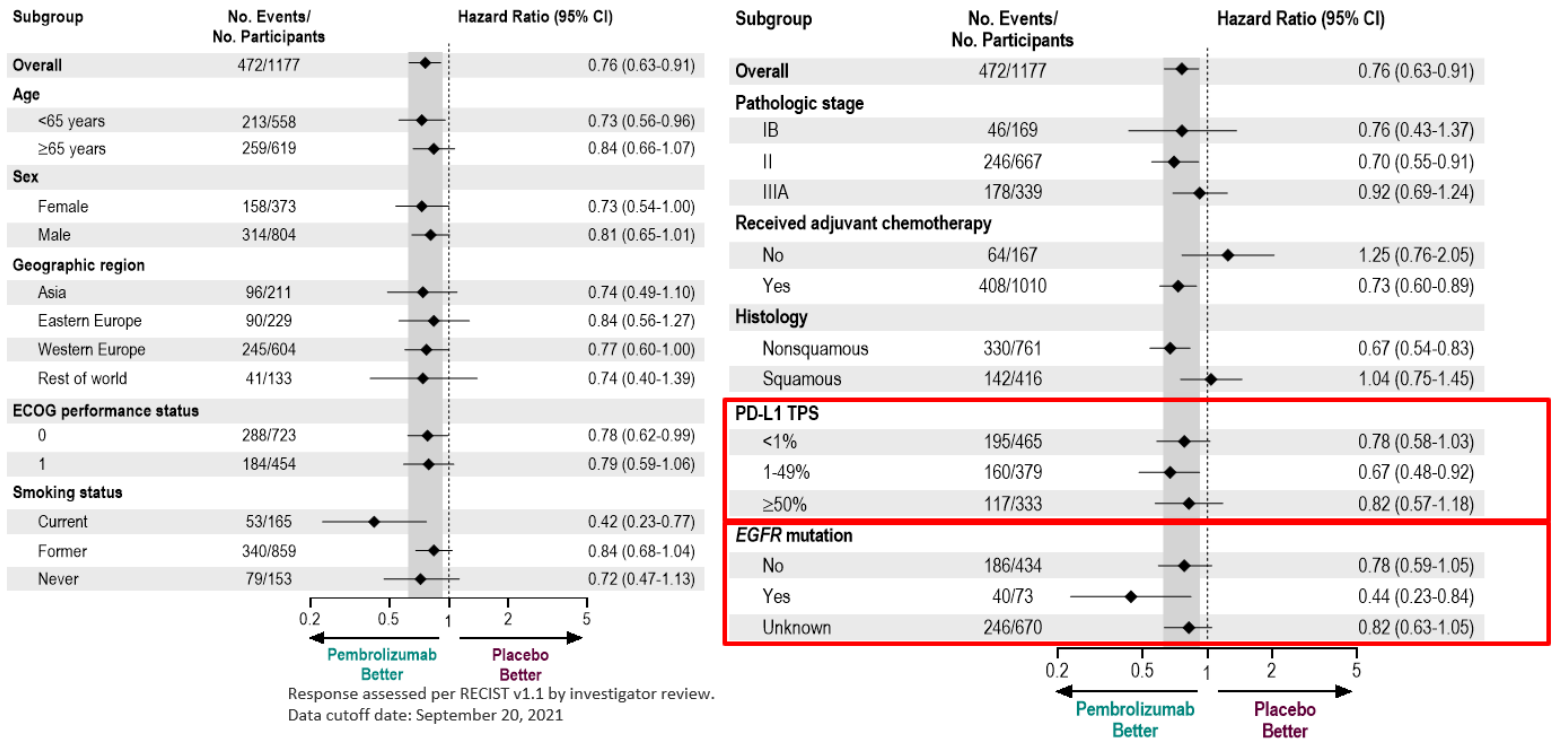




O'Brien ASCO 2022

KHDAK'de Adjuvan İmmünoterapi

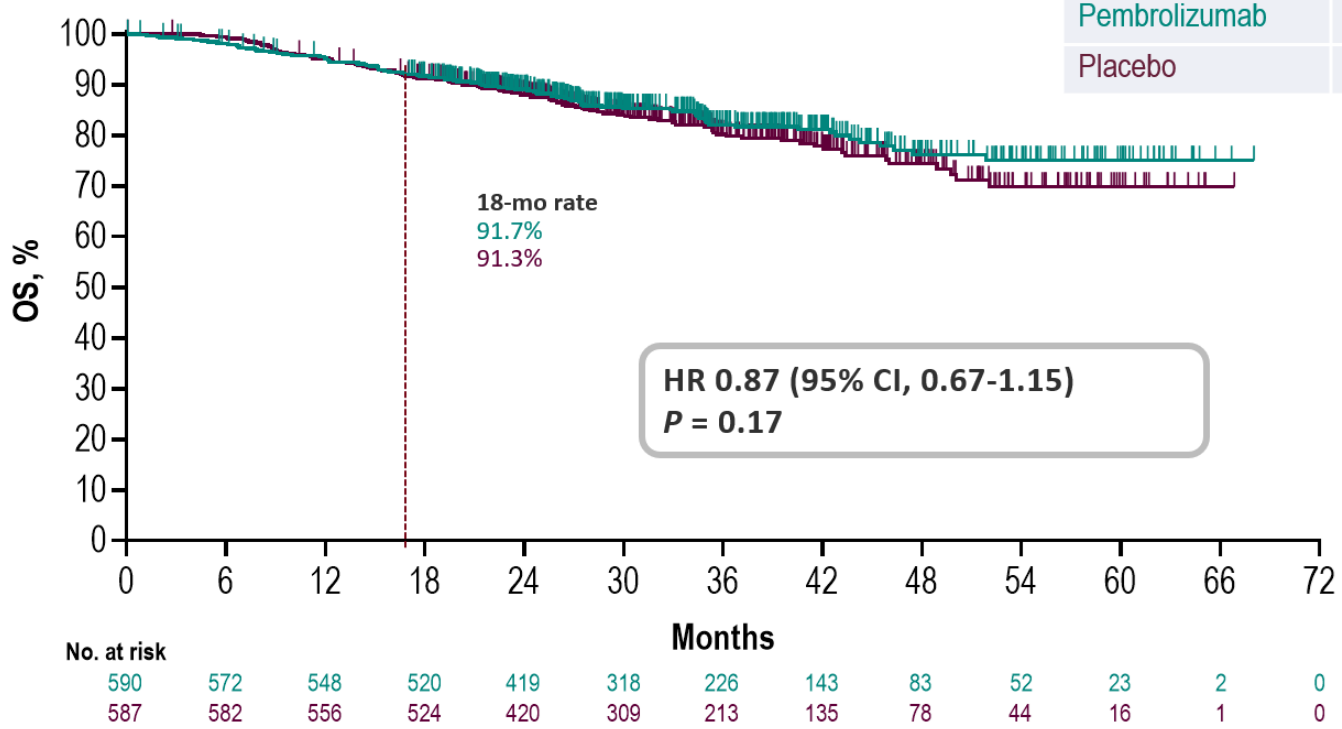
KN-091 DFS in Key Subgroups, Overall Population



KHDAK'de Adjuvan İmmünoterapi

KN-091 OS, Overall Population

	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	16.6%	NR (NR-NR)
Placebo	18.9%	NR (NR-NR)

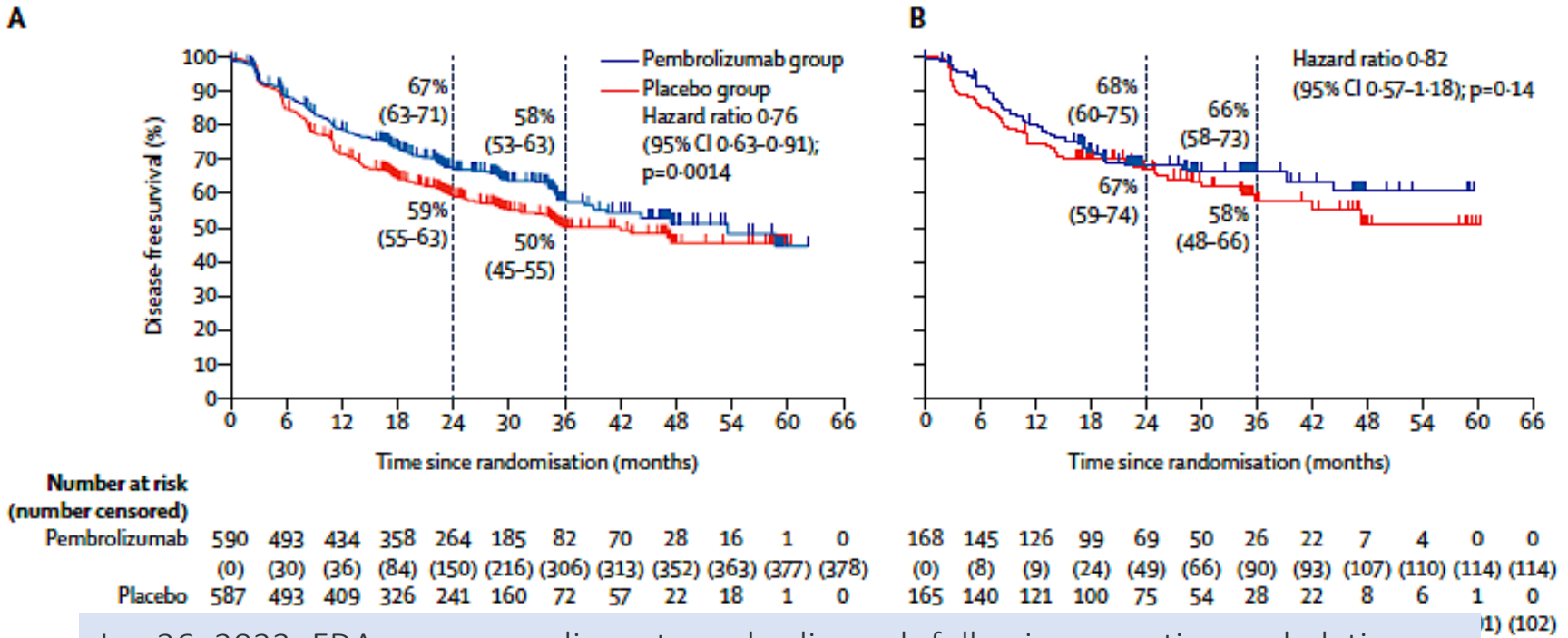


Data cutoff date: September 20, 2021

KEYNOTE-091/PEARLS RP3 study of adjuvant pembrolizumab vs BSC for resectable NSCLC

Stage IB-IIIA
HR=0.76 (P=.0014,
95% CI 0.63-0.91)

PD-L1>50%
HR=0.82 (P=.14,
95% CI , 0.57-1.18)



Jan 26, 2023: FDA approves adjuvant pembrolizumab following resection and platinum-based chemotherapy for stage IB (T2a ≥4 cm), II, or IIIA NSCLC

O'Brien et al, Lancet Oncology 2022

Erken Evre KHDAK'de RT+İmmünoterapi

What about IO after definitive RT? The I-SABR RP2 study for early-stage or isolated lung parenchymal recurrent node-negative NSCLC

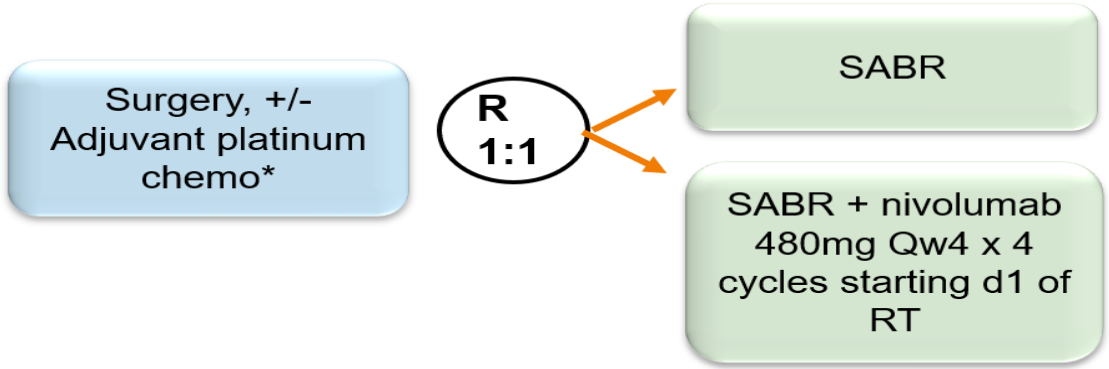
N=156 randomized

Key eligibility

- Stage IA-IIB, AJCC 8th ed. Or isolated parenchymal recurrence (node-negative)
- Medically inoperable or refused surgery

Stratification:

- ECOG PS (0–1 vs 2), tumor size (≤3 cm vs >3 to 5 cm vs >5 to 7 cm), histology (squamous vs non-squamous), and lung cancer history (primary vs recurrent disease)

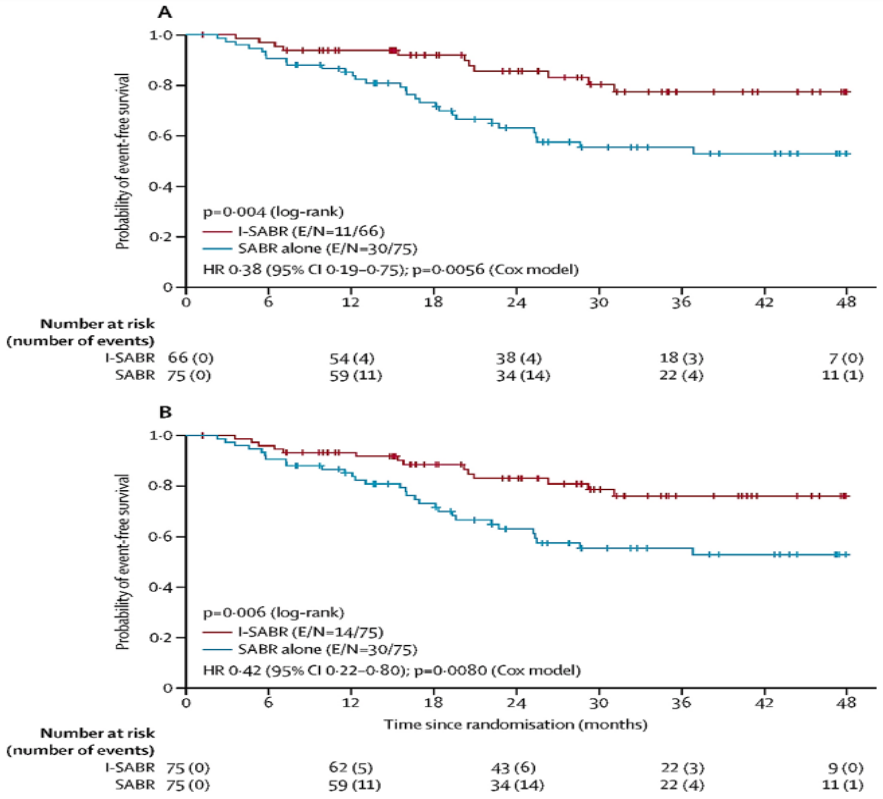


Primary endpoint : 4Y EFS (events include recurrence, new primary, or death), both ITT and treatment per-protocol

Chang et al, Lancet 2023

Erken Evre KHDAK'de RT+İmmünoterapi

I-SABR RP2 study for early-stage or isolated lung parenchymal recurrent node-negative NSCLC: primary results



Chang et al, Lancet 2023

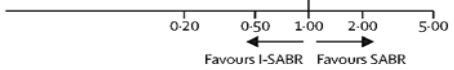
Per protocol treated
HR 0.38 (95% CI 0.19-.75; p=.0056)

ITT population
HR 0.42 (95% CI 0.22-.80; p=.006)

Erken Evre KHDAK'de RT+İmmünoterapi

I-SABR RP2 study for early-stage or isolated lung parenchymal recurrent node-negative NSCLC: subgroup analyses

	Number of participants (events)	Number of participants (events)	Hazard ratio	Hazard ratio (95% CI) I–SABR vs SABR	p value
All patients	66 (11)	75 (30)		0·38 (0·19–0·75)	0·0056
Sex					
Female	46 (7)	41 (9)		0·63 (0·24–1·71)	0·37
Male	20 (4)	34 (21)		0·29 (0·10–0·85)	0·024
Age (years)					
≤72	40 (6)	41 (17)		0·32 (0·12–0·80)	0·016
>72	26 (5)	34 (13)		0·46 (0·16–1·29)	0·141
Smoking					
Current or former	59 (11)	68 (30)		0·38 (0·19–0·75)	0·0056
Never*	7 (0)	7 (0)		..	..
Lung cancer history					
No	50 (7)	63 (24)		0·32 (0·14–0·74)	0·0077
Yes	16 (4)	12 (6)		0·52 (0·15–1·85)	0·31
ECOG score					
0–1	62 (11)	68 (27)		0·39 (0·19–0·79)	0·0092
2†	4 (0)	7 (3)		..	..
Histology					
Non-squamous	55 (11)	61 (22)		0·48 (0·23–0·99)	0·046
Squamous†	11 (0)	14 (8)		..	..
Tumour size					
0 to ≤2 cm	35 (6)	51 (21)		0·35 (0·14–0·86)	0·023
>2 to 5 cm	31 (5)	24 (9)		0·40 (0·14–1·20)	0·10
SABR regimen					
50 Gy in four fractions	59 (10)	63 (24)		0·42 (0·20–0·88)	0·022
70 Gy in ten fractions	7 (1)	12 (6)		0·18 (0·02–1·52)	0·12
PD-L1 status					
<1%	27 (4)	34 (16)		0·27 (0·09–0·81)	0·019
≥1%†	15 (0)	16 (5)		..	..
Unknown	24 (7)	25 (9)		0·84 (0·31–2·27)	0·74
EGFR status					
Wild type	25 (2)	22 (10)		0·17 (0·04–0·80)	0·025
Mutated†	1 (0)	3 (1)		..	..
Unknown	40 (9)	50 (19)		0·51 (0·23–1·14)	0·10



Chang et al, Lancet 2023

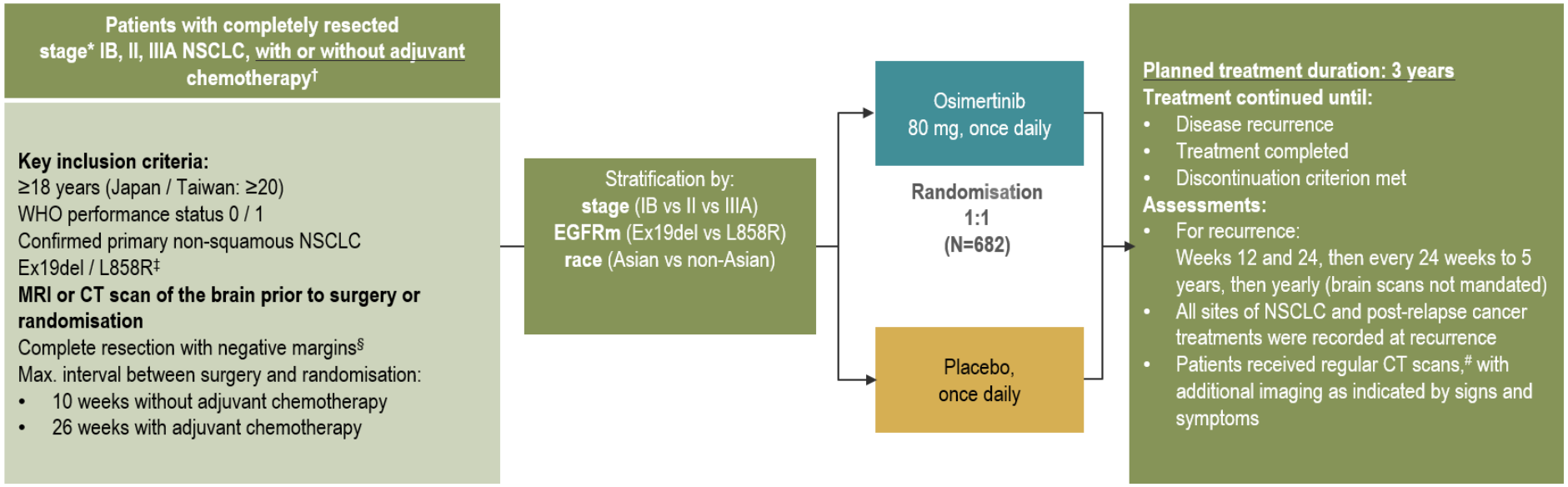
KHDAK'de Adjuvan İmmünoterapi

Adjuvant PD-1/PD-L1 IO trials

Drug/Trial	Description	Stages entered	Description	Primary endpoint
Nivolumab ANVIL arm of ALCHEMIST	US, NCI (ECOG), Observational control	IB (4cm)-IIIA After Adj Chemo +/- radiation	Phase 3 Allows PD-L1 +/-	OS/DFS
Atezolizumab IMPOWER010	Global, Placebo controlled	IB (4cm)-IIIA After Adj Chemo	Phase 3 Allows PD-L1 +/-	DFS
Durvalumab	Global, Placebo controlled	IB (4cm)-IIIA After Adj Chemo	Phase 3 Allows PD-L1 +/-	DFS
Pembrolizumab PEARLS KN-091	ETOP/EORTC, Placebo Controlled	IB (4cm)-IIIA After Adj Chemo	Phase 3 Allows PD-L1 +/-	DFS

KHDAK'de Adjuvan Hedefe Yönelik Tedavi

ADAURA: Phase III double-blind study design



- The primary and key secondary endpoints of DFS¶ in stage II/IIIA patients and the overall population, respectively, have been reported previously[1]
- **Here we report results from a pre-specified exploratory analysis of disease recurrence patterns in ADAURA, including CNS**

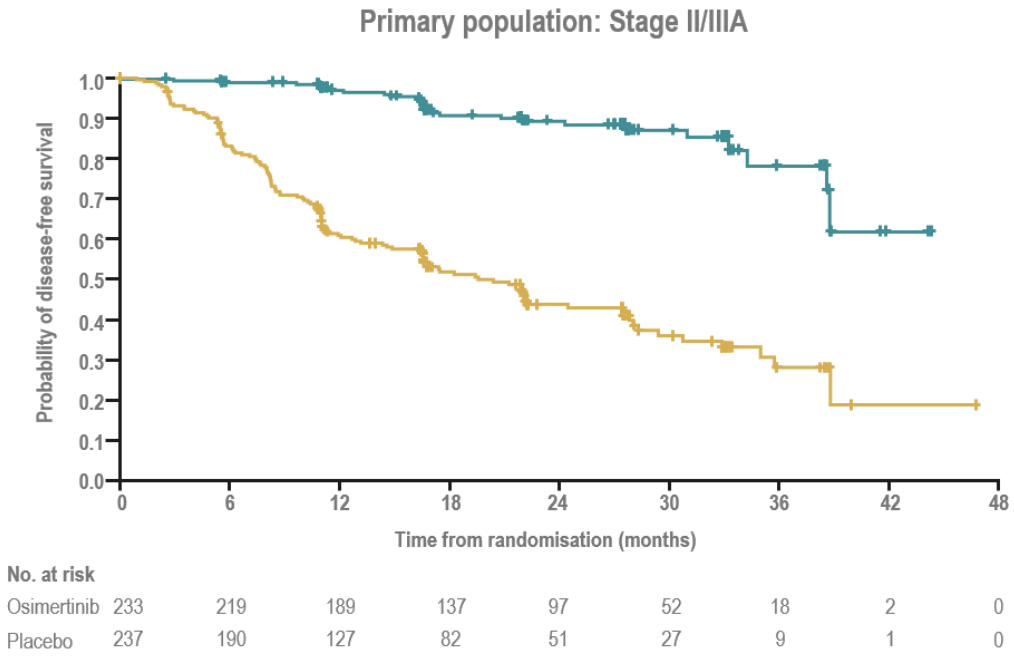
CT, computed tomography; MRI, magnetic resonance imaging; WHO, World Heath Organization; ex19del, exon 19 deletion; *AJCC 7th edition; †Prior, post, or planned radiotherapy was not allowed; ‡Centrally confirmed in tissue; §Patients received a CT scan after resection and within 28 days prior to treatment; ¶ By investigator assessment; #CT scans of the chest and abdomen, including liver and adrenal glands.

1. Herbst et al. J Clin Oncol 2020;38:18_suppl.LBA5.

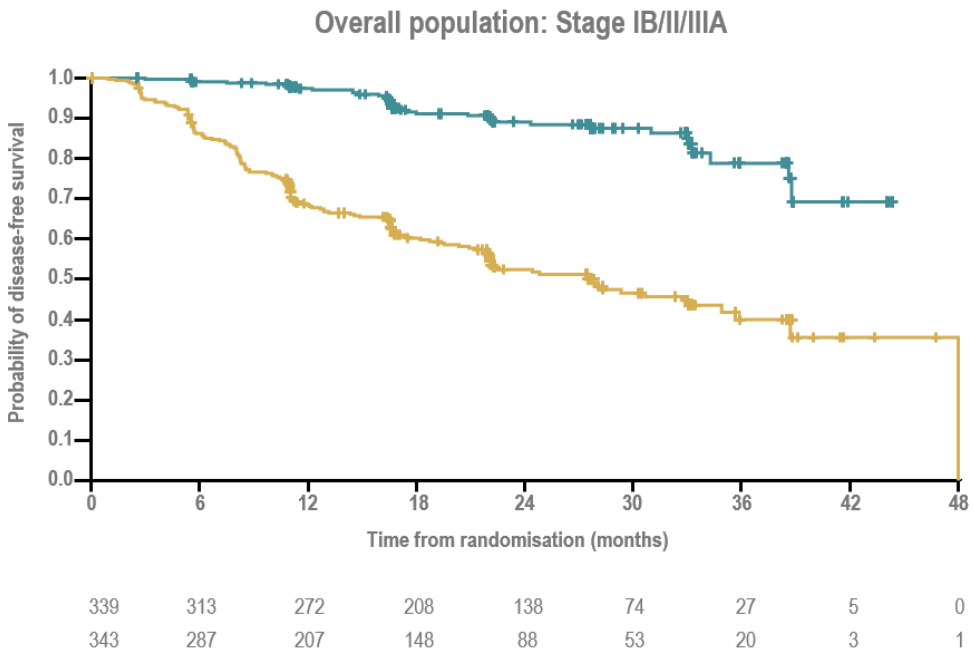
ADAURA data cut-off: 17 January, 2020

KHDAK'de Adjuvan Adjuvan Hedefe Yönelik Tedavi

ADAURA: A positive breakthrough for some patients
Osimertinib improves DFS in pts w resected EGFRmut NSCLC



	Median DFS, months (95% CI)	HR (99.06% CI)
– Osimertinib	NR (38.8, NC)	0.17 (0.11, 0.26) P<0.0001
– Placebo	19.6 (16.6, 24.5)	



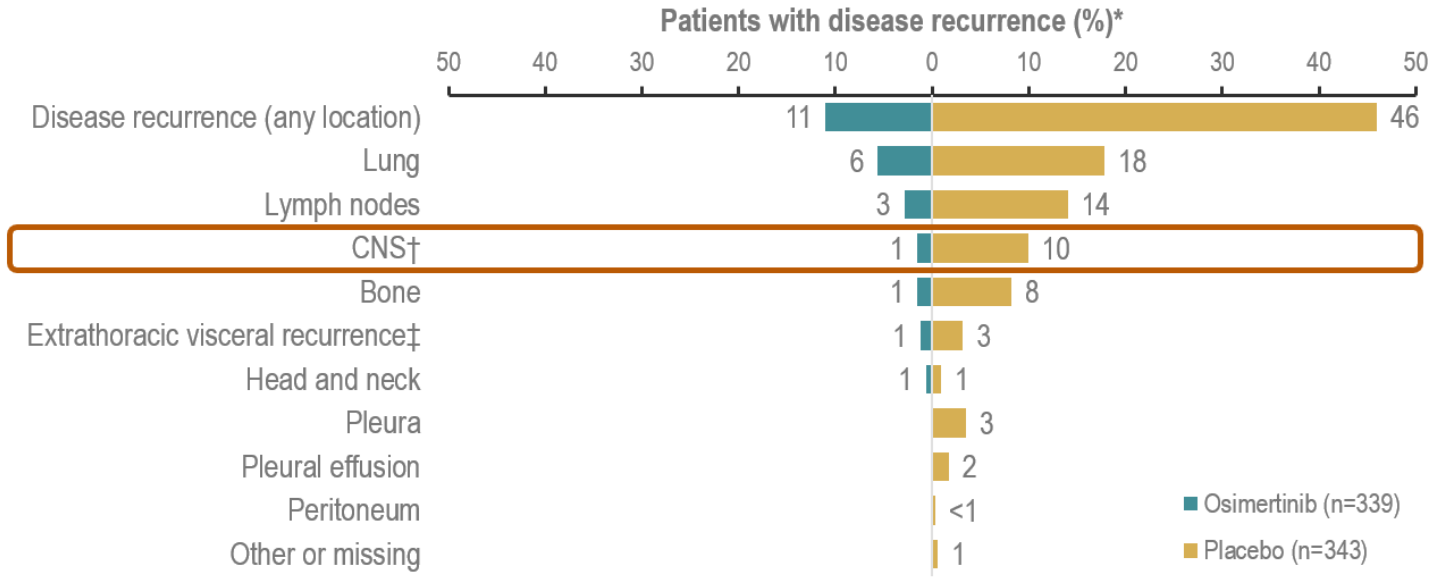
	Median DFS, months (95% CI)	HR (99.12% CI)
– Osimertinib	NR (NC, NC)	0.20 (0.14, 0.30) P<0.0001
– Placebo	27.5 (22.0, 35.0)	

CI, confidence interval; NC, not calculable; HR, hazard ratio; NR, not reached
ADAURA data cut-off: 17 January, 2020

Tsuboi ESMO 2020, Yu WCLC 2020, Wu NEJM 2020

KHDAK'de Adjuvan Adjuvan Hedefe Yönelik Tedavi

Sites of disease recurrence

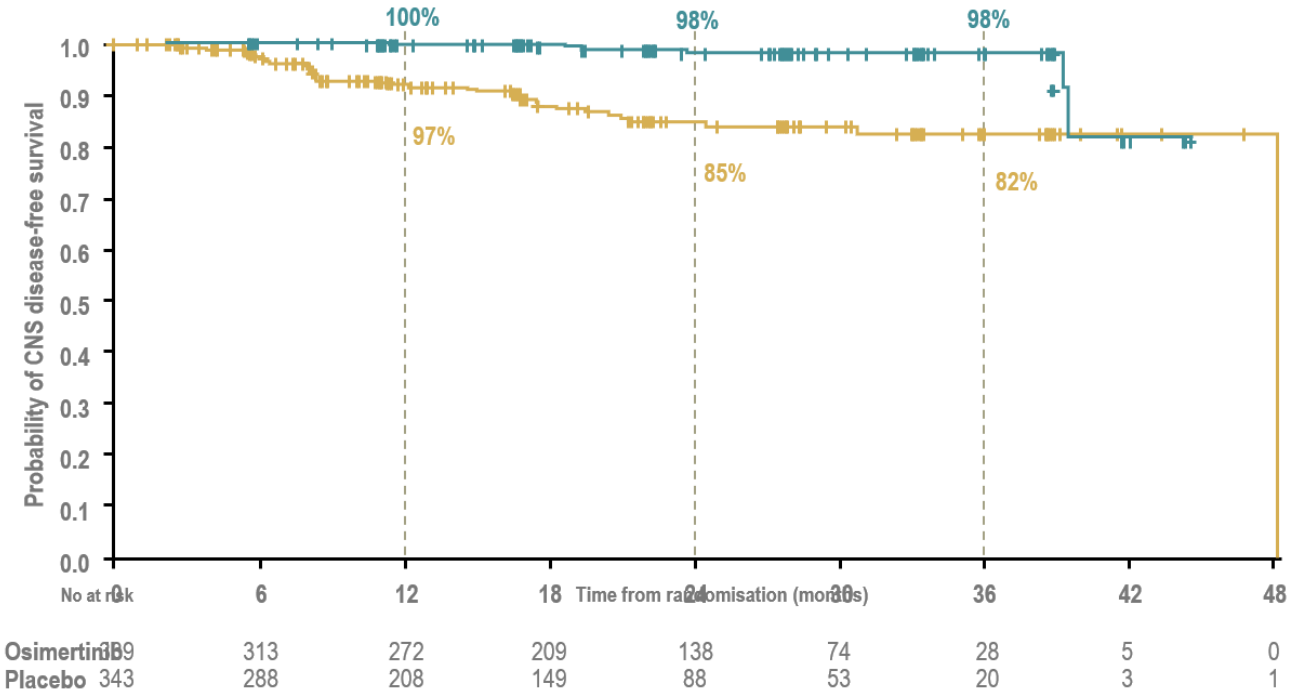


*Number of patients with disease recurrence regardless of pathology results of the tumour recurrence location;
†Includes CNS only (osimertinib n=4 [1%]; placebo n=25 [7%]) and CNS plus other locations (osimertinib n=1 [<1%]; placebo n=9 [3%]).
One patient in the osimertinib arm and one patient in the placebo arm had CNS metastases at baseline; therefore, these two patients were censored on Day 1 and excluded from the CNS DFS efficacy analysis;
‡Includes disease recurrence in liver, renal and adrenal systems and pancreas.
ADAURA data cut-off: 17 January, 2020

Tsuboi ESMO 2020

KHDAK'de Adjuvan Adjuvan Hedefe Yönelik Tedavi

CNS DFS in the overall population



Median CNS DFS, months (95% CI)	
Osimertinib	NR (39, NC)
Placebo	48.2 (NC, NC)
HR* (95% CI)	**0.18 (0.10, 0.33); p<0.0001**

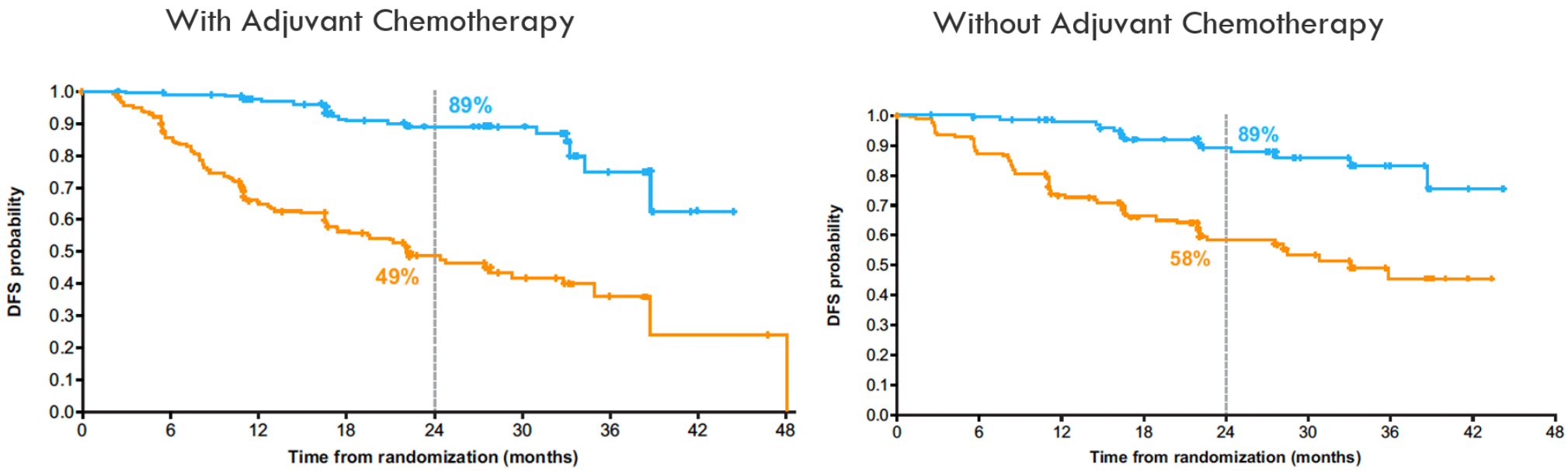
Maturity 7%:
osimertinib 2%, placebo 11%

Tsuboi ESMO 2020, Wu NEJM 2020

Median follow-up: osimertinib 22.1 months, placebo 16.6 months;
*A hazard ratio of <1 favours osimertinib.
ADAURA data cut-off: 17 January, 2020

KHDAK'de Adjuvan Adjuvan Hedefe Yönelik Tedavi

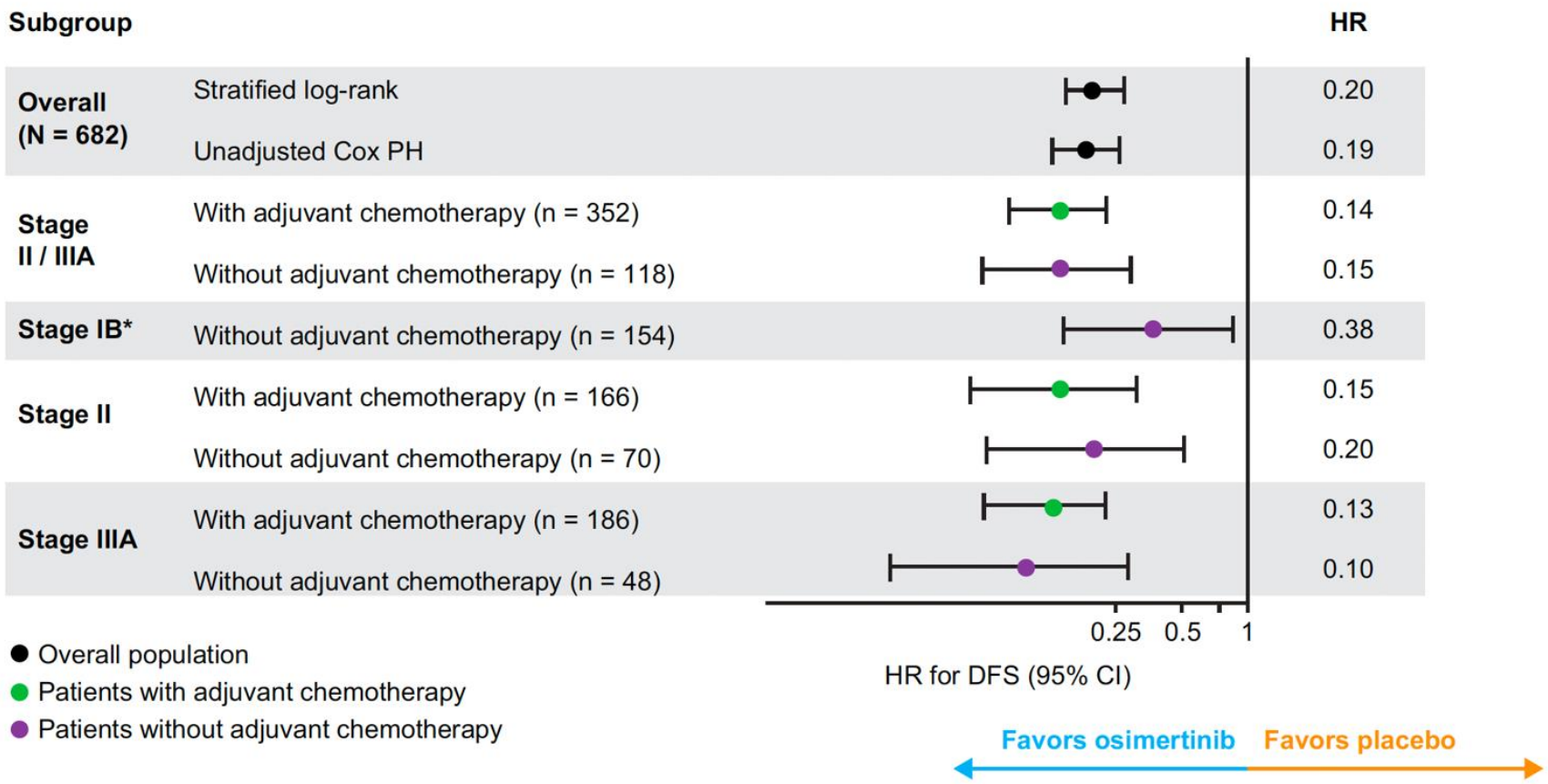
ADAURA: DFS with Adjuvant Osimertinib for Patients Receiving and Not Receiving Adjuvant Chemotherapy



Wu YL et al. *J Thorac Oncol* 2022;17(3):423-33.

KHDAK'de Adjuvan Adjuvan Hedefe Yönelik Tedavi

ADAURA: DFS with Adjuvant Osimertinib for Patients Receiving and Not Receiving Adjuvant Chemotherapy — Subgroups

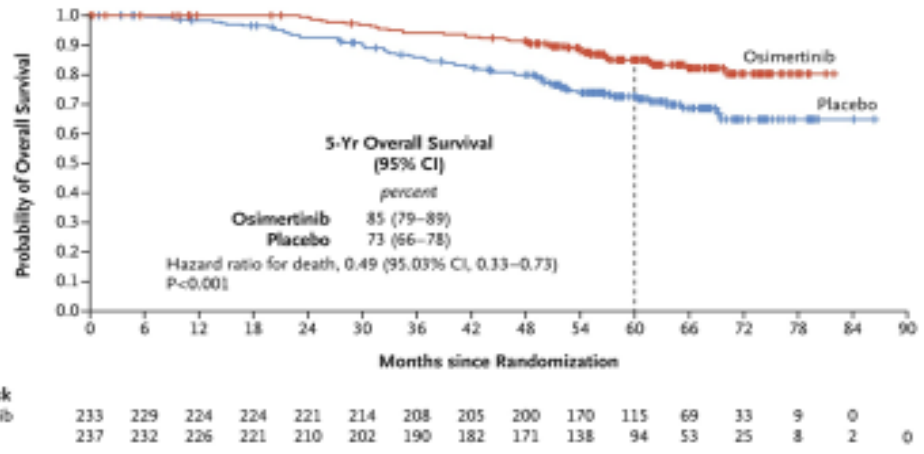


Wu YL et al. *J Thorac Oncol* 2022;17(3):423-33.

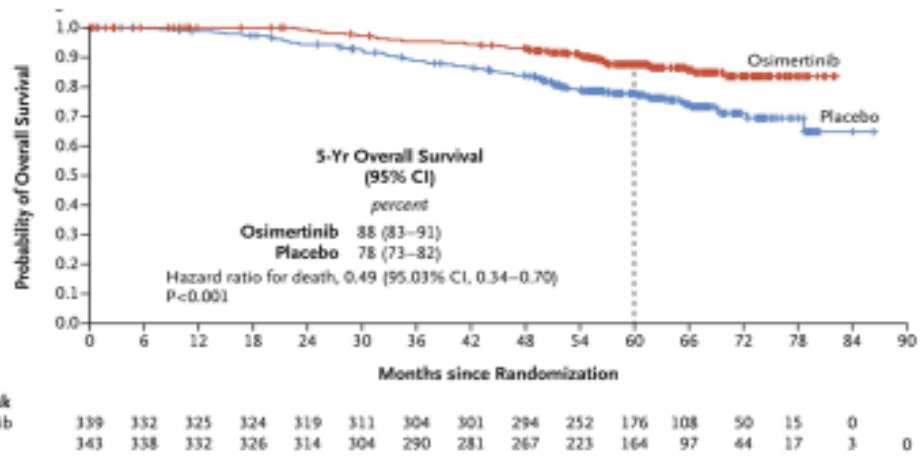
KHDAK'de Adjuvan Adjuvan Hedefe Yönelik Tedavi

ADAURA adjuvant osimertinib for resectable EGFR mutant NSCLC: Updated OS results

Stage II-IIIA (primary endpoint)
OS HR 0.49 (95.03%% CI, 0.33-.73)
P<.001



Stage IB-IIIA (overall population)
HR 0.49 (95.03% CI, 0.34-.70)
P<.001

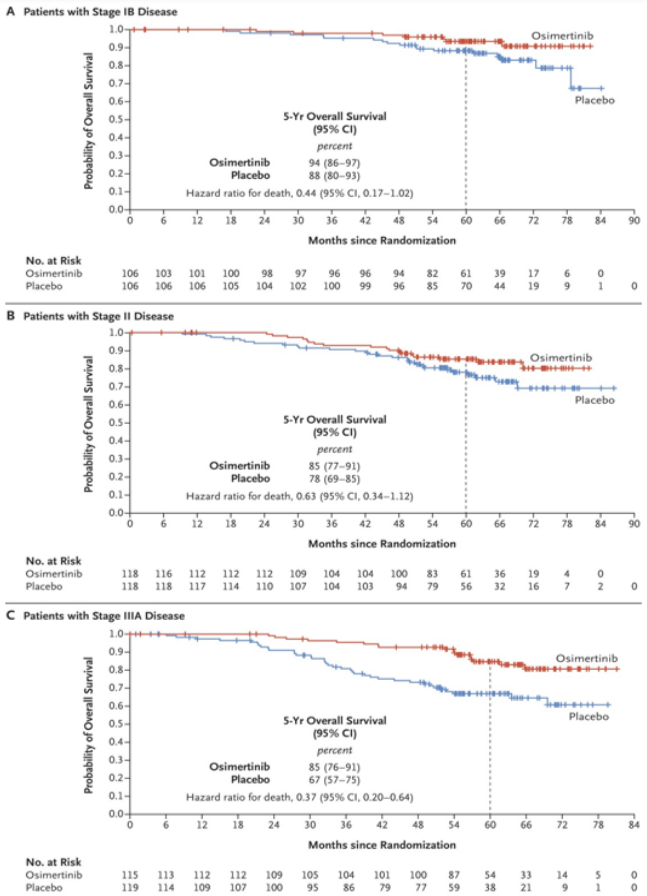


THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Tsuboi M et al. N Engl J Med 2023;389:137-147

KHDAK'de Adjuvan Hedefe Yönelik Tedavi

ADAURA OS data among patients with stage IB, II, and IIIA disease



Stage IB
HR 0.44 (95% CI, 0.17-1.02)

Stage II
HR 0.63 (95% CI, 0.34-1.12)

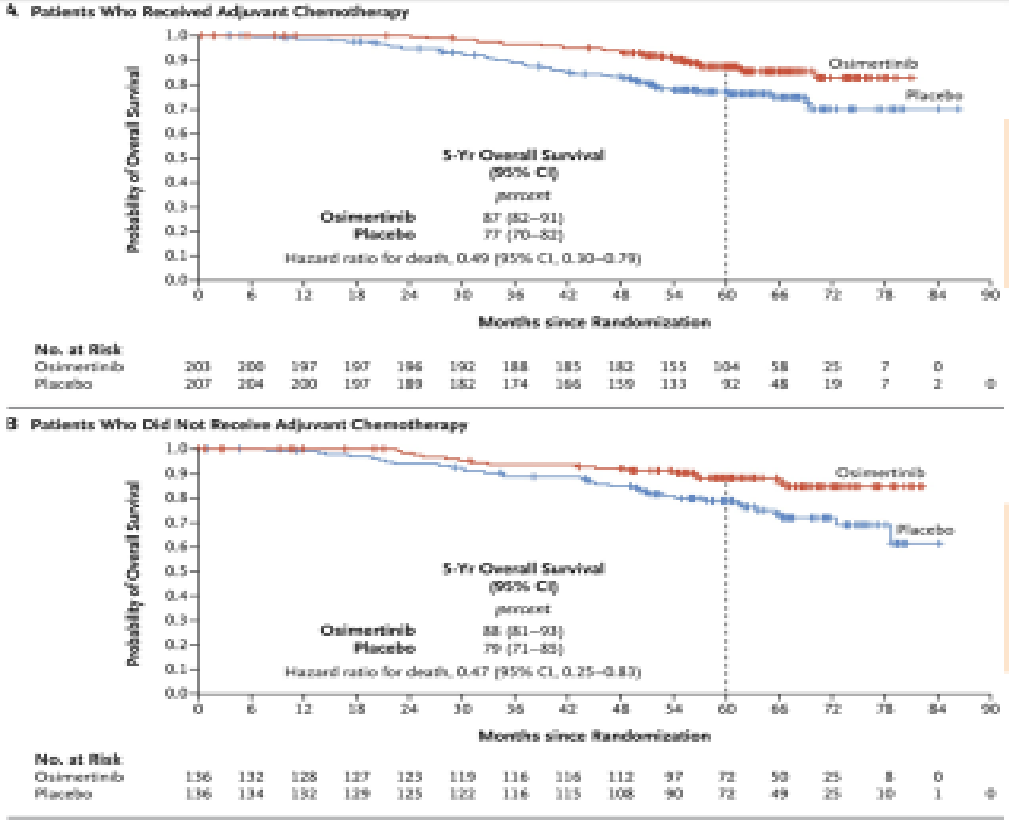
Stage IIIA
HR 0.37 (95% CI, 0.20-.64)

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Tsuboi M et al. N Engl J Med 2023;389:137-147

KHDAK'de Adjuvan Adjuvan Hedefe Yönelik Tedavi

ADAURA OS benefit among those who did or did not receive adjuvant chemotherapy



Received adjuvant chemo
HR 0.49 (95% CI, 0.30–.79)

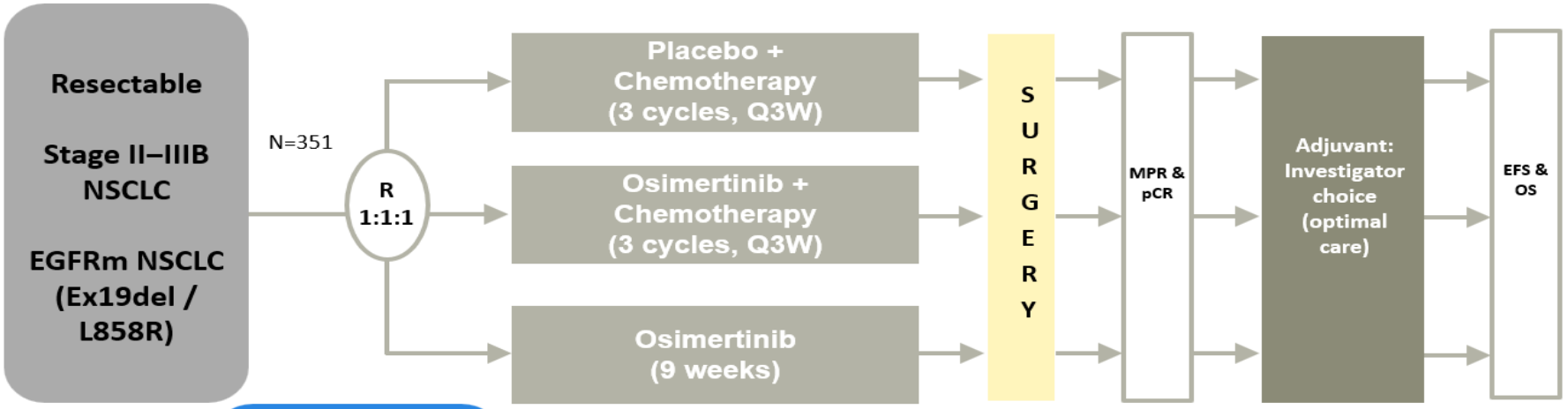
Did not receive adjuvant chemo
HR 0.47 (95% CI, 0.25–.83)

Tsuboi M et al. N Engl J Med 2023;389:137-147

Gelecek Perspektif; Neoadjuvan/Adjuvan

NeoADAURA (NCT 04351555)

Phase III, Randomized, Controlled, Multicenter Study of Neoadjuvant Osimertinib



Stratification:
Stage II/III
Non-Asian/ Chinese/ other Asian
Ex19del/L858R

Double-blind treatment arms:
1. Placebo + pemetrexed 500 mg/m^2 plus carboplatin AUC5 mg/ml.min or cisplatin 75 mg/m^2
2. Osimertinib 80 mg qd + pemetrexed 500 mg/m^2 plus carboplatin AUC5 mg/ml.min or cisplatin 75 mg/m^2

Open-label (sponsor-blind) treatment arm:
3. Osimertinib 80 mg qd

Adjuvant therapy at investigator's discretion:
- Up to 5 years
- Osimertinib will be offered for up to 3 years

KHDAK'de Adjuvan Hedefe Yönelik Tedavi

ALINA study design: adjuvant alectinib for resectable ALK mutant NSCLC

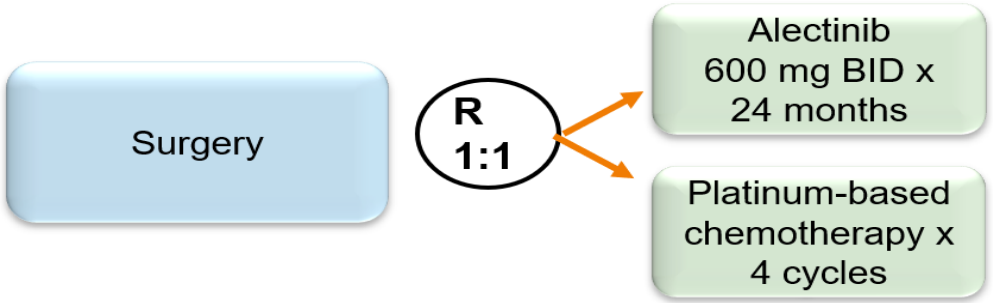
N=257

Key eligibility

- Stage IB-IIIA (>4cm)
- ALK fusion
- Complete resection with negative margins

Stratification:

- Stage (IB vs II vs IIIA)
- race (Asian vs non-Asian)



Primary endpoint : DFS, by investigator assessment

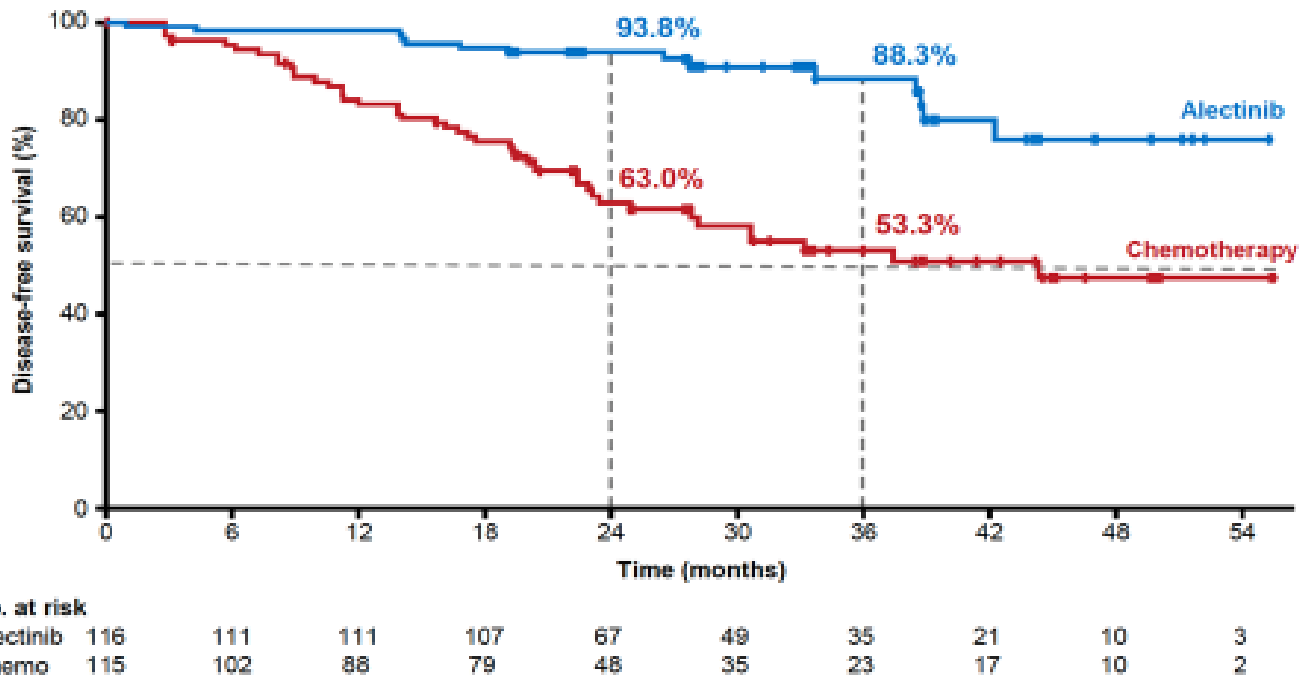
Secondary endpoints include: OS; safety; PK

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Solomon et al, Proc ASCO 2019

ALK pozitif KHDAK'de Adjuvan Hedefe Yönelik Tedavi

Disease-free survival: stage II–IIIA*

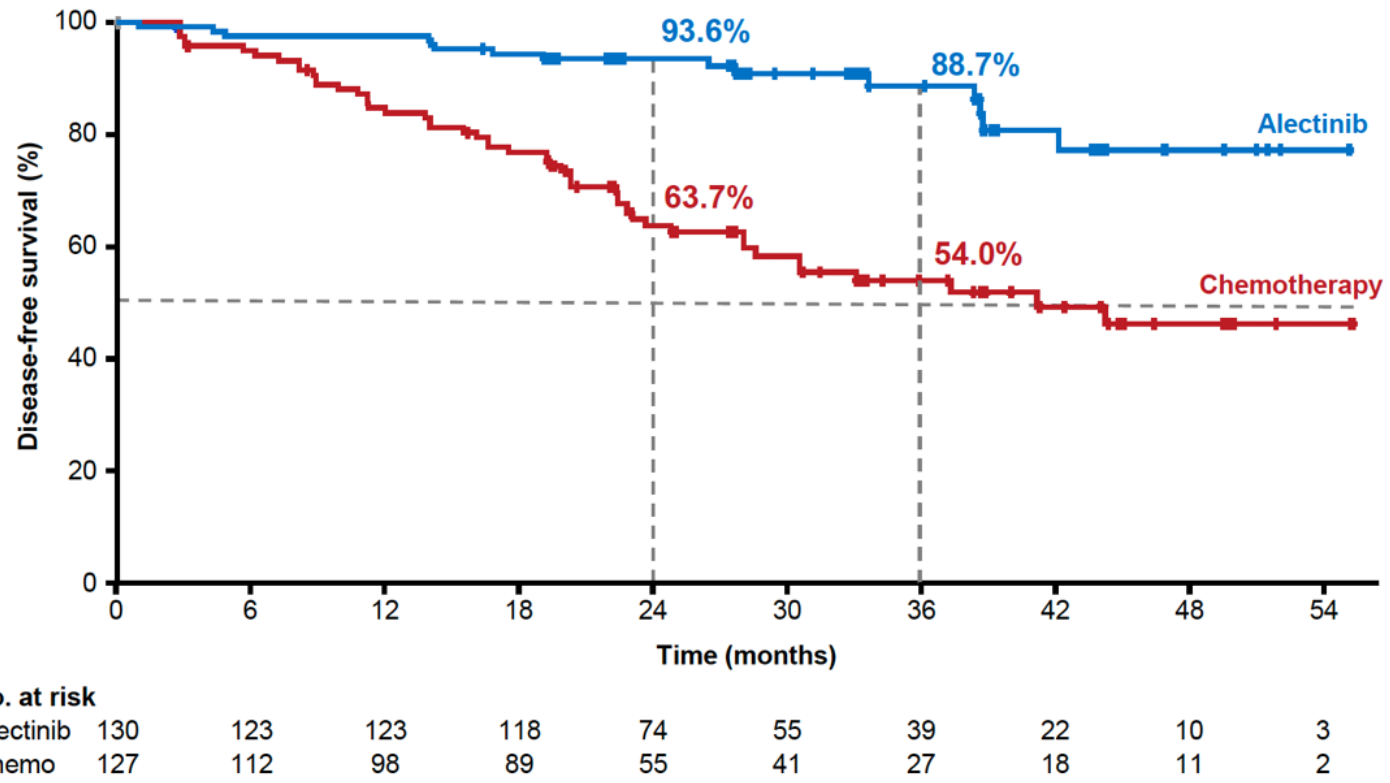


	Alectinib (N=116)	Chemotherapy (N=115)
Patients with event Death Recurrence	14 (12%) 0 14	45 (39%) 1 44
Median DFS, months (95% CI)	Not reached	44.4 (27.8, NE)
DFS HR (95% CI)	**0.24** (0.13, 0.45) p†<0.0001	

Median survival follow up: alectinib, 27.9 months; chemotherapy, 27.8 months

ALK pozitif KHDAK'de Adjuvan Hedefe Yönelik Tedavi

Disease-free survival: ITT (stage IB–IIIA)*



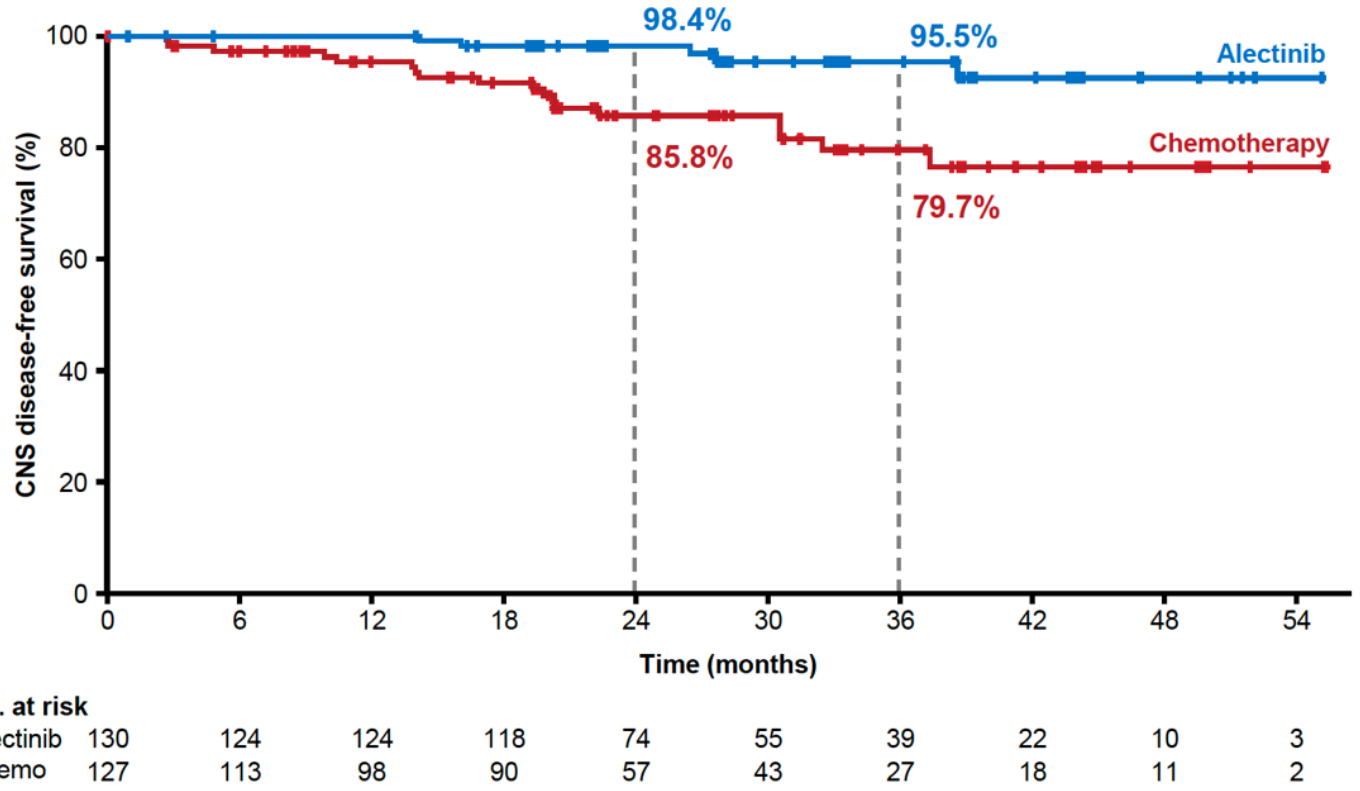
	Alectinib (N=130)	Chemotherapy (N=127)
Patients with event Death Recurrence	15 (12%) 0 15	50 (39%) 1 49
Median DFS, months (95% CI)	Not reached	41.3 (28.5, NE)
DFS HR (95% CI)	**0.24** (0.13, 0.43) p†<0.0001	

At the data cutoff date, **OS data were immature** with only 6 (2.3%) OS events reported‡

Median survival follow up: alectinib, 27.8 months; chemotherapy, 28.4 months

ALK pozitif KHDAK'de Adjuvan Hedefe Yönelik Tedavi

CNS disease-free survival in the ITT population

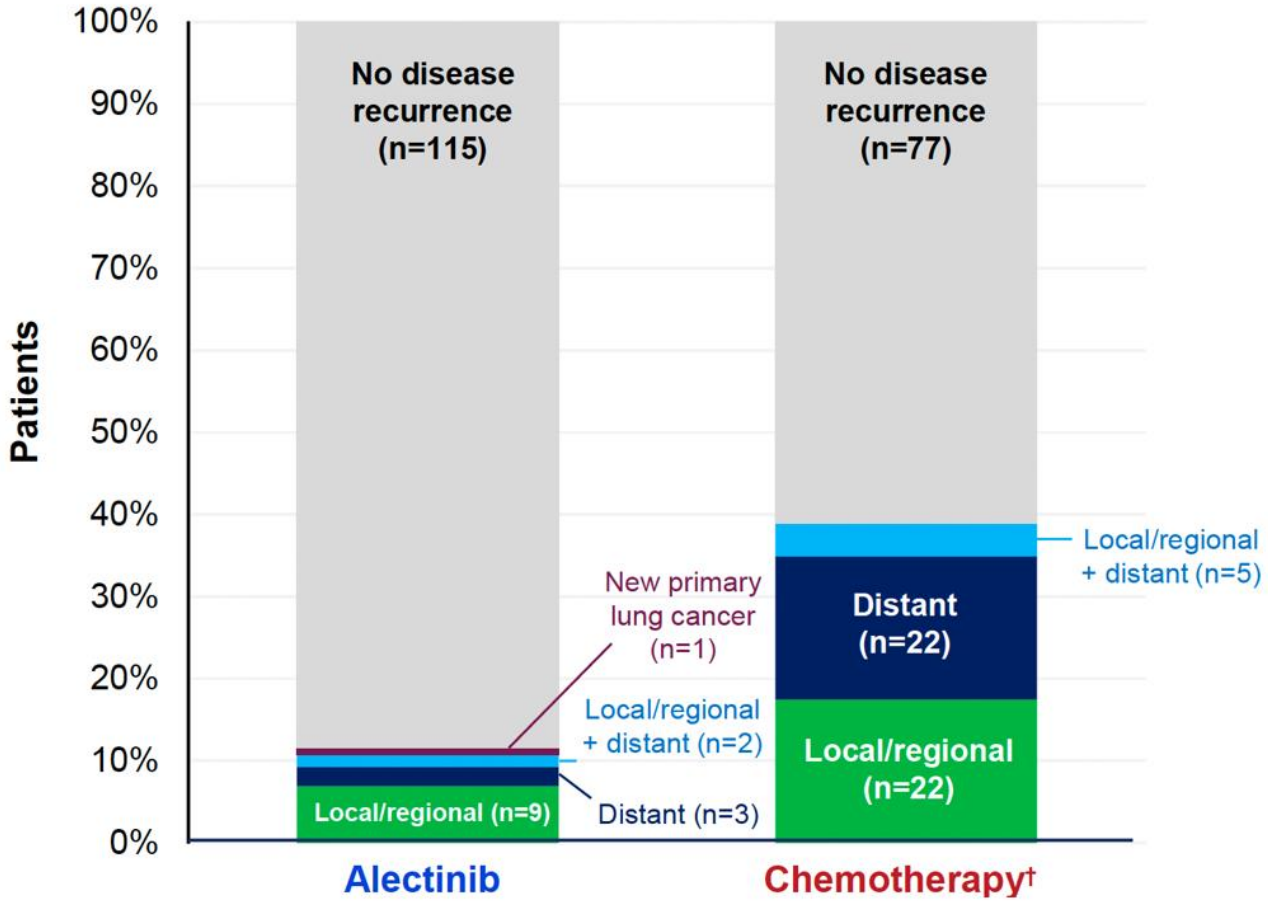


	Alectinib (N=130)	Chemotherapy (N=127)
Patients with event	5	18
Death	1	4
Brain recurrence	4	14
CNS-DFS HR* (95% CI)	**0.22** (0.08, 0.58)	

Median survival follow up: alectinib, 27.8 months; chemotherapy, 28.4 months

ALK pozitif KHDAK'de Adjuvan Hedefe Yönelik Tedavi

Sites of disease recurrence (ITT)



Site(s) of distant recurrence*	Alectinib (n=130)	Chemotherapy (n=127)
Brain	4	14
Bone	1	8
Adrenal gland	0	3
Lymph node	0	2
Kidney	0	1
Peritoneum	0	1
Other	1	0

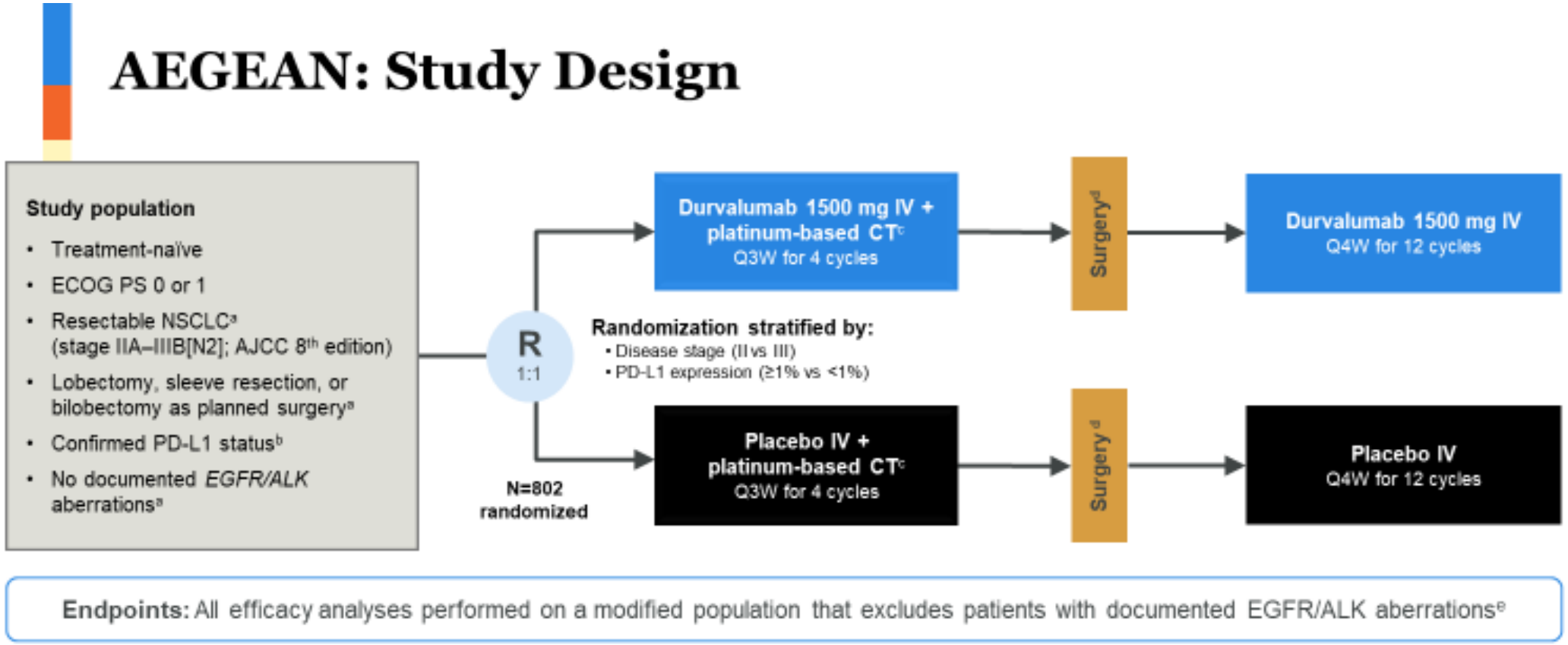
ALK pozitif KHDAK'de Adjuvan Hedefe Yönelik Tedavi

Summary

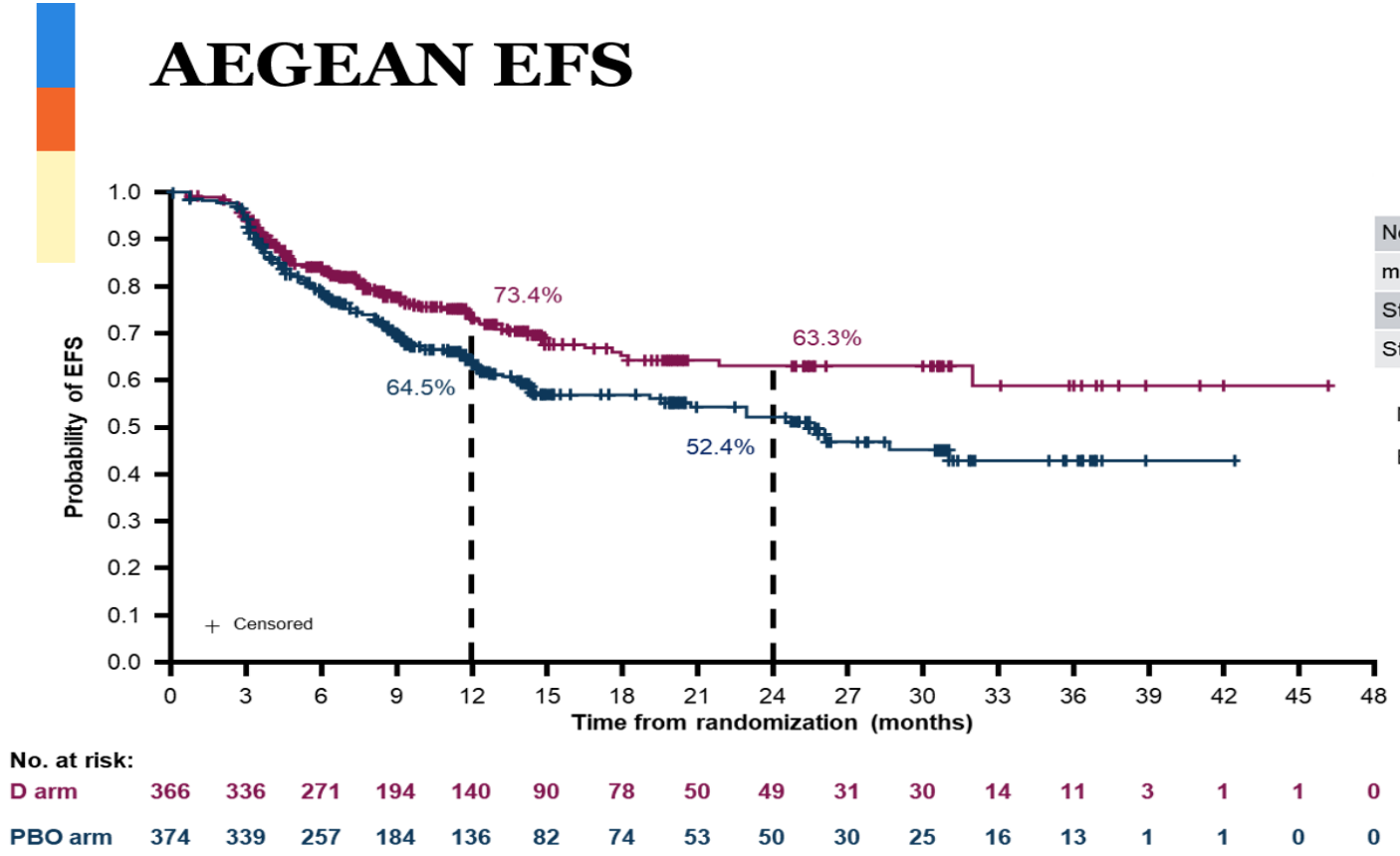
- ALINA is the first and only positive phase III trial of an ALK inhibitor in resected, stage IB–IIIA NSCLC
- Treatment with adjuvant alectinib resulted in a statistically significant and clinically meaningful improvement in DFS compared with chemotherapy (HR 0.24; 95% CI 0.13, 0.43; p<0.0001)
  - The DFS benefit was seen consistently across subgroups
- An improvement in CNS-DFS was observed (HR 0.22; 95% CI 0.08, 0.58)
- Adjuvant alectinib was tolerable and in line with the known safety profile of alectinib

Adjuvant alectinib represents an important new treatment strategy for patients with resected, stage IB–IIIA, *ALK*+ NSCLC

Gelecek Perspektif; Neoadjuvan/Adjuvan İmünoterapi



Gelecek Perspektif; Neoadjuvan/Adjuvan İmünoterapi



	D arm	P arm
No. events / no. patients (%)	98/366 (26.8)	138/374 (36.9)
mEFS, months (95% CI)	NR (31.9–NR)	25.9 (18.9–NR)
Stratified HR* (95% CI)	0.68 (0.53–0.88)	
Stratified log-rank P-value	0.003902	

Median follow-up (range) in censored patients: 11.7 months (0.0–46.1)

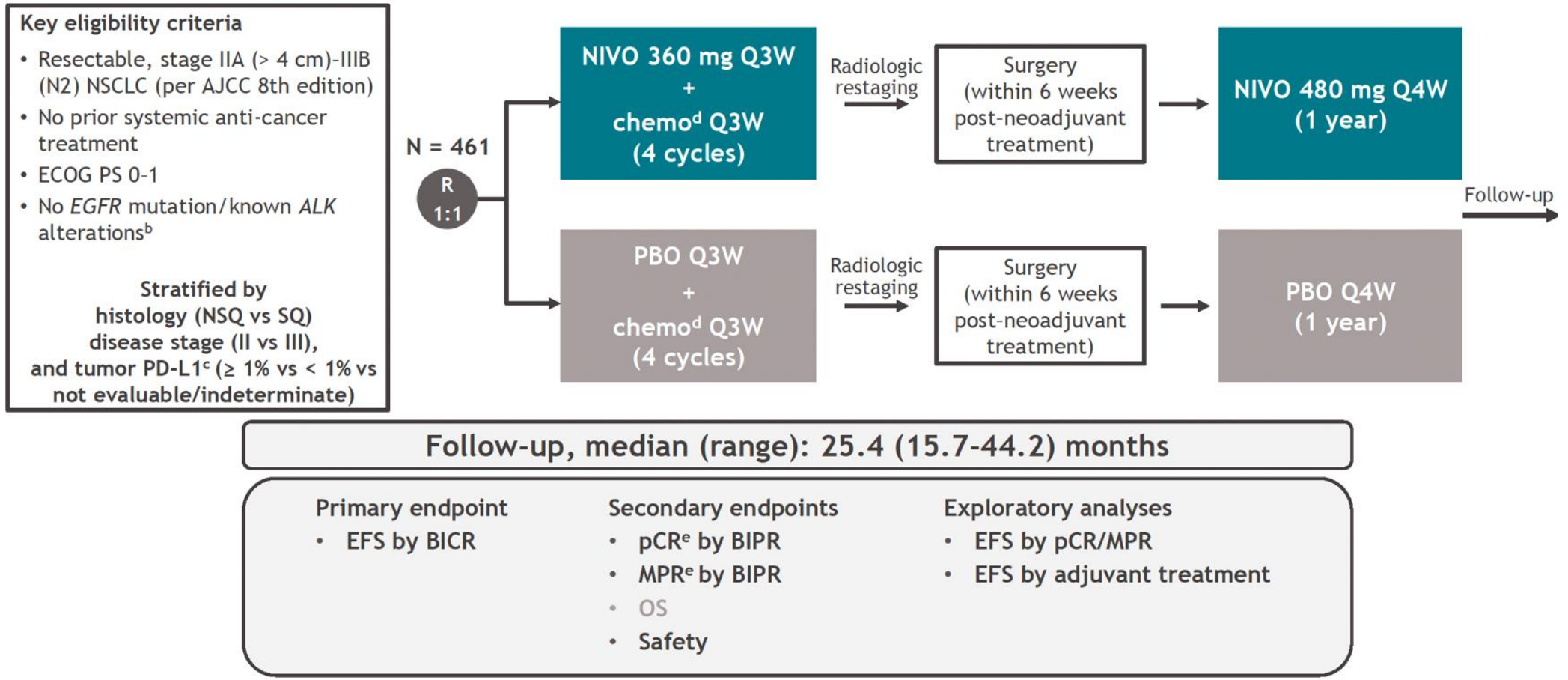
EFS maturity: 31.9%

Heymach, J. AACR April 2023.

Memorial Sloan Kettering Cancer Center

Gelecek Perspektif; Neoadjuvan/Adjuvan İmünoterapi

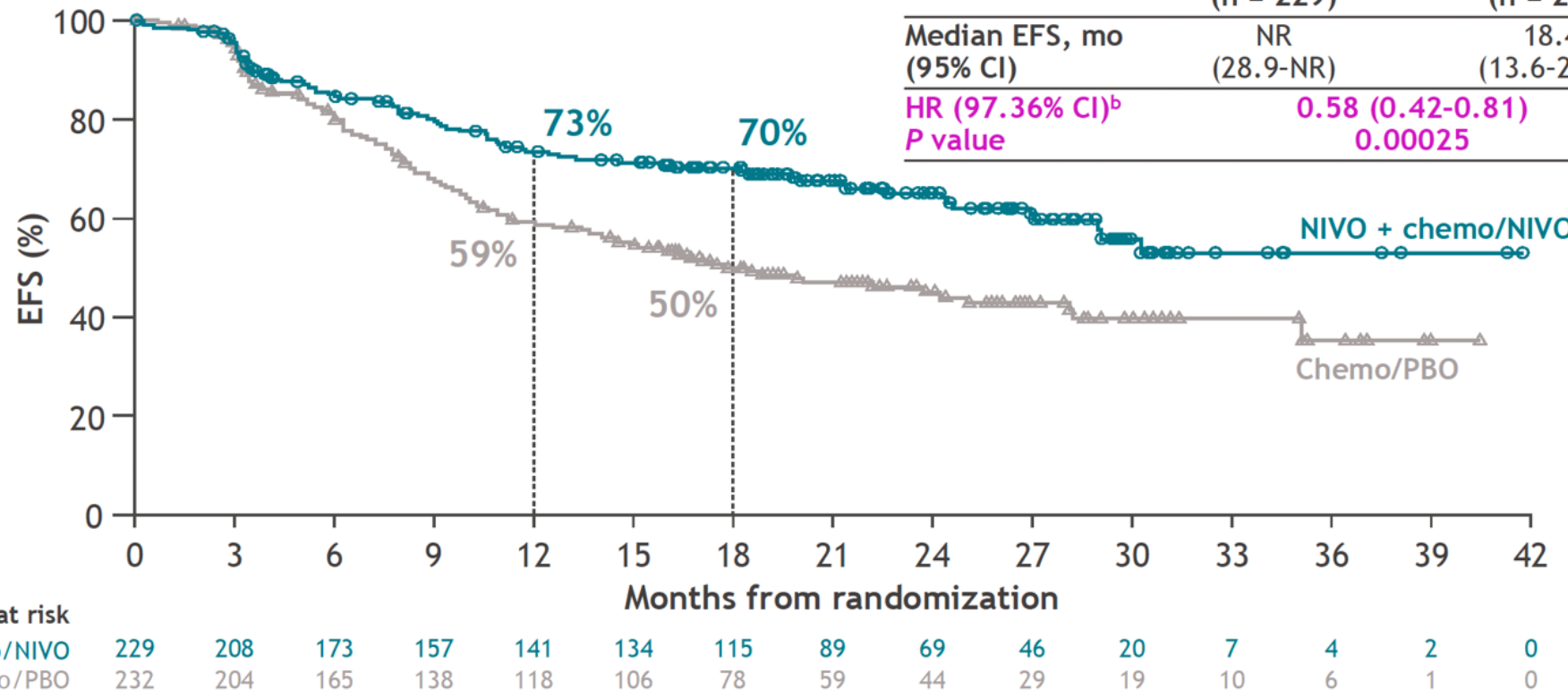
CheckMate 77T[a] study design



Database lock date: September 6, 2023.

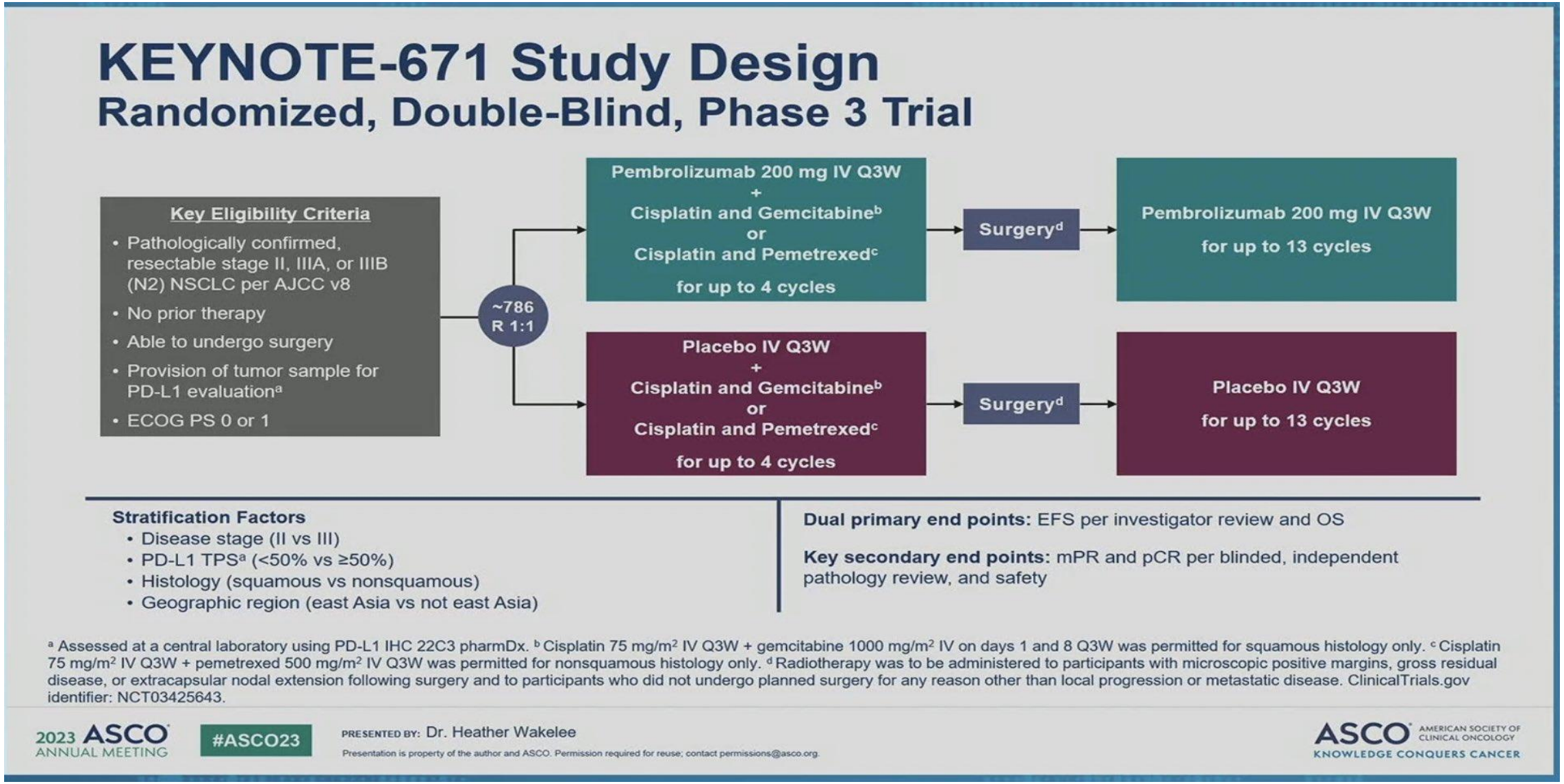
Gelecek Perspektif; Neoadjuvan/Adjuvan İmünoterapi

Primary endpoint:
EFS[a] per BICR with neoadjuvant NIVO + chemo/adjuvant NIVO vs chemo/PBO



- EFS per investigator assessment, NIVO + chemo/NIVO vs chemo/PBO: HR, 0.56; 95% CI, 0.41-0.76

Gelecek Perspektif; Neoadjuvan/Adjuvan İmünoterapi

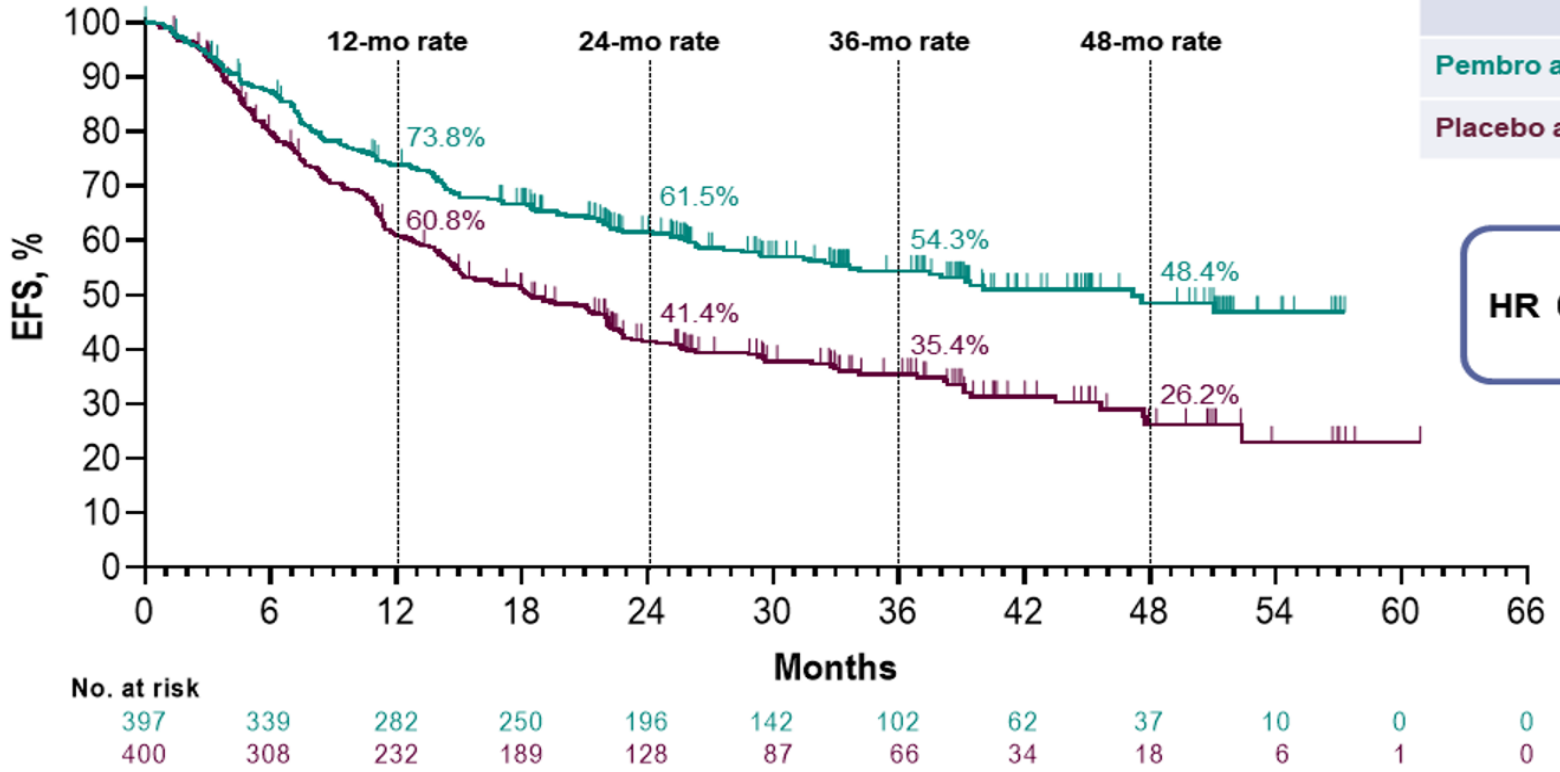


Gelecek Perspektif; Neoadjuvan/Adjuvan İmünoterapi

Spicer KN671 IA2 ESMO 2023

Event-Free Survival, IA2

Median Follow-Up: 36.6 months (range, 18.8-62.0)



	Pts w/ Event	Median (95% CI), mo
Pembro arm	43.8%	47.2 (32.9-NR)
Placebo arm	62.0%	18.3 (14.8-22.1)

HR 0.59 (95% CI, 0.48-0.72)

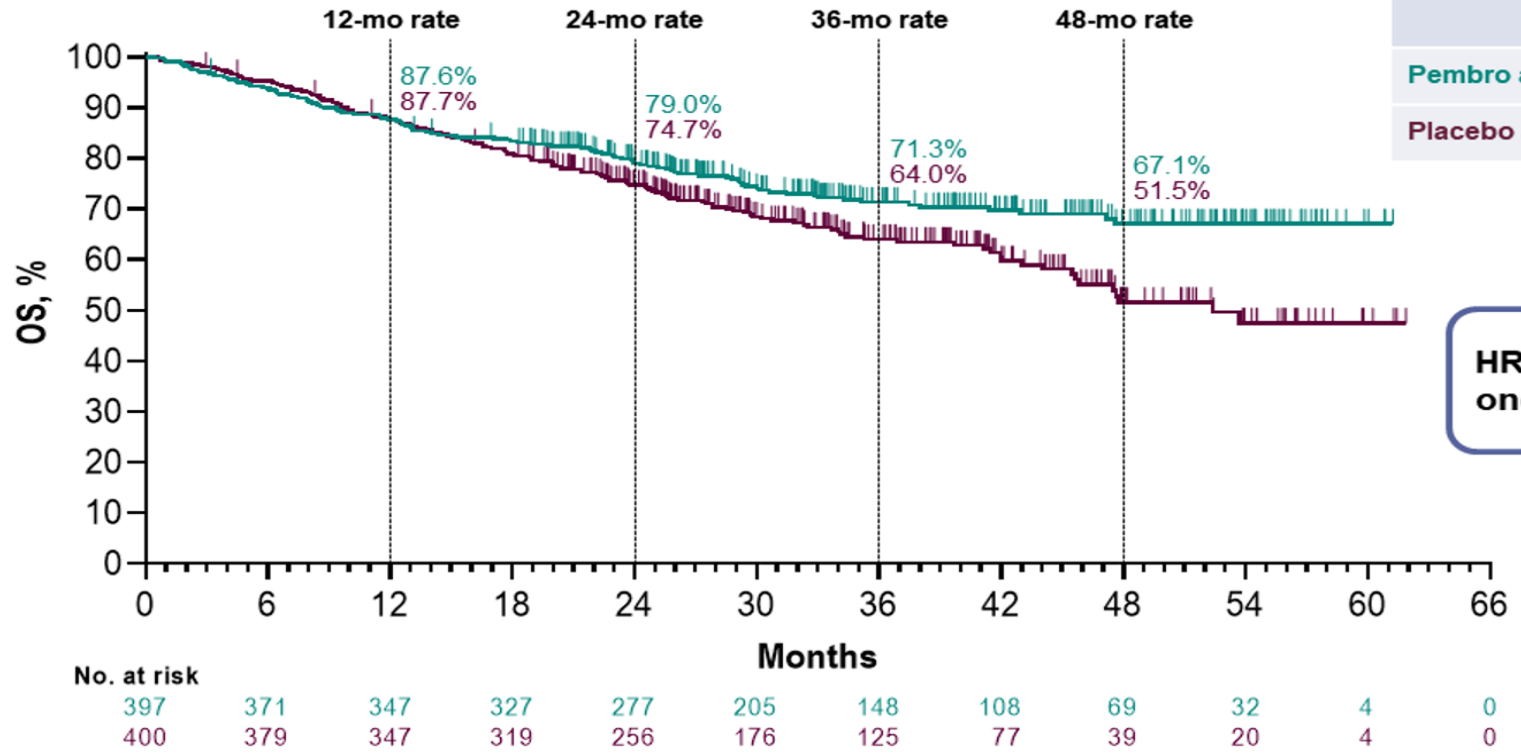
EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause. Data cutoff date for IA2: July 10, 2023.

Gelecek Perspektif; Neoadjuvan/Adjuvan İmünoterapi

Spicer KN671 IA2 ESMO 2023

Overall Survival, IA2

Median Follow-Up: 36.6 months (range, 18.8-62.0)



	Pts w/ Event	Median (95% CI), mo
Pembro arm	27.7%	NR (NR-NR)
Placebo arm	36.0%	52.4 (45.7-NR)

HR 0.72 (95% CI, 0.56-0.93)
one-sided *P* = 0.00517[a]

OS defined as time from randomization to death from any cause. [a] Significance boundary at IA2, one-sided *P* = 0.00543.
Data cutoff date for IA2: July 10, 2023.

KHDAK'de Adjuvan Adjuvan Hedefe Yönelik Tedavi

Ongoing trials

Neoadjuvant and Adjuvant **Tiragolumab** Plus Atezolizumab, With or Without Platinum-Based Chemotherapy, in Participants With Previously Untreated Locally Advanced Resectable Stage II, IIIA, or Select IIIB Non-Small Cell Lung Cancer

Neo-ADAURA: Osimertinib in Treating Participants With Stage I-IIIA EGFR-mutant Non-small Cell Lung Cancer Before Surgery

ALCHEMIST: Adjuvant Crizotinib for ALK+ NSCLC

A Study of Multiple Therapies in Biomarker-Selected Patients With Resectable Stages IB-III Non-Small Cell Lung Cancer (Drugs: Alectinib Entrectinib; Vemurafenib; Cobimetinib; Pralsetinib; Atezolizumab)

KHDAK'de Adjuvan Hedefe Yönelik Tedavi ve İmmünoterapi

National Comprehensive Cancer Network®

NCCN Guidelines Version 5.2022
Non-Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion

SYSTEMIC THERAPY REGIMENS FOR NEOADJUVANT AND ADJUVANT THERAPY

Preferred (nonsquamous)
- Cisplatin 75 mg/m² day 1, pemetrexed 500 mg/m² day 1 every 21 days for 4 cycles[1]

Preferred (squamous)
- Cisplatin 75 mg/m² day 1, gemcitabine 1250 mg/m² days 1 and 8, every 21 days for 4 cycles[2]
- Cisplatin 75 mg/m² day 1, docetaxel 75 mg/m² day 1 every 21 days for 4 cycles[3]

Other Recommended
- Cisplatin 50 mg/m² days 1 and 8; vinorelbine 25 mg/m² days 1, 8, 15, and 22, every 28 days for 4 cycles[4]
- Cisplatin 100 mg/m² day 1, vinorelbine 30 mg/m² days 1, 8, 15, and 22, every 28 days for 4 cycles[5,6]
- Cisplatin 75–80 mg/m² day 1, vinorelbine 25–30 mg/m² days 1 and 8, every 21 days for 4 cycles
- Cisplatin 100 mg/m² day 1, etoposide 100 mg/m² days 1–3, every 28 days for 4 cycles[5]

Useful in Certain Circumstances
- Chemotherapy Regimens for Patients with Comorbidities or Patients Not Able to Tolerate Cisplatin
- Carboplatin AUC 6 day 1, paclitaxel 200 mg/m² day 1, every 21 days for 4 cycles[7]
- Carboplatin AUC 5 day 1, gemcitabine 1000 mg/m² days 1 and 8, every 21 days for 4 cycles[8]
- Carboplatin AUC 5 day 1, pemetrexed 500 mg/m² day 1 every 21 days for 4 cycles[9] (non-squamous histology)

All chemotherapy regimens listed above can be used for sequential chemotherapy/RT.

Neoadjuvant Systemic Therapy
- Nivolumab 360 mg and platinum-doublet chemotherapy every 3 weeks for 3 cycles[10,*]
  - Platinum-doublet chemotherapy options include:
    - ◊ Carboplatin AUC 5 or AUC 6 day 1, paclitaxel 175 mg/m² or 200 mg/m² day 1 (any histology)
    - ◊ Cisplatin 75 mg/m² day 1, pemetrexed 500 mg/m² day 1 (non-squamous histology)
    - ◊ Cisplatin 75 mg/m² day 1, gemcitabine 1000 mg/m² or 1250 mg/m² days 1 and 8 (squamous histology)
    - ◊ Cisplatin 75 mg/m² day 1, paclitaxel 175 mg/m² or 200 mg/m² day 1 (any histology)
  - Chemotherapy Regimens for Patients with Comorbidities or Patients Not Able to Tolerate Cisplatin
    - ◊ Carboplatin AUC 5 or AUC 6 day 1, pemetrexed 500 mg/m² day 1 (non-squamous histology)
    - ◊ Carboplatin AUC 5 or AUC 6 day 1, gemcitabine 1000 mg/m² or 1250 mg/m² days 1 and 8 (squamous histology)

Adjuvant Systemic Therapy
- Osimertinib 80 mg daily[11]
  - Osimertinib for patients with completely resected stage IB–IIIA *EGFR* (*exon 19* deletion, *L858R*) NSCLC who received previous adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy.
- Atezolizumab 840 mg every 2 weeks, 1200 mg every 3 weeks, or 1680 mg every 4 weeks for up to 1 year[12]
  - Atezolizumab for patients with completely resected stage IIB–IIIA or high risk stage IIA PD-L1 ≥1% NSCLC who received previous adjuvant chemotherapy.

KHDAK'de Adjuvan Hedefe Yönelik Tedavi ve İmmünoterapi

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2023
Non-Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion

PERIOPERATIVE SYSTEMIC THERAPY

Adjuvant Systemic Therapy
- Test for PD-L1 status, *EGFR* mutations, and *ALK* rearrangements (stages IB–IIIA, IIIB [T3,N2]). Principles of Molecular and Biomarker Analysis (NSCL-H).

Preferred (nonsquamous)
- Cisplatin 75 mg/m² day 1, pemetrexed 500 mg/m² day 1 every 21 days for 4 cycles[2]

Preferred (squamous)
- Cisplatin 75 mg/m² day 1, gemcitabine 1250 mg/m² days 1 and 8, every 21 days for 4 cycles[3]
- Cisplatin 75 mg/m² day 1, docetaxel 75 mg/m² day 1 every 21 days for 4 cycles[4]

Other Recommended
- Cisplatin 50 mg/m² days 1 and 8; vinorelbine 25 mg/m² days 1, 8, 15, and 22, every 28 days for 4 cycles[5]
- Cisplatin 100 mg/m² day 1, vinorelbine 30 mg/m² days 1, 8, 15, and 22, every 28 days for 4 cycles[6,7]
- Cisplatin 75–80 mg/m² day 1, vinorelbine 25–30 mg/m² days 1 and 8, every 21 days for 4 cycles
- Cisplatin 100 mg/m² day 1, etoposide 100 mg/m² days 1–3, every 28 days for 4 cycles[6]

Useful in Certain Circumstances
- Chemotherapy Regimens for Patients Not Candidates for Cisplatin-Based Therapy
  - Carboplatin AUC 6 day 1, paclitaxel 200 mg/m² day 1, every 21 days for 4 cycles[8]
  - Carboplatin AUC 5 day 1, gemcitabine 1000 mg/m² days 1 and 8, every 21 days for 4 cycles[9]
  - Carboplatin AUC 5 day 1, pemetrexed 500 mg/m² day 1 every 21 days for 4 cycles[10] (nonsquamous histology)

All chemotherapy regimens listed above can be used for sequential chemotherapy/RT.

Systemic Therapy Following Previous Adjuvant Systemic Therapy
- Osimertinib 80 mg daily[11]
  - Osimertinib for patients with completely resected stage IB–IIIA or stage IIIB (T3, N2) NSCLC and positive for *EGFR* (exon 19 deletion, exon 21 L858R) mutations who received previous adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy.
- Atezolizumab 840 mg every 2 weeks, 1200 mg every 3 weeks, or 1680 mg every 4 weeks for up to 1 year[12]
  - Atezolizumab for patients with completely resected stage IIB–IIIA, stage IIIB (T3, N2), or high-risk stage IIA NSCLC with PD-L1 ≥1% and negative for *EGFR* exon 19 deletion or exon 21 L858R mutations or *ALK* rearrangements who received previous adjuvant chemotherapy and with no contraindications to immune checkpoint inhibitors.*
- Pembrolizumab 200 mg every 3 weeks or 400 mg every 6 weeks for up to 1 year[13]
  - Pembrolizumab for patients with completely resected stage IIB–IIIA, stage IIIB (T3, N2), or high-risk stage IIA NSCLC and negative for *EGFR* exon 19 deletion or exon 21 L858R mutations or *ALK* rearrangements who received previous adjuvant chemotherapy and with no contraindications to immune checkpoint inhibitors.*

Sonuç

- Evre [IB(4 cm>)-IIIA] ve EGFR mutasyonu(Ekzon 19,21) olan hastalarda 4 kür adjuvan KT sonrası adjuvan Osimertinib(3 yıl)
- Evre [IB(4 cm>)-IIIA] ve ALK mutasyonu(Ekzon 19,21) olan hastalarda adjuvan Alectinib(2 yıl)
- Evre [II-IIIA] ve PD-L1>%1 olan hastalarda 4 kür adjuvan KT sonrası adjuvan immünoterapi(1 yıl)
- Devam eden çok sayıda çalışmalarla daha bireyselleşmiş uygun tedavi seçenekleri