

Akciğer Kanseri Tedavisinde Adjuvan Hedefe Yönelik Tedavi ve İmmunoterapi

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Tıbbi Onkoloji

Ders Planı

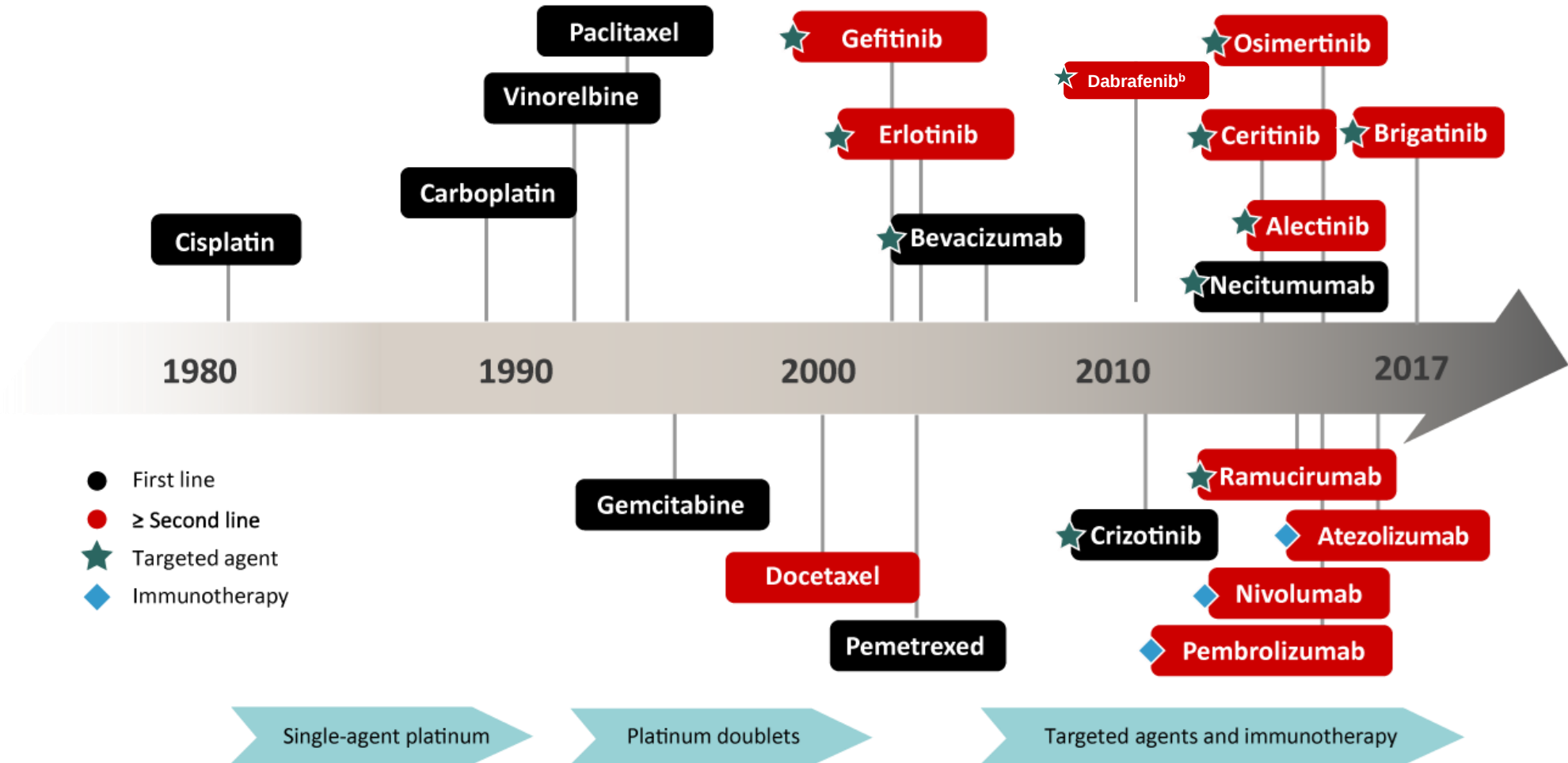
Giriş

Küçük hücreli dışı akciğer kanserinde

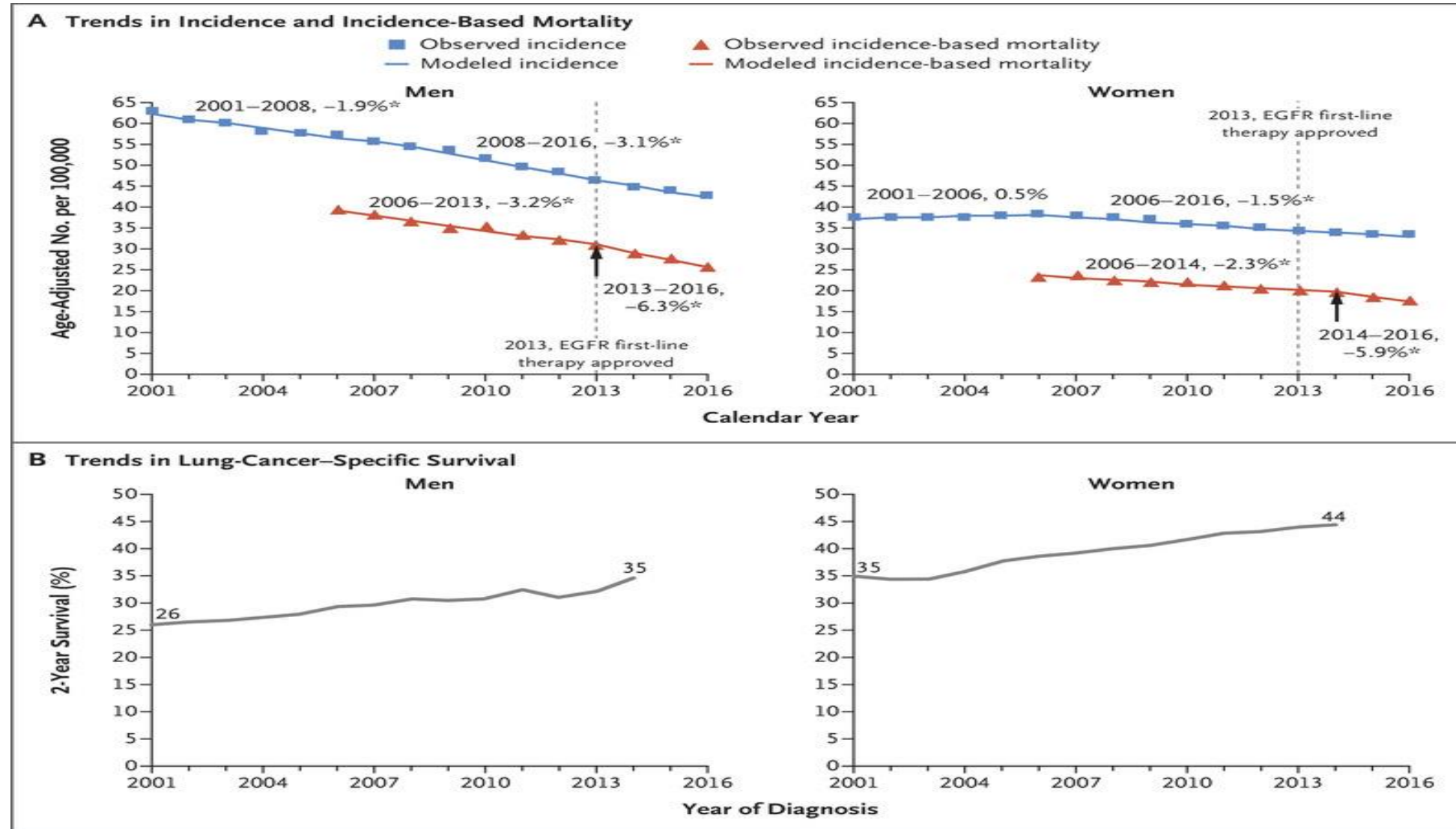
- Adjuvan immünoterapi
- Adjuvan Hedefe Yönelik Tedavi

Sonuç

KHDAK'de Sistemik Tedavilerin Tarihsel Yolculuğu



Evre IV Akciğer Kanseri İnsidans ve Mortalite



Histoloji ve Genomik Özelliklere Göre Tedavi



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NCCN Guidelines Version 7.2021 Non-Small Cell Lung Cancer

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CLINICAL PRESENTATION

Advanced
or
metastatic
disease

- Establish histologic subtype^a with adequate tissue for molecular testing (consider rebiopsy^{II} if appropriate)
- Smoking cessation counseling
- Integrate palliative care^C ([See NCCN Guidelines for Palliative Care](#))

HISTOLOGIC SUBTYPE^a

- Adenocarcinoma
- Large cell
- NSCLC not otherwise specified (NOS)

Squamous cell
carcinoma

BIOMARKER TESTING^{mm}

- Molecular testing, including:
 - *EGFR* mutation (category 1), *ALK* (category 1), *KRAS*, *ROS1*, *BRAF*, *NTRK1/2/3*, *MET*ex14 skipping, *RET*
 - Testing should be conducted as part of broad molecular profilingⁿⁿ
- PD-L1 testing (category 1)

- Consider molecular testing, including:^{oo}
 - *EGFR* mutation, *ALK*, *KRAS*, *ROS1*, *BRAF*, *NTRK1/2/3*, *MET* exon 14 skipping, *RET*
 - Testing should be conducted as part of broad molecular profilingⁿⁿ
- PD-L1 testing (category 1)

[See Testing
Results
\(NSCL-19\)](#)

[See Testing
Results
\(NSCL-19\)](#)

Histoloji ve Genomik Özelliklere Göre Tedavi



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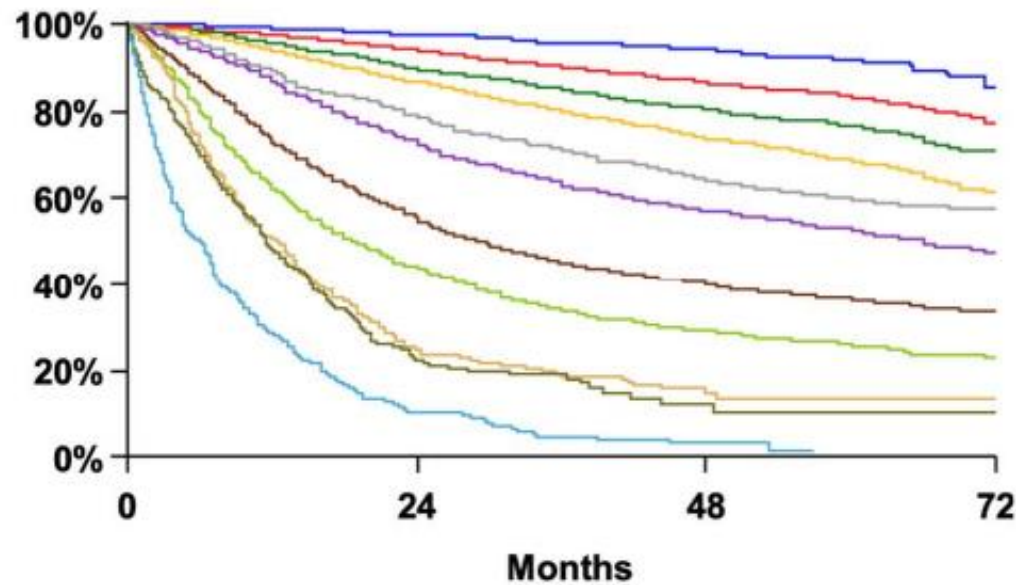
NCCN Guidelines Version 1.2022 Non-Small Cell Lung Cancer

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TESTING RESULTS^{11,mm}

<i>EGFR</i> exon 19 deletion or <i>L858R</i> mutation positive	NSCL-20
<i>EGFR</i> S768I, L861Q, and/or G719X mutation positive	NSCL-23
<i>EGFR</i> exon 20 insertion mutation positive	NSCL-24
<i>KRAS</i> G12C mutation positive	NSCL-25
<i>ALK</i> rearrangement positive	NSCL-26
<i>ROS1</i> rearrangement positive	NSCL-29
<i>BRAF</i> V600E mutation positive	NSCL-31
<i>NTRK1/2/3</i> gene fusion positive	NSCL-32
<i>MET</i> ex14 skipping mutation positive	NSCL-33
<i>RET</i> rearrangement positive	NSCL-34
PD-L1 ≥50% and negative for actionable molecular biomarkers above	NSCL-35
PD-L1 ≥1%–49% 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 (8 th 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%

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

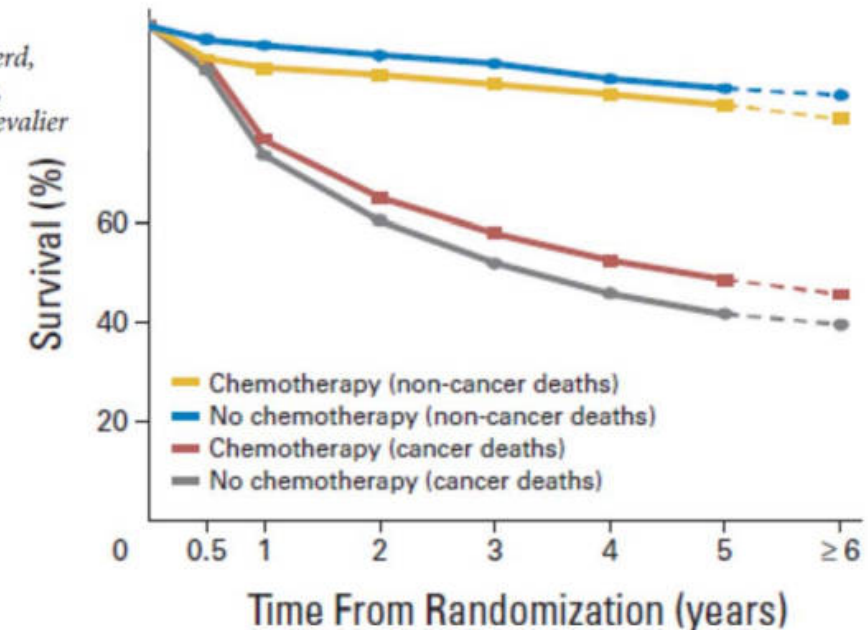
KHDAK'de Sistemik Tedavilerin Tarihsel Yolculuğu

What is the role for adjuvant systemic therapy? Chemotherapy

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

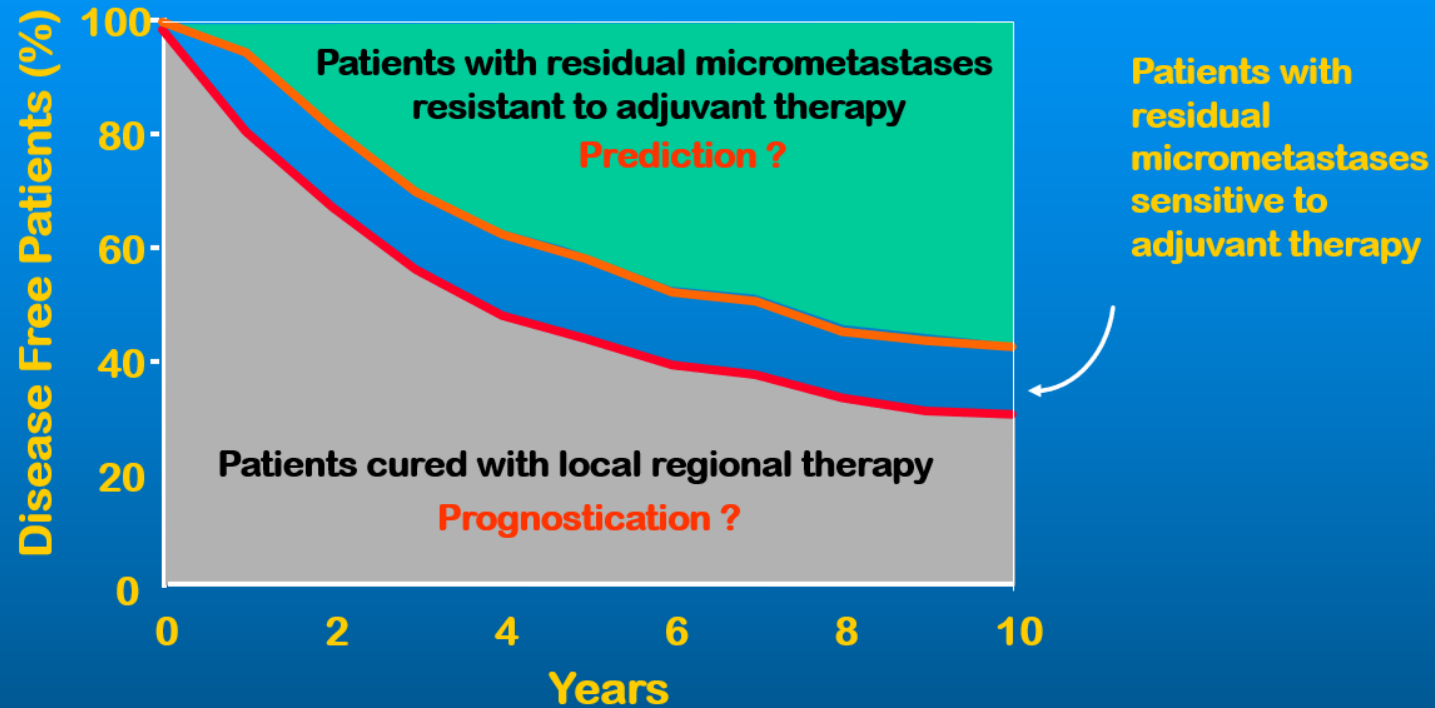
Jean-Pierre Pignon, Hélène Tribodet, Giorgio V. Scagliotti, Jean-Yves Douillard, Frances A. Shepherd, Richard J. Stephens, Ariane Dunant, Valter Torri, Rafael Rosell, Lesley Seymour, Stephen G. Spiro, Estelle Rolland, Roldano Fossati, Delphine Aubert, Keyue Ding, David. Waller, and Thierry Le Chevalier

- 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)**



Metastatik Olmayan KHDAK'de Sistemik Tedaviye İhtiyaç Varmı

Potential Benefit from Adjuvant Systemic Therapy



Devam eden 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	

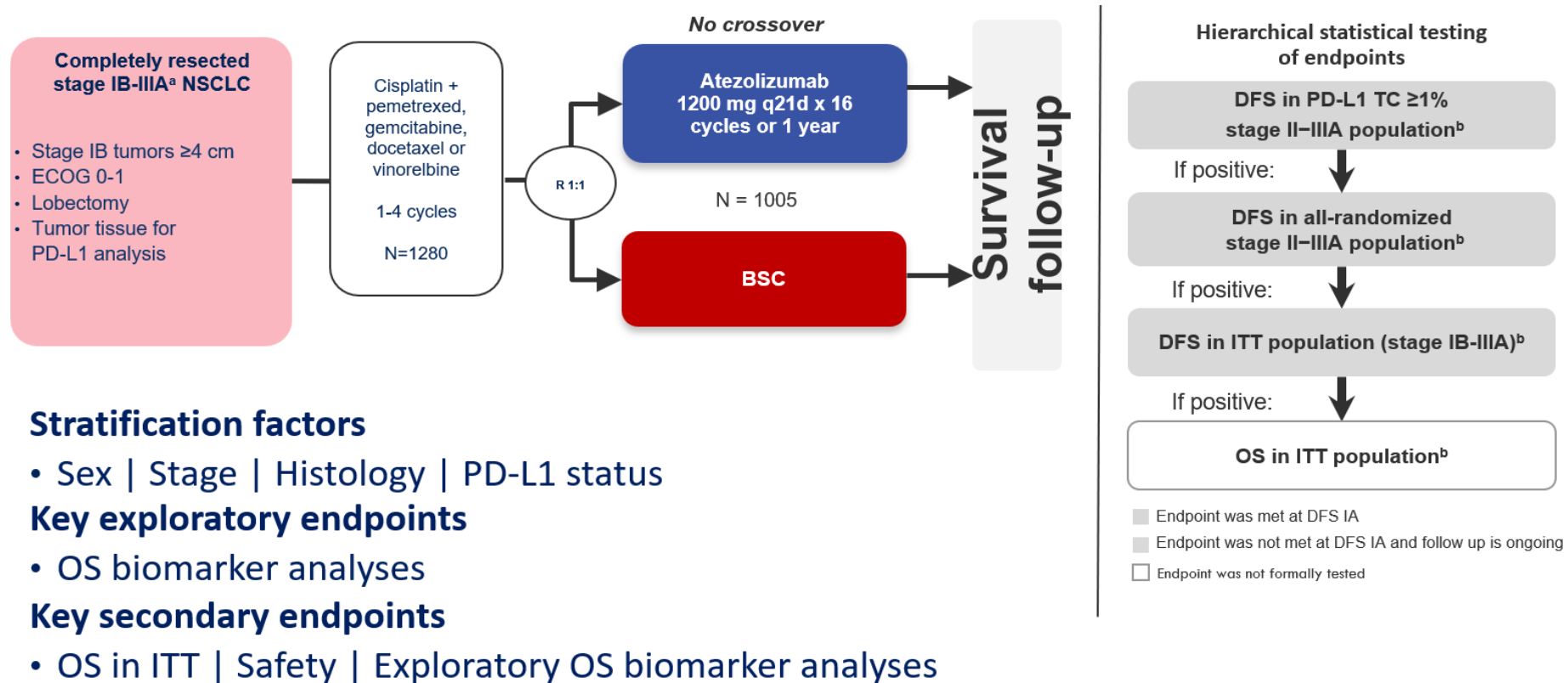
Immunotherapy + chemotherapy				
CheckMate 816	NCT02998528	IB-IIIa, neoadjuvant	nivolumab + chemotherapy	2017-2028
KEYNOTE-671	NCT03425643	II-IIIB, both neo/adjuvant	pembrolizumab + chemotherapy	2018-2026
IMpower030	NCT03456063	IB-IIa, neoadjuvant	atezolizumab + platinum chemotherapy	2018-2026
AEGEAN	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

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

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



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 $\alpha=0.05$.

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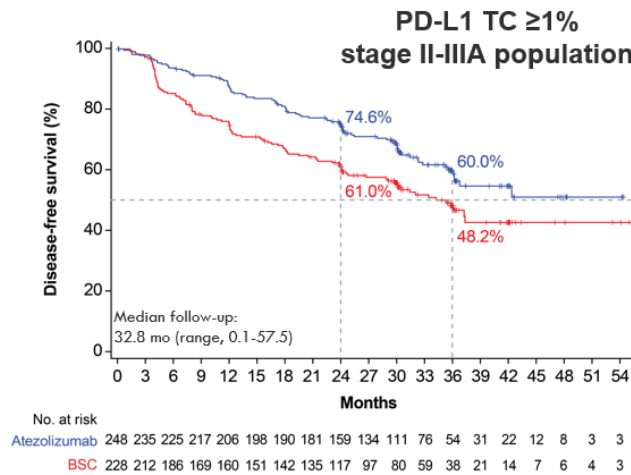
IMpower010: baseline characteristics

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)

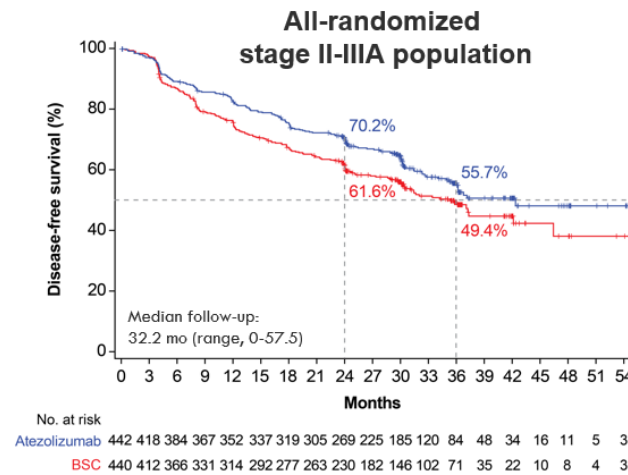
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IMpower010: DFS in the PD-L1 TC $\geq 1\%$ ^a stage II-III A, all-randomized stage II-III A and ITT pop (primary endpoint)

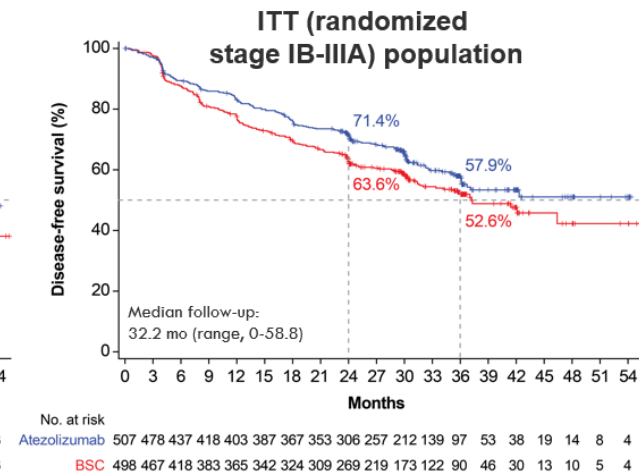
US FDA approval Oct 15, 2021



	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	



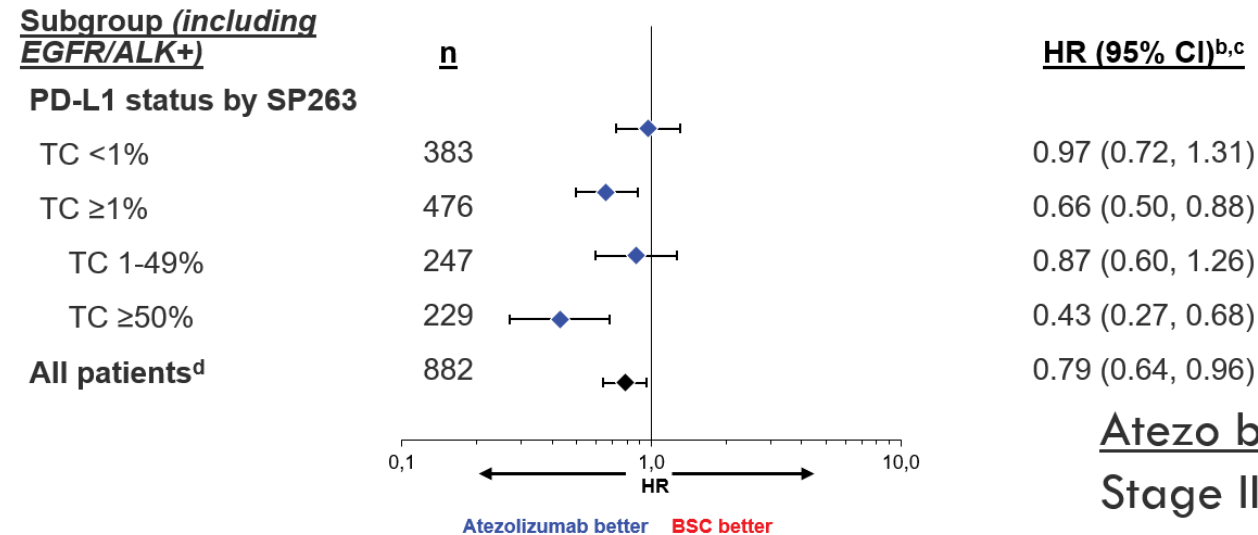
	Atezolizumab (n=507)	BSC (n=498)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value ^b	0.04 ^d	

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.

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IMpower010 DFS by PD-L1 status^a

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



Atezo best:

Stage IIIa

Non-Sq

Never-smoke

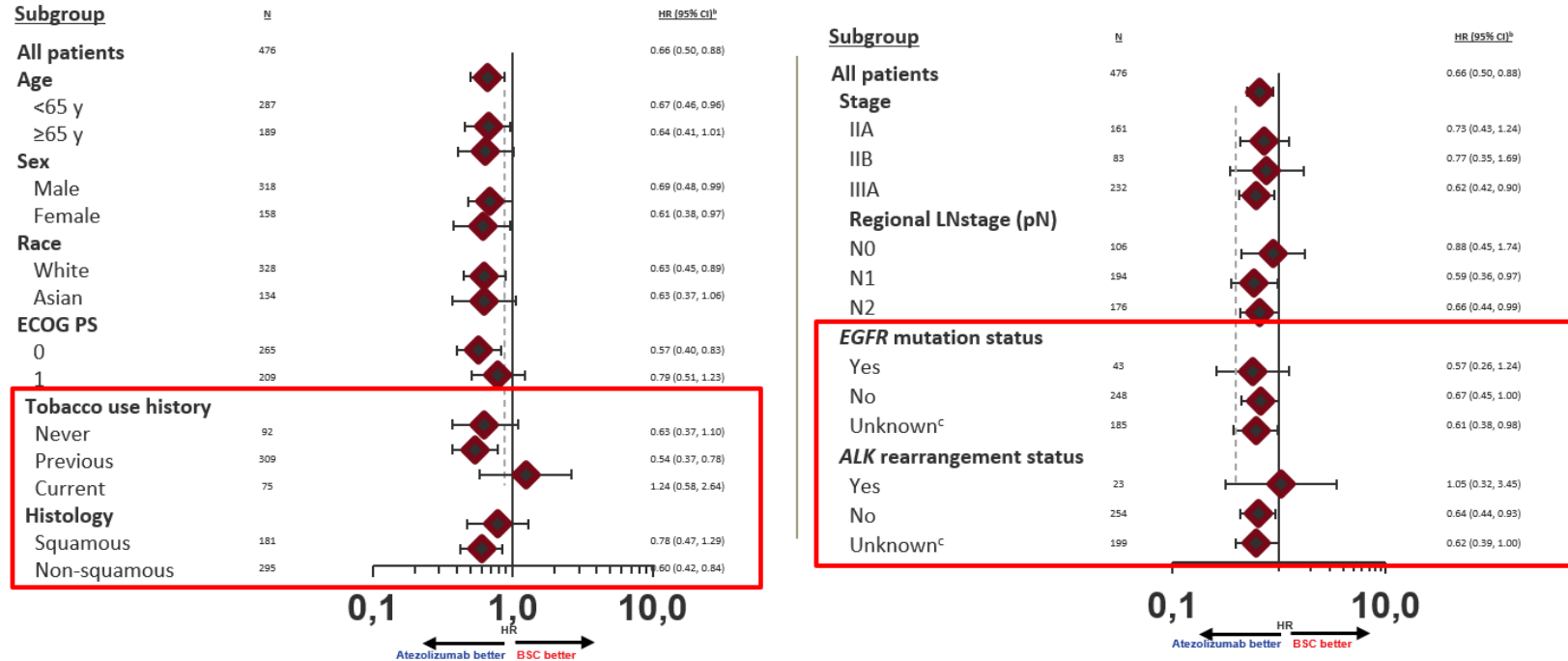
PD-L1 ≥50%

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.

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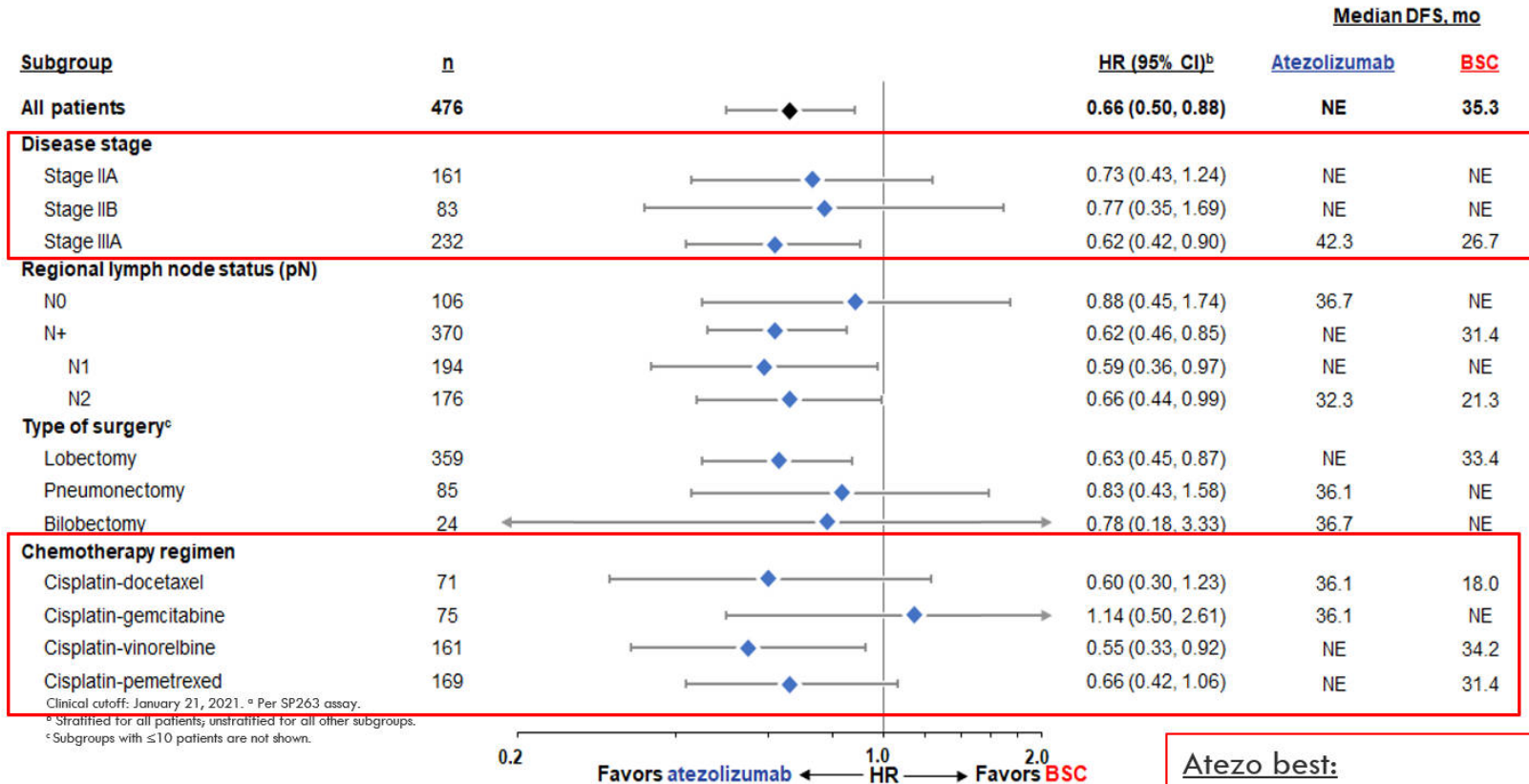
IMpower010: DFS in key subgroups of the PD-L1 TC $\geq 1\%$ ^a stage II-IIIa population



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.

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IMpower010: PD-L1 TC $\geq 1\%$ ^a stage II-IIIa population: DFS by disease and treatment characteristics

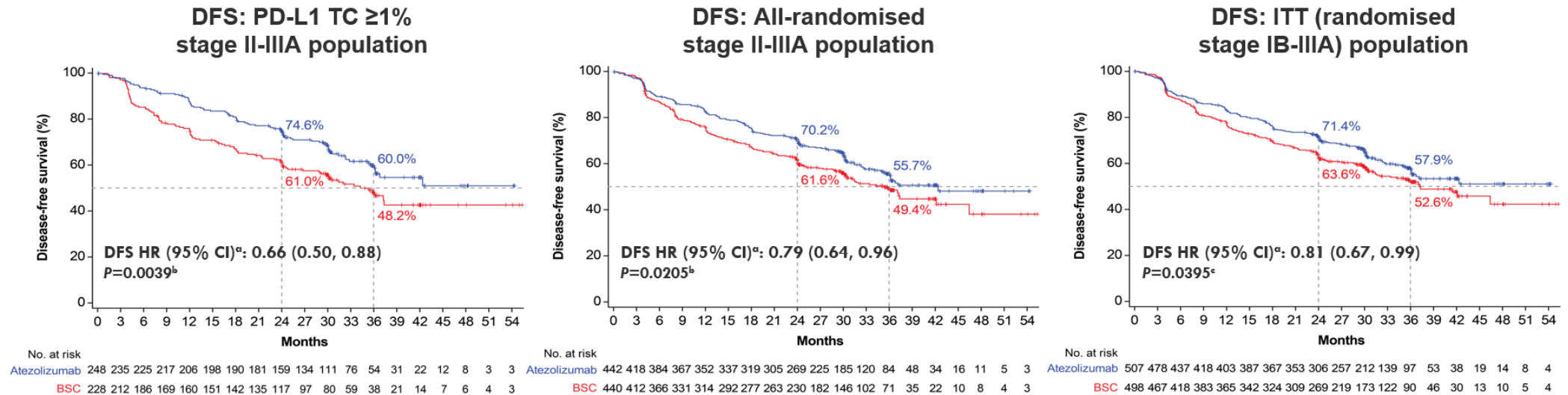


^a Stratified for all patients, unstratified for all other subgroups.
^b Clinical cutoff: January 21, 2021. ^c Per SP263 assay.
^d Subgroups with ≤ 10 patients are not shown.

Atezo best:
 Stage IIIA
 Non-Sq
 Prev smoking history
 PD-L1 $\geq 50\%$

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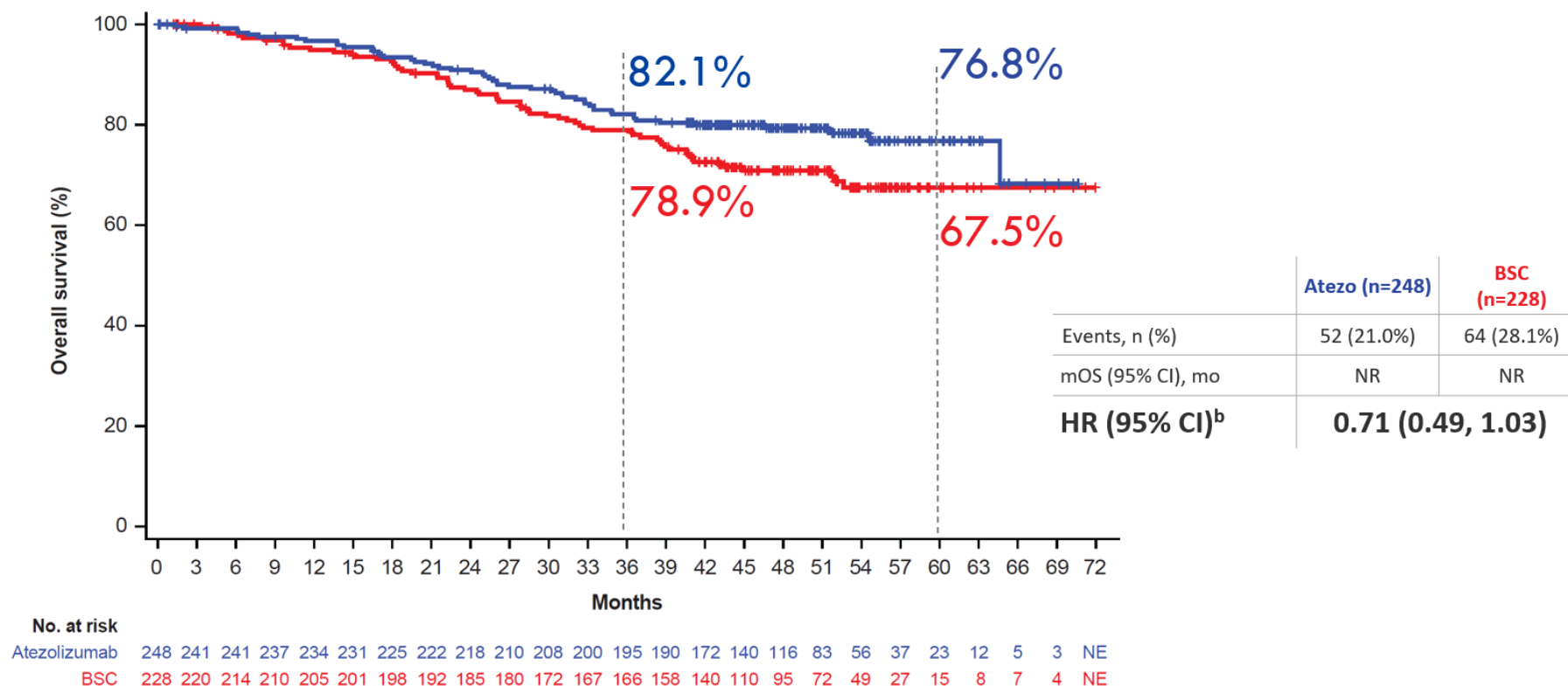
Recap of DFS and OS data from the DFS IA^{1,2} (data cutoff: 21 Jan '21, median follow-up: 32 months)



- OS data not mature (event to patient ratio in ITT was 19% in atezolizumab arm, 18% in BSC arm)
 - PD-L1 TC $\geq 1\%$ 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

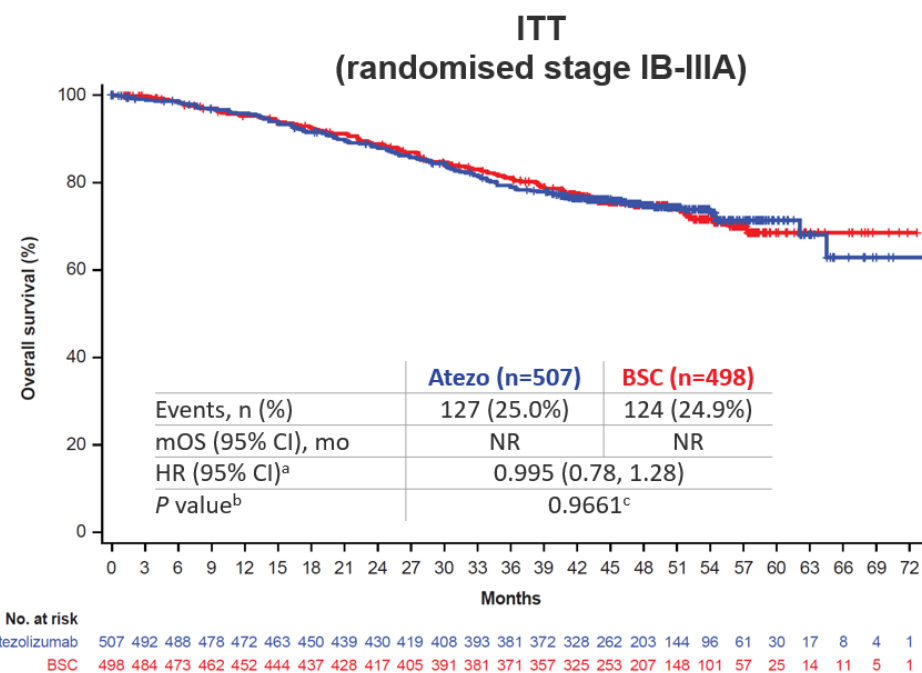
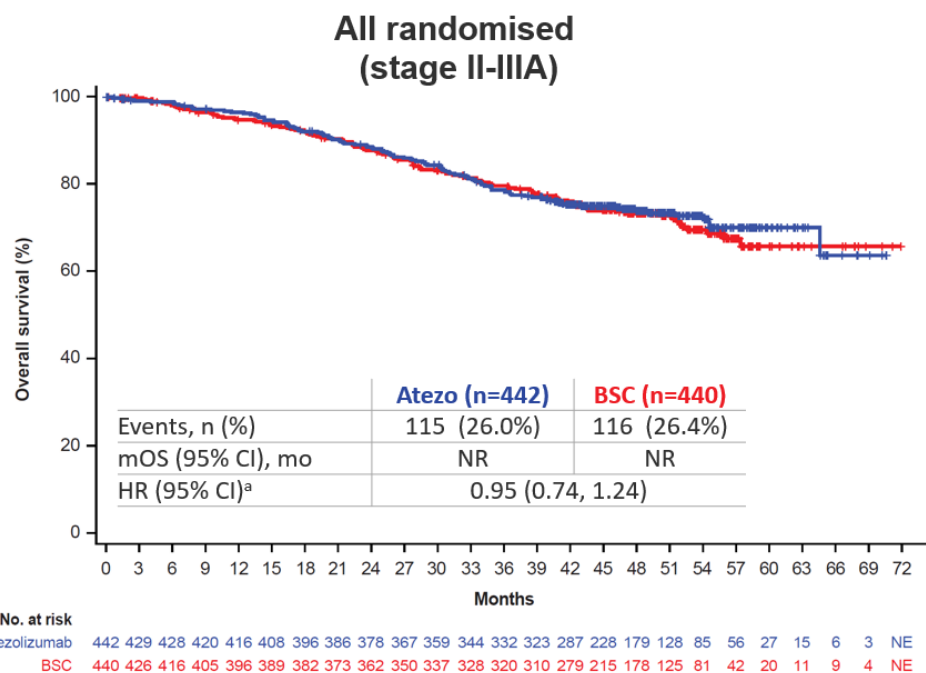
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IMpower010: Results of OS IA_(data cut 4/18/22: 46 mo med f/up) PD-L1 TC $\geq 1\%$ ^a (stage II-IIIA)



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

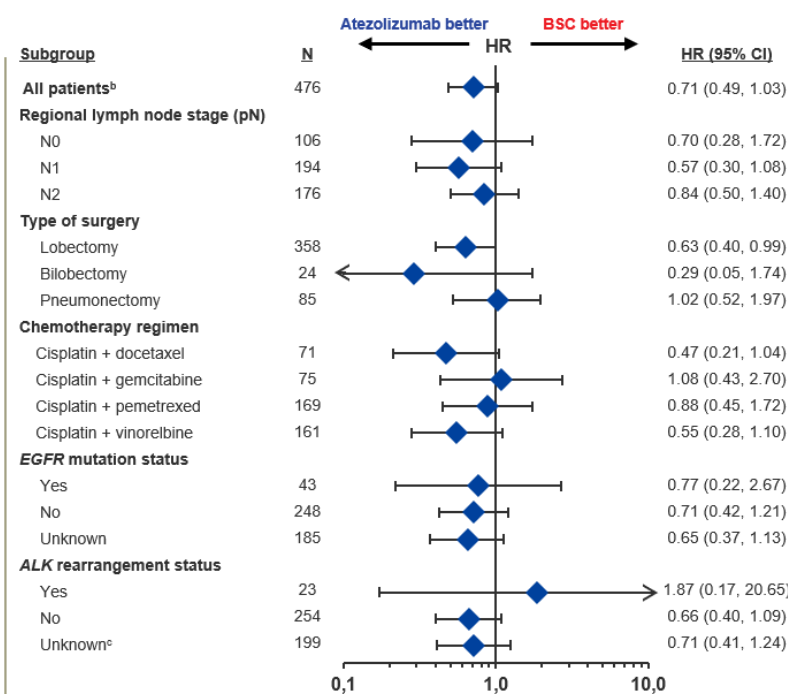
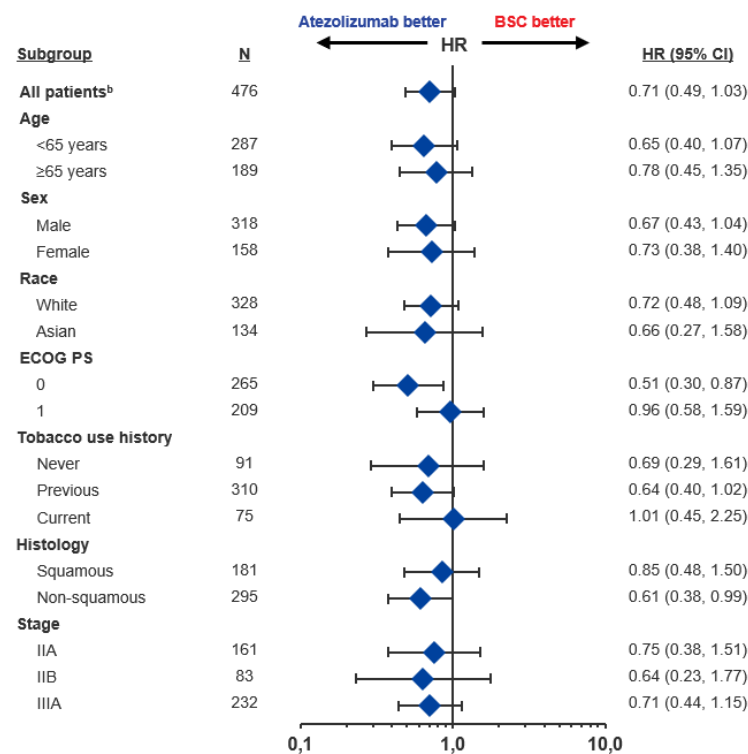


Clinical cutoff: 18 April 2022.^aStratified. ^bNo formal testing until statistical significance observed for DFS in the ITT population due to the prespecified testing hierarchy.

^cDescriptive purposes only.

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Subgroup analysis of OS in PD-L1 TC $\geq 1\%$ ^a (stage II-III A) (data cutoff: 18 Apr '22, median follow-up: 46 months)

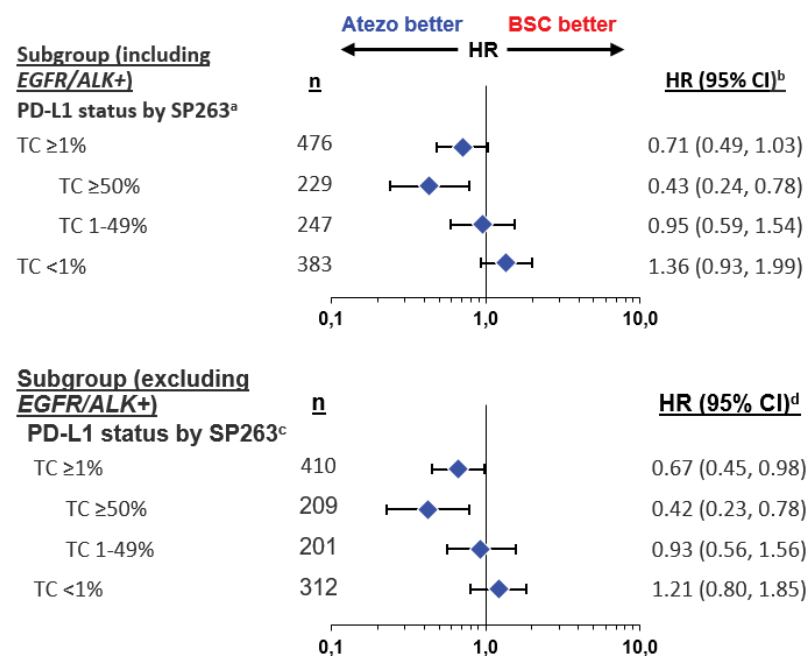


Clinical cutoff: 18 April 2022 (event to patient ratio, 25% [ITT]). ^aBy SP263 assay. ^bStratified.

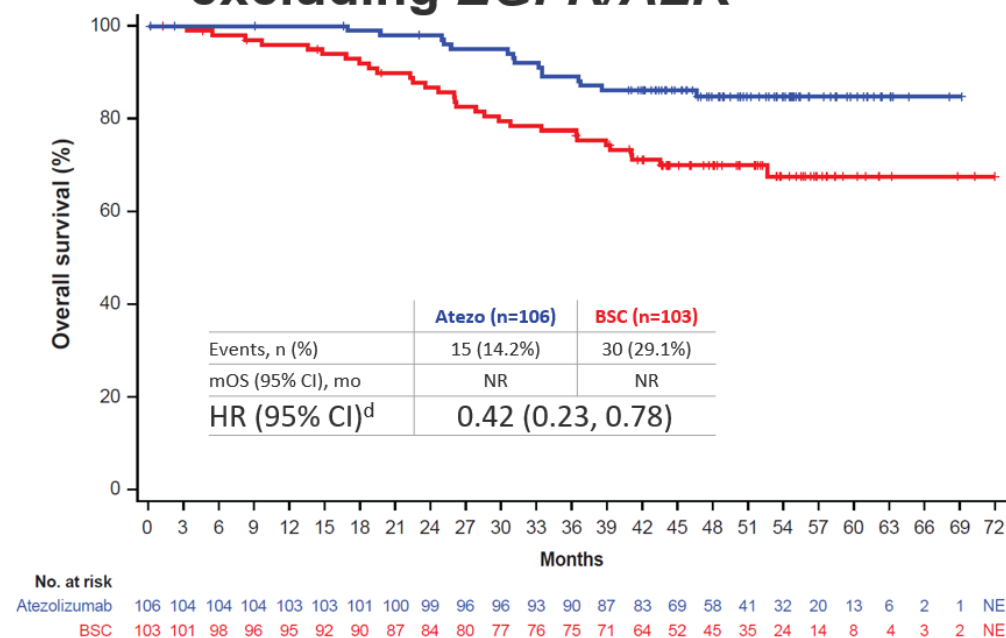
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OS by Biomarkers (stage II-III A)

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



OS: PD-L1 TC ≥50% (stage II-III A) excluding EGFR/ALK+



^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.

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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%

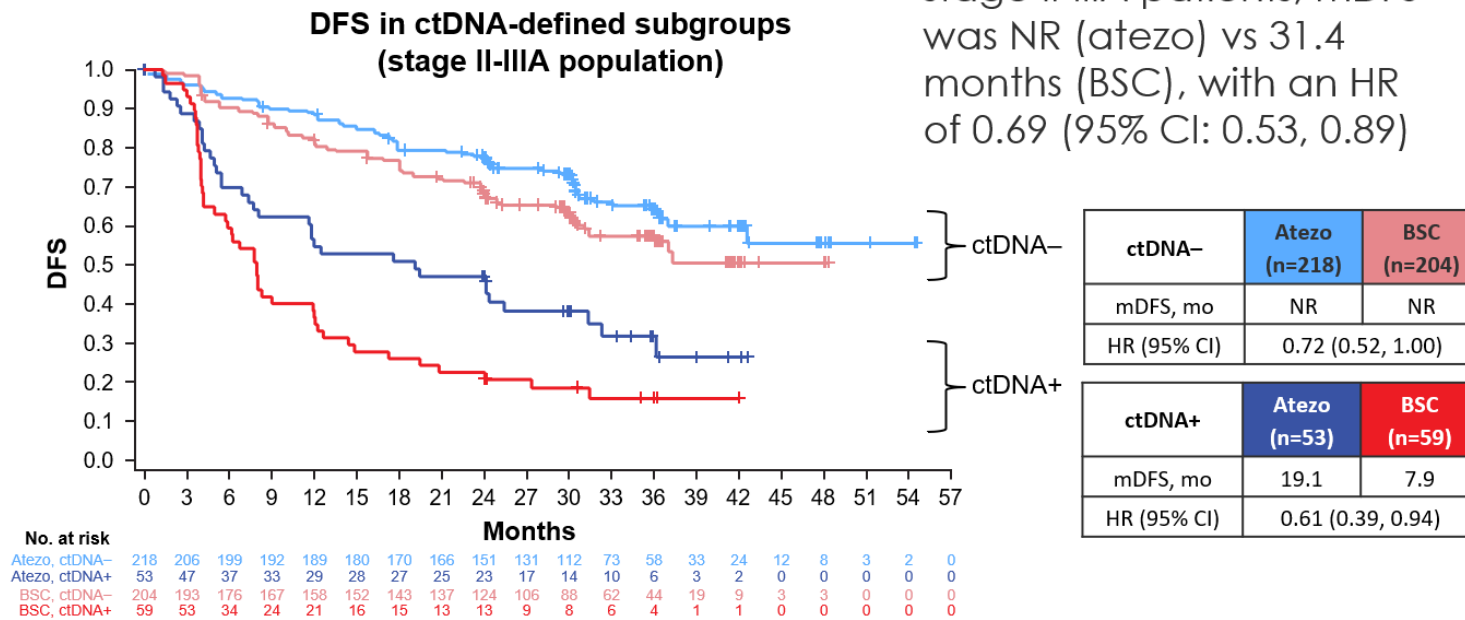
AESI, AE of special interest; SAE, serious AE. ^a No new deaths due to AEs occurred since the DFS IA clinical cutoff date; a previous 'other' death was updated to a Grade 5 AE.

^b No new AESI medical concepts noted at OS IA vs DFS IA.

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IMpower010 – Exploratory ctDNA results

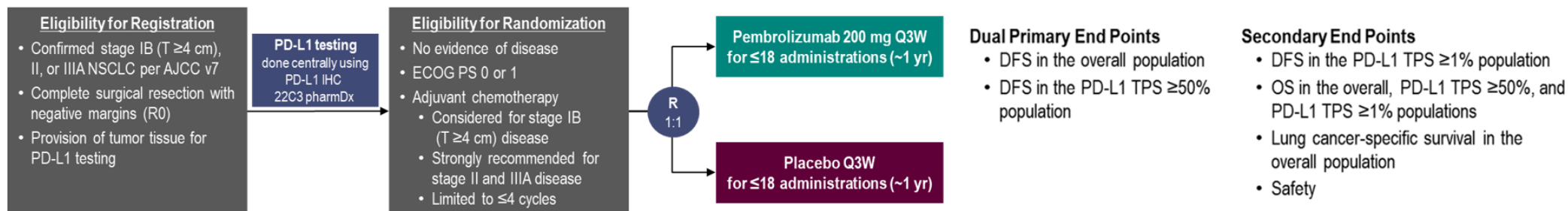
- In all ctDNA-evaluable stage II-IIIa patients, mDFS was NR (atezo) vs 31.4 months (BSC), with an HR of 0.69 (95% CI: 0.53, 0.89)



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PEARLS/KEYNOTE-091 Study Design

Global, Randomized, Triple-Blind Phase 3 Study



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%

*2 (0.3%) participants in the placebo arm had stage IV disease; neither had TPS ≥50%.

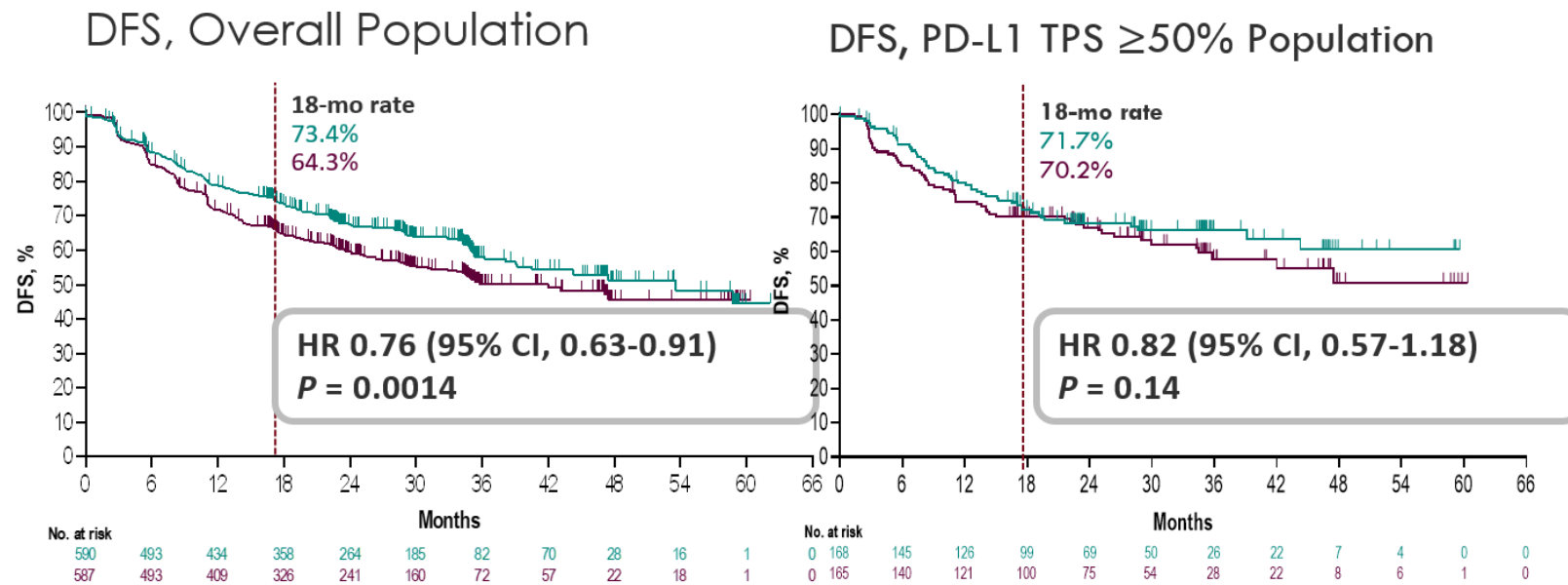
^bEGFR mutation status was unknown for 670 (63.5%) in the overall population and 198 (59.5%) in the TPS ≥50% population.

^cALK translocation status was unknown for 747 (63.5%) in the overall population and 217 (65.2%) in the TPS ≥50% population.

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%

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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)

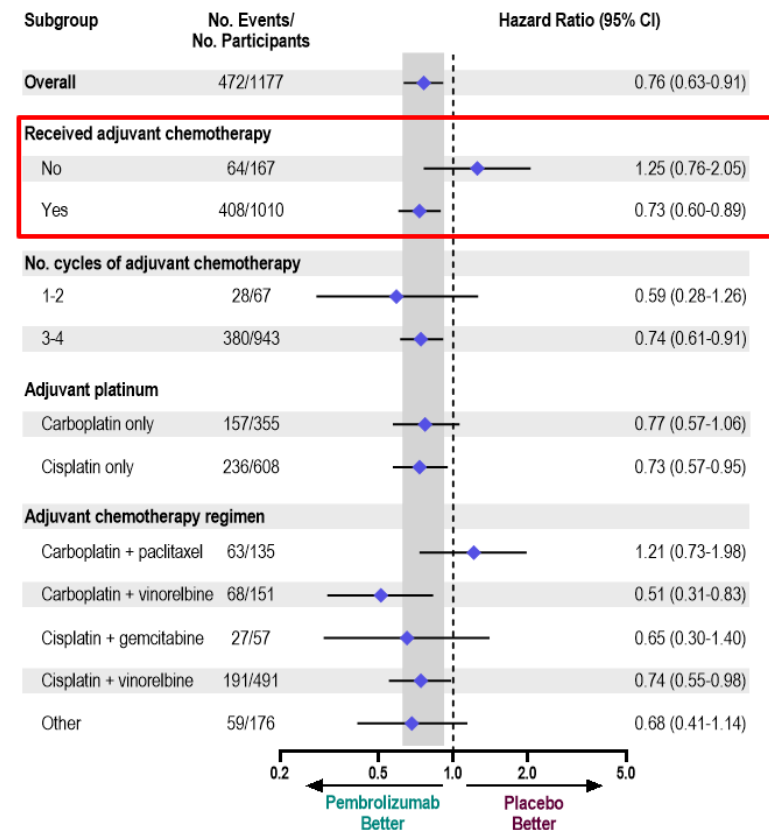
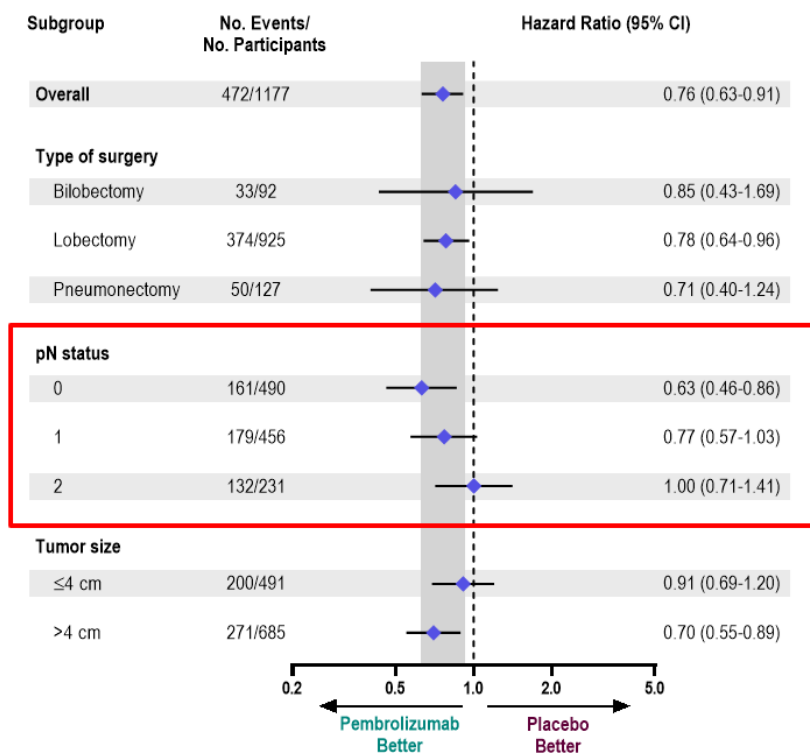
Response assessed per RECIST v1.1 by investigator review.
 Data cutoff date: September 20, 2021

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

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

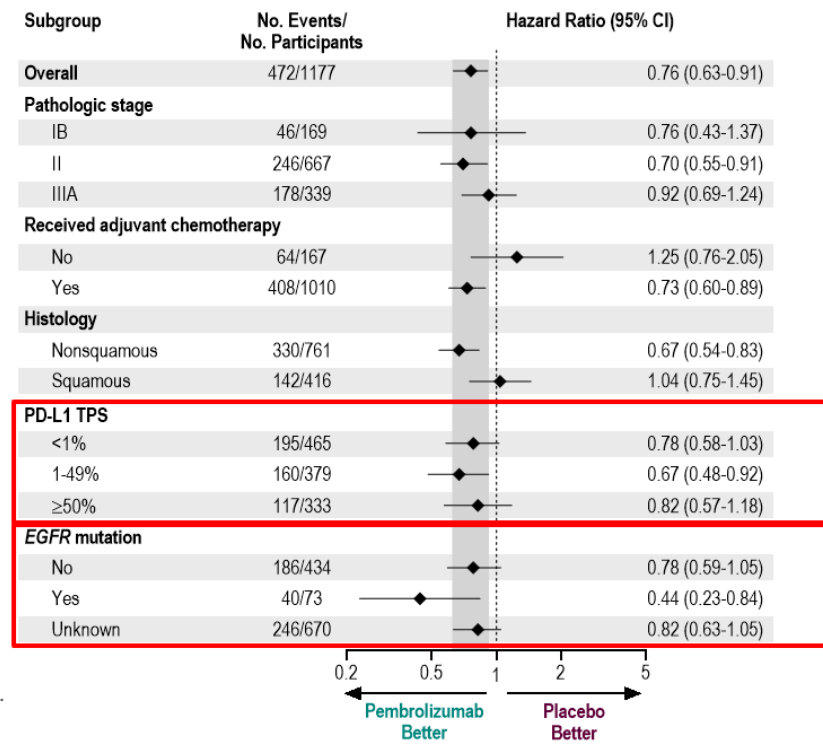
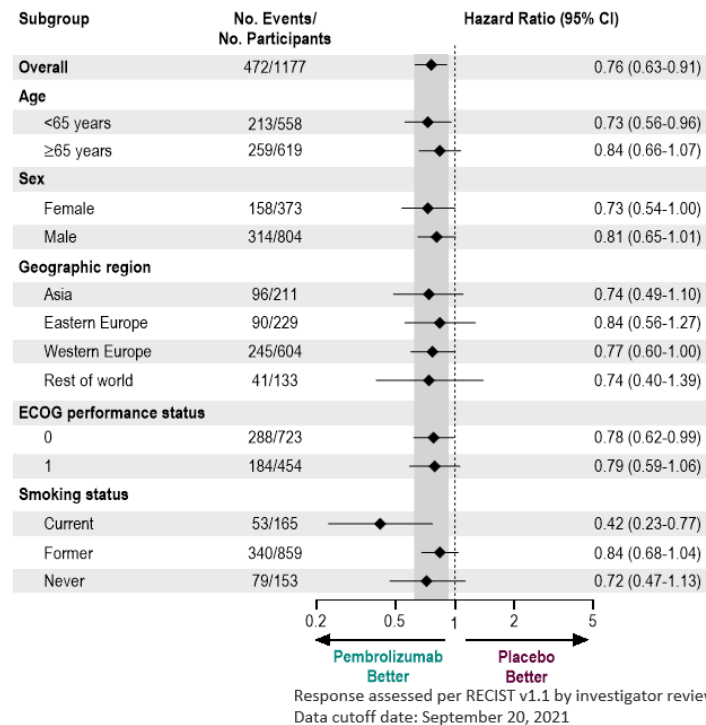
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KN-091 Results: DFS Related to Surgical Resection, Disease Burden, and Use of Adjuvant Chemotherapy



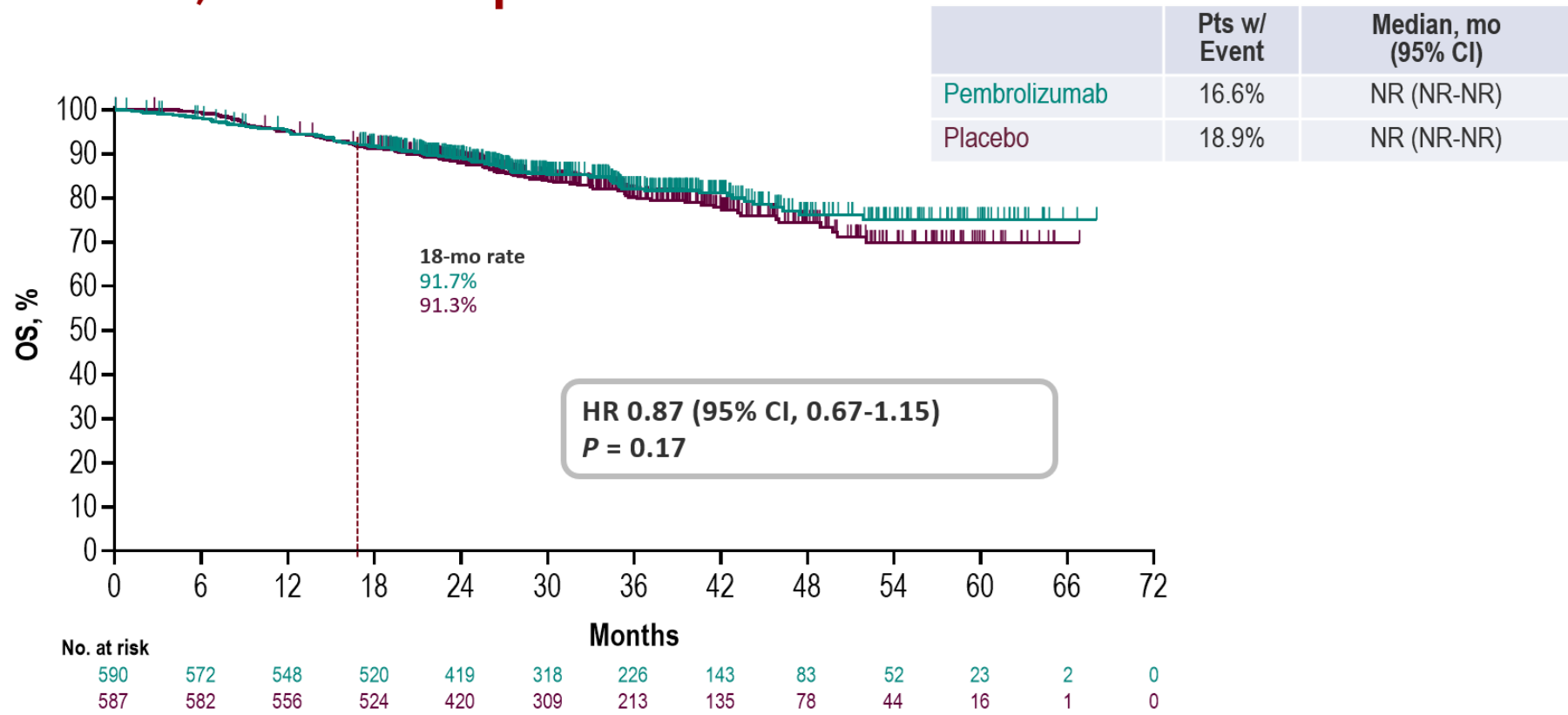
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KN-091 DFS in Key Subgroups, Overall Population



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KN-091 OS, Overall Population



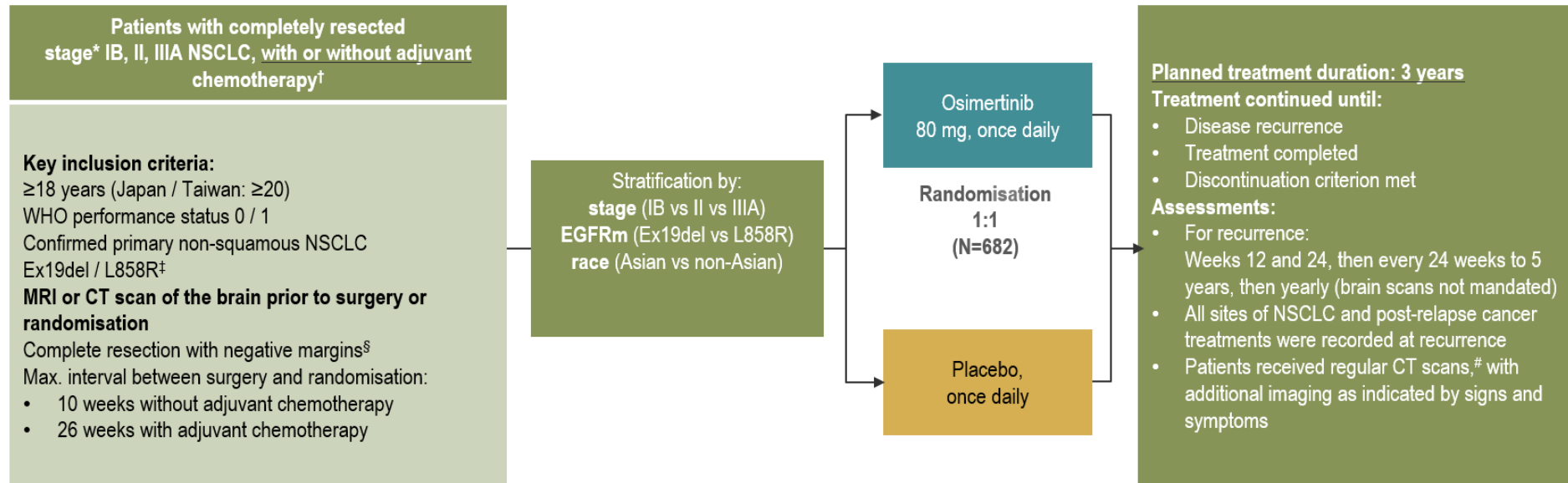
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Adjuvant PD-1/PD-L1 IO trials

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

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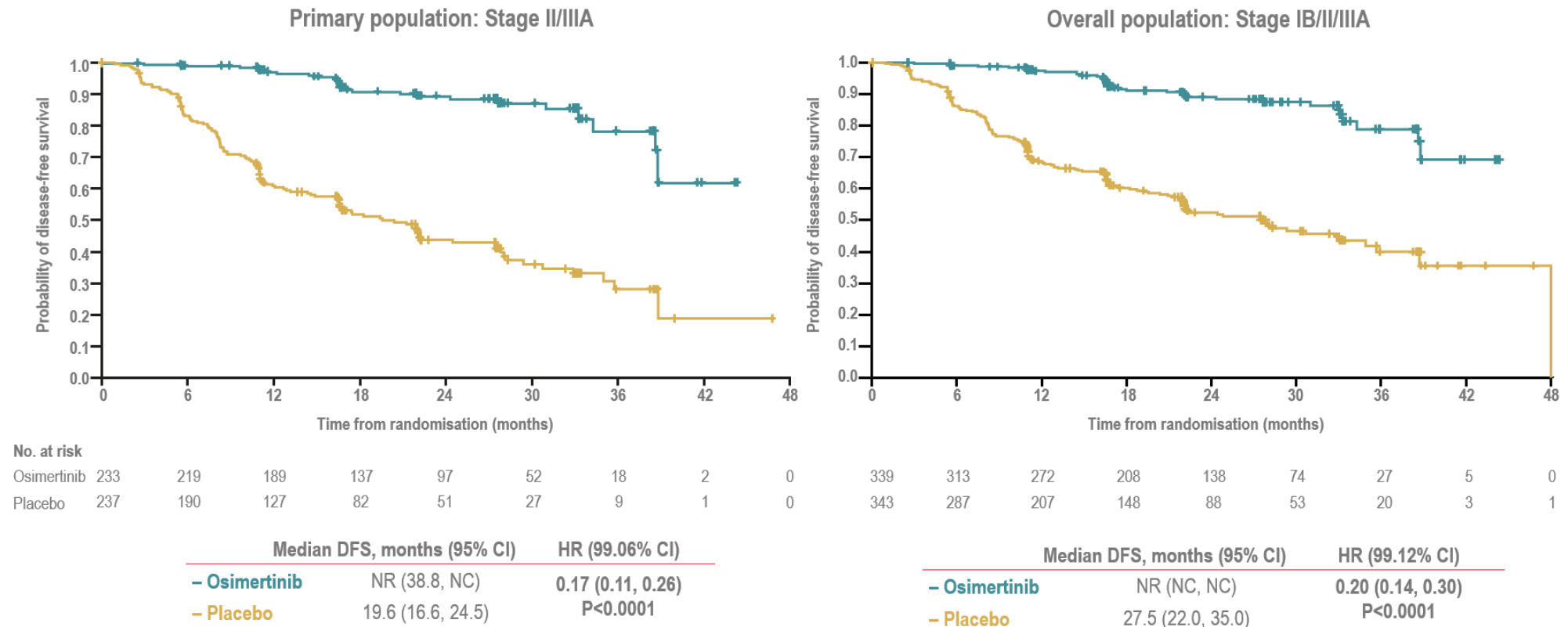
ADAURA: Phase III double-blind study design



- The primary and key secondary endpoints of DFS¶ in stage II/IIIA patients and the overall population, respectively, have been reported previously¹
- Here we report results from a pre-specified exploratory analysis of disease recurrence patterns in ADAURA, including CNS

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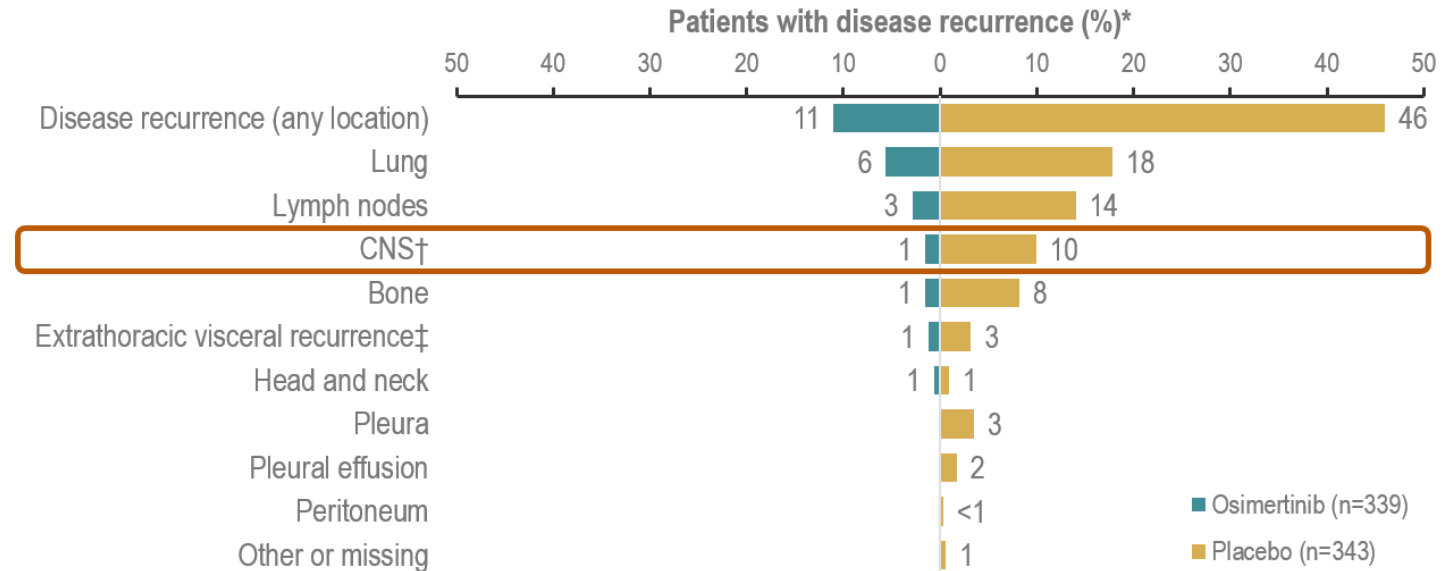
ADAURA: A positive breakthrough for some patients Osimertinib improves DFS in pts w resected EGFRmut NSCLC



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

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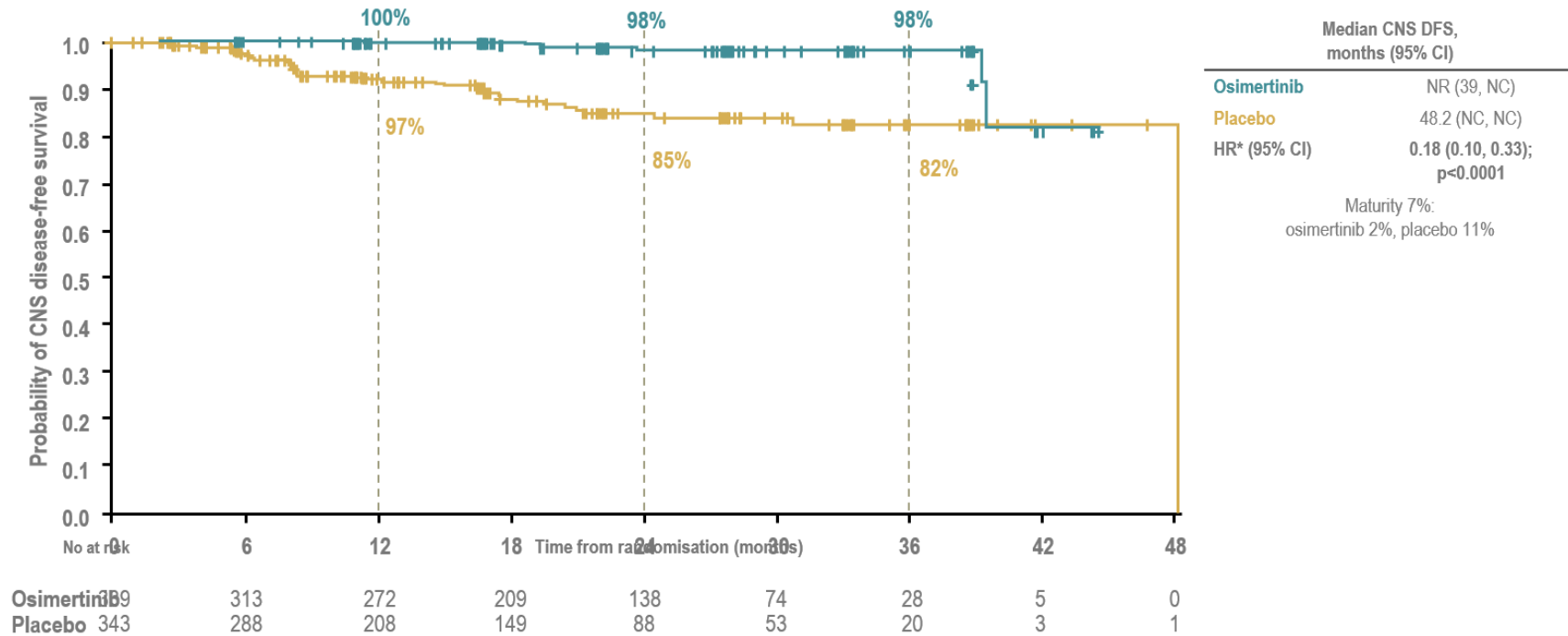
Sites of disease recurrence



*Number of patients with disease recurrence regardless of pathology results of the tumour recurrence location;
†Includes CNS only (osimertinib n=4 [1%]; placebo n=26 [7%]) and CNS plus other locations (osimertinib n=1 [<1%]; placebo n=9 [3%]).
‡Includes disease recurrence in liver, renal and adrenal systems and pancreas.
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;
ADAURA data cut-off: 17 January, 2020

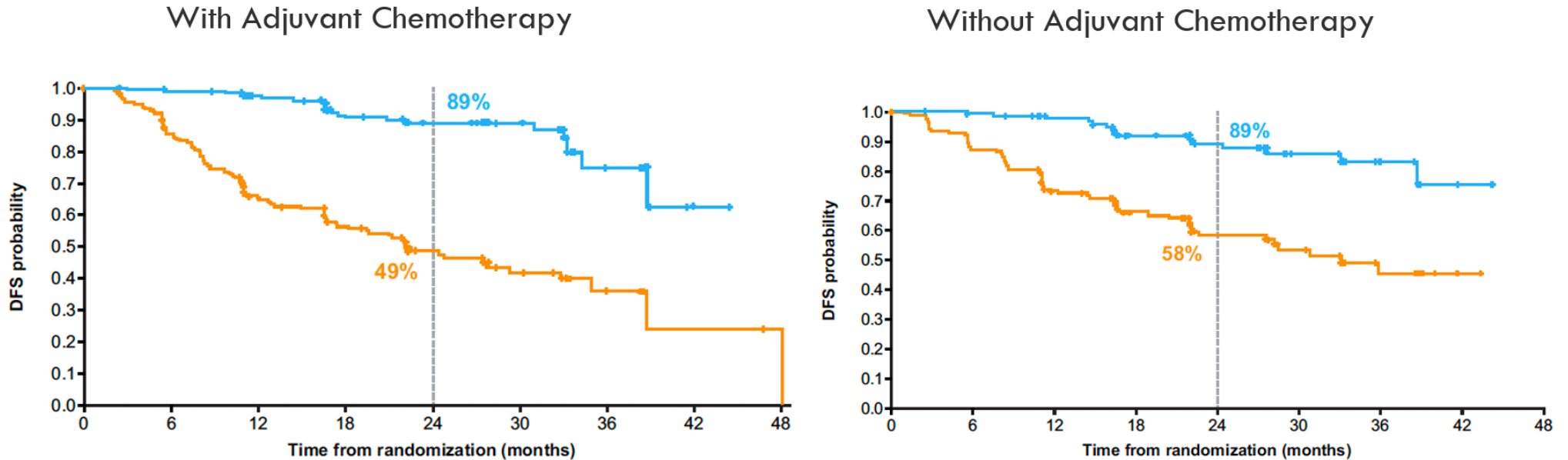
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CNS DFS in the overall population



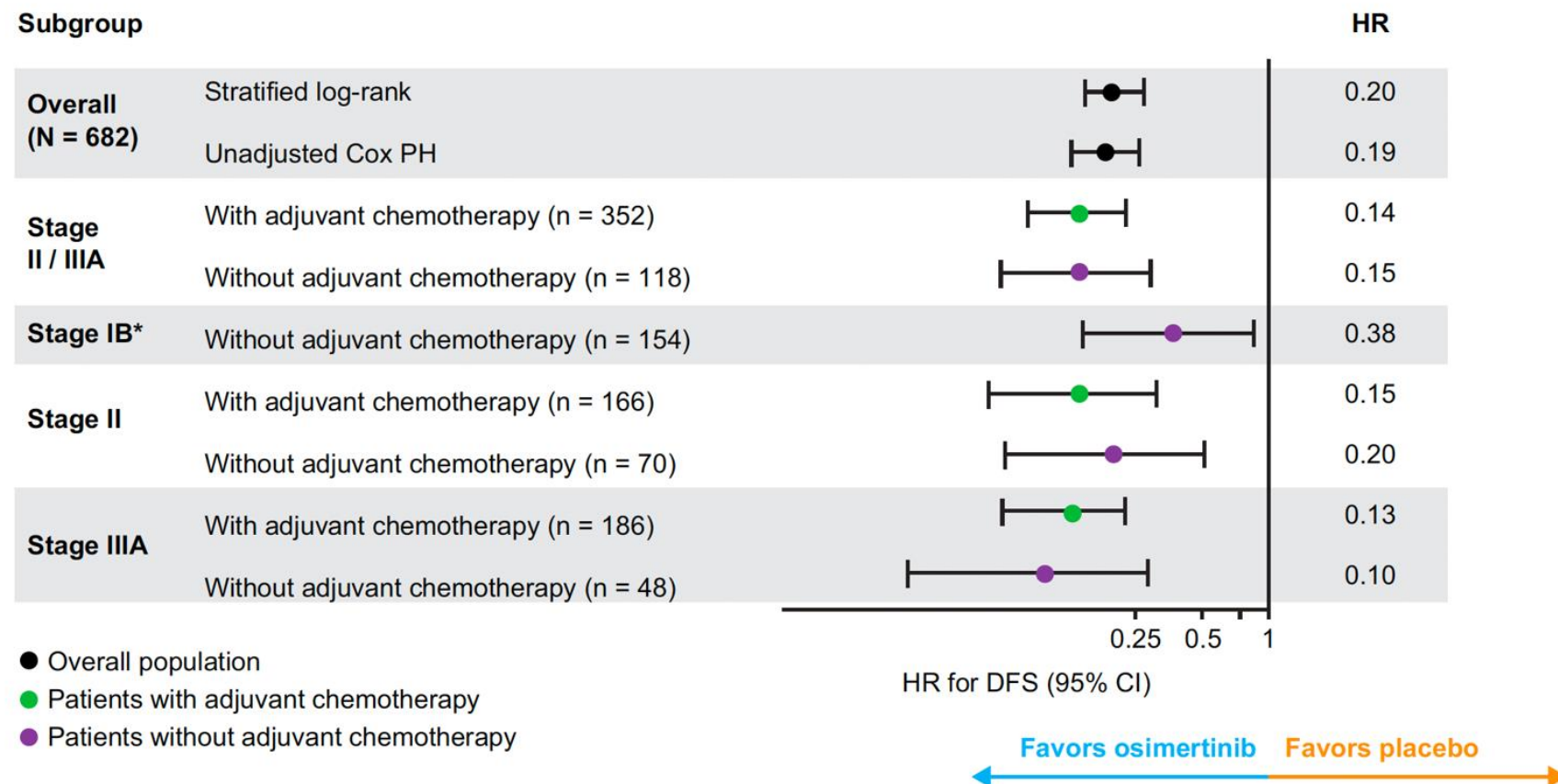
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ADAURA: DFS with Adjuvant Osimertinib for Patients Receiving and Not Receiving Adjuvant Chemotherapy



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



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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-III A 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)

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National
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NCCN Guidelines Version 5.2022 Non-Small Cell Lung Cancer

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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 cycles¹

Preferred (squamous)

- Cisplatin 75 mg/m² day 1, gemcitabine 1250 mg/m² days 1 and 8, every 21 days for 4 cycles²
- Cisplatin 75 mg/m² day 1, docetaxel 75 mg/m² day 1 every 21 days for 4 cycles³

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 cycles⁴
- 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 cycles⁵

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 cycles⁷
- Carboplatin AUC 5 day 1, gemcitabine 1000 mg/m² days 1 and 8, every 21 days for 4 cycles⁸
- Carboplatin AUC 5 day 1, pemetrexed 500 mg/m² day 1 every 21 days for 4 cycles⁹ (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 daily¹¹
 - ▶ 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 year¹²
 - ▶ Atezolizumab for patients with completely resected stage IIB–IIIA or high risk stage IIA PD-L1 ≥1% NSCLC who received previous adjuvant chemotherapy.

Sonuç

- ❑ Evre [IB(4 cm>)-IIIA] ve EGFR mutasyonu(Ekzon 19,21) olan hastalarda 4 kür adjuvan KT sonrası adjuvan Osimertinib(3 yıl)
- ❑ Evre [II-III A] 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