Nuove strategie nel trattamento del tumore del polmone

Giovanni Maria Fadda

SC Oncologia – AOU SS

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Primo punto: il miglioramento della sopravvivenza

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Cancer. 2024;1–7.

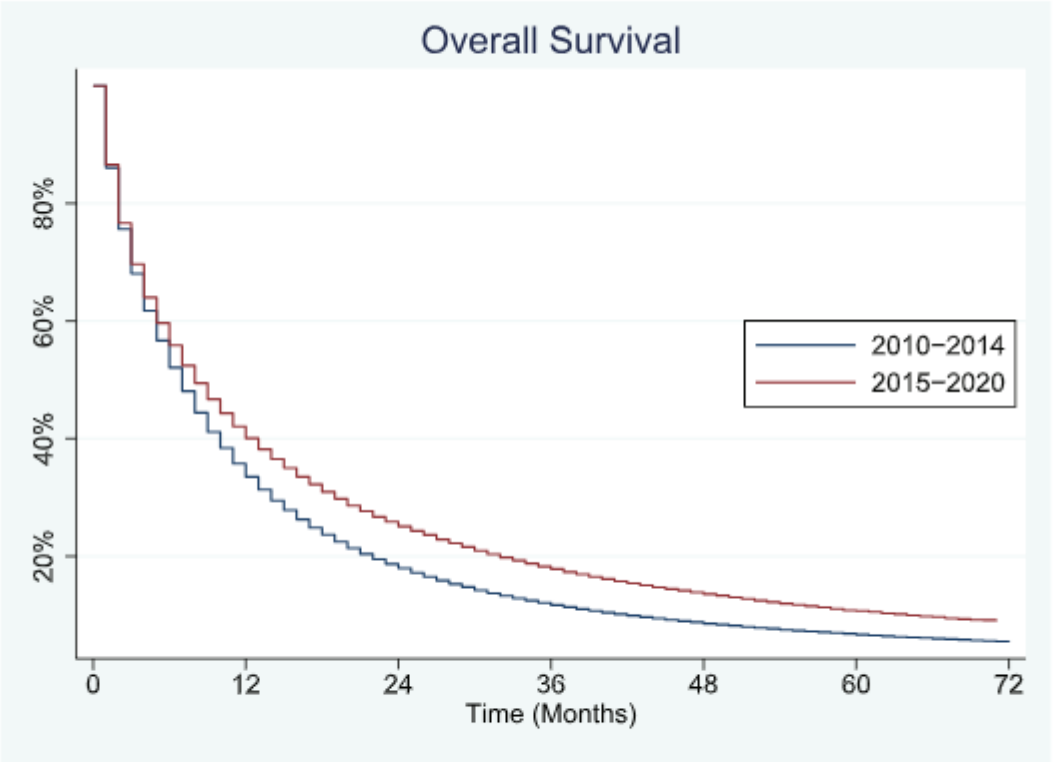

FIGURE 1 Kaplan–Meier curves comparing survival in the preimmunotherapy and immunotherapy er
40.1% vs. 33.5%; 3-year OS, 17.8% vs. 11.7%; 5-year OS, 10.7% vs. 6.8%; median OS, 8 vs. 7 months; $p <$

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Cancer. 2024;1–7.

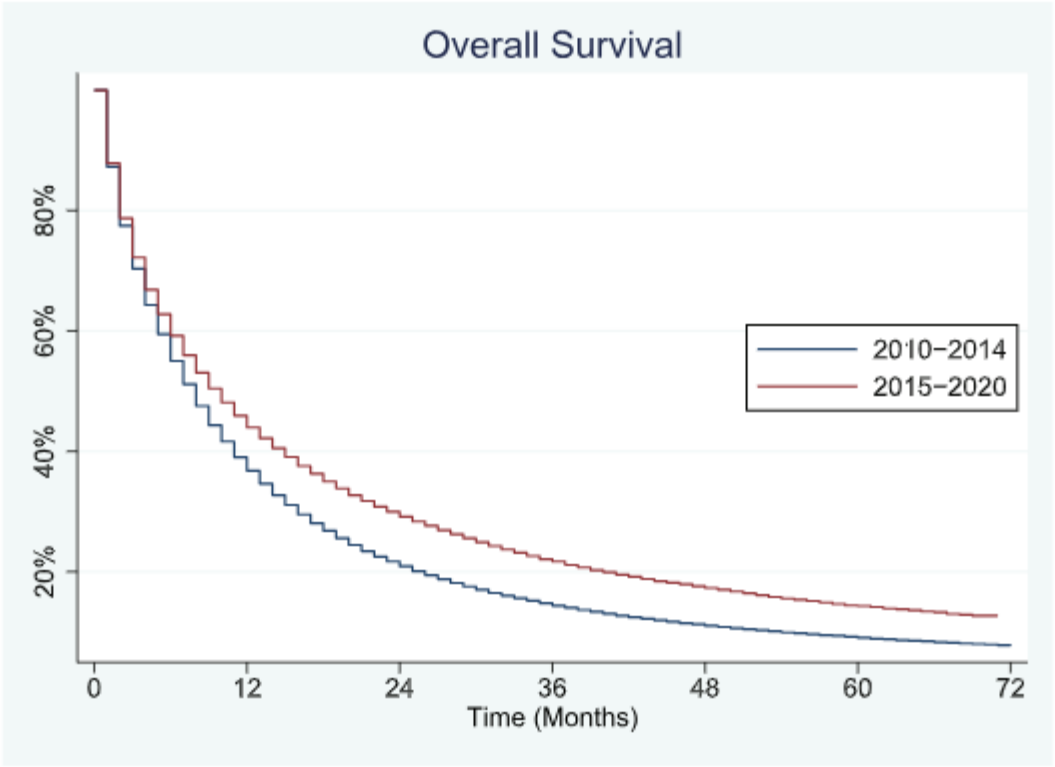

FIGURE 2 Kaplan–Meier curves comparing cancer-specific survival in the preimmunotherapy and immu
44.0% vs. 36.8%; 3-year survival, 21.7% vs. 14.4%; 5-year survival, 14.3% vs. 9.0%; median overall survival,
rank test).

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Cancer. 2024;1–7.

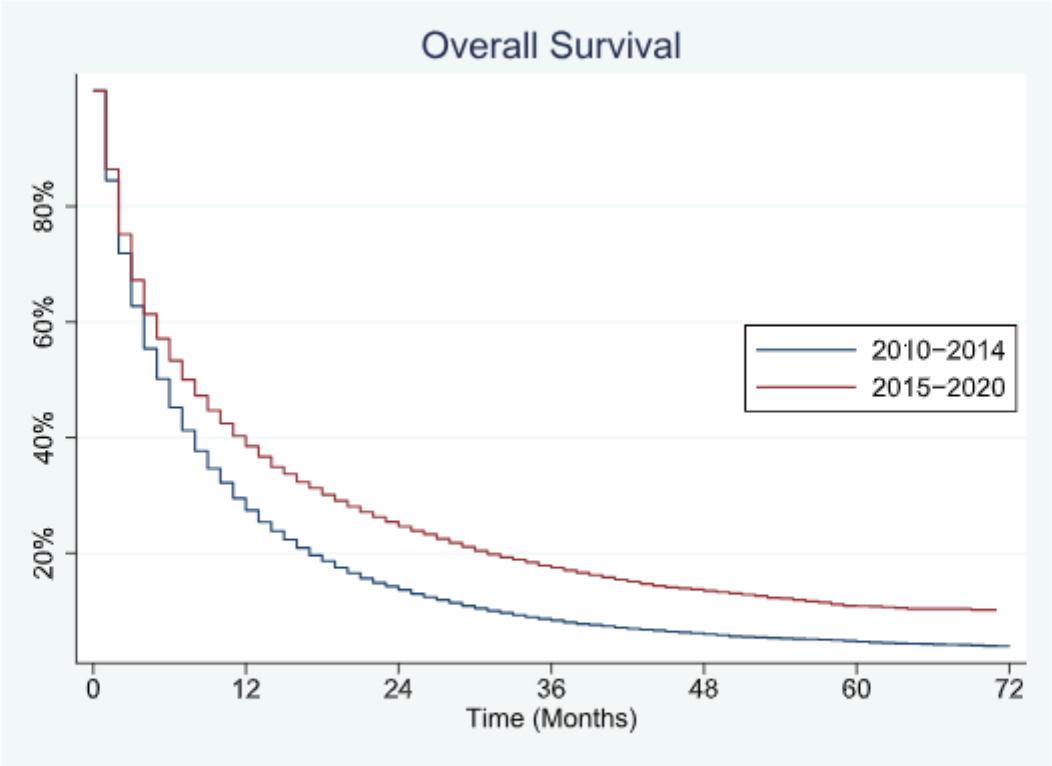

FIGURE 3 Kaplan–Meier curves comparing cancer-specific survival of patients with brain metastases
immunotherapy eras (8 vs. 6 months; $p < .001$ by log-rank test).

Secondo punto: il contributo dell'immunoterapia nella malattia avanzata

Malattia «non oncogene addicted» senza driver molecolari sfruttabili

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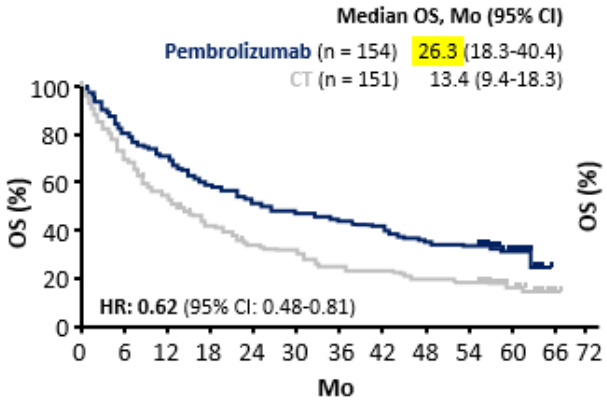
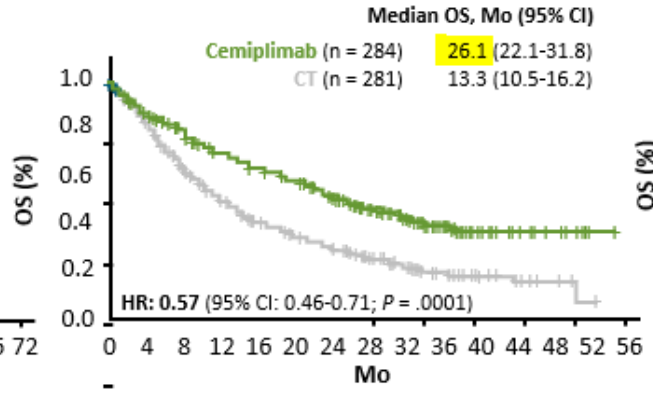
FDA-Approved ICI Monotherapies for PD-L1–High Advanced or Metastatic NSCLC

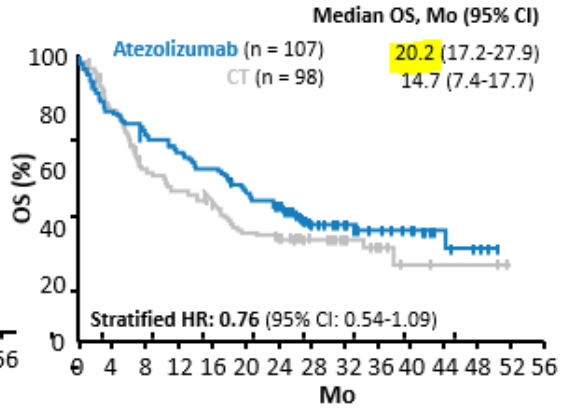
KEYNOTE-024[1,2] (N = 305): Pembrolizumab vs CT
(PD-L1 TPS ≥50%*)



EMPOWER-Lung 1[4] (n = 565†): Cemiplimab vs CT
(PD-L1 TPS ≥50%*)



IMpower110[5] (n = 205‡): Atezolizumab vs CT
(PD-L1 ≥50% [TC] or ≥10% [IC])



- Pembrolizumab indication as monotherapy for metastatic NSCLC was expanded to tumors with PD-L1 TPS ≥1% based on KEYNOTE-042.[3]

*PD-L1 IHC by 22C3. †712 patients enrolled in overall ITT population.
‡572 patients enrolled in overall population; PD-L1 IHC by SP142.

1. Reck. JCO. 2021;39:2339. 2. Reck. NEJM. 2016;375:1823 3. Castro. JCO. 2023;41:1986.
4. Ozguroglu. Lancet Oncol. 2023;24:989. 5. Jassem. J Thorac Oncol. 2021;16:1872.

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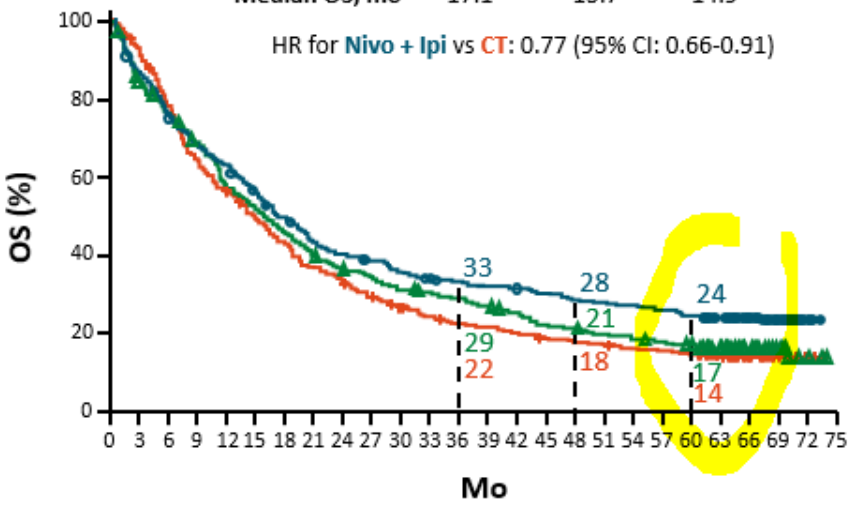
CheckMate 227: First-line Nivolumab + Ipilimumab vs Chemotherapy for Advanced NSCLC

5-Yr OS: PD-L1 ≥1%

	Nivo + Ipi (n = 396)	Nivo (n = 396)	CT (n = 397)
Median OS, mo	17.1	15.7	14.9

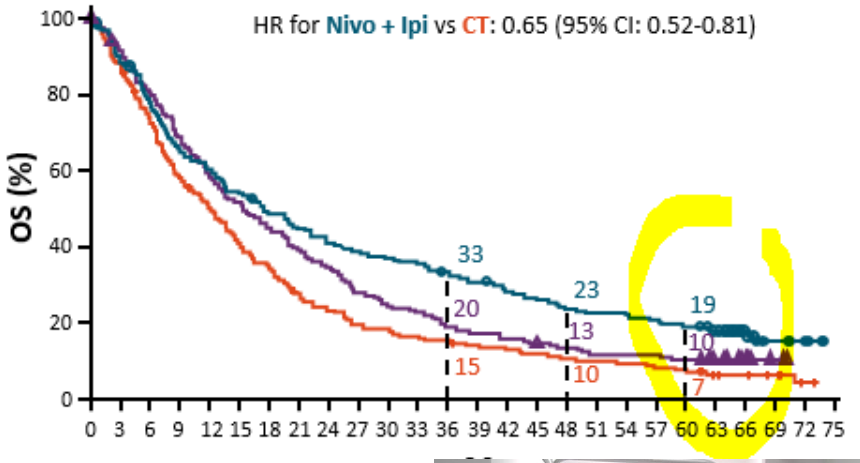
HR for Nivo + Ipi vs CT: 0.77 (95% CI: 0.66-0.91)



5-Yr OS: PD-L1 <1%*

	Nivo + Ipi (n = 187)	Nivo + CT (n = 177)	CT (n = 186)
Median OS, mo	17.4	15.2	12.2

HR for Nivo + Ipi vs CT: 0.65 (95% CI: 0.52-0.81)



*Not FDA approved indication.

Brahmer. J Clin Oncol. 2023;41:1200.

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Terzo punto: il contributo dell'immuno-chemioterapia nella malattia avanzata

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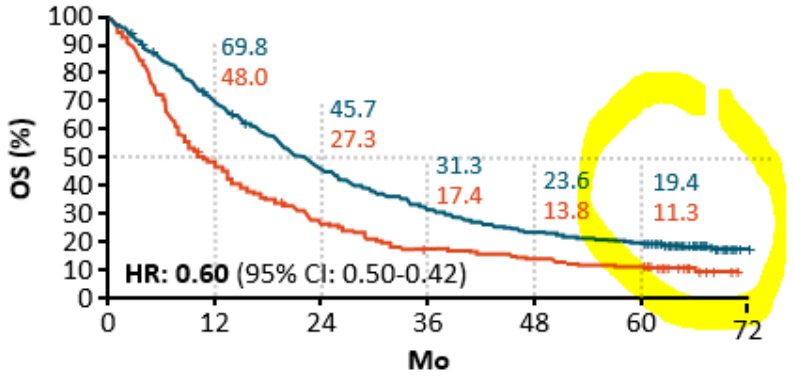
First-line Pembrolizumab Plus Chemotherapy in Advanced NSCLC

KEYNOTE-189:
Pembrolizumab vs CT in Nonsquamous NSCLC

OS in ITT (N = 616)

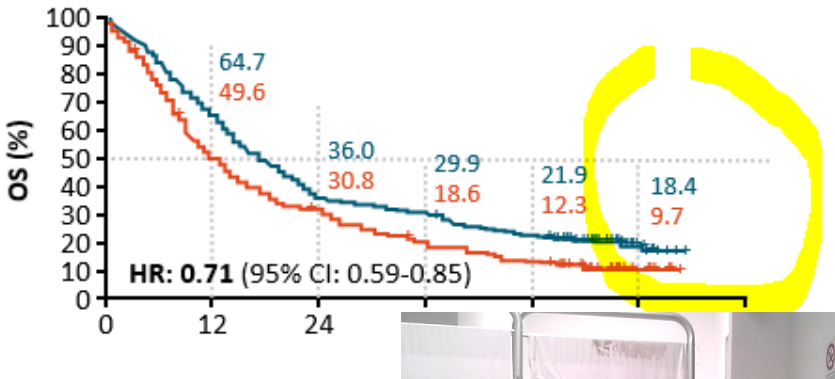
Treatment Group	Median OS, mo (95% CI)
Pembro + CT	19.4 (15.7-23.4)
Placebo + CT	11.3 (7.4-16.1)



KEYNOTE-407:
Pembrolizumab vs CT in Squamous NSCLC

OS in ITT (N = 563)

Treatment Group	Median OS, mo (95% CI)
Pembro + CT	18.4 (13.8-23.4)
Placebo + CT	9.7 (6.5-13.7)



Garassino. JCO. 2023;41:1992. Novello. ESMO 2022. Abstr 974MO. Novello. JCO. 2023;41:1999.

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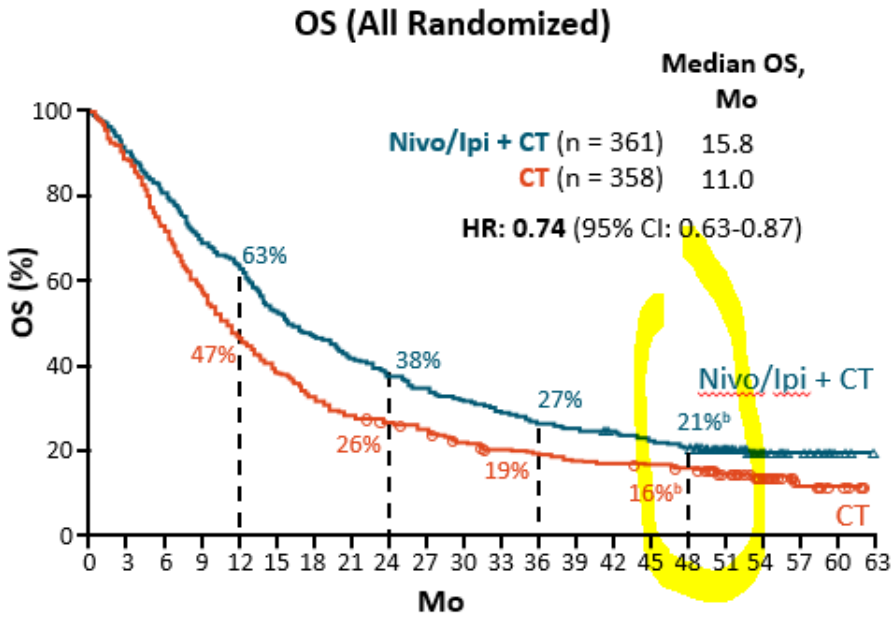
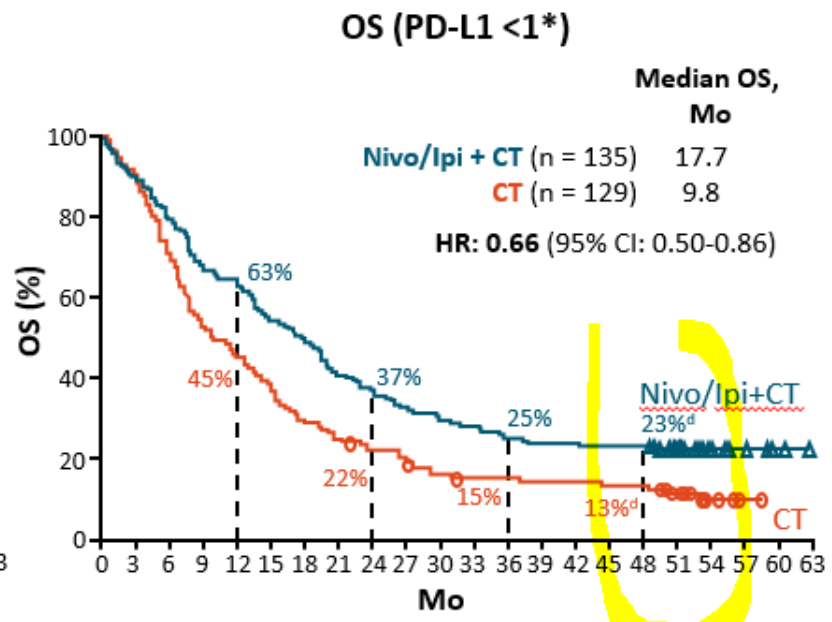
CheckMate 9LA: Nivolumab + Ipilimumab + CT vs CT in Advanced NSCLC





*Measured by IHC (28-8 Pharm

Carbone. ASCO 2023. Abstr LBA9023. Paz-Ares. J Thorac Oncol. 2023;18:204.

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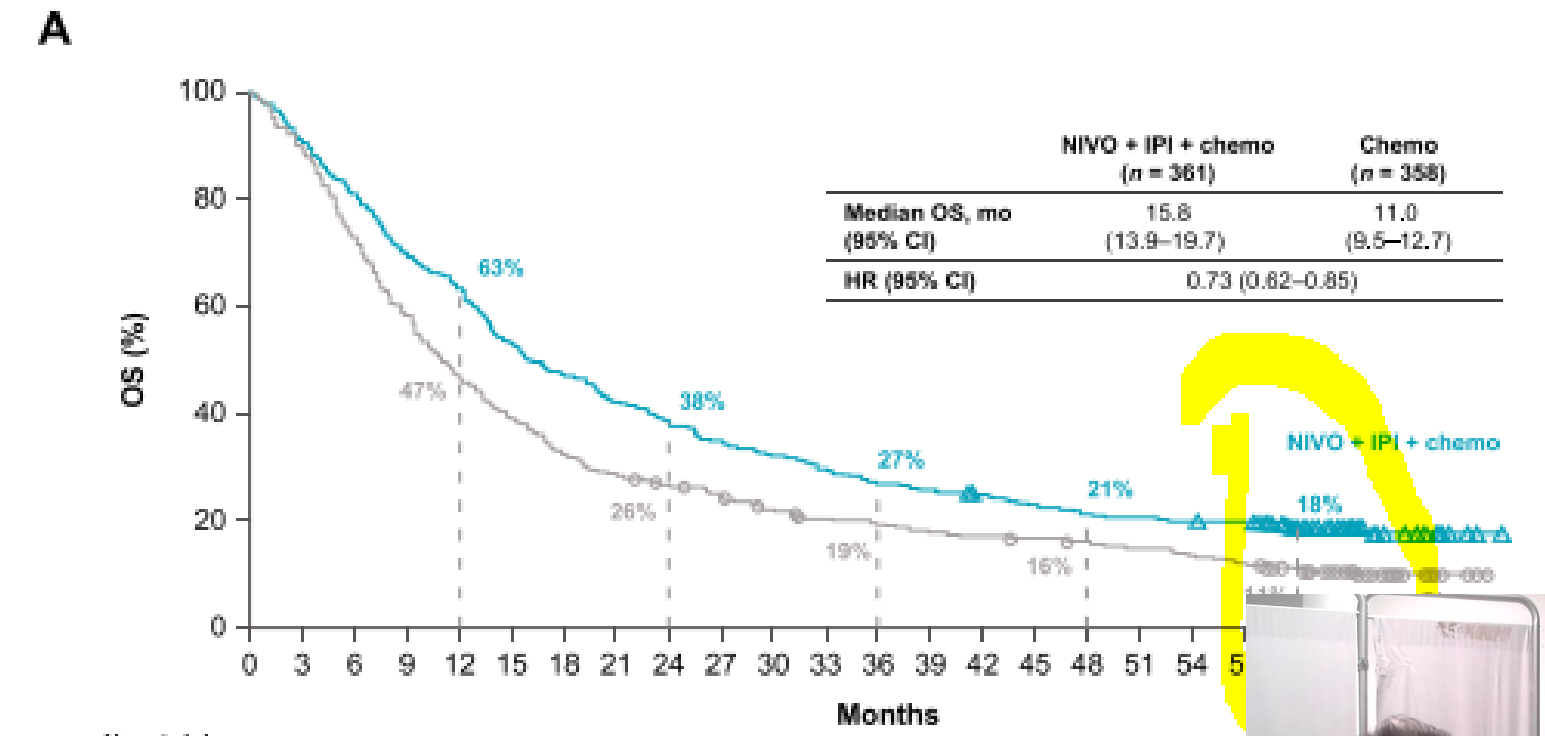
Five-year outcomes with first-line nivolumab plus ipilimumab with 2 cycles of chemotherapy versus 4 cycles of chemotherapy alone in patients with metastatic non-small cell lung cancer in the randomized CheckMate 9LA trial

Martin Reck [a,*,1], Tudor-Eliade Ciuleanu [b], Michael Schenker [c], Stephanie Bordenave [d], Manuel Cobo [e], Oscar Juan-Vidal [f], Niels Reinmuth [g], Eduardo Richardet [h], Enriqueta Felip [i], Juliana Menezes [j], Ying Cheng [k], Hideaki Mizutani [l], Bogdan Zurawski [m], Aurelia Alexandru [n], David P. Carbone [o], Shun Lu [p], Thomas John [q], Takekazu Aoyama [r], Diederik J. Grootendorst [r], Nan Hu [r], Laura J. Eccles [r], Luis G. Paz-Ares [s]

European Journal of Cancer 211 (2024) 114296



	NIVO + IPI + chemo (*n* = 361)	Chemo (*n* = 358)
Median OS, mo (95% CI)	15.8 (13.9–19.7)	11.0 (9.5–12.7)
HR (95% CI)	0.73 (0.62–0.85)	

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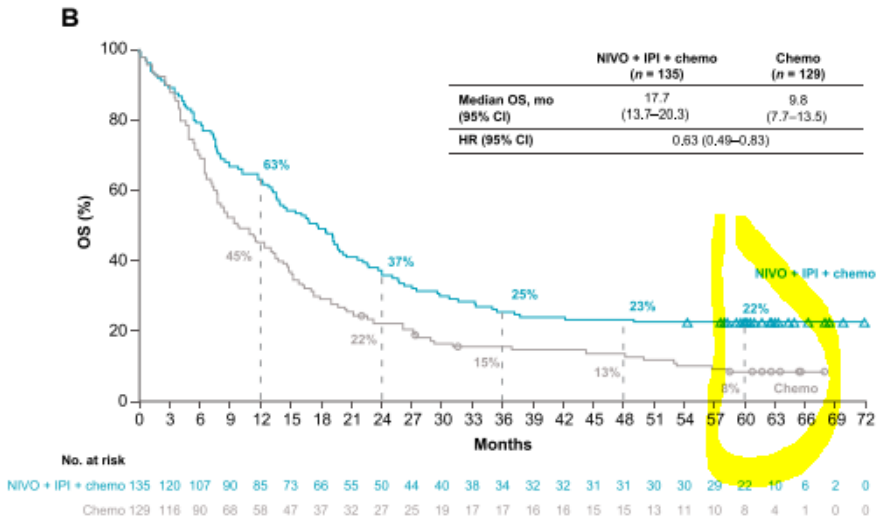

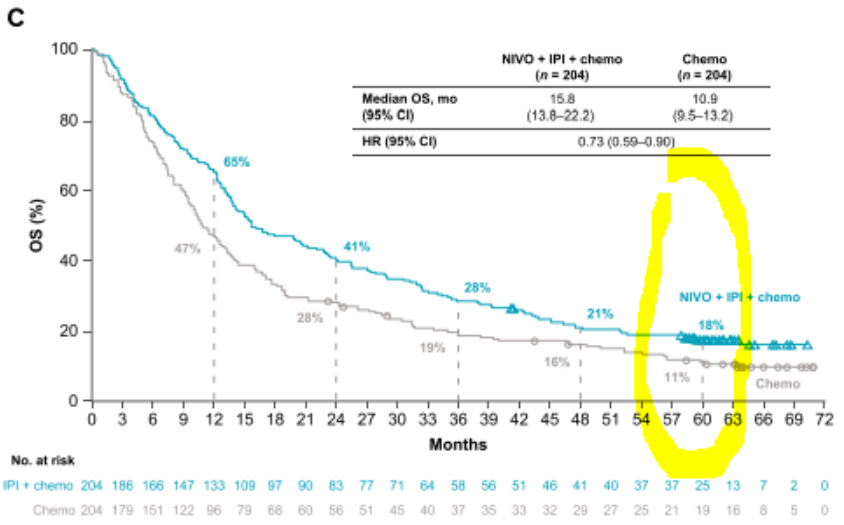

OS (PD-L1 <1*)

OS (P

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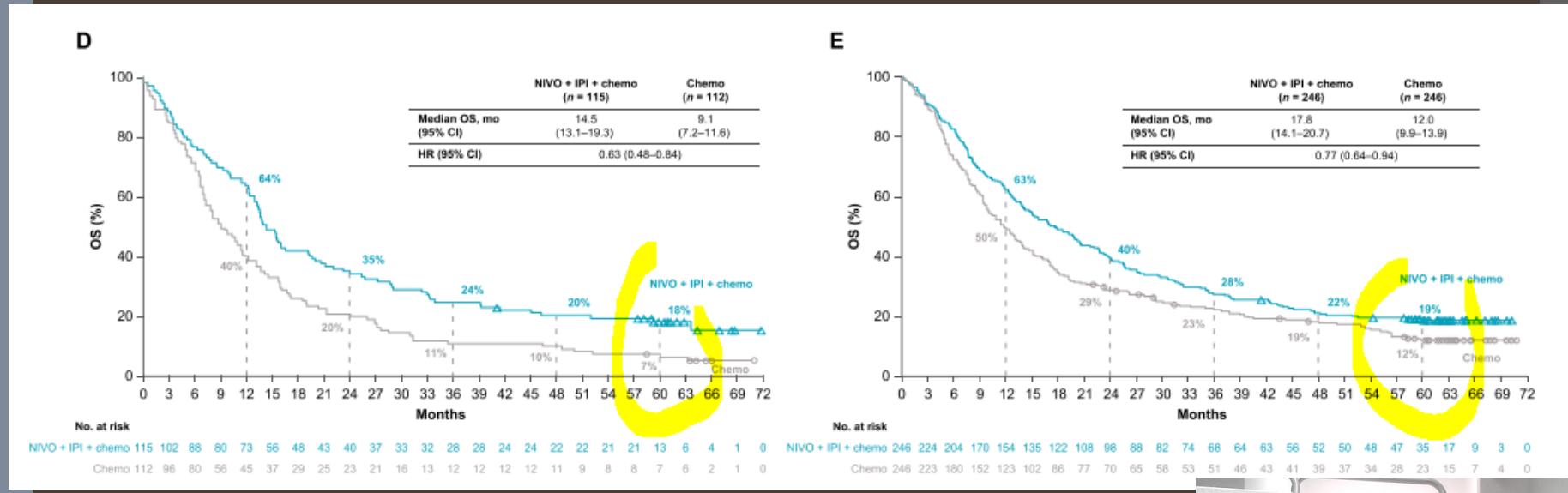

OS (SQ)

OS

Quarto punto: il contributo dell'immuno-chemioterapia nella malattia localmente avanzata

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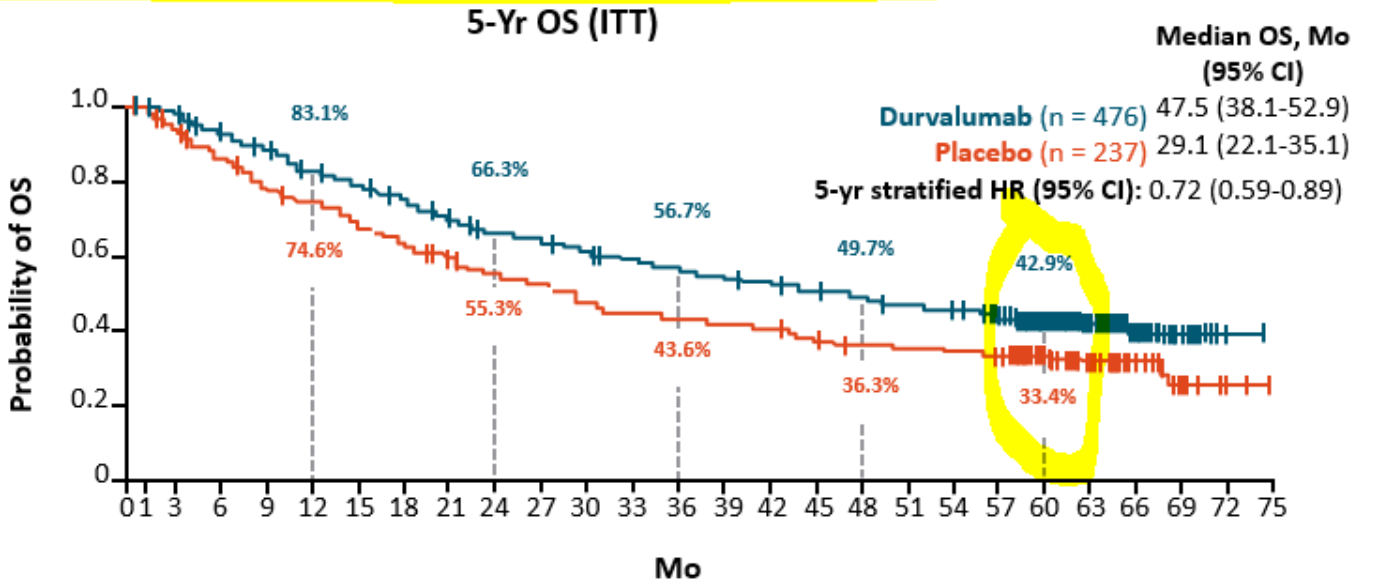
PACIFIC: Consolidation Durvalumab After Concurrent CRT for Locally Advanced, Unresectable, Stage III NSCLC



In February 2018, the FDA approved durvalumab for the treatment of unresectable stage III NSCLC without disease progression following

Spigel. J Clin Oncol. 2022;40:1301.

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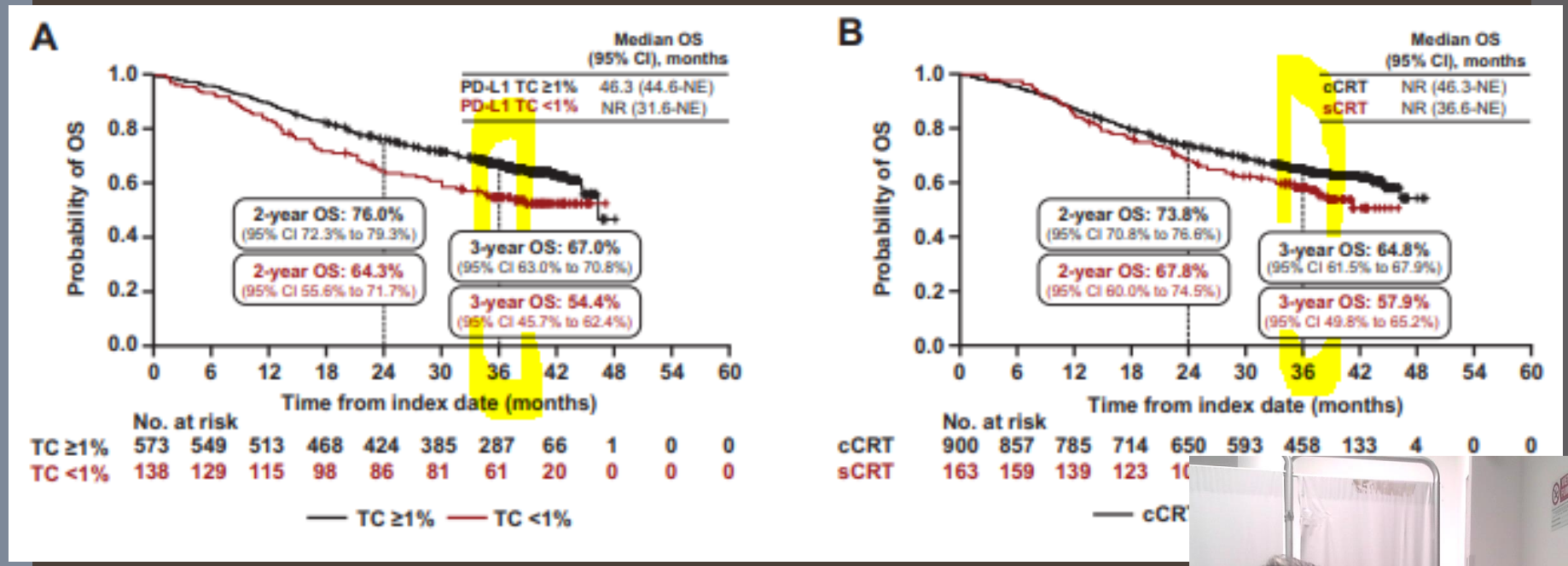
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

ORIGINAL RESEARCH

Real-world outcomes with durvalumab after chemoradiotherapy in patients with unresectable stage III NSCLC: interim analysis of overall survival from PACIFIC-R

A. R. Filippi[1,†], J. Bar[2,3], C. Chouaid[4], D. C. Christoph[5], J. K. Field[6], R. Fietkau[7], M. C. Garassino[8], P. Garrido[9], V. D. Haakensen[10], S. Kao[11], B. Markman[12], F. McDonald[13], F. Mornex[14], M. Moskovitz[15†], S. Peters[16], A. Sibille[17], S. Siva[18], M. van den Heuvel[19], P. Vercauter[20], S. Anand[21], P. Chander[21], M. Licour[22], A. R. de Lima[21], Y. Qiao[21] & N. Girard[23,24]



Quarto punto: il contributo dell'immuno-chemioterapia nella malattia resecabile

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Terapia neoadiuvante

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Considerations for Integrating IO Into the Care of Resectable Lung Cancer

Neoadjuvant

- Shorter treatment time
- Better treatment compliance
- Allows response assessment
- Option to tailor further therapy to response
- Potential downstaging
- Better antigen priming?
- Early reduction of micrometastases

Perioperative

- Eradicate micrometastases before and after surgery
- Risk of overtreatment
- Allows response assessment
- Longer treatment time

Adjuvant

- No risk of surgical delay
- No increased perioperative risks due to preop therapy
- Complete pathologic staging
- Longer treatment time

Desai. JAMA Oncol. 2023;9:135. Duan. Transl Lung Cancer Res. 2022;11:1247.

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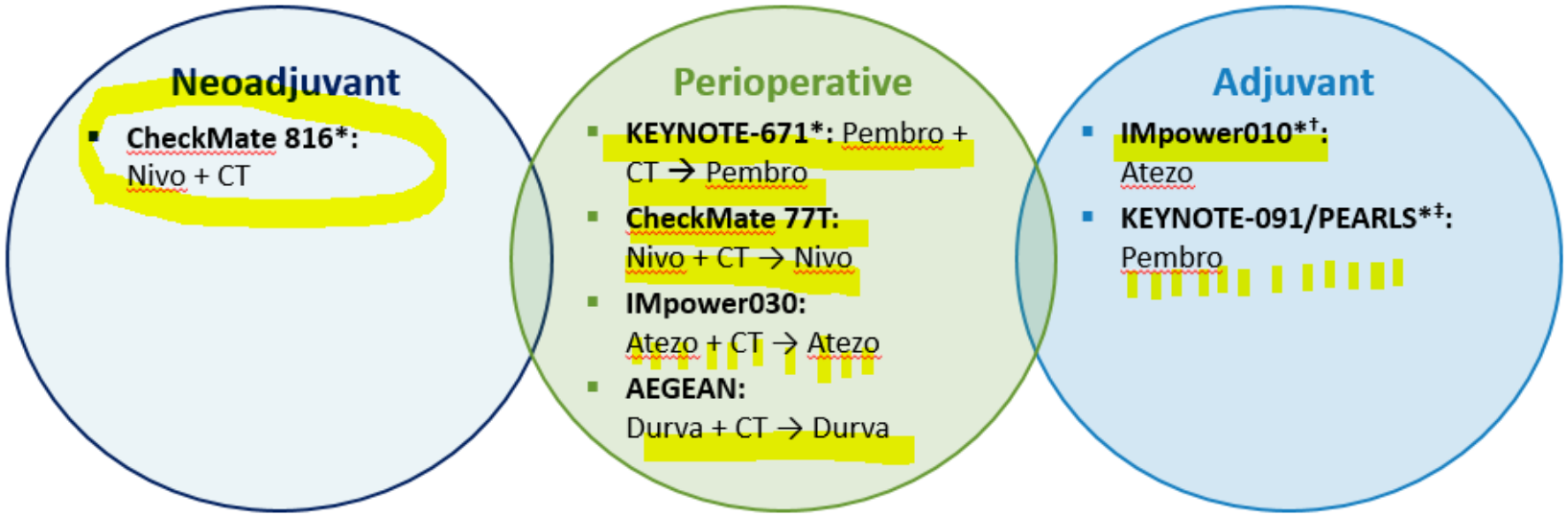
Evolving Immunotherapy-Based Treatment Landscape in Resectable NSCLC



*Trials leading to FDA approvals of denoted treatment regimen. †Mandatory chemotherapy. ‡Chemotherapy not mandatory.

NCT02998528. NCT03425643. NCT04025879. NCT03456063. NCT03800134. NCT02486718. NCT02504372.

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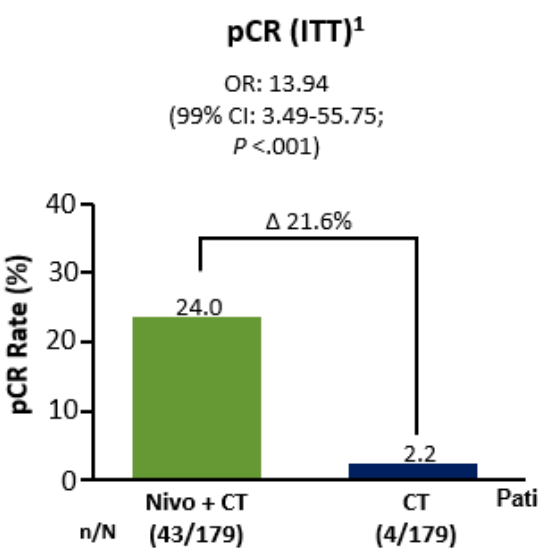
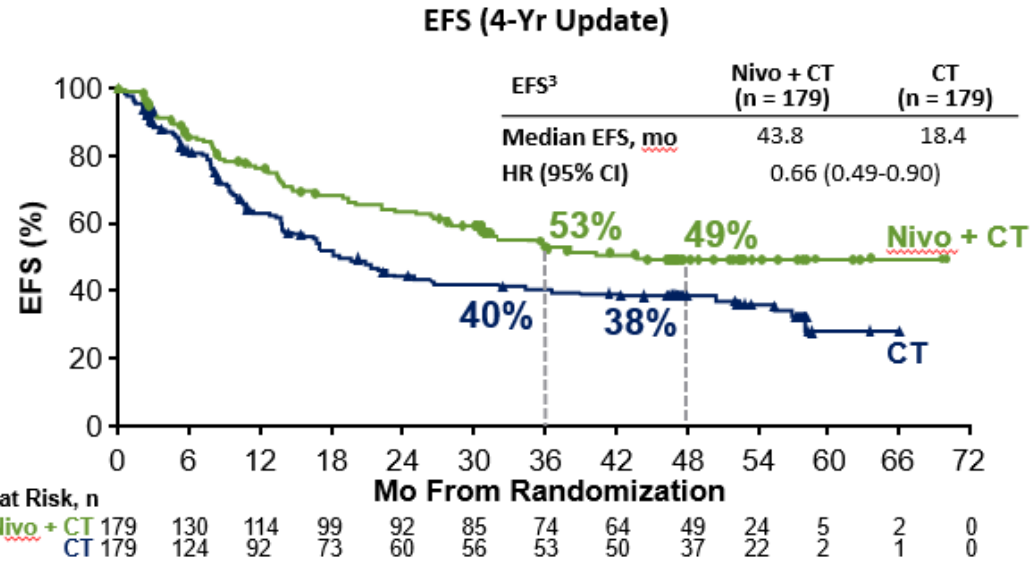
CheckMate 816: Neoadjuvant Nivolumab + CT for Resectable Stage IB-IIIA NSCLC

Phase III CheckMate 816: pCR and Updated 4-Yr EFS





FDA-approved in March 2022 for adults with resectable NSCLC (tumors ≥4 cm or N+) in combination with platinum doublet CT in the neoadjuvant setting[2]

1. Forde. NEJM. 2022;386:1973. 2. Nivolumab PI. 3. Spicer. ASCO 2024. Abstr LBA8010.

CheckMate 816: Neoadjuvant Nivolumab + CT for Resectable Stage IB-IIIA NSCLC

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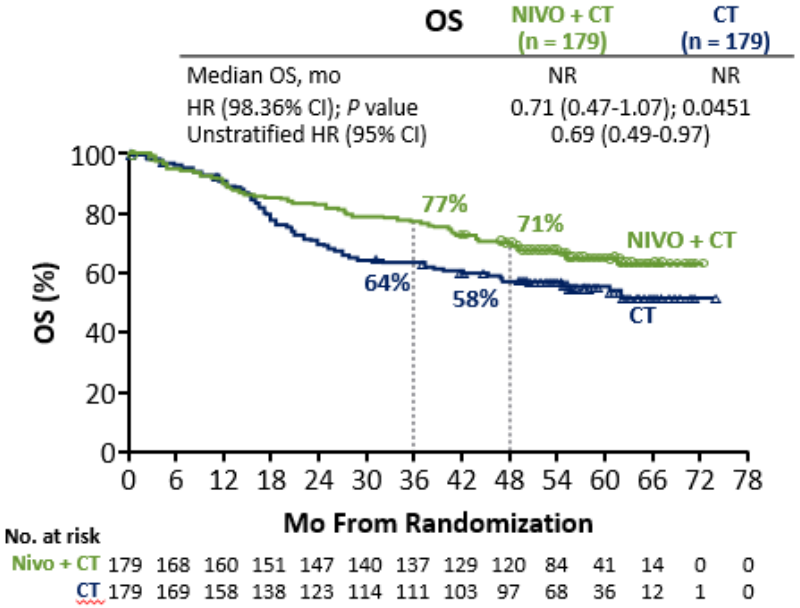
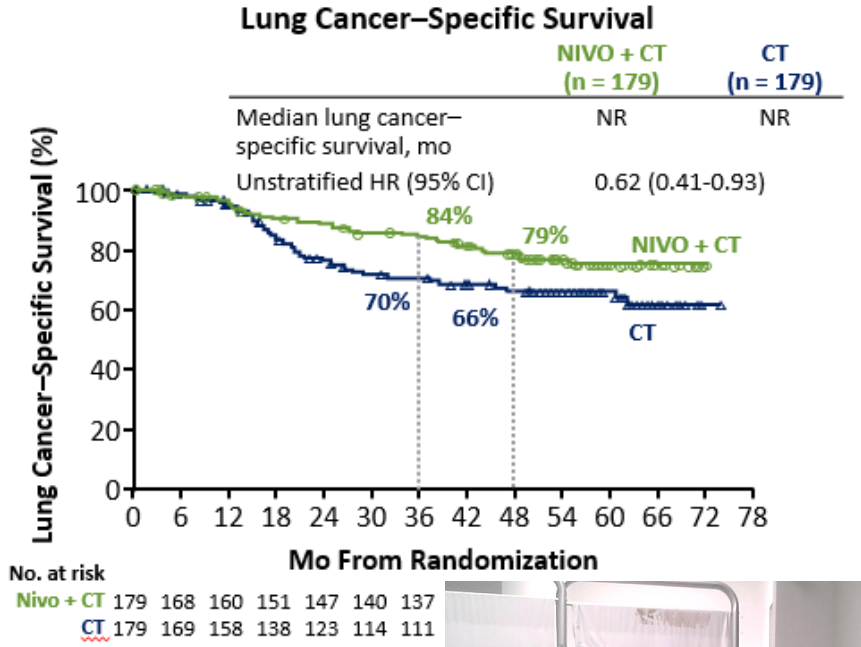
Phase III CheckMate 816: 4-Yr OS

- Patients who received NIVO + CT and had pCR continued to have improved OS vs those who did not (HR [95% CI]: 0.08 [0.02-0.34]; **4-yr OS rates: 95% vs 63%**)





Quarto punto: il contributo dell'immuno-chemioterapia nella malattia resecabile

Terapia adiuvante

IMpower010: Atezolizumab After CT in Adjuvant Setting for Resected Stage IB-IIIA NSCLC

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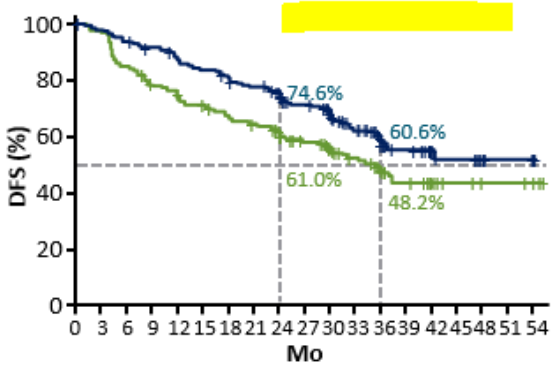
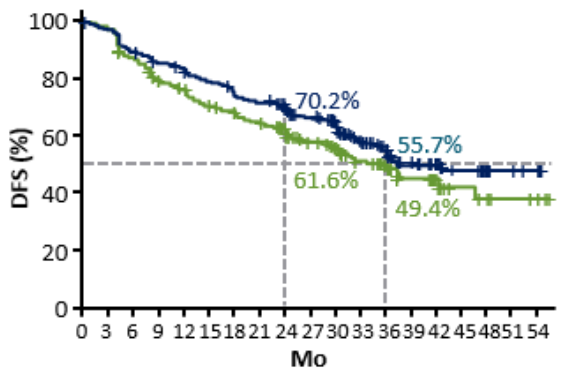
IMpower010: DFS

Stage II-IIIA NSCLC With PD-L1 TC ≥1%



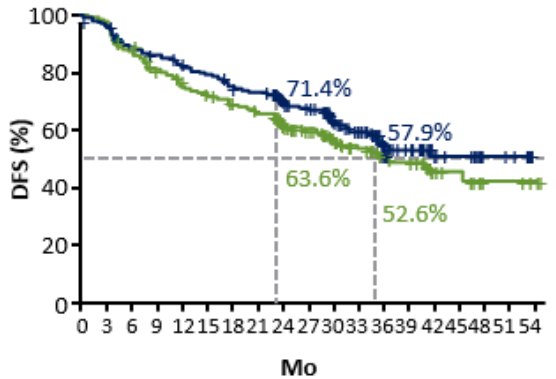
	Atezo (n = 248)	BSC (n = 228)
Median DFS, mo	NE	35.3
HR* (95% CI)	0.66 (0.50-0.88)	
P value	.0039	

All Stage II-IIIA NSCLC



	Atezo (n = 442)	BSC (n = 440)
Median DFS, mo	42.3	35.3
HR* (95% CI)	0.79 (0.64-0.96)	
P value	.0205	

ITT (Randomized Stage IB-IIIA NSCLC)



	Atezo (n = 507)	BSC (n = 498)
Median DFS, mo	NE	37.2
HR* (95% CI)	0.81 (0.67-0.99)	
P value	.0395†	

- DFS benefit seen across subgroups but primarily in patients with stage II-IIIA NS

*Stratified. †Did not cross the prespecified boundary for significance.

Felip. Lancet. 2021;398:1344. Wakelee. ASCO 2021. Abstr 8500.

IMpower010: Atezolizumab After CT in Adjuvant Setting for Resected Stage IB-IIIA NSCLC

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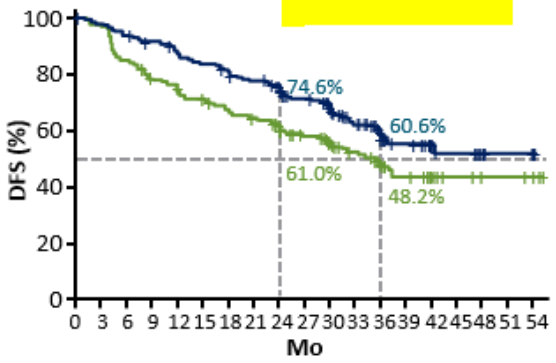
IMpower010: DFS

Stage II-IIIA NSCLC With PD-L1 TC ≥1%

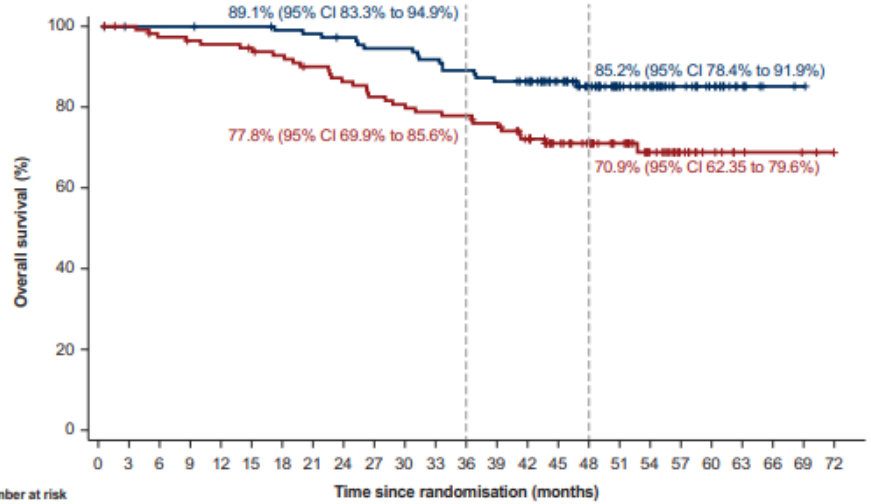


	Atezo (n = 248)	BSC (n = 228)
Median DFS, mo	NE	35.3
HR* (95% CI)	0.66 (0.50-0.88)	
P value	.0039	

Stage II-IIIA NSCLC With PD-L1 TC ≥50%

D

	Events, *n* (%)	Patients, *n*	Median overall survival, months (95% CI)	HR (95% CI)[a]
Atezolizumab group	16 (13.9)	115	NE (NE)	0.43 (0.24-0.78); *P* = 0.0045
Best supportive care group	32 (28.1)	114	NE (NE)	



Number at risk (number censored)																								
Atezolizumab	115 (0)	113 (2)	113 (2)	113 (2)	112 (3)	112 (3)	110 (4)	109 (4)	107 (5)	104 (5)	104 (5)	101 (5)	98 (5)	95 (5)	91 (9)	77 (23)	64 (35)	45 (54)	36 (63)	23 (76)	16 (83)	7 (92)	2 (97)	1 (98)	NE (NE)
Best supportive care	114 (0)	112 (2)	108 (3)	106 (4)	105 (4)	101 (6)	99 (6)	96 (7)	92 (7)	88 (7)	85 (7)	84 (7)	83 (7)	79 (8)	71 (13)	57 (26)	49 (34)	39 (44)	26 (56)	14 (68)	8 (74)	4 (78)	3 (79)	2 (80)	NE (NE)

- DFS benefit seen across subgroups but primarily in patients with stage II-IIIA NS

*Stratified. [†]Did not cross the prespecified boundary for significance.

Felip. Lancet. 2021;398:1344. Wakelee. ASCO 2021. Abstr 8500.

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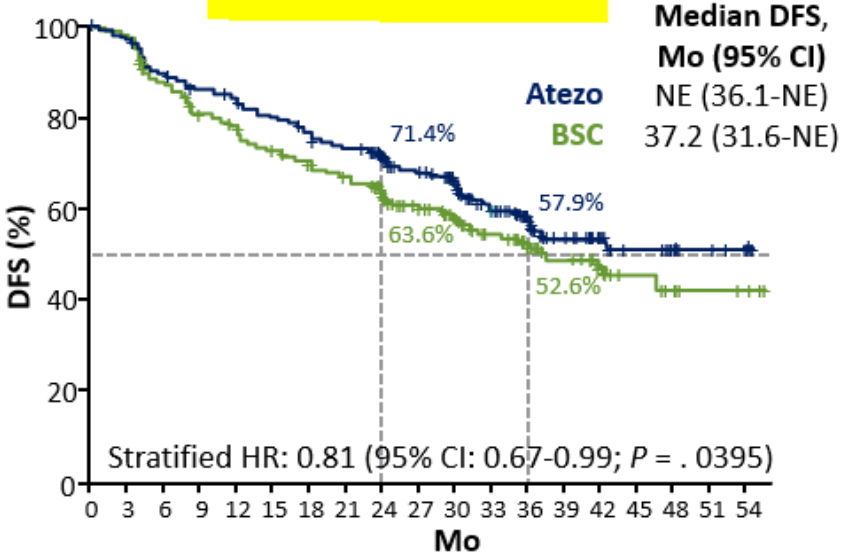
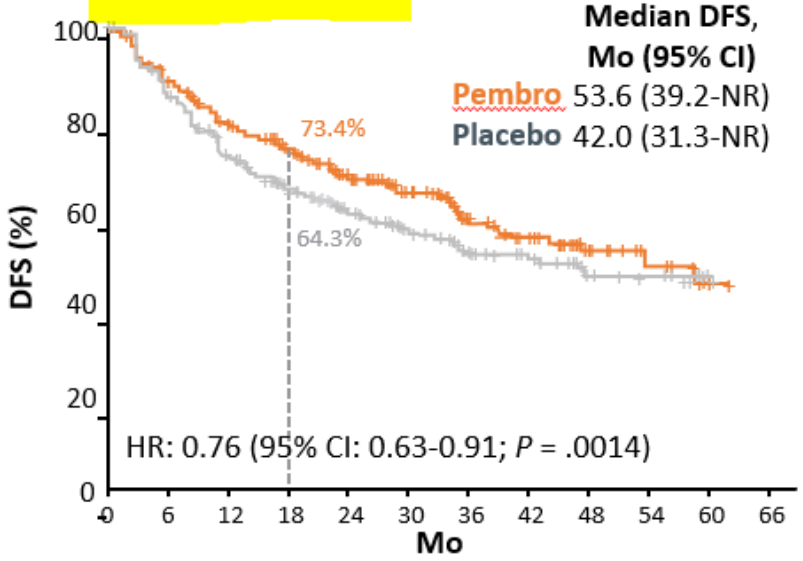
Adjuvant IO Trials: DFS in Overall Population (ITT)

IMpower010: ITT Population[1,2]



FDA-approved in October 2021 as **adjuvant treatment** following resection and platinum-based CT for adults with stage II-IIIA NSCLC and PD-L1 expression on ≥1% of tumor cells[3]

PEARLS/KEYNOTE-091: Overall Population[4,5]



FDA-approved in January 2023 as **adjuvant treatment** following resection and platinum-bas… IB-IIIA, includi…

1. Felip. Lancet. 2021;398:1344. 2. Wakelee. ASCO 2021. Abstr 8500. 3. Atezolizumab PI. 4. Paz-Ares. ESMO Virtual 2022. Abstr VP3-2022. 5. O'Brien. Lancet Oncol. 2022;23:1274. 6. Pembrolizumab PI.

Quarto punto: il contributo dell'immuno-chemioterapia nella malattia resecabile

Terapia «perioperatoria»

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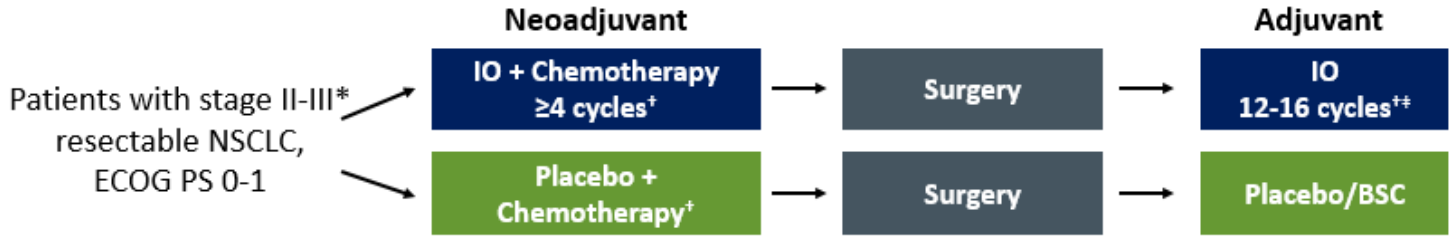
Ongoing Phase III Perioperative Studies in Resectable NSCLC



	KEYNOTE-671[1,2]	AEGEAN[3,4]	CheckMate 77T[5,6]	IMpower030[7,8]
IO agent	Pembrolizumab	Durvalumab	Nivolumab	Atezolizumab
Primary endpoint(s)	EFS, OS	pCR, EFS	EFS	EFS
Disease stage (TNM 8th ed.)	II-IIIB§	IIA-IIIB§	II-IIIB§	II-IIIB§
N	797	826	482	453
EGFR or *ALK* mut allowed	Yes	Amended to exclude	No	No
Chemotherapy backbone	≥4 cycles of cis/(gem or pemetrexed)	4 cycles of carbo/pac, carbo/pemetrexed, cis/gem, or cis/pemetrexed	≥4 cycles carbo/pac, cis/doc, carbo/pemetrexed, cis/pemetrexed, or carbo/pac	4 cycles of carbo/pemetrexed, carbo/*nab*-pac, cis/pemetrexed, or cis/gem

*Stages included differ between trials. †Dosage, timing, duration, and chemotherapy backbones differ between trials. ‡In contrast, Che
± RT. §Includes stages IIIB patients with N2 disease that is considered resectable. Cross trial comparisons are not intended. ‖Molecular

1. Spicer. ESMO 2023. Abstr LBA56. 2. NCT03425643. 3. Heymach. NEJM. 2023;389:1672. 4. NCT03800134.
5. Cascone. ESMO 2023. Abstr LBA1. 6. NCT04025879 7. Peters. Annal Oncol. 2019;30:Suppl 2. 8. NCT03456063.

KEYNOTE-671: Neoadjuvant and Adjuvant Pembrolizumab in Resectable NSCLC

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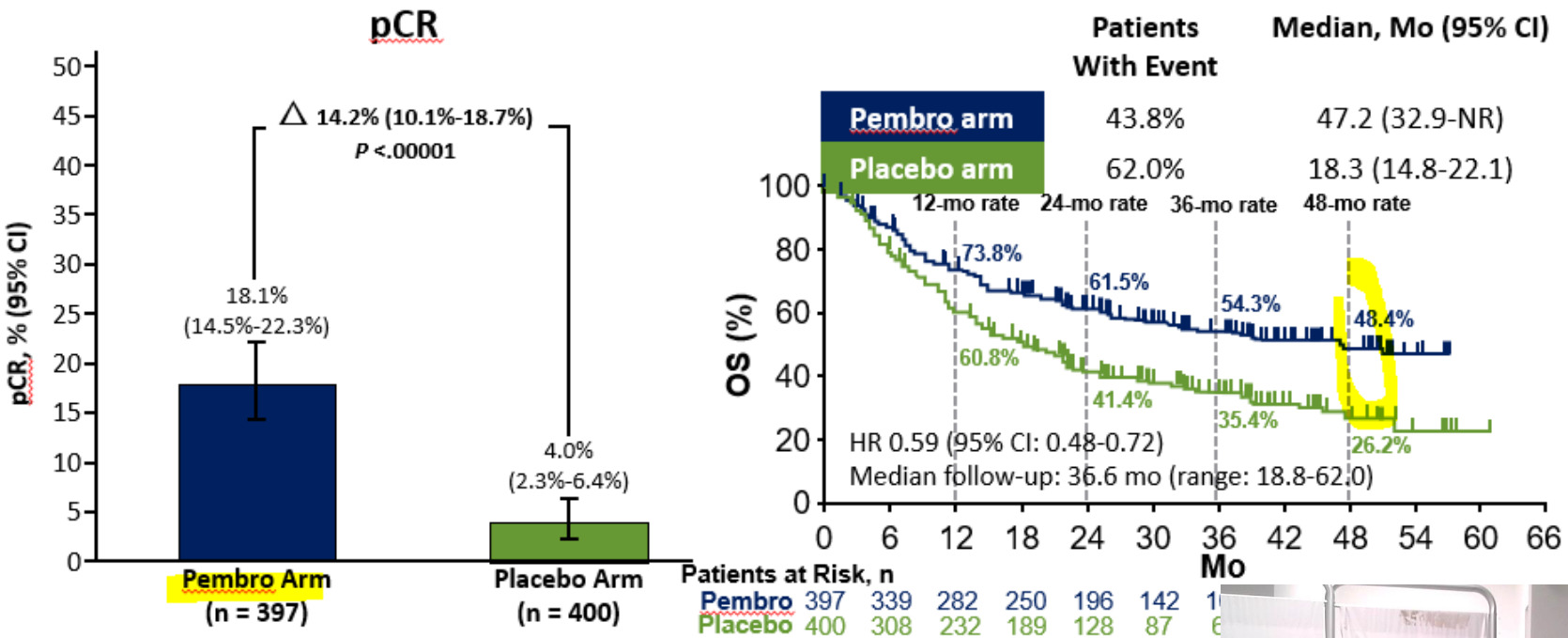
KEYNOTE-671: pCR and EFS



Wakelee. ASCO 2023. Abstr LBA100. Wakelee. NEJM. 2023;389:491. Spicer. ESMO 2023. Abstr LBA56.

KEYNOTE-671: Neoadjuvant and Adjuvant Pembrolizumab in Resectable NSCLC

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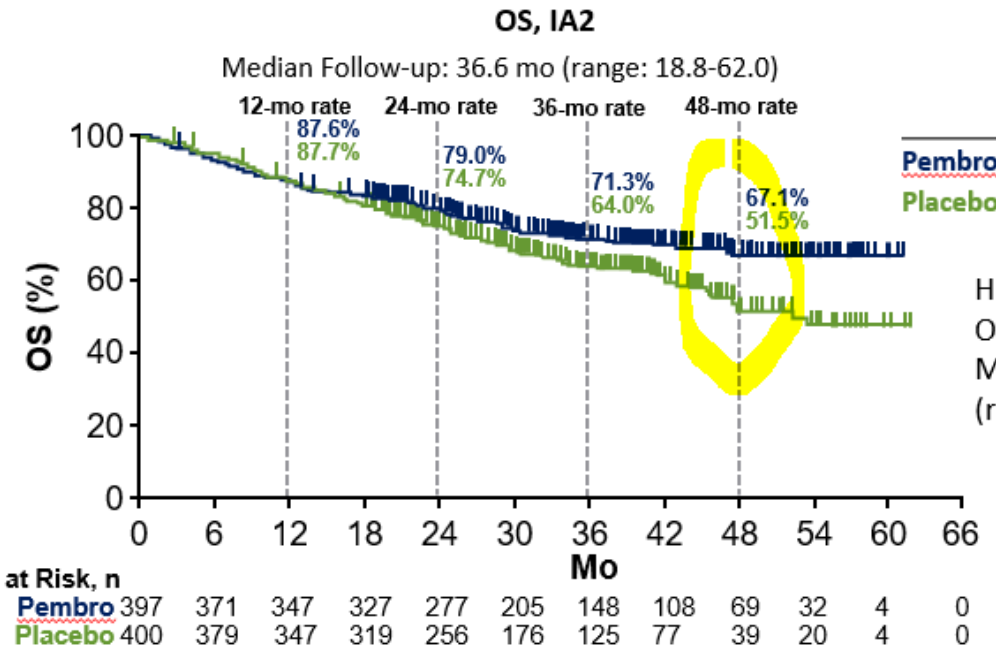
KEYNOTE 671: OS



	Patients With 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* = .00517
Median follow-up: 36.6 mo
(range: 18.8-62.0)

Spicer. ESMO 2023. Abstr LBA56.

CheckMate 77T: Neoadjuvant and Adjuvant Nivolumab in Resectable NSCLC

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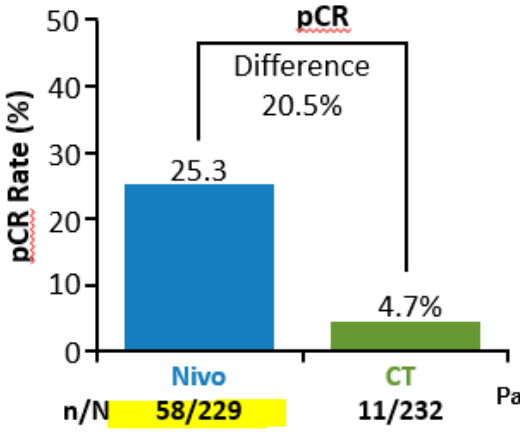
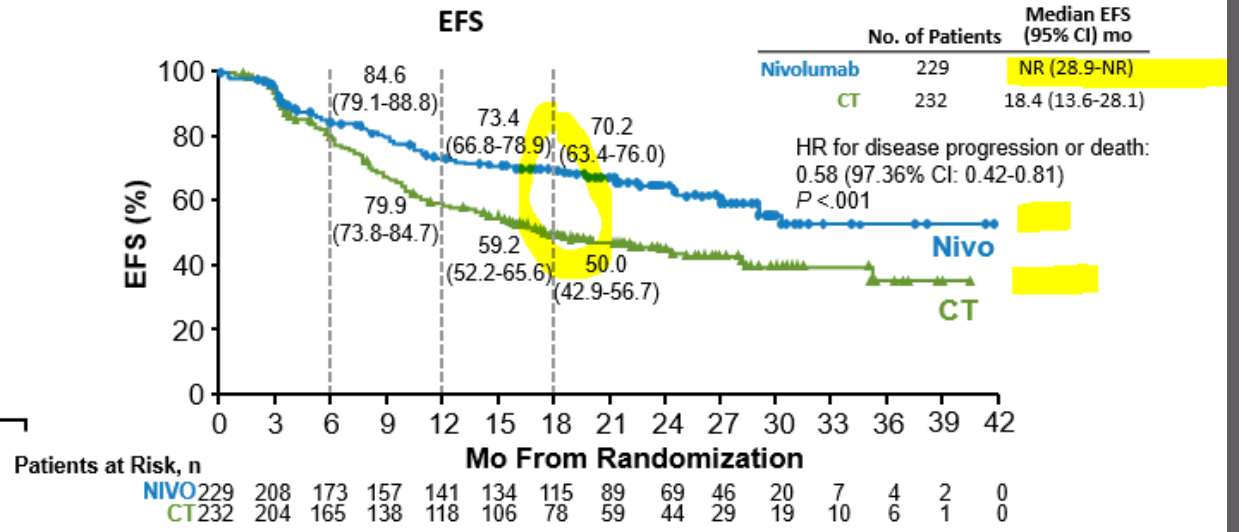
CheckMate 77T: pCR and EFS





Odds Ratio: 6.64 (95% CI: 3.40-12.97)

Cascone. NEJM. 2024;390:1756. Cascone. ESMO 2023. Abstr LBA1.

AEGEAN: Neoadjuvant and Adjuvant Durvalumab in Resectable NSCLC

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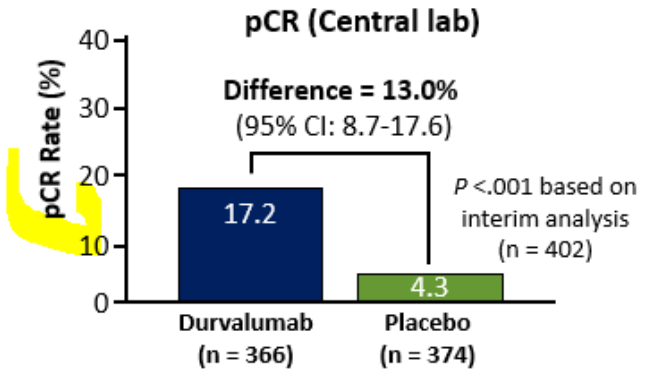
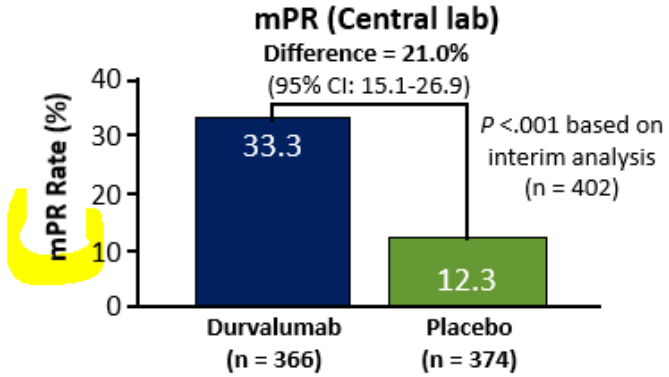
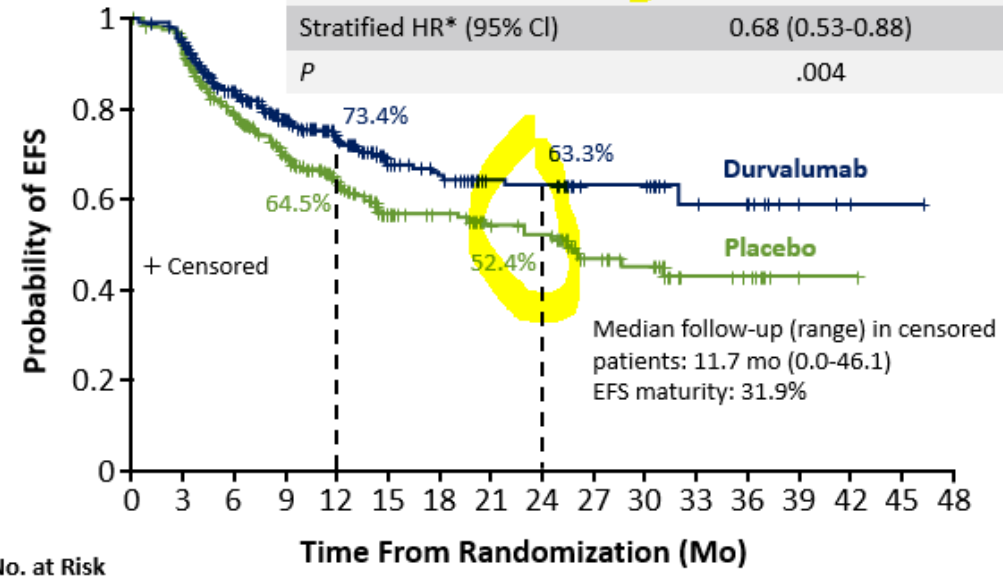
AEGEAN: pCR, mPR, and EFS





	Durvalumab	Placebo
No. events/no. patients (%)	98/366 (26.8)	138/374 (36.9)
mEFS, mo (95% CI)	NR (31.9-NR)	25.9 (18.9-NR)
Stratified HR* (95% CI)	0.68 (0.53-0.88)	
P	.004	



No. at Risk

Durvalumab	366	336	271	194	140	90	78	50	49	3
Placebo	374	339	257	184	136	82	74	53	50	3

Heymach. AACR 2023. Abstr CT005. Heymach. NEJM. 2023;389:1672.

Quinto punto: la malattia con mutazione di EGFR

Malattia «oncogene addicted» con driver molecolari sfruttabili

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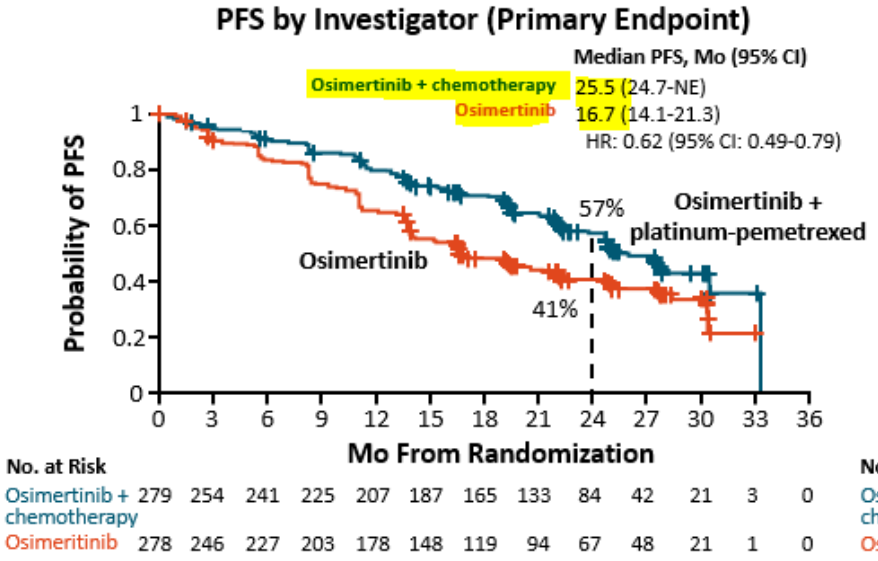
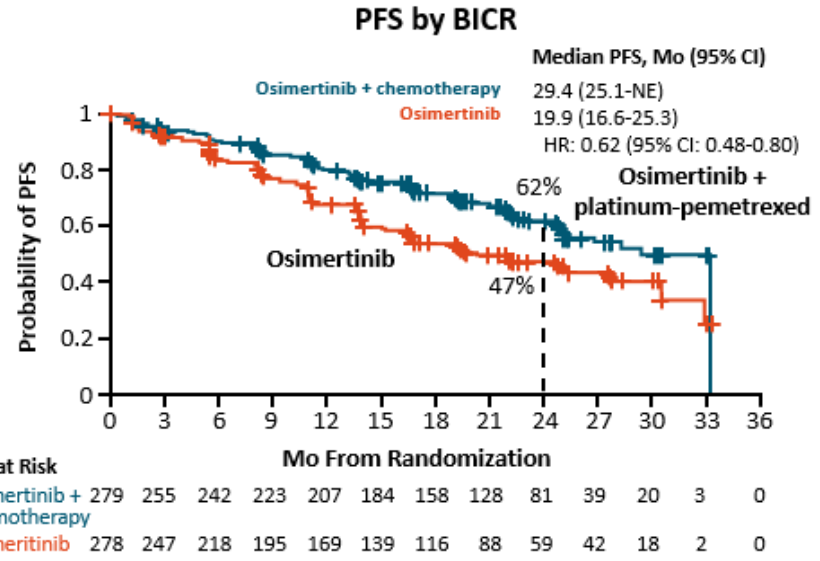
FLAURA2: Osimertinib ± Platinum-Based Chemotherapy in *EGFR*-Mutated Advanced NSCLC

FLAURA2: PFS





- PFS data per investigator currently 51% mature
  - Median follow-up 19.5 mo in osimertinib + chemotherapy arm, 16.5 mo in osimertinib monoth
- PFS benefit with addition of chemotherapy to osimertinib observed across all predefine

Planchard. NEJM. 2023;389:1935.

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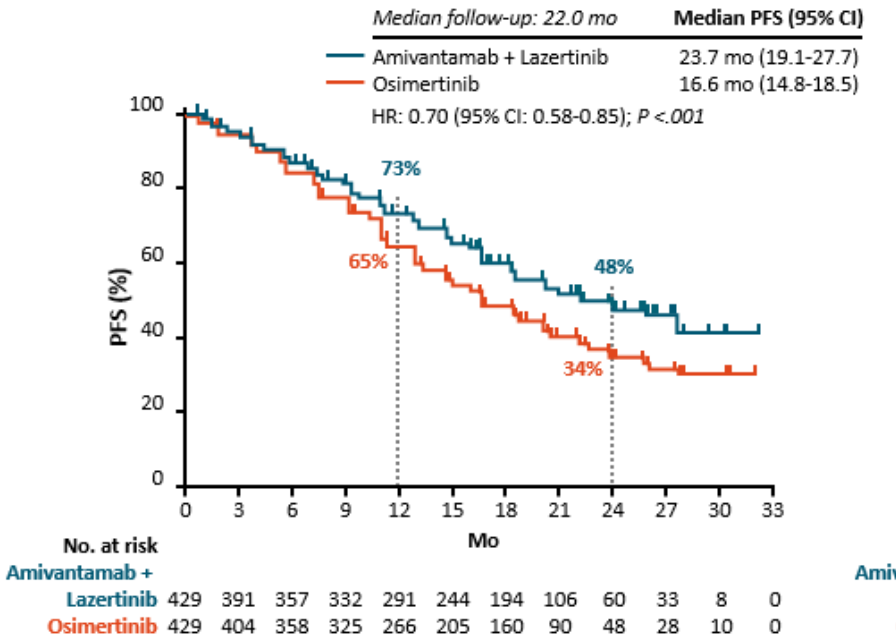
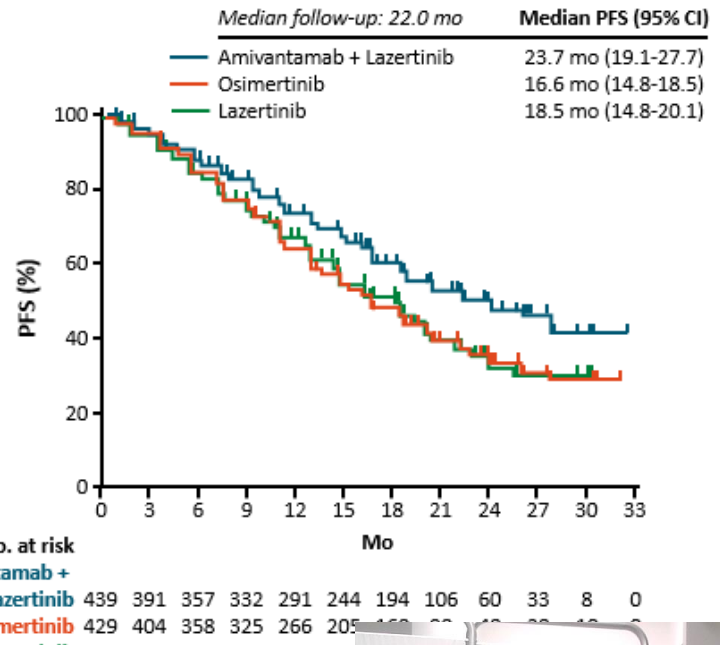
MARIPOSA: PFS by BICR (Primary Endpoint)





Cho. ESMO 2023. LBA14. Felip. ASCO 2024. Abstr 8504.

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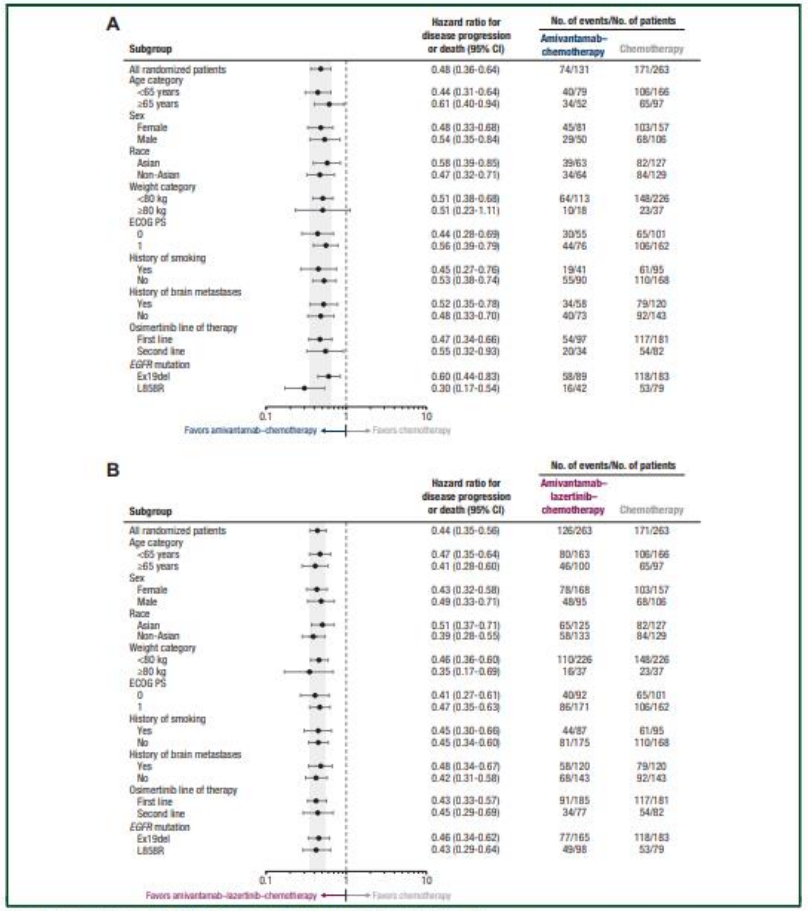

Figure 2. Progression-free survival by blinded independent central review of patient subgroups.
Shown are forest plots of progression-free survival in patient subgroups assessed by blinded independent central review for amivantamab—chemotherapy versus chemotherapy (A) and for amivantamab—lazertinib—chemotherapy versus chemotherapy (B). The efficacy analysis set included all randomized patients. The shaded areas indicate the 95% CI for the overall hazard ratio (all patients). CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status.

Annals of Oncology A. Passaro et al.

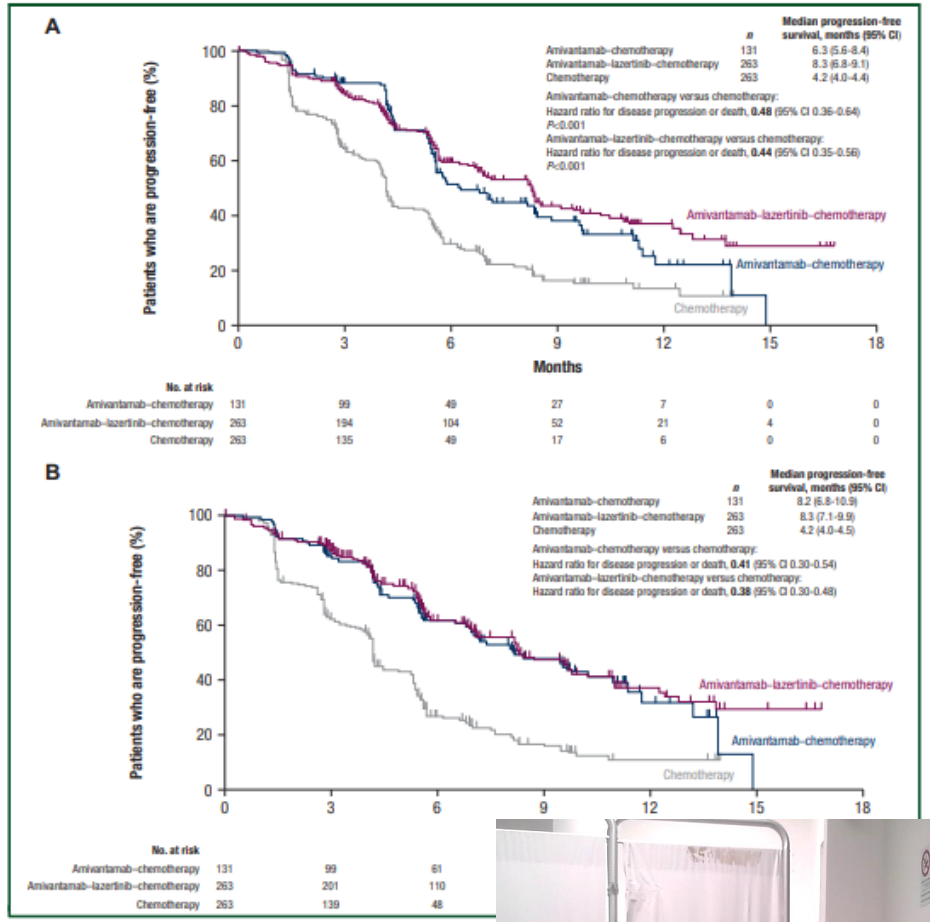

Figure 1. Progression-free survival by blinded independent central review and by inv
Shown are Kaplan—Meier estimates of progression-free survival assessed by blinded i
analysis set included all randomized patients. Tick marks indicate censoring of data. CI,

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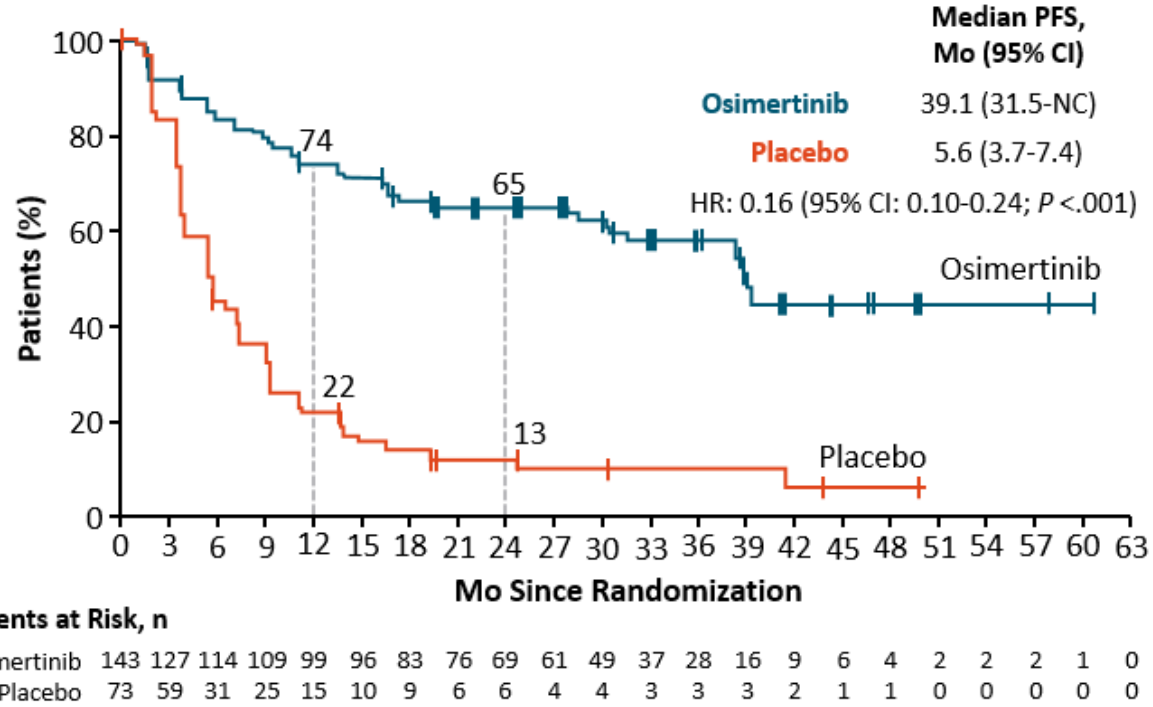
LAURA: Osimertinib vs Placebo After Definitive CRT in Unresectable Stage III *EGFR*-Mutated NSCLC

LAURA: PFS by BICR (Primary Endpoint)



Lu. NEJM. 2024;[Epub]. Ramalingam. ASCO 2024. Abstr LBA4.

- Median follow-up for PFS, mo (range):
  - Osimertinib: 22.0 (<0.1-60.6)
  - Placebo: 5.6 (<0.1-49.7)
- PFS favored osimertinib across all patient subgroups

ADAURA: Adjuvant Osimertinib for Early-Stage *EGFR*-Mutated NSCLC

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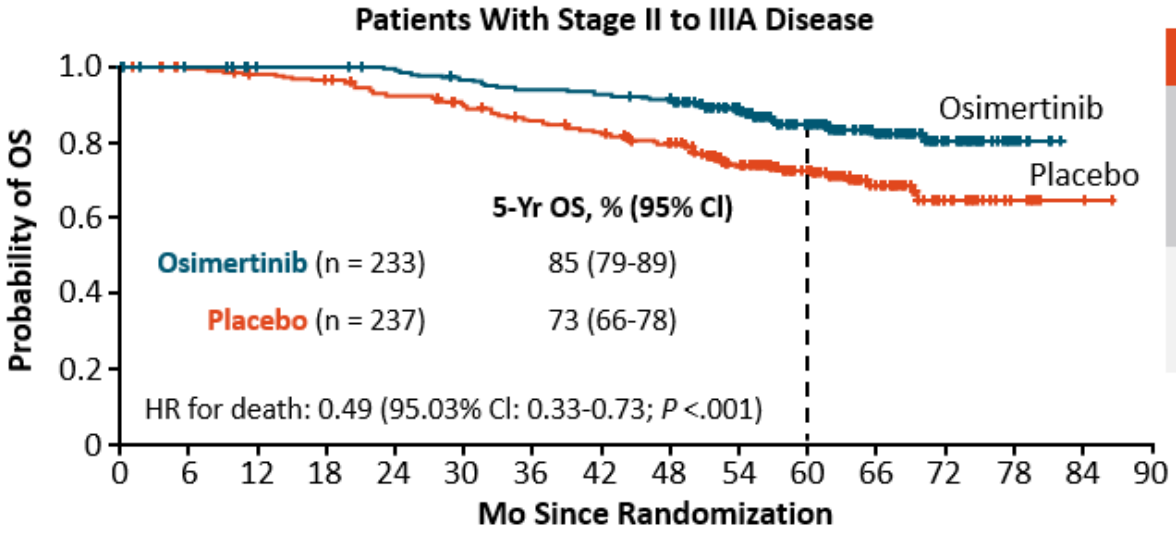
ADAURA: Overall Survival in Patients With Stage II-IIIA NSCLC

- Median follow-up for OS: 61.5 mo



5-Yr OS, %	Osi	Pbo	HR
Disease stage			
▪ IB	94	88	0.44
▪ II	85	78	0.63
▪ IIIA	85	67	0.37
Adjuvant CT			
▪ Yes	87	77	0.49
▪ No	88	79	0.47

Tsuboi. NEJM. 2023;389:137. Herbst. ASCO 2023. Abstr LBA3.

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ADAURA: Adjuvant Osimertinib for Early-Stage *EGFR*-Mutated NSCLC

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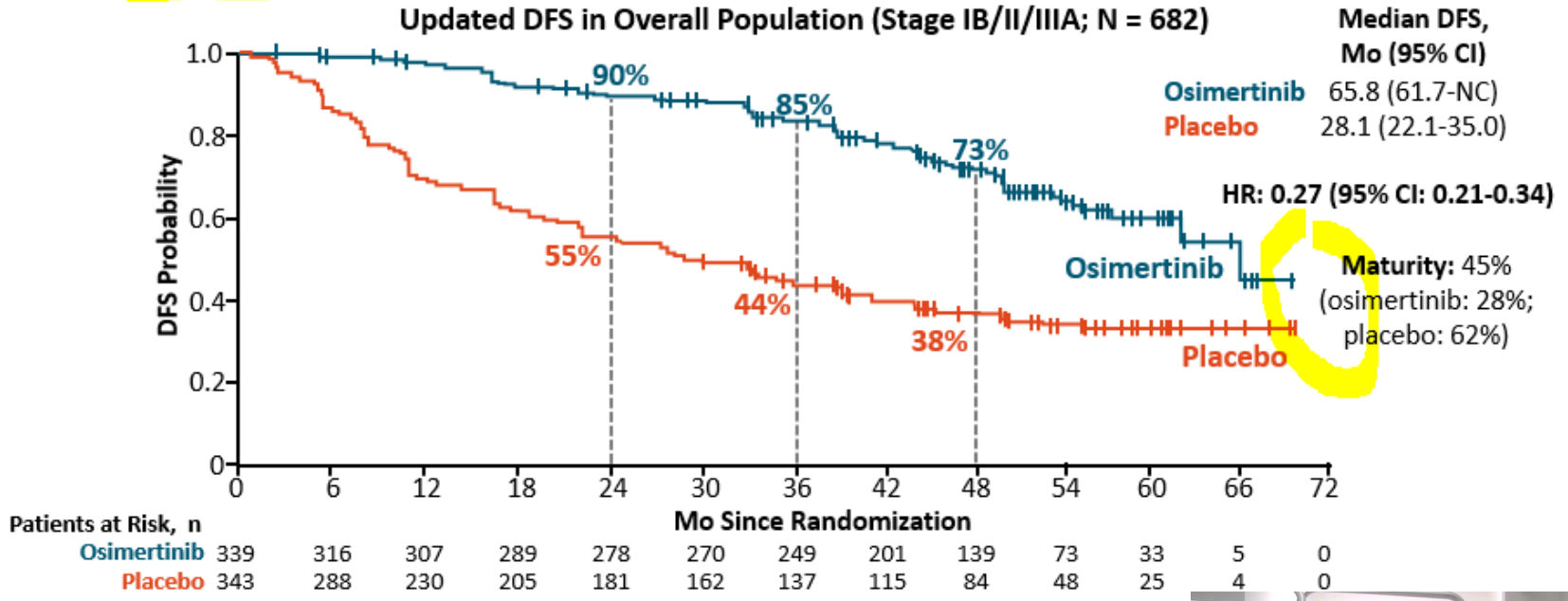
ADAURA: Disease-Free Survival in Patients With Stage IB-IIIA NSCLC



- FDA approved in December 2020 for adjuvant treatment of adults with s
  EGFR+ (del19 or L585R) NSCLC following tumor resection ± adjuvant che

Herbst. J Clin Oncol. 2023;41:1830. Osimertinib PI.

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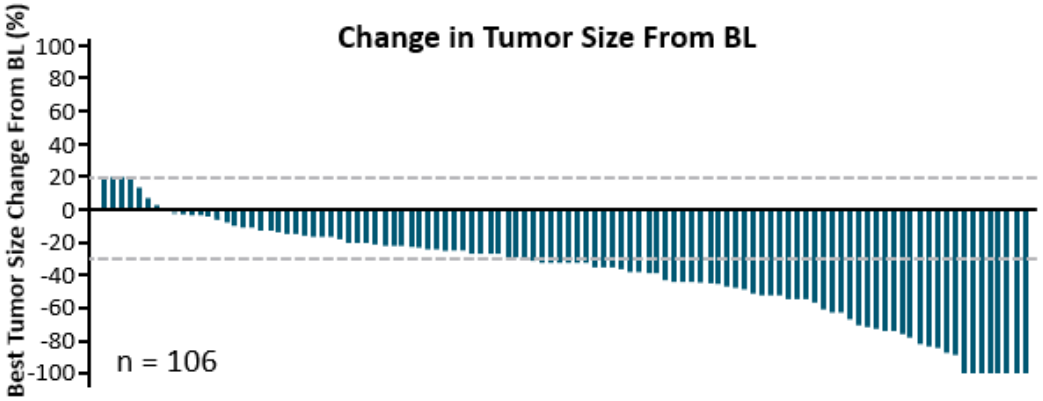
WU-KONG1: Antitumor Activity



Tumor Response per IRC	All Patients (n = 107)	
	Overall	Confirmed
ORR, % (97.5% CI)	53.3 (42.0-64.3)	44.9 (34.0-56.1)
CR, n (%)	3 (2.8)	2 (1.9)
PR, n (%)	54 (50.5)	46 (43.0)
SD, n (%)	44 (41.1)	--
PD, n (%)	8 (7.5)	--
Not evaluable, n (%)	3 (2.8)	--

- Median DoR not reached
- 9-month DoR rate: 57%
- Sunvozertinib activity noted regardless of previous amivantamab therapy
  - ORR in patients with prior amivantamab: 50%
  - ORR in patients without prior amivantamab: 53.8%

Yang. ASCO 2024. Abstr 8513. Reproduced with permission.

Sesto punto: la malattia con fusione di ALK

Malattia «oncogene addicted» con driver molecolari sfruttabili

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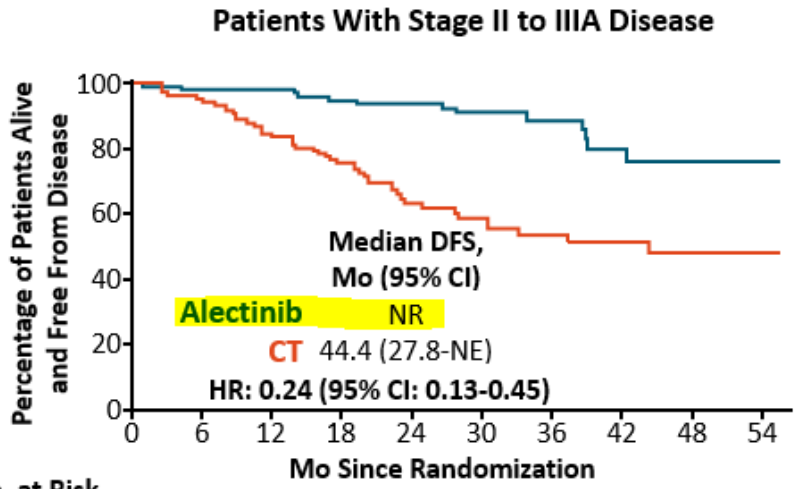
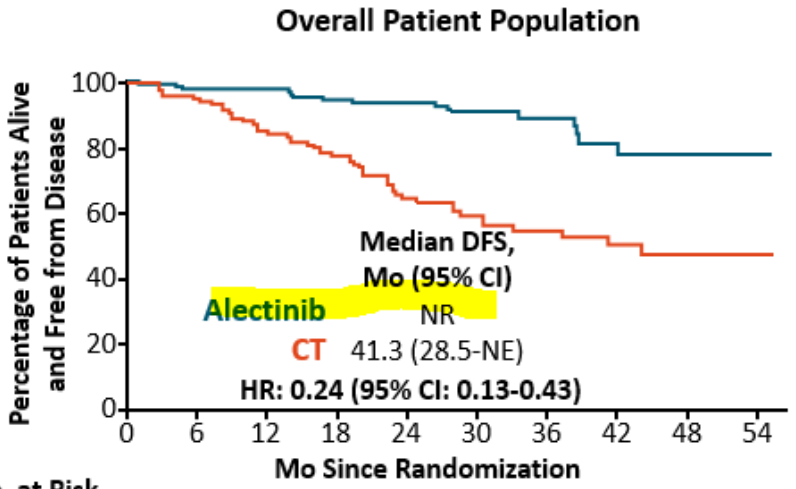
ALINA: Adjuvant Alectinib for Early-Stage *ALK* Fusion–Positive NSCLC

ALINA: Disease-Free Survival (Primary Endpoint)





No. at Risk										
Alectinib	116	111	111	107	67	49	35	21	10	3
CT	115	102	88	79	48	35	23	17	10	2

No. at Risk										
Alectinib	130	123	123	118	74	55	39	22	10	3
CT	127	112	98	89	55	41	27	18	11	2

- DFS benefit with alectinib vs chemotherapy observed across all subgroups of the ITT population, including age, sex, race, baseline ECOG PS, tobacco use history, tumor stage, ar

Wu. NEJM. 2024;390:1265.

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ALINA: Adjuvant Alectinib for Early-Stage *ALK* Fusion–Positive NSCLC

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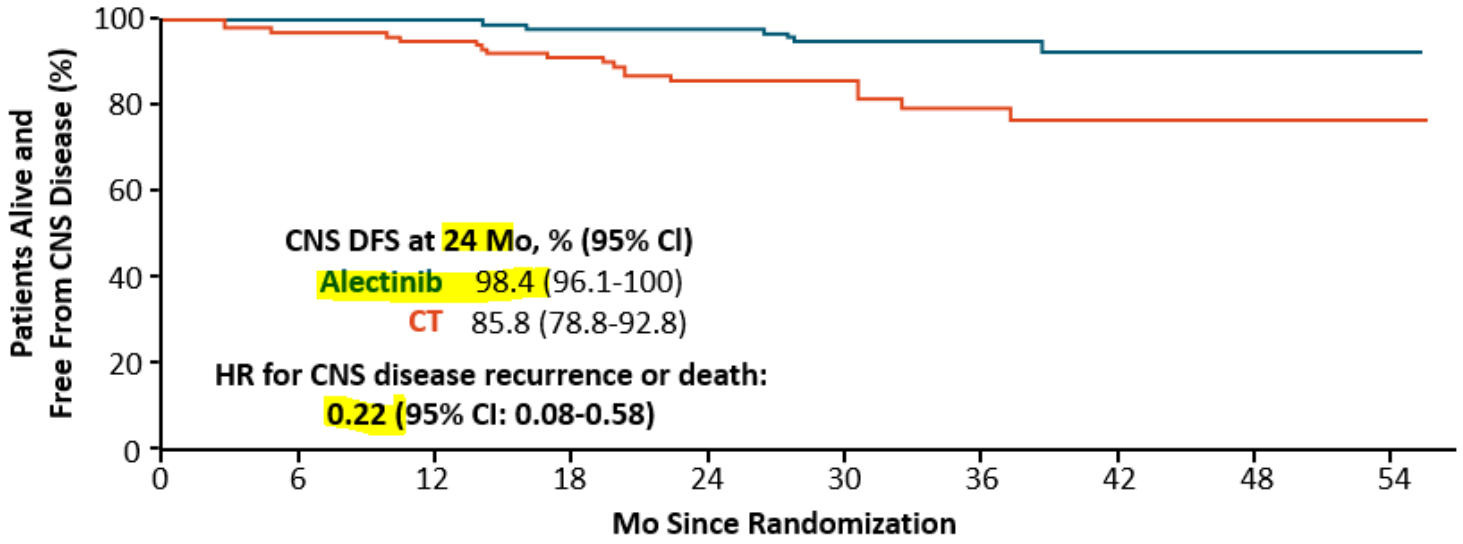
ALINA: CNS Disease-Free Survival



No. at Risk										
Alectinib	130	124	124	118	74	55	39	22	10	3
CT	127	113	98	90	57	43	27	18		

Wu. NEJM. 2024;390:1265.

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CROWN 5-Yr Update: First-line Lorlatinib vs Crizotinib in *ALK*-Positive NSCLC

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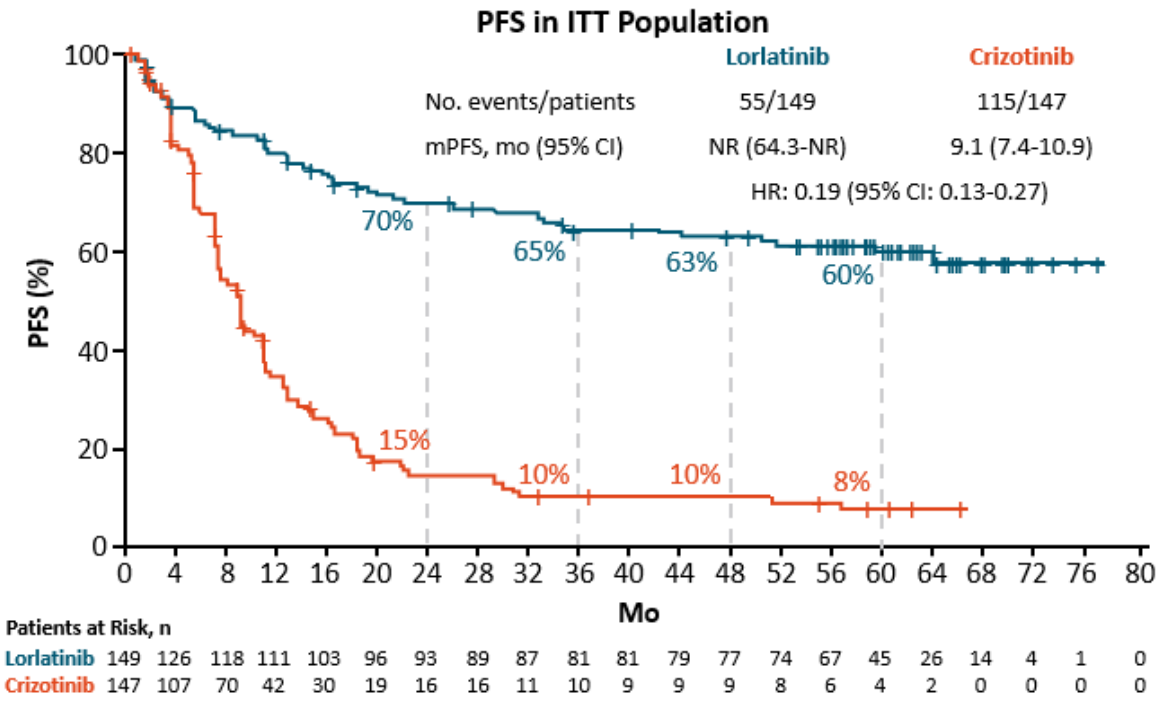
CROWN 5-Yr Update: PFS by Investigator



- PFS favored lorlatinib vs crizotinib among all patient subgroups, including with/without BL brain metastases or poor prognostic biomarkers*
- HR for PFS (95% CI):
  - With BL brain mets: **0.08** (0.04-0.19)
  - Without BL brain mets: **0.24** (0.16-0.36)
- OS events needed for assessment NR; follow-up ongoing

*EML4::AL

Solomon. ASCO 2024. Abstr LBA8503. Solomon. JCO. 2024;[Epub].

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Sesto punto: la malattia con fusione di ROS

Malattia «oncogene addicted» con driver molecolari sfruttabili

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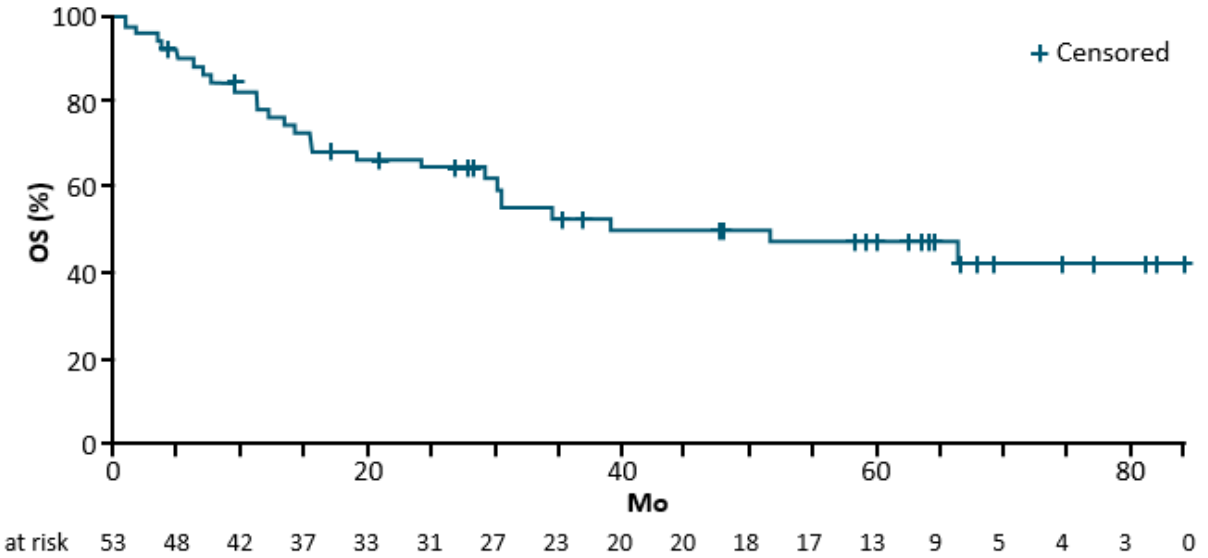
Crizotinib in *ROS1*-Rearranged NSCLC (Update): OS



- **Median OS:** 51.4 mo (95% CI: 29.3-NR)
- **Median follow-up period:** 62.6 mo
- **48-mo OS rate:** 51%

Shaw. Ann Oncol. 2019.390;1121.

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Guideline Recommendations for the Management of *ROS1*-Rearranged NSCLC

***ROS1* Rearrangement Confirmed**

Rearrangement confirmed prior to 1L systemic therapy

Preferred
- Crizotinib
- Entrectinib
- Repotrectinib

Other recommended
- Ceritinib

Progression (Subsequent Therapy)

Rearrangement confirmed during 1L systemic therapy

Complete planned systemic therapy (including maintenance therapy), or interrupt then →
- Crizotinib (preferred)
- Entrectinib (preferred)
- Repotrectinib (preferred)
- Ceritinib

NCCN clinical practice guidelines in oncology: NSCLC. v7.2024. nccn.org.

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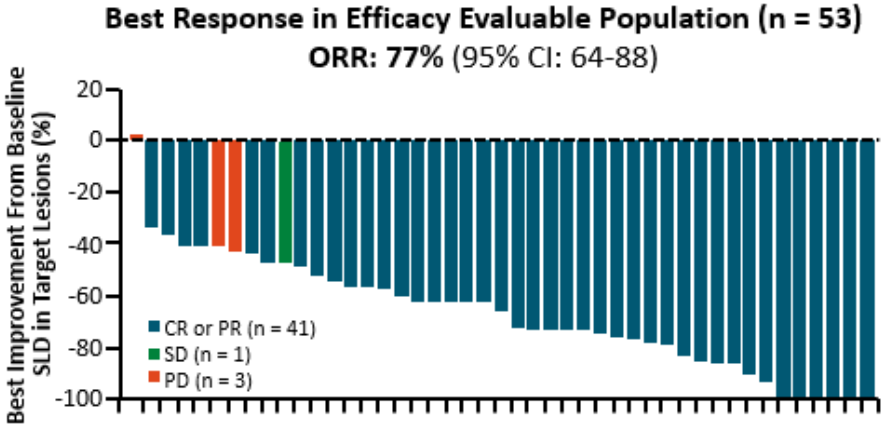
Entrectinib in *ROS1*-Rearranged NSCLC: Efficacy



Parameter[2]	Median, mo	95% CI
DoR	20	13.9-28.6
PFS	15.7	11.0-21.1
OS	47.8	44.1-NR

- In 25 patients with measurable baseline CNS disease:
  - Intracranial ORR: 80% (95% CI: 59.3-93.2)
  - Median intracranial DoR: 12.9 mo
  - Median intracranial PFS: 8.8 mo

1. Drilon. Lancet Oncol. 2020;21:261. 2. Drilon. J Thorac Oncol Clin Res Rep. 2022;3:100332.

Repotrectinib in *ROS1*-Rearranged NSCLC (TRIDENT-1)

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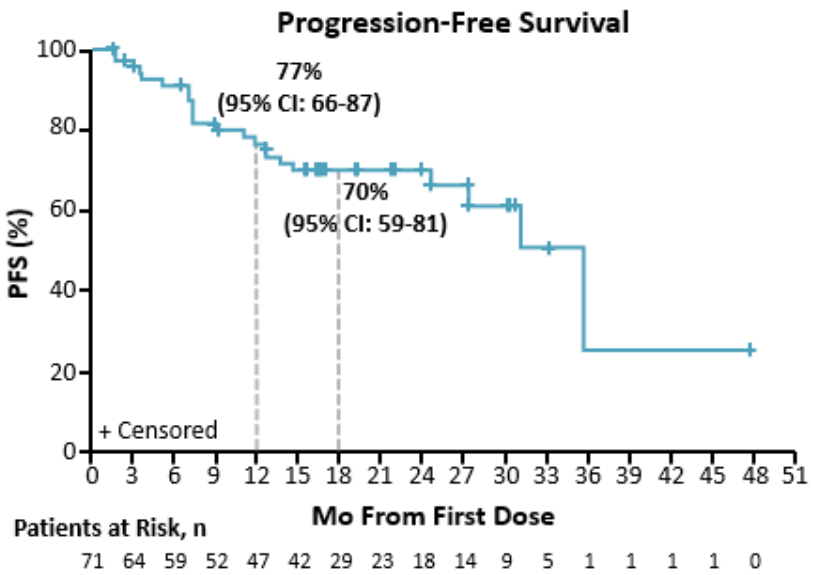
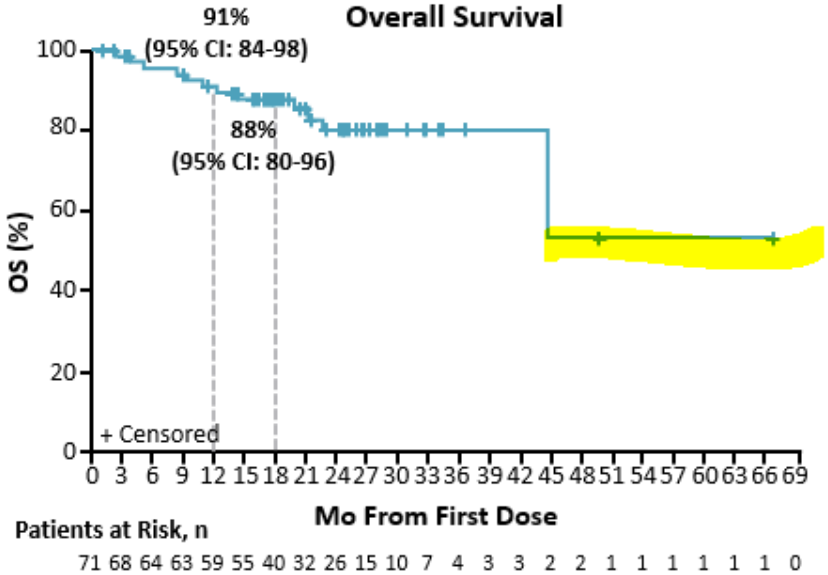
TRIDENT-1 (ROS1 TKI–Naive Cohort): PFS and OS



Patient Subgroup	mPFS, mo (95% CI)
All (n = 71)	35.7 (27.4-NE)
Prior CT (n = 20)	31.1 (24.6-NE)
No prior CT (n = 51)	NE (27.4-NE)



Patient Subgroup	mOS, mo (95% CI)
All (n = 71)	NE (44.4-NE)
Prior CT (n = 20)	
No prior CT (n = 51)	

Cho. WCLC 2023. Abstr OA03.06. Drilon. NEJM. 2024;390:118.

Median follow-up: 24.0 mo (range: 14.2-66.6).

Repotrectinib in *ROS1*-Rearranged NSCLC (TRIDENT-1)

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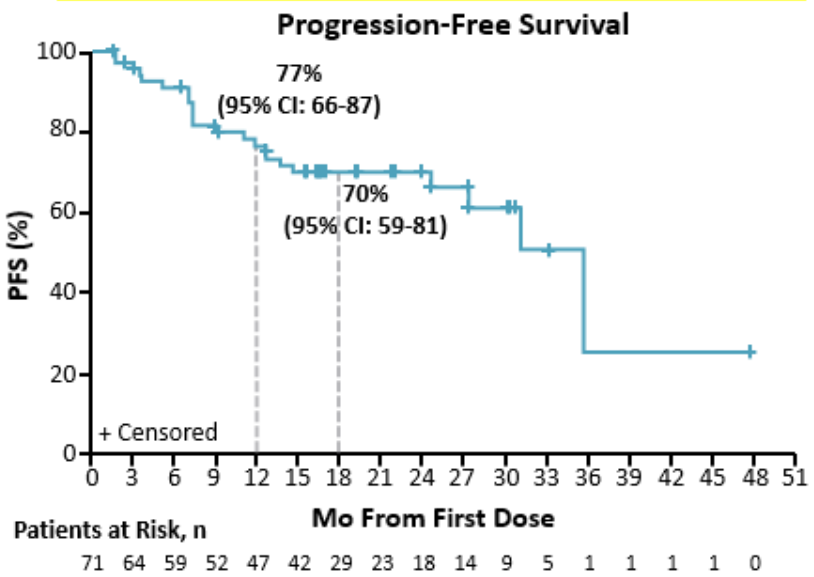

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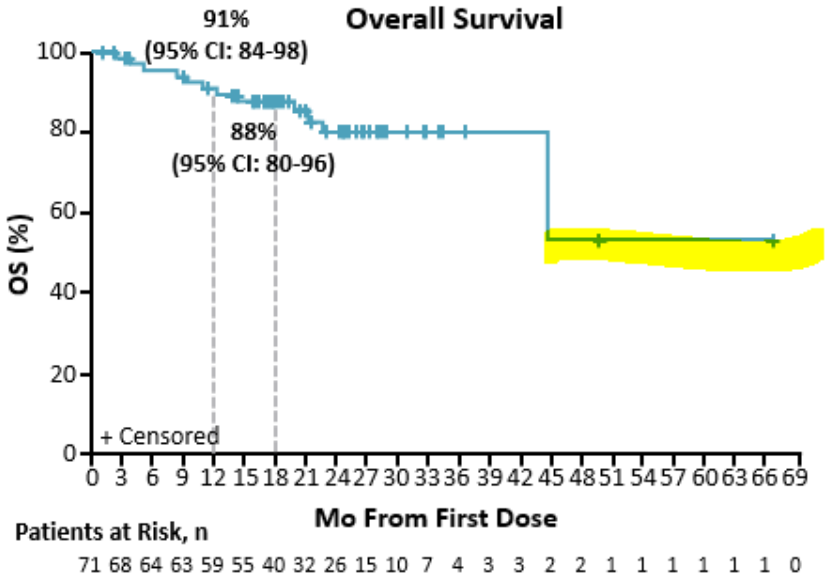

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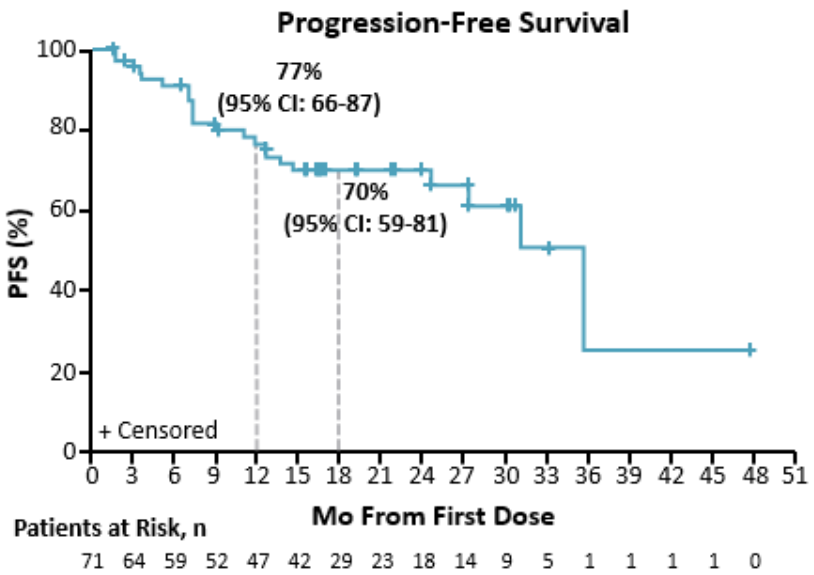

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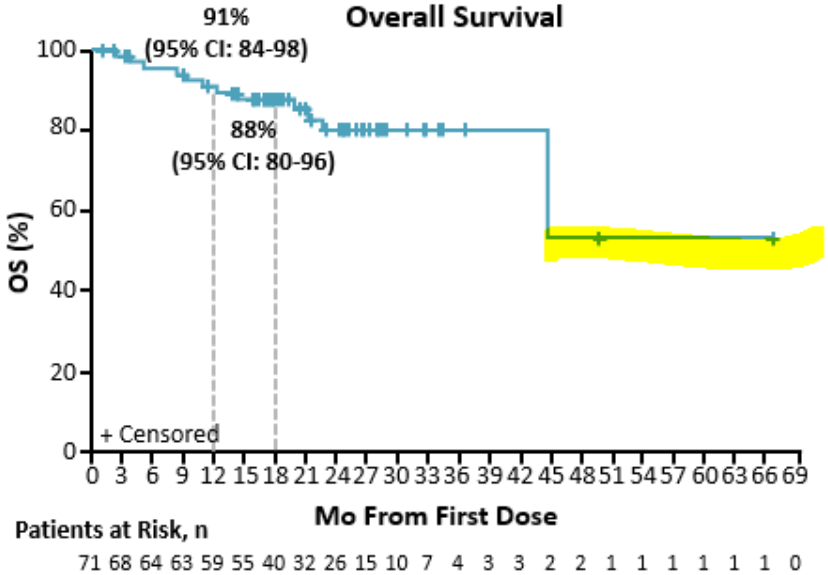

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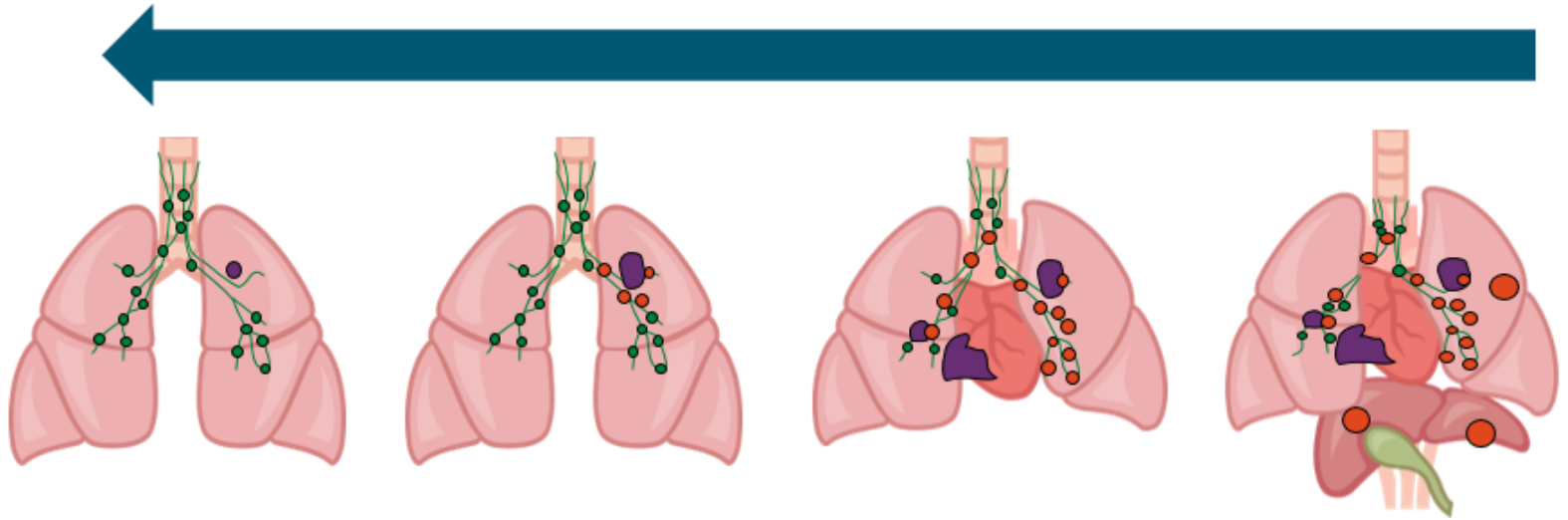
Moving Targeted Therapy and Immunotherapy Earlier in Disease Course



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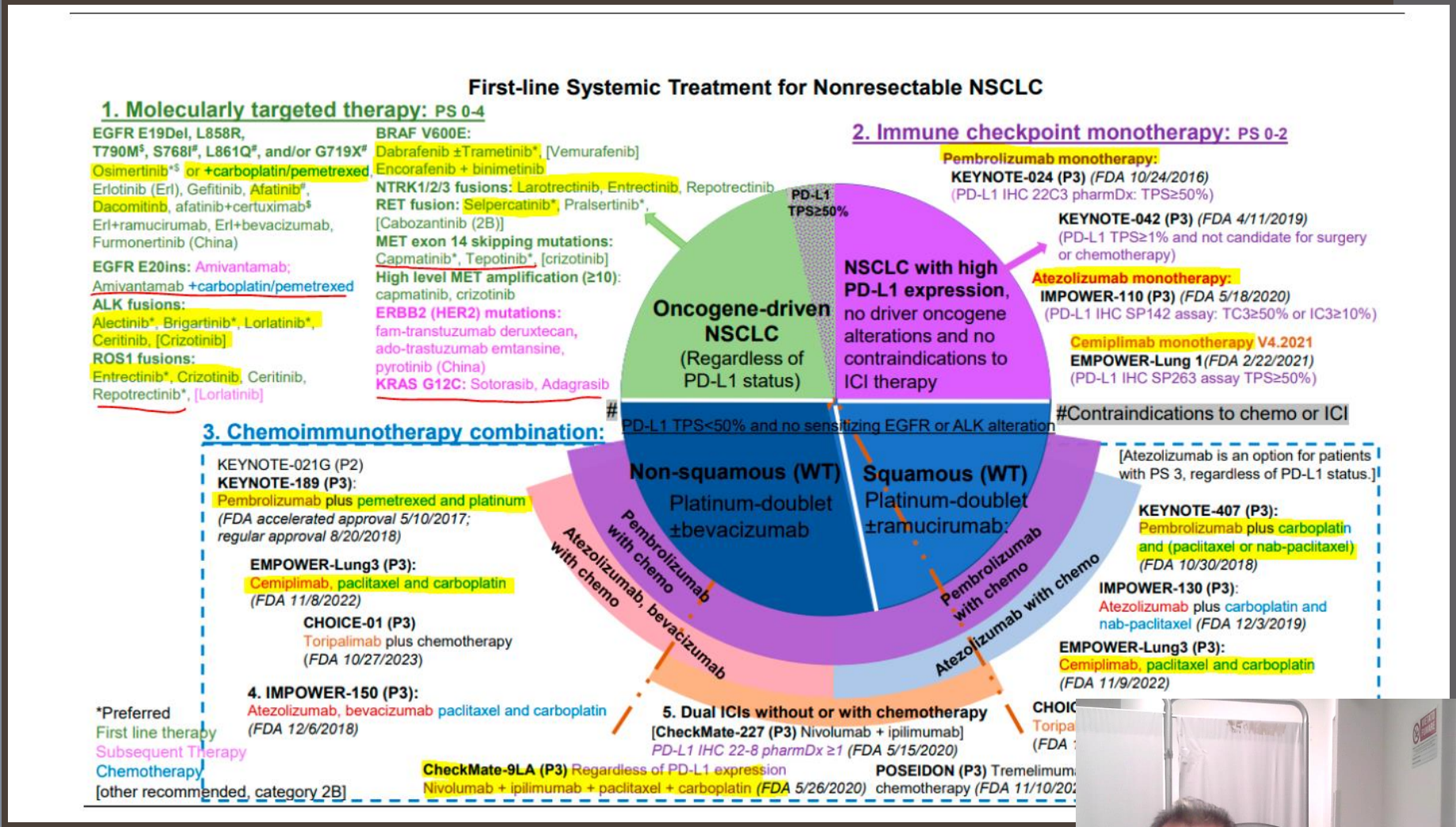

Grazie per l'attenzione

Giovanni Maria Fadda