Continued Evolution of Immunotherapy-Based Treatment in NSCLC: Multidisciplinary Perspectives for Clinical Practice

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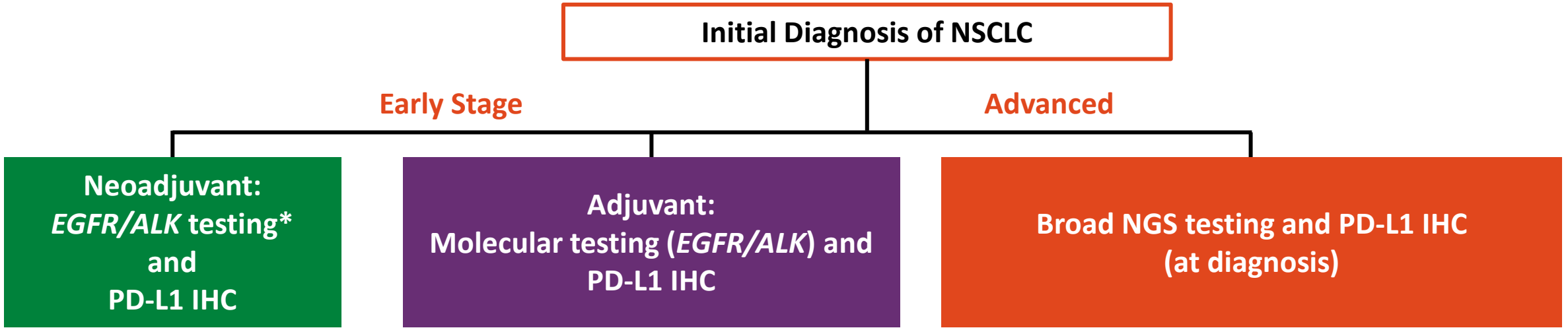
- I have no financial disclosures regarding this presentation.

Molecular and PD-L1 Testing at Initial Diagnosis to Guide Treatment in NSCLC



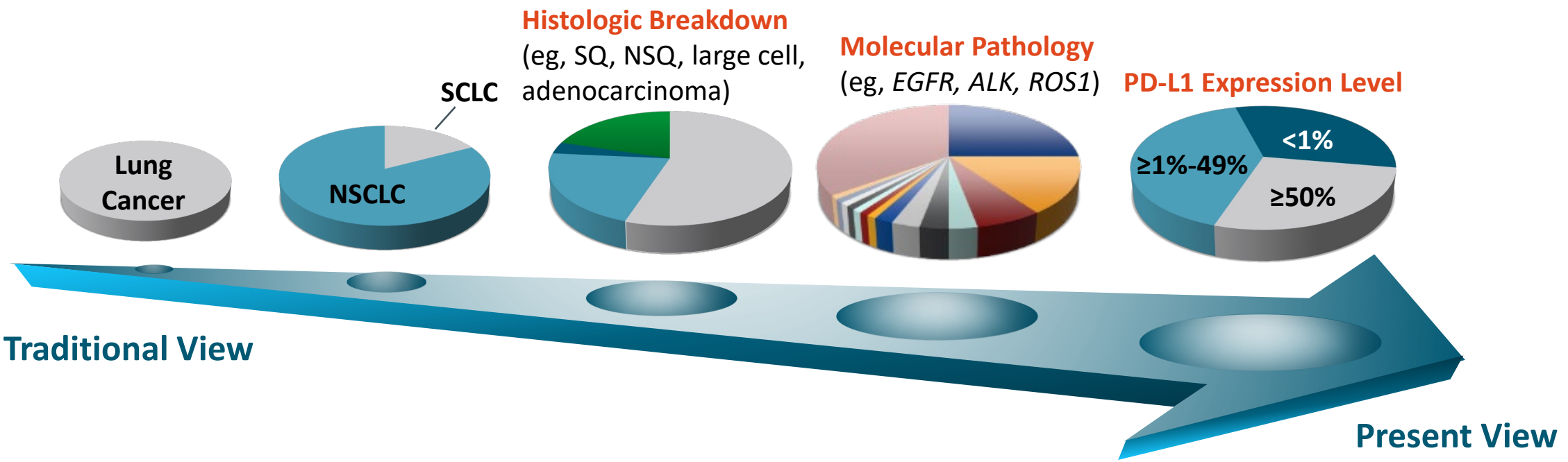
*NSQ or young, never-smoker SQ

- Test for PD-L1 expression required for all advanced NSCLC
- Broad molecular testing for all cases of advanced **nonsquamous** NSCLC should include *EGFR*, *ALK, ROS1, BRAF* V600E*, NTRK, RET, MET*ex14 skipping, *KRAS* G12C, and *HER2* mutation
  - For squamous NSCLC, consider testing in young, never/light smokers, and female patients, or if biopsy specimen is of mixed histology
- Biomarker results should be obtained before starting checkpoint inhibitor therapy

Pennell. ASCO Educ Book. 2019;39:351. Godoy. Biomark Res. 2023;11:7.

Slide credit: clinicaloptions.com

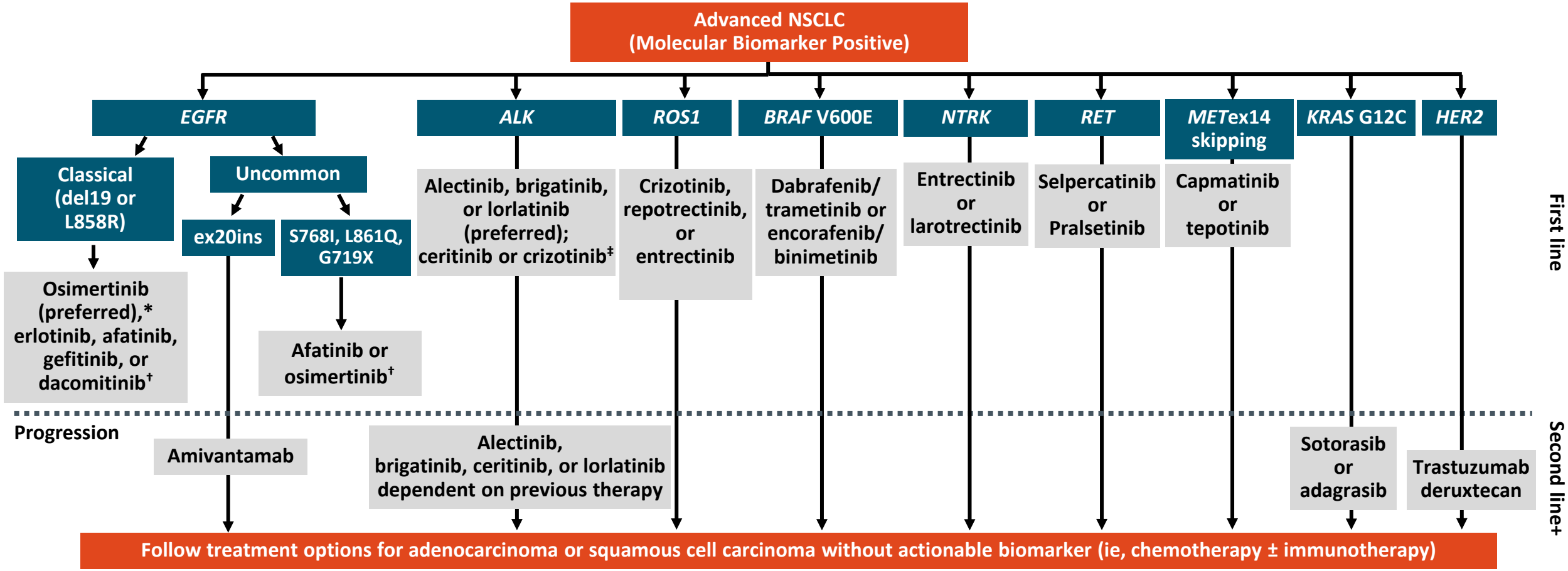
Evolution of Therapy in Lung Cancer



de Jong. Cancers (Basel). 2023;15:2855.

Slide credit: clinicaloptions.com

Targeted Therapy in Advanced NSCLC With Actionable Driver Mutations (2024)



*Osimertinib also approved as second-line therapy for *EGFR* T790M–positive disease after an earlier-generation EGFR TKI. †Afatinib, dacomitinib, erlotinib (alone or in combination with ramucirumab or bevacizumab), gefitinib, and osimertinib approved for *EGFR* exon19del, exon 21 L858R; afatinib for *EGFR* G719X, S768I, L861Q. Osimertinib also a preferred option for *EGFR* G719X, S768I, L861Q per NCCN guidelines. ‡Or as second-line after CT.

Adagrasib PI. Afatinib PI. Alectinib PI. Amivantamab PI. Capmatinib PI. Ceritinib PI. Crizotinib PI. Dabrafenib PI. Dacomitinib PI. Entrectinib PI. Erlotinib PI. Gefitinib PI. Lorlatinib PI. Larotrectinib PI. Osimertinib PI. Pralsetinib PI. Selpercatinib PI. Sotorasib PI. Trametinib PI. Trastuzumab deruxtecan PI. NCCN. Clinical practice guidelines in oncology: NSCLC. v.3.2024.

Indications for ICIs in Advanced NSCLC

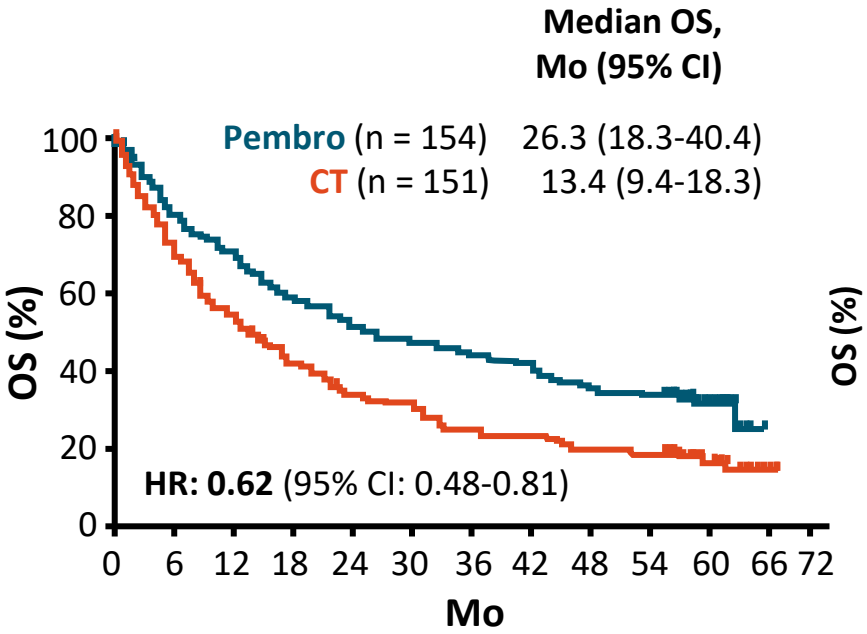
	ICI Regimen	Indication (FDA Approval)
Monotherapy	**Atezolizumab**	1L metastatic NSCLC, no *EGFR* or *ALK* aberrations (PD-L1 ≥50% or IC ≥10%)
	Cemiplimab	1L for locally advanced or metastatic NSCLC, no *EGFR*, *ALK*, or *ROS1* aberrations (PD-L1 ≥50%)
	Pembrolizumab*	1L for metastatic† NSCLC (PD-L1 ≥1%), no *EGFR* or *ALK* aberrations or 2L for metastatic NSCLC (PD-L1 ≥1%), no *EGFR* or *ALK* aberrations after platinum CT

*Single-agent pembrolizumab approved for ≥1% PD-L1 but not broadly recommended by experts; guideline recommended for PD-L1 1%-49% if poor PS or contraindications to combining with CT.
†Also indicated as 1L treatment for patients with stage III NSCLC who are not candidates for surgical resection or definitive chemoradiation.

Atezolizumab PI. Cemiplimab PI. Pembrolizumab PI.

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

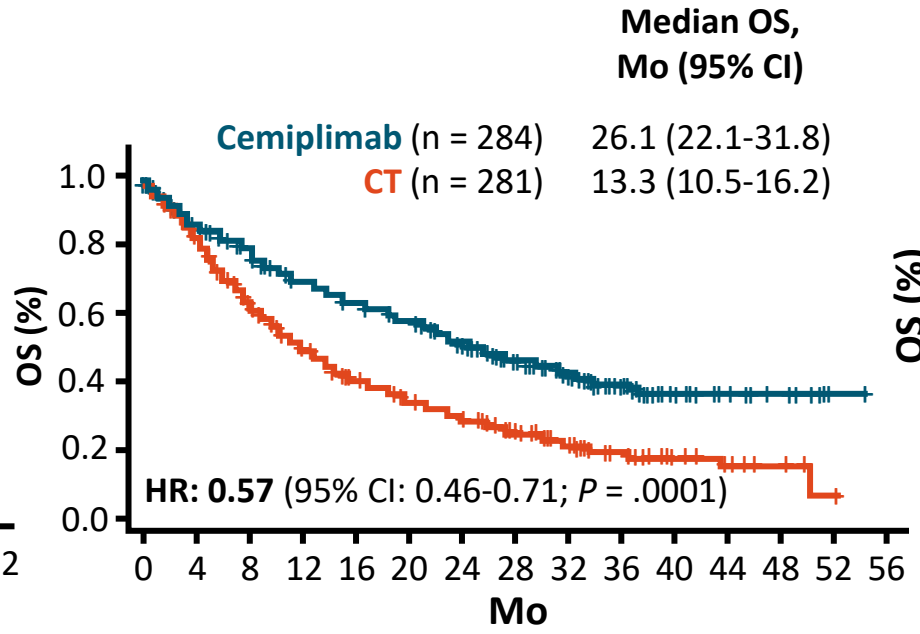
KEYNOTE-024 (N = 305)[1]:
Pembro vs CT (PD-L1 TPS ≥50%*)



*PD-L1 IHC by 22C3.

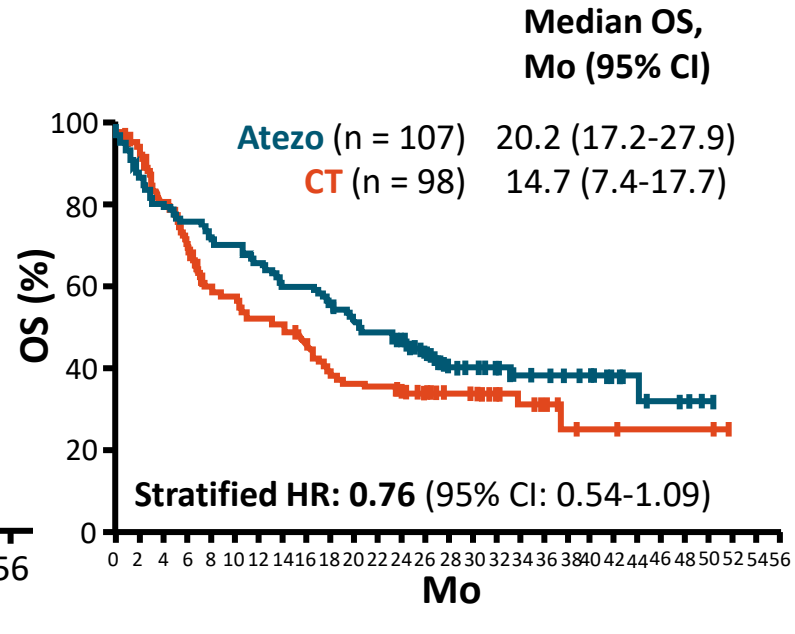
Pembrolizumab's approval as a single-agent treatment for metastatic NSCLC was expanded to tumors with PD-L1 TPS ≥1% based on the KEYNOTE-042 trial.[2]

EMPOWER-Lung 1 (N = 565†)[3]:
Cemiplimab vs CT (PD-L1 TPS ≥50%*)



†712 patients enrolled in overall ITT population.

IMpower110 (N = 205‡)[4]:
Atezo vs CT (PD-L1 ≥50% [TC] or ≥10% [IC])



‡572 patients with PD-L1 ≥1% on TC or IC (per SP142) enrolled in overall population.

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

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	Pembrolizumab*	1L for metastatic† NSCLC (PD-L1 ≥1%), no *EGFR* or *ALK* aberrations or 2L for metastatic NSCLC (PD-L1 ≥1%), no *EGFR* or *ALK* aberrations after platinum CT
Combination Regimens	***Nonsquamous***	
	Atezolizumab + bevacizumab + carboplatin + paclitaxel	1L for metastatic nonsquamous NSCLC, no *EGFR* or *ALK* aberrations
	Atezolizumab + carboplatin + *nab*-paclitaxel	1L for metastatic nonsquamous NSCLC, no *EGFR* or *ALK* aberrations
	Pembrolizumab + pemetrexed + platinum CT	1L for metastatic nonsquamous NSCLC, no *EGFR* or *ALK* aberrations
	Squamous	
	Pembrolizumab + carboplatin + (*nab*-)paclitaxel	1L for metastatic squamous NSCLC
	Any histology	
	Cemiplimab + platinum-based CT	1L for locally advanced or metastatic NSCLC, no *EGFR*, *ALK*, or *ROS1* aberrations
	Durvalumab + tremelimumab + platinum-based CT	Metastatic NSCLC, no sensitizing *EGFR* or *ALK* aberrations
	Nivolumab + Ipilimumab	1L for metastatic NSCLC (PD-L1 ≥1%), no *EGFR* or *ALK* aberrations
	Nivolumab† + ipilimumab + platinum-doublet CT	1L for metastatic/recurrent NSCLC, no *EGFR* or *ALK* aberrations

*Single-agent pembrolizumab approved for ≥1% PD-L1 but not broadly recommended by experts; guideline recommended for PD-L1 1%-49% if poor PS or contraindications to combining with CT. †Also indicated as 1L treatment for patients with stage III NSCLC who are not candidates for surgical resection or definitive chemoradiation.

Atezolizumab PI. Cemiplimab PI. Durvalumab PI. Nivolumab PI. Pembrolizumab PI.

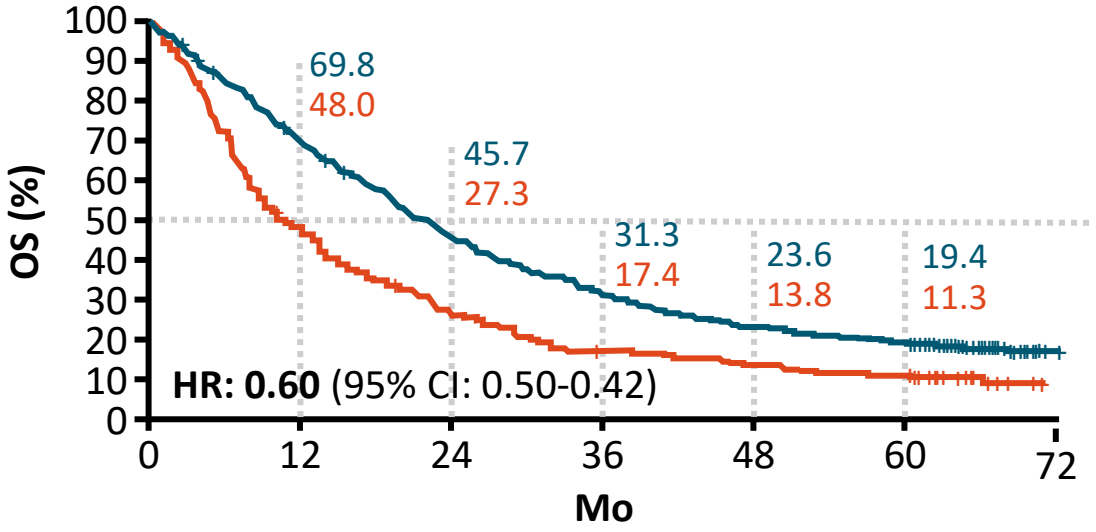
Slide credit: clinicaloptions.com

First-line Pembrolizumab Plus Chemotherapy in Advanced NSCLC

KEYNOTE-189:
Pembrolizumab vs CT in Nonsquamous NSCLC

OS in ITT (N = 616)

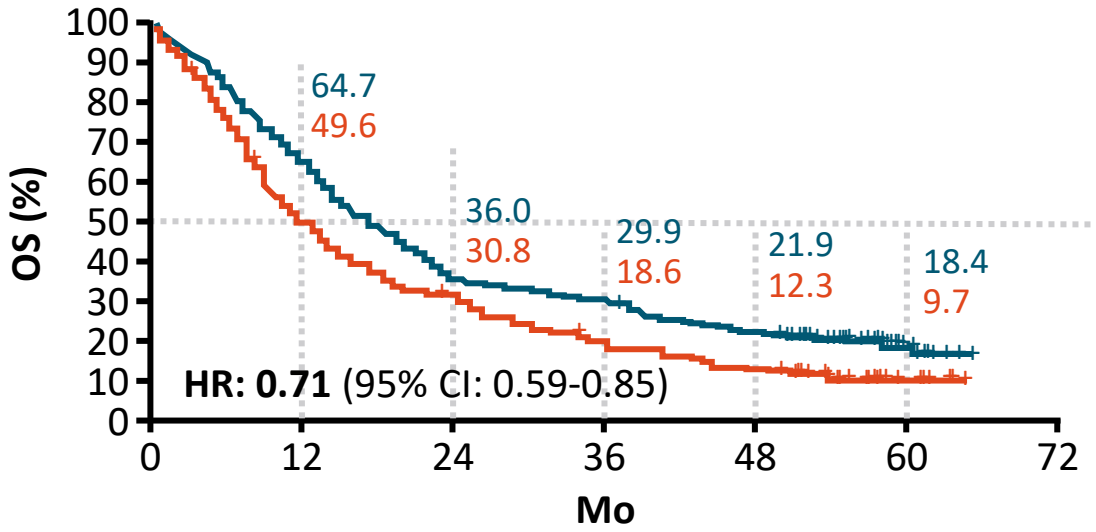
Treatment Group	Median OS, mo (95% CI)
Pembro + CT	19.4 (15.7-23.4)
Placebo + CT	11.3 (7.4-16.1)



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.

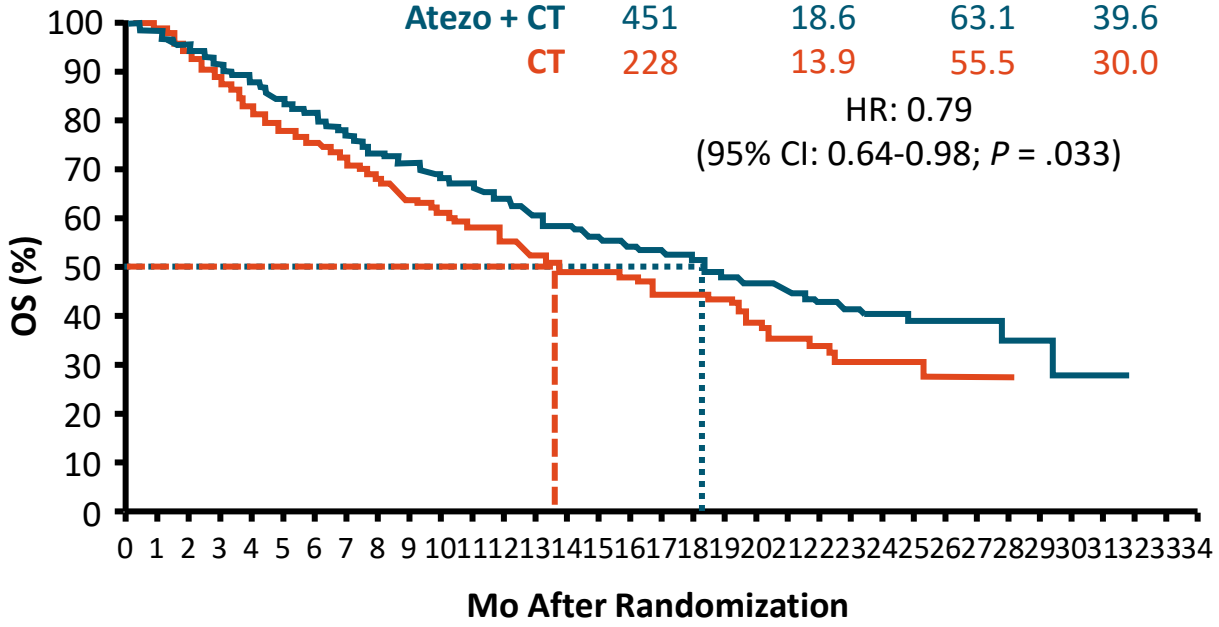
First-line Atezolizumab Plus Chemotherapy in Nonsquamous Advanced NSCLC

IMpower130: Atezolizumab ± Carbo/*nab*-Paclitaxel vs CT

OS in ITT WT* (N = 723)

	Patients, n	Median OS, Mo	12-Mo OS, %	24-Mo OS, %
Atezo + CT	451	18.6	63.1	39.6
CT	228	13.9	55.5	30.0

HR: 0.79
(95% CI: 0.64-0.98; *P* = .033)

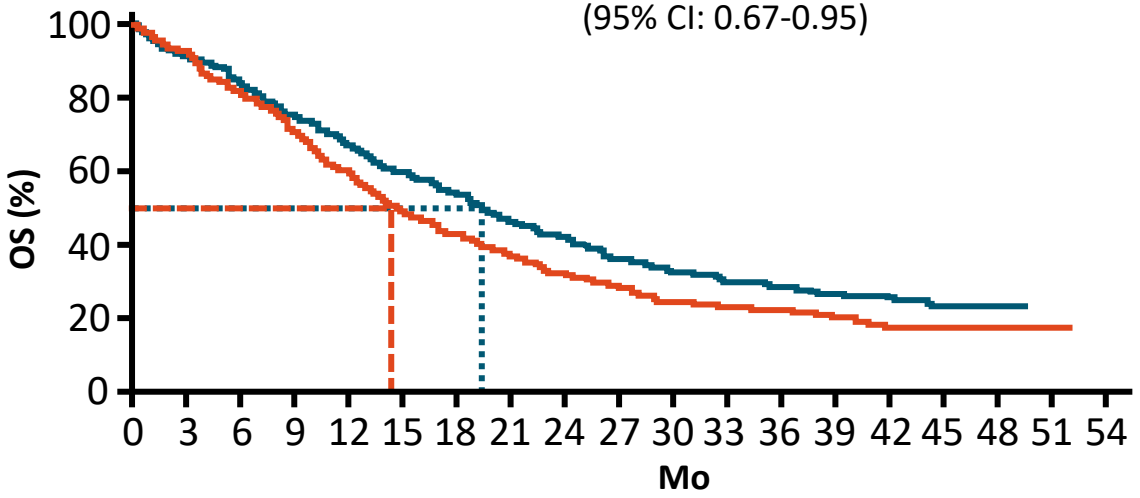


IMpower150: Atezolizumab + Carbo/Pac + Bev vs Carbo/Pac + Bev

OS in ITT WT* (N = 697)

	Patients, n	Median OS, Mo	12-Mo OS, %	24-Mo OS, %
Atezolizumab + Carbo/Pac + Bev	359	19.5	67	42
Carbo/Pac + Bev	338	14.7	60	32

HR: 0.80
(95% CI: 0.67-0.95)

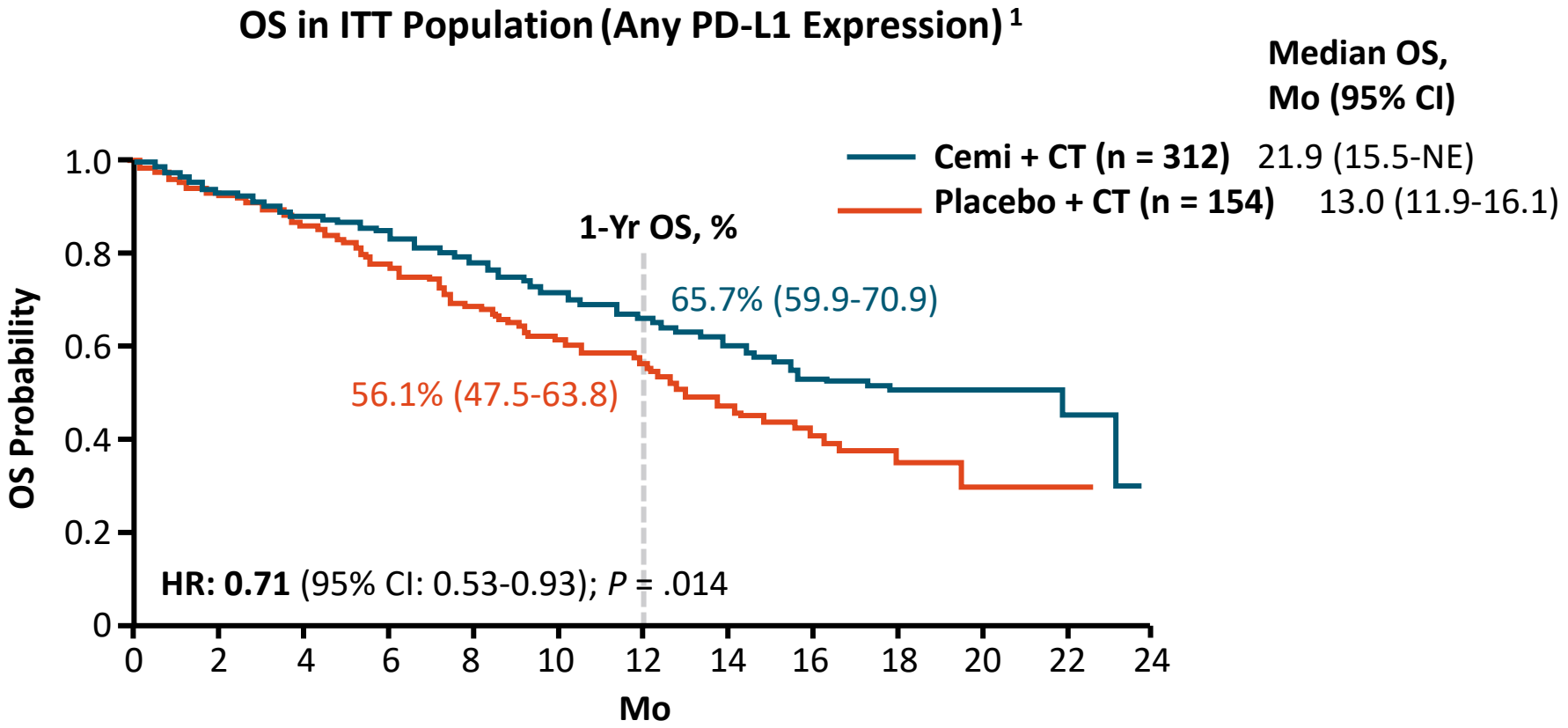


*ITT WT: patients without *EGFR* or *ALK* alterations.

Socinski. J Thorac Oncology. 2021;16:1909. West. Lancet Oncol. 2019;20:924.

Slide credit: clinicaloptions.com

EMPOWER-Lung 3: First-line Cemiplimab + Platinum CT vs Placebo + CT in Advanced NSCLC of Any Histology



- Although the study was not powered to determine efficacy within subgroups, there were median OS improvements in the cemiplimab arm vs CT in both squamous (21.9 mo vs 13.8 mo) and nonsquamous (15.8 mo vs 13.0 mo) histology[1]
- In PD-L1 ≥1% population, median OS was 23.5 mo vs 12.1 mo (HR: 0.52 (95% CI: 0.38-0.69); *P* <.0001)[2]

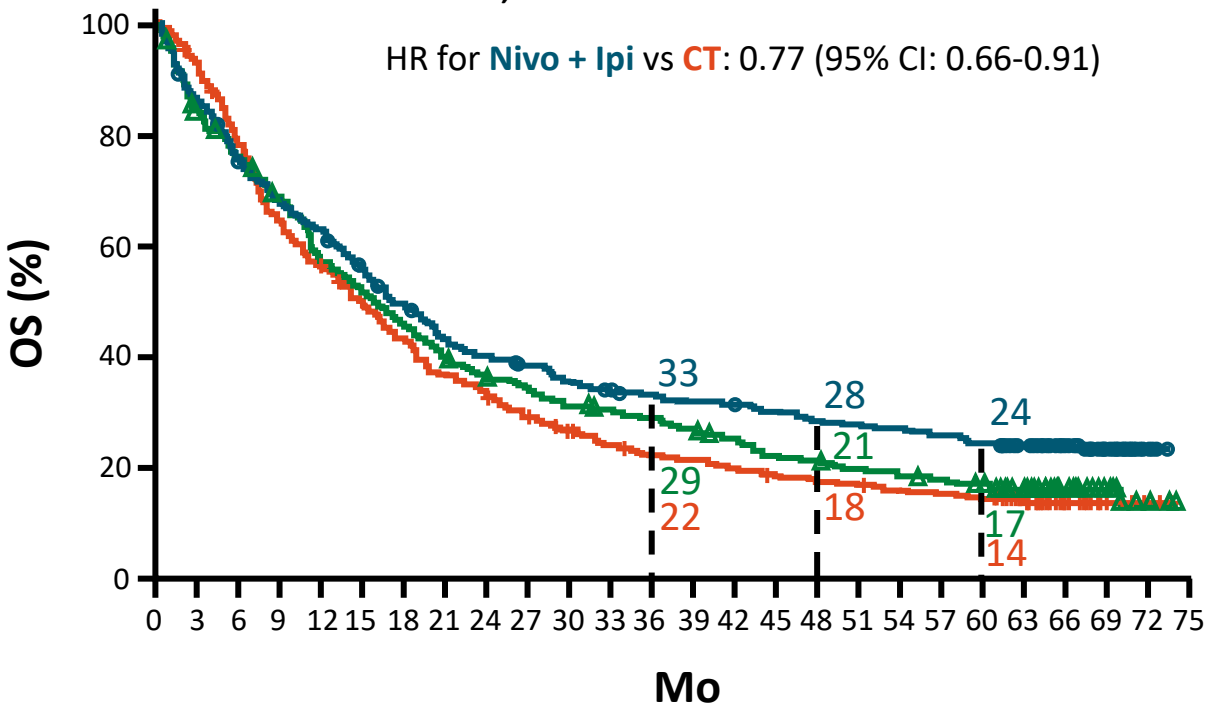
1. Gogishvili. Nat Med. 2022;28:2374. 2. Baramidze. ESMO 2023. Abstr 1495P.

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

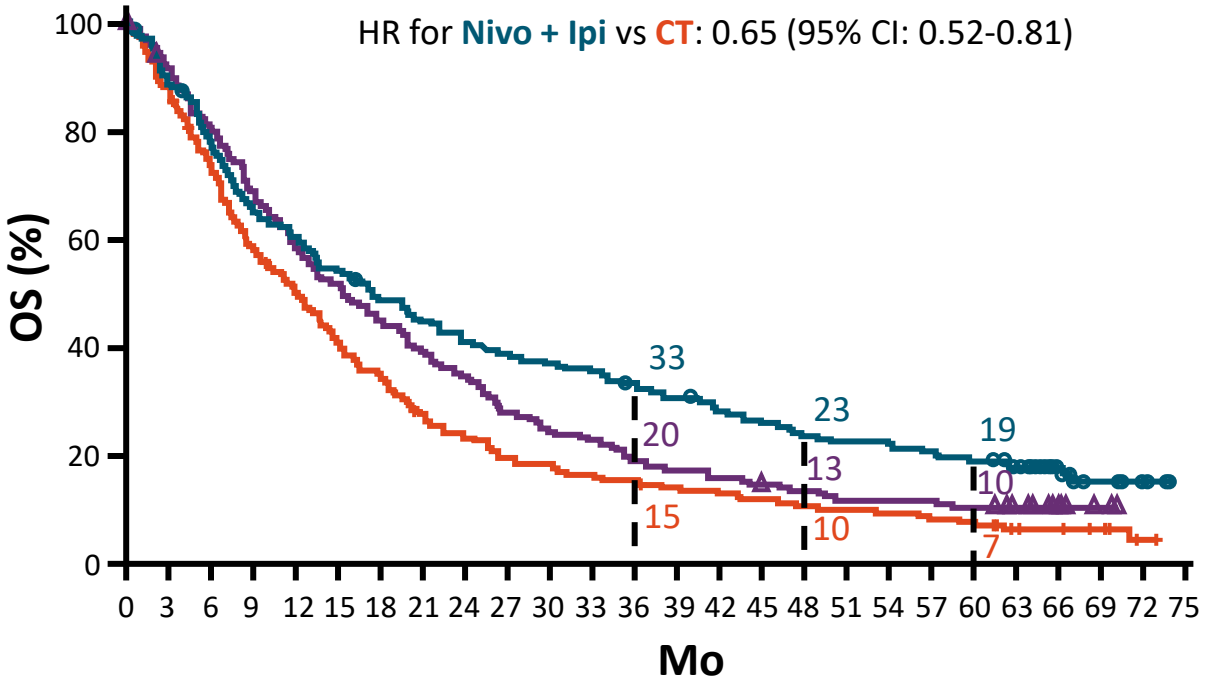
HR for Nivo + Ipi vs CT: 0.77 (95% CI: 0.66-0.91)



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)



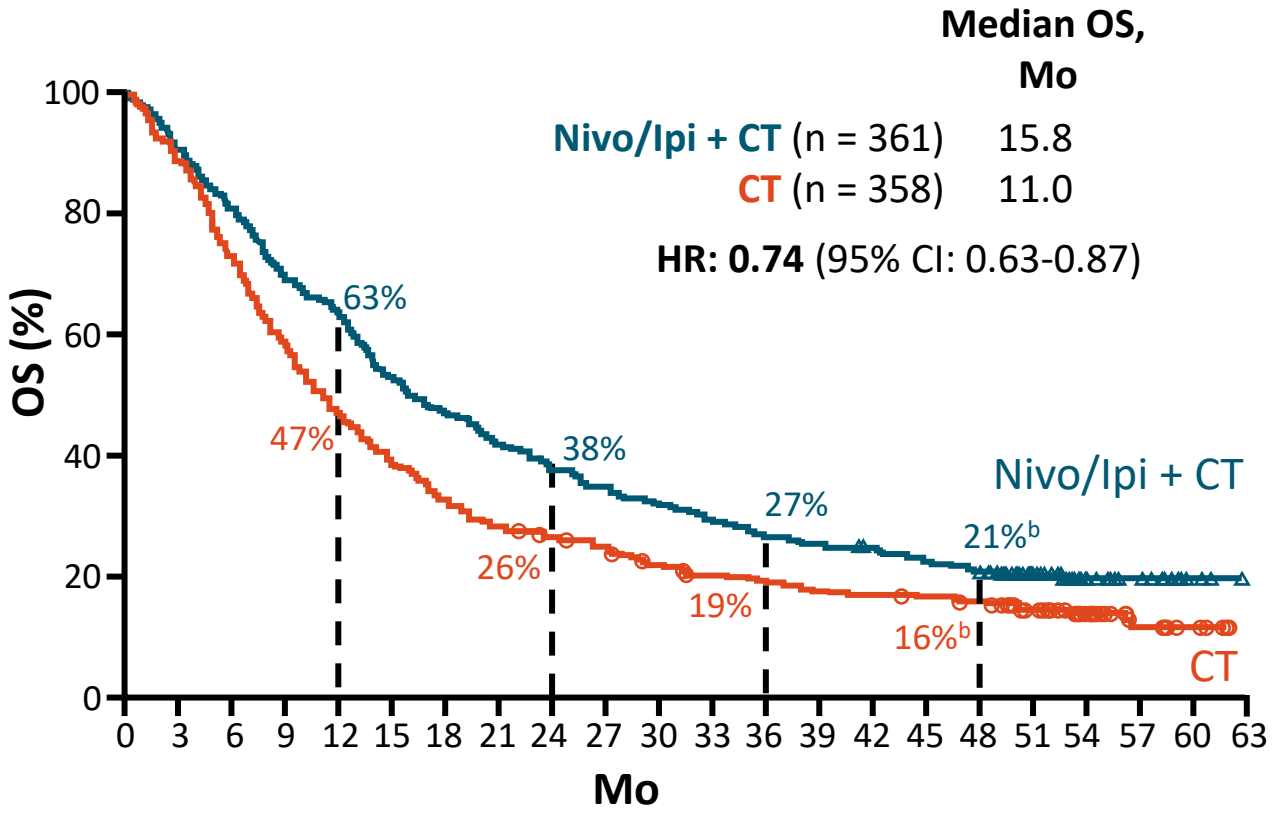
*Not FDA approved indication.

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

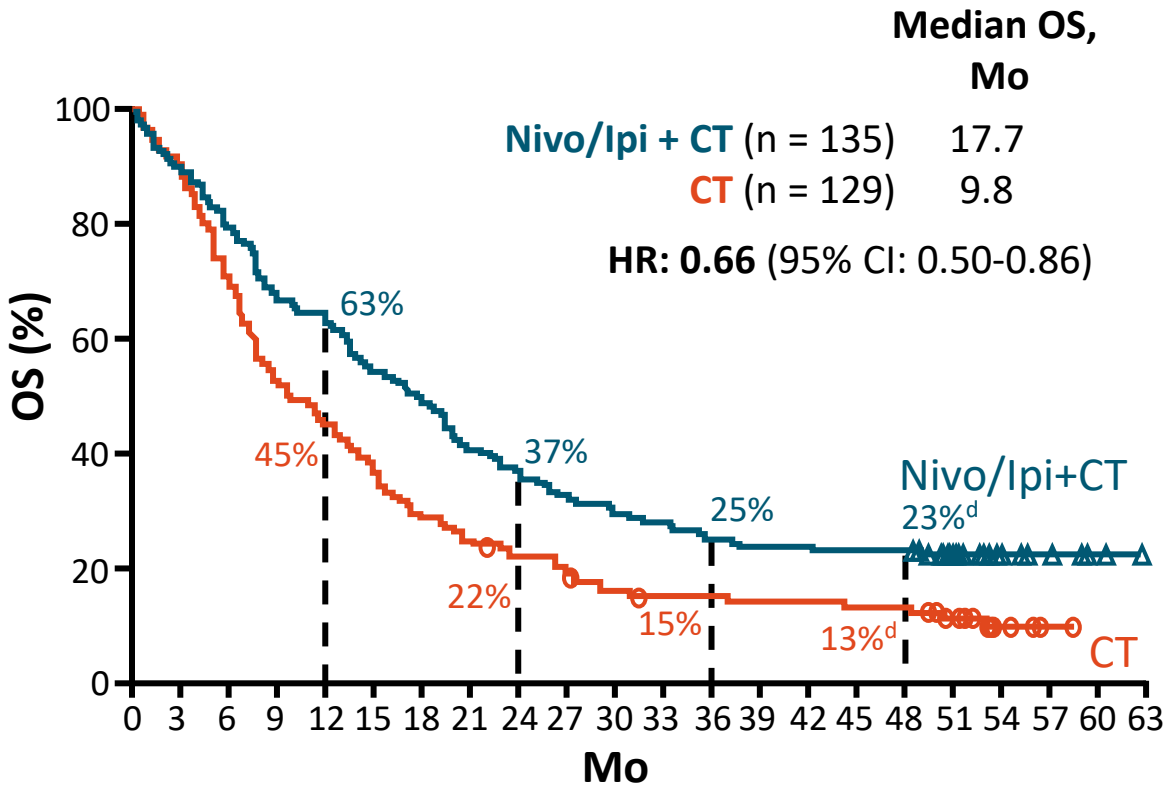
Slide credit: clinicaloptions.com

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

OS (All Randomized)



OS (PD-L1 <1*)



*Measured by IHC (28-8 PharmDx assay).

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

Slide credit: clinicaloptions.com

POSEIDON: 1L Durvalumab ± Tremelimumab + Platinum Chemotherapy in Stage IV NSCLC

- Open-label, multicenter, randomized phase III trial

Stratified by PD-L1 (≥50% vs <50%), disease stage (IVA vs IVB), histology

Patients with stage IV NSCLC, no *EGFR* or *ALK* alterations, ECOG PS 0/1, treatment-naive for metastatic disease (N = 1013)

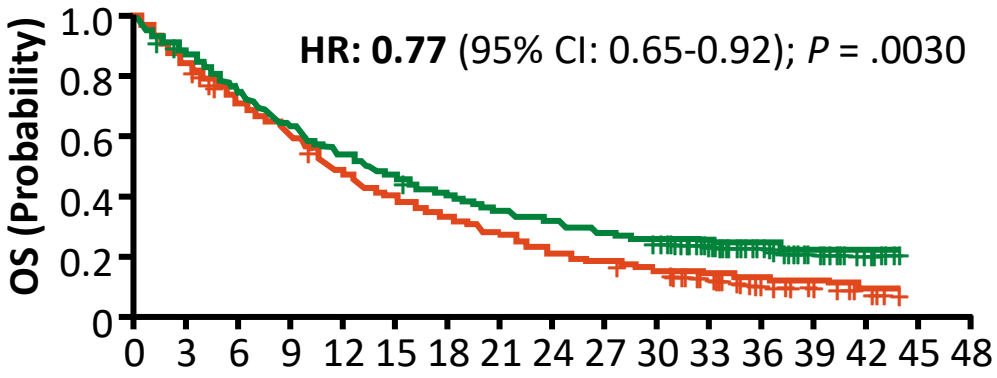
Durva 1500 mg + **CT*** Q3W (4 cycles) (n = 338)	**Durva** 1500 mg Q4W + **Pemetrexed**†
Durva 1500 mg + **Treme** 75 mg (4 cycles) + **CT*** Q3W (4 cycles) (n = 338)	**Durva** 1500 mg Q4W + **Treme** 75 mg (Wk 16 only‡) + **Pemetrexed**†
CT* Q3W (up to 6 cycles) (n = 337)	**Pemetrexed**†

*Gem + carbo or cis (squamous), pemetrexed + carbo or cis (nonsquamous), or *nab*-pac + carboplatin (either histology). †Maintenance pemetrexed only given to patients with nonsquamous NSCLC who received first-line pemetrexed. ‡218 patients received 5 doses of tremelimuab.

OS With D + T + CT vs CT

	Median OS, Mo (95% CI)
T+ D + CT	14.0 (11.7 to 16.1)
CT	11.7 (10.5 to 13.1)

HR: 0.77 (95% CI: 0.65-0.92); *P* = .0030



- **Primary endpoints**: PFS by BICR, OS (D + CT vs CT); positivity for either triggered analysis of key secondary endpoints

Genomic Biomarkers for Immunotherapy Response

Immunotherapy Plus Chemotherapy in *EGFR*-Mutated NSCLC After Progression on TKIs

Trial	Treatment	Patient Population	Results
IMpower150[1]	ACP (atezo + carbo/pac) vs ABCP (atezo + bev + carbo/pac) vs BCP (bev + carbo/pac)	*EGFR*+ advanced, NSCLC* (n = 124)	In patients with *EGFR* sensitizing mutation: OS HR (ACP vs BCP): 0.90 (95% CI: 0.47-1.74)
CheckMate 722[2,†]	Nivo/Ipi or Nivo + CT vs CT	*EGFR*-mutated, metastatic NSCLC after PD on *EGFR* TKI (N = 294)	mOS, mo (Nivo + CT vs CT): 19.4 vs 15.9 HR: 0.82 (95% CI: 0.61-1.10) mPFS, mo (Nivo + CT vs CT): 5.6 vs 5.4 HR: 0.75 (95% CI: 0.56-1.00); *P* = .0528
KEYNOTE-789[3]	Pembrolizumab + CT vs CT	TKI resistant, *EGFR*-mutated, metastatic NSQ NSCLC (N = 492)	mOS: 15.9 mo vs 14.7 mo HR: 0.84 (95% CI: 0.69-1.02); *P* = .0362[‡]
ORIENT-31[4]	Sintilimab + bevacizumab[§] + CT vs sintilimab + CT vs CT	*EGFR*-mutated, advanced or metastatic, NSQ NSCLC after PD on EGFR TKI (N = 476)	mOS: 21.1 vs 20.5 vs 19.2 HR (sintilimab + bevacizumab + CT vs CT): 0.98 (95% CI: 0.72-1.34) HR (sintilimab + CT vs CT): .97 (95% CI: 0.71-1.32)
IMpower151[5]	ABCP vs BCP	Metastatic NSQ NSCLC with sensitizing *EGFR* or *ALK* alterations with PD after ≥1 prior TKI (n = 163)	mPFS, mo: (*EGFR/ALK+)* 8.5 vs 8.3 HR: 0.86 (95% CI: 0.61-1.21)
ATTLAS[6]	ABCP vs PC (pemetrexed + carbo or cis)	*EGFR*- or *ALK*-mutated, metastatic NSCLC after EGFR or ALK inhibitor (N = 228)	mOS: 20.63 vs 20.27; HR: 1.01 (95% CI: 0.69-1.46); *P* = .975

*Patient subgroup. [†]Trial was underpowered to differentiate between treatment arms due to reduced sample size due to the COVID-19 pandemic. [‡]Did not reach prespecified threshold for statistical significance of *P* = .0117). [§]Study used a bevacizumab biosimilar IBI305.

1. Reck. Lancet Respir Med. 2019;7:387. 2. Mok. ESMO Asia 2022. Abstr LBA8. 3. Yang. ASCO 2023. Abstr LBA9000. 4. Lu. Lancet Respir Med. 2023;11:624. 5. Zhou. WCLC 2023. Abstr OA09.06. 6. Park. JCO. 2023;[EPub]

Potential Toxicity With Sequential Use of Immunotherapy Followed by a TKI

- Retrospective review of patient records to identify severe toxicity with ICI and EGFR TKI, regardless of sequence, in patients with *EGFR*-mutated NSCLC (N = 126)
  - Of 41 patients treated with ICI followed by osimertinib, 6 developed a severe irAE
  - Of 21 patients treated with osimertinib within 3 mo of ICI, 24% developed a severe irAE; conversely, no severe irAEs were identified if osimertinib was given before ICI

Pt No.	ICI	Days on ICI	Days Between ICI and Osi	Days to irAE Onset After 1st Osi Dose	irAE	Hospitalized?	Response to Steroids?
1	Nivolumab	14	29	24	G3 pneumonitis	Yes	Yes
2	Pembrolizumab + CT*	21	23	15	G3 pneumonitis	No	Yes
3	Nivolumab + ipilimumab	392	22	167	G3 pneumonitis	Yes	Yes
4	Pembrolizumab	126	28	14	G3 colitis	Yes	No
5	Pembrolizumab	126	314	15	G3 pneumonitis	Yes	Yes
6	Nivolumab	68	39	39	G4 hepatitis	Yes	No

*Carboplatin plus pemetrexed.

Schoenfeld. Ann Oncol. 2019;30:839.

Slide credit: clinicaloptions.com

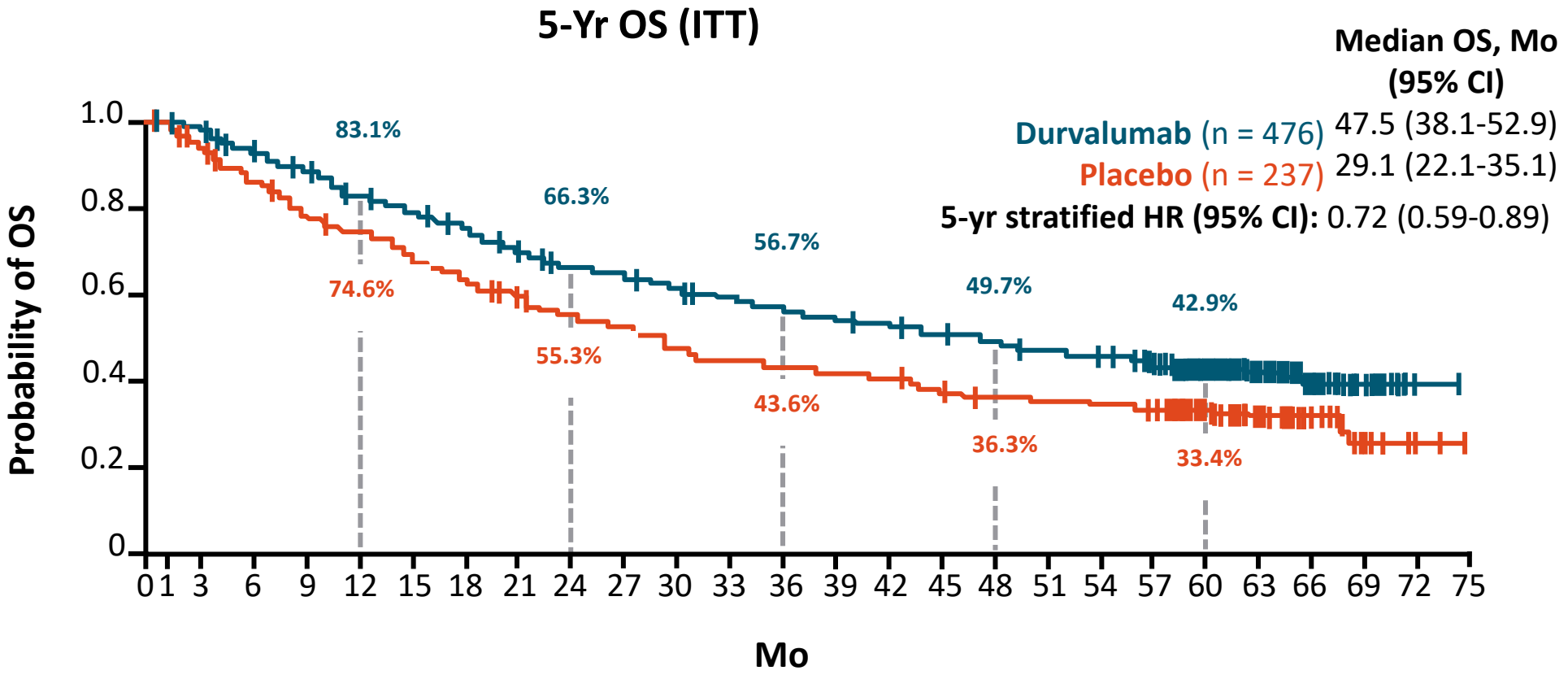
Practical Considerations for IO in Advanced NSCLC

- For PD-L1–high disease, single-agent PD-1 or PD-L1 antibodies remain mainstay of treatment
  - Chemo/IO combinations increase response, but survival is similar to single-agent PD-1 blockade
- For PD-L1–negative disease, either chemo/IO, or IO/IO/chemo
  - IO/IO combinations without chemo can be considered for off-label use in select patients
- For PD-L1 1%-49%, either chemo/IO, IO/IO, or IO/IO/chemo are options
- Although long-term survival is possible, it is only realized in a subset of patients
- Sequencing of IO therapy and chemo remains an open question

Akinboro. ASCO 2022. Abstr 9000.

Role of Immunotherapy in the Management of Stage I-III NSCLC

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

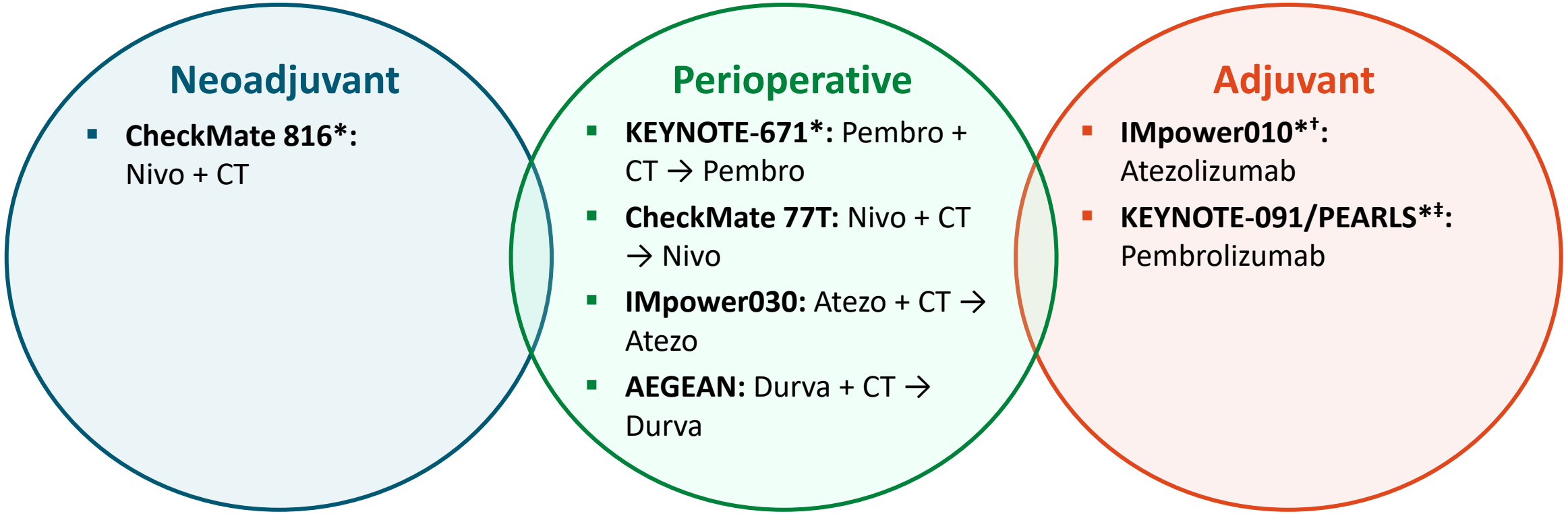


In February 2018, the FDA approved durvalumab for the treatment of unresectable stage III NSCLC without disease progression following concurrent CRT

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

Slide credit: clinicaloptions.com

Evolving Immunotherapy-Based Treatment Landscape in Resectable NSCLC



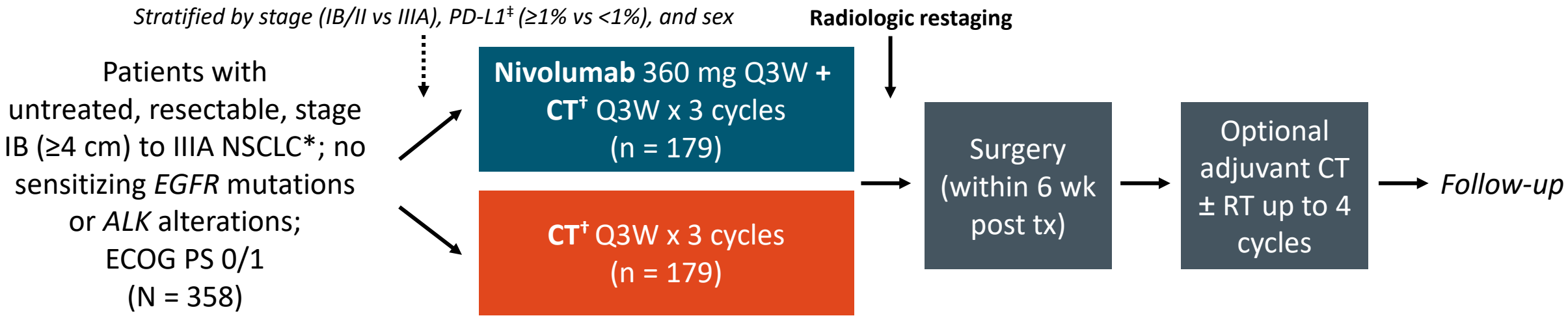
*Trials leading to FDA approvals of denoted treatment regimen
†Mandatory chemotherapy. ‡Chemotherapy not mandatory.

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

Slide credit: clinicaloptions.com

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

- Randomized, open-label phase III trial



*By TNM 7th edition. †NSQ: cisplatin/pemetrexed; SQ: cisplatin/gemcitabine; both: carboplatin/paclitaxel; if receiving adjuvant chemotherapy: cisplatin/vinorelbine, cisplatin/docetaxel. ‡PD-L1 28-8 pharmDx IHC assay.

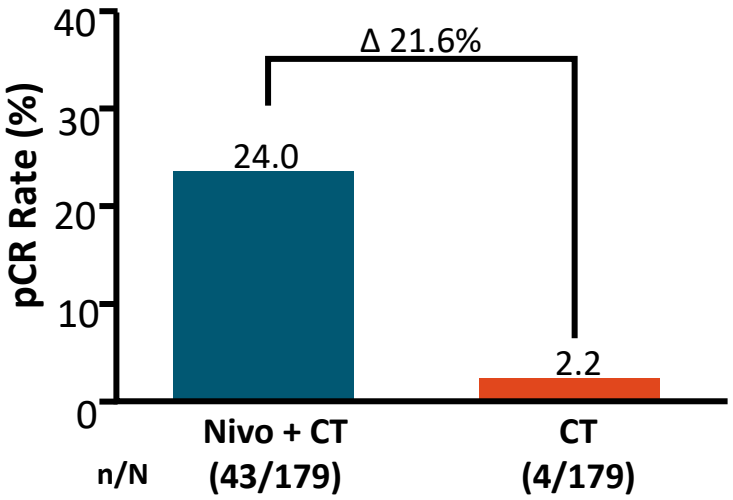
- **Primary endpoints:** pCR (by BIPR) and EFS (by BICR)
- **Key secondary endpoints:** OS, MPR (by BIPR), time to death or distant metastasis
- **Key exploratory endpoints:** ORR (by BICR), feasibility of surgery, peri- and postoperative surgery related AEs

Forde. NEJM. 2022;386:1973. Girard. AACR 2022. Abstr CT012. Spicer. ASCO 2021. Abstr 8503.

Phase III CheckMate 816: pCR and EFS

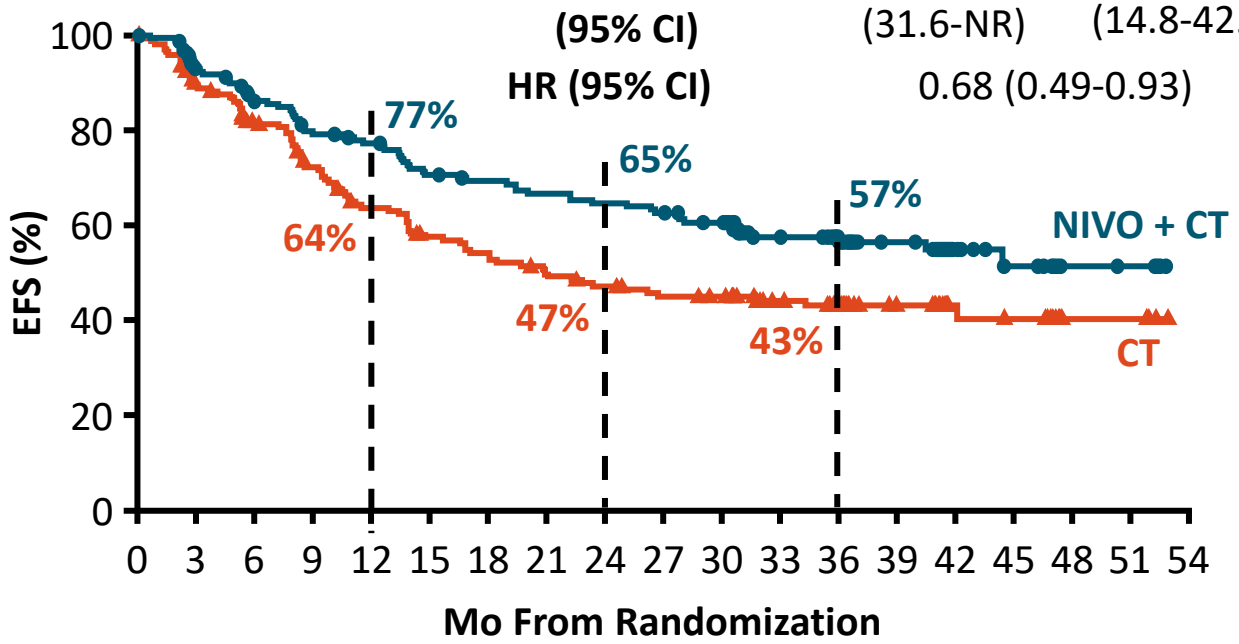
pCR (ITT; ypT0N0)[1]

OR: 13.94
(99% CI: 3.49-55.75;
P <.0001)



Event-free Survival[2]

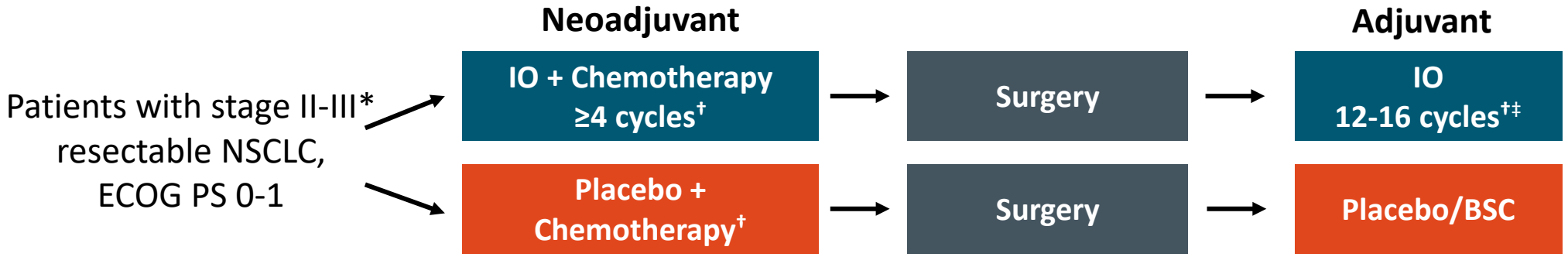
	NIVO + CT (n = 179)	CT (n = 179)
Median EFS, mo (95% CI)	NR (31.6-NR)	21.1 (14.8-42.1)
HR (95% CI)	0.68 (0.49-0.93)	



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[3]

1. Forde. NEJM. 2022;386:1973. 2. Girard. ELCC 2023. Abstr 840. 3. Nivolumab PI.

Ongoing Phase III Perioperative Studies in Resectable NSCLC

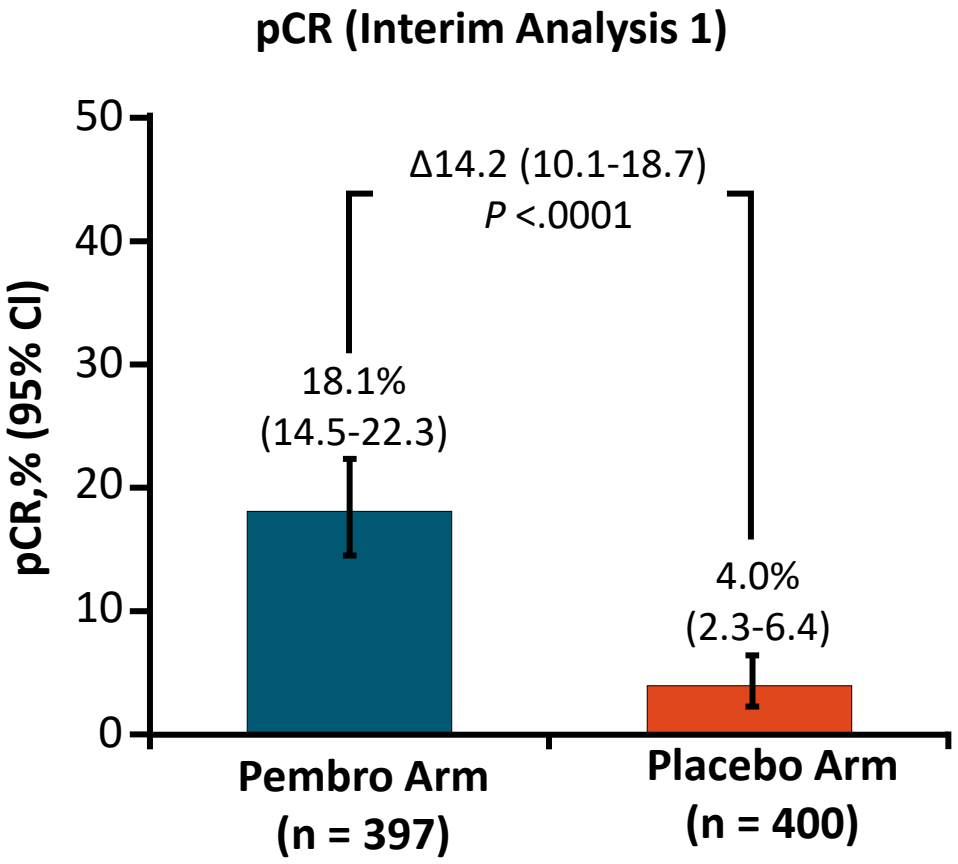


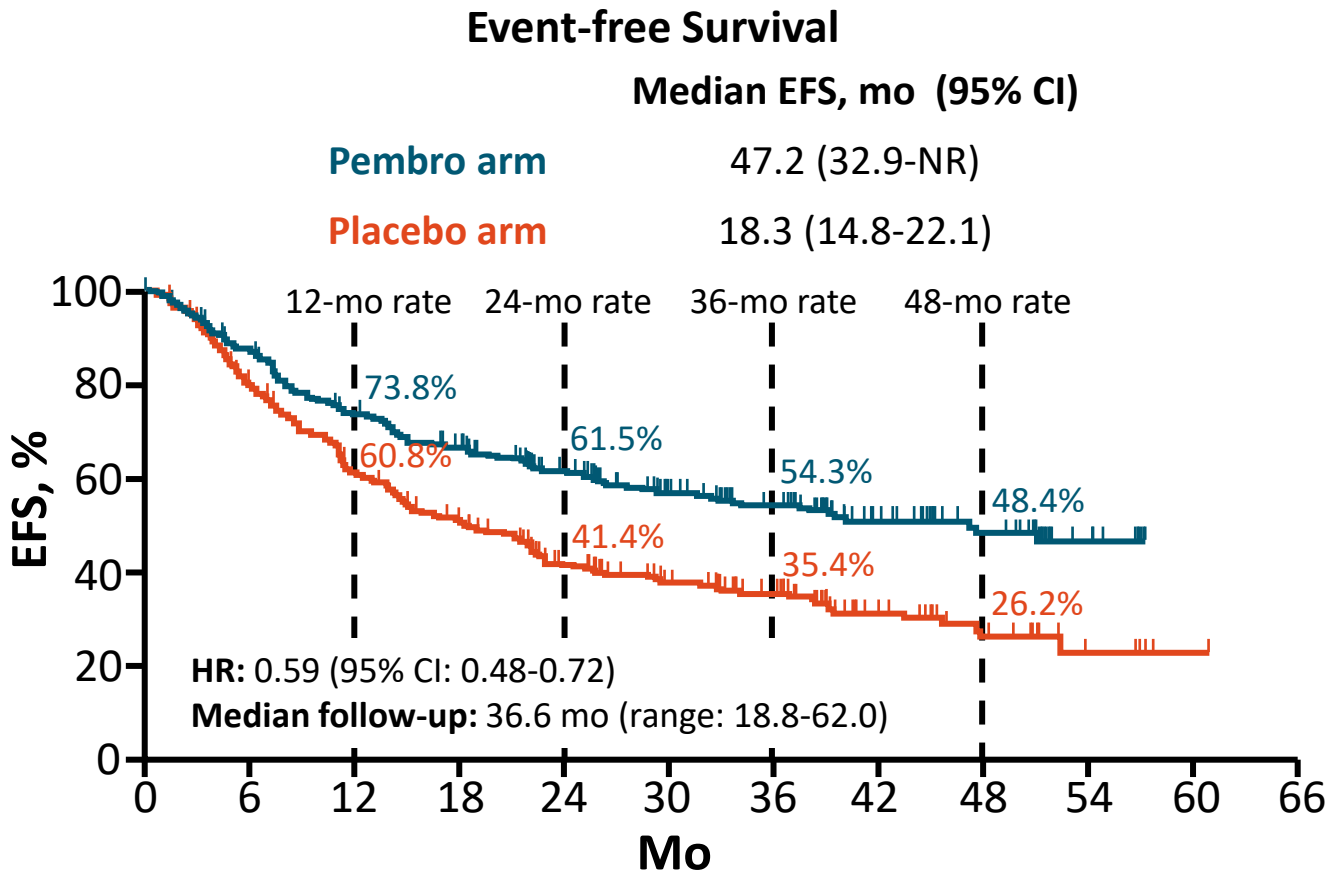
	KEYNOTE-671[1,2]	AEGEAN[3,4]	CheckMate 77T[5,6]	IMpower030[7,8]
IO agent	Pembrolizumab	Durvalumab	Nivolumab	Atezolizumab
Primary endpoint(s)	EFS, OS	pCR, EFS	EFS	EFS
Disease stage (TNM 8th ed.)	II-IIIB§	IIA-IIIB§	II-IIIB§	II-IIIB§
Target N	797 (actual)	826 (actual)	452	453 (actual enrollment)
EGFR or *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, CheckMate 816 allowed optional adjuvant CT ± RT. §Includes stages IIIB patients with N2 disease that is considered resectable. Cross trial comparisons are not intended. ‖Molecular testing no mandated

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: Perioperative Pembrolizumab in Resectable NSCLC — pCR and Event Free Survival



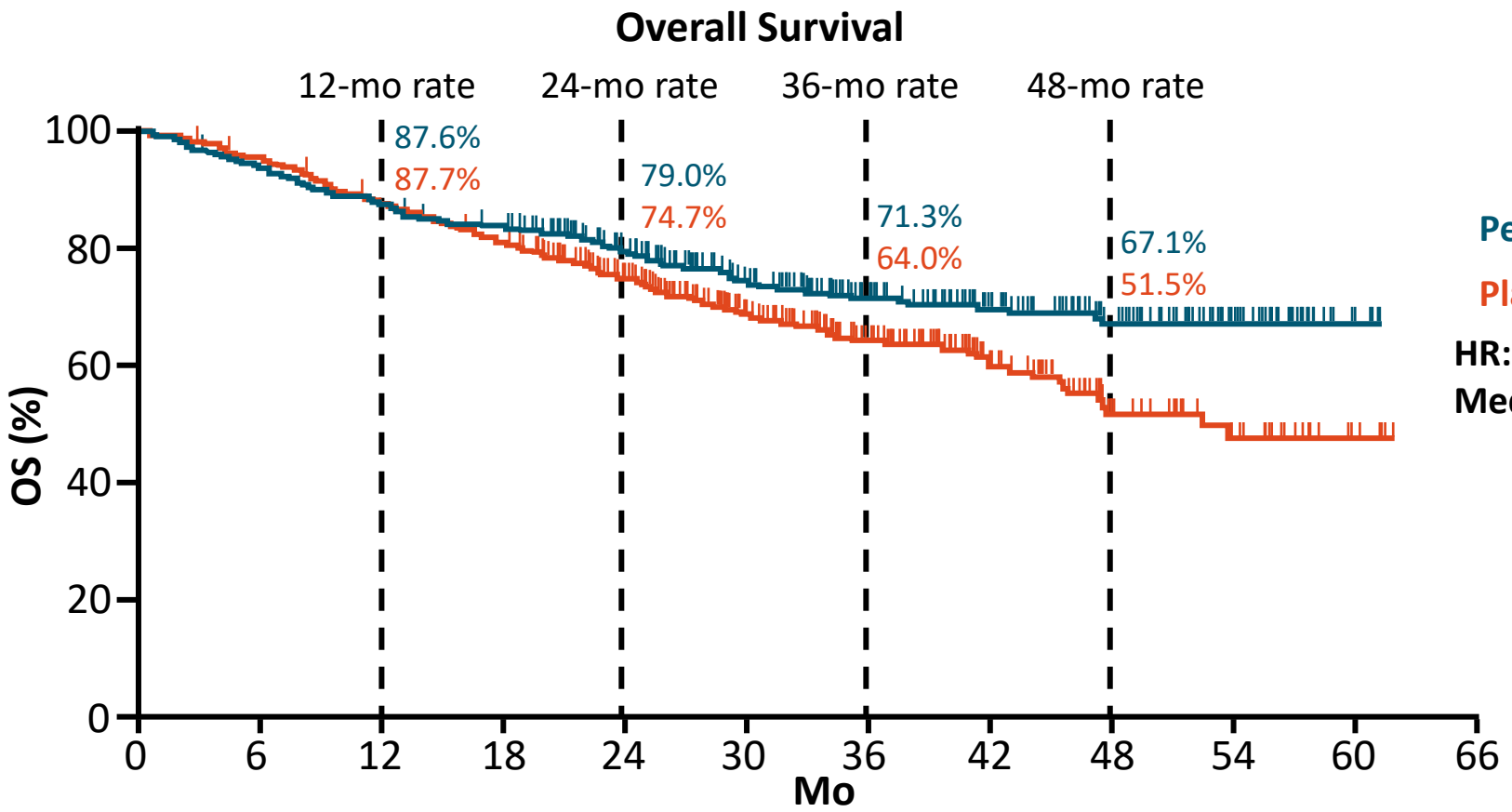


- In subgroup analysis, PD-L1 TPS ≥1% was linked to greater EFS and OS benefit from perioperative pembrolizumab

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

Slide credit: clinicaloptions.com

KEYNOTE-671: Overall Survival



	Median OS, mo (95% CI)
Pembro arm	NR (NR-NR)
Placebo arm	52.4 (45.7-NR)

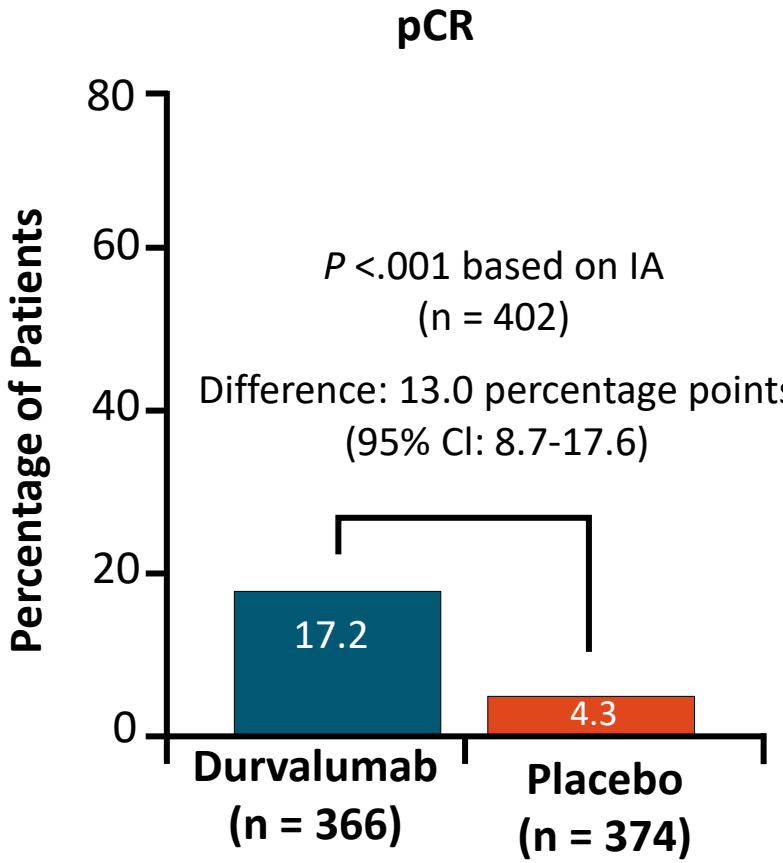
HR: 0.72 (95% CI: 0.56-0.93); *P* = .00517
Median f/u: 36.6 mo (range: 18.8-62.0)

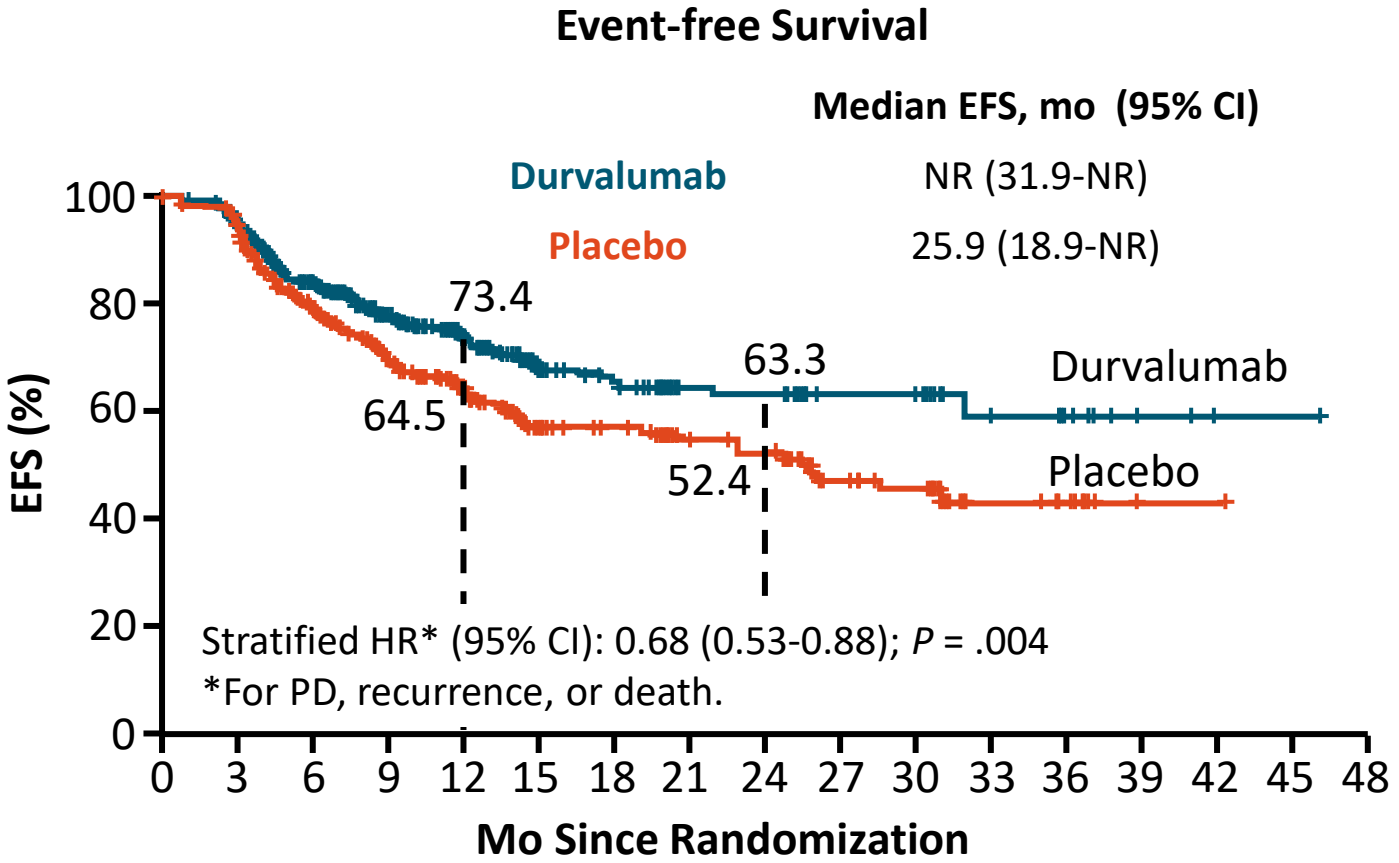
FDA-approved in October 2023 for resectable (tumors ≥4 cm or node-positive) NSCLC in combination with platinum-containing CT **as neoadjuvant treatment**, and then **continued as a single agent as adjuvant treatment** after surgery

Spicer. ESMO 2023. Abstr LBA56.

Slide credit: clinicaloptions.com

AEGEAN: Perioperative Durvalumab in Resectable NSCLC — pCR and EFS



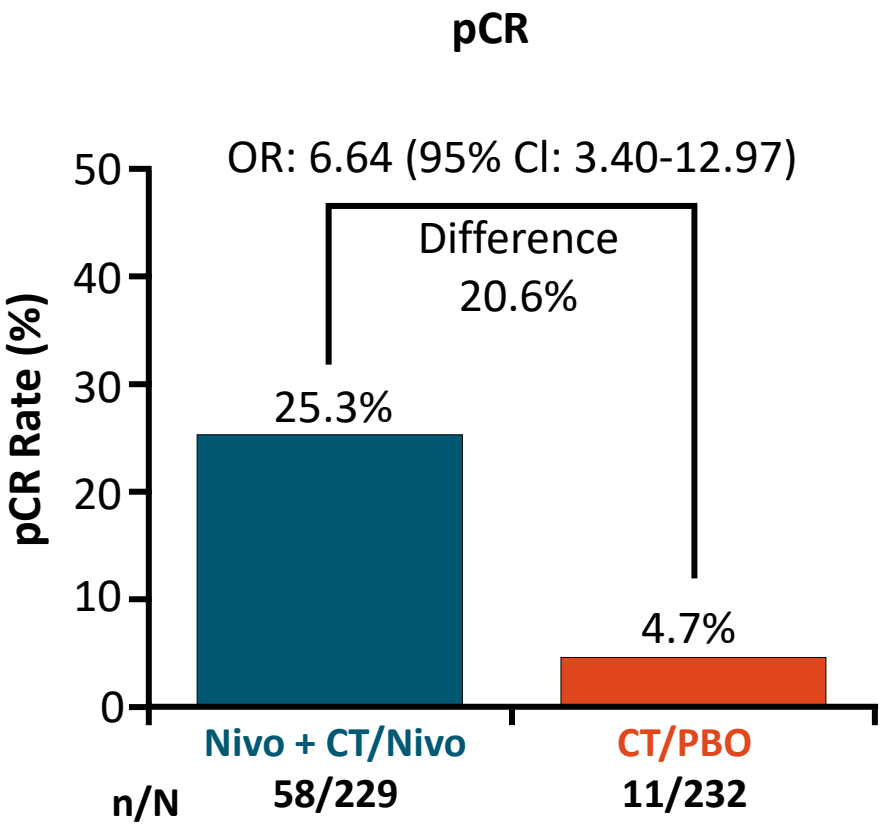


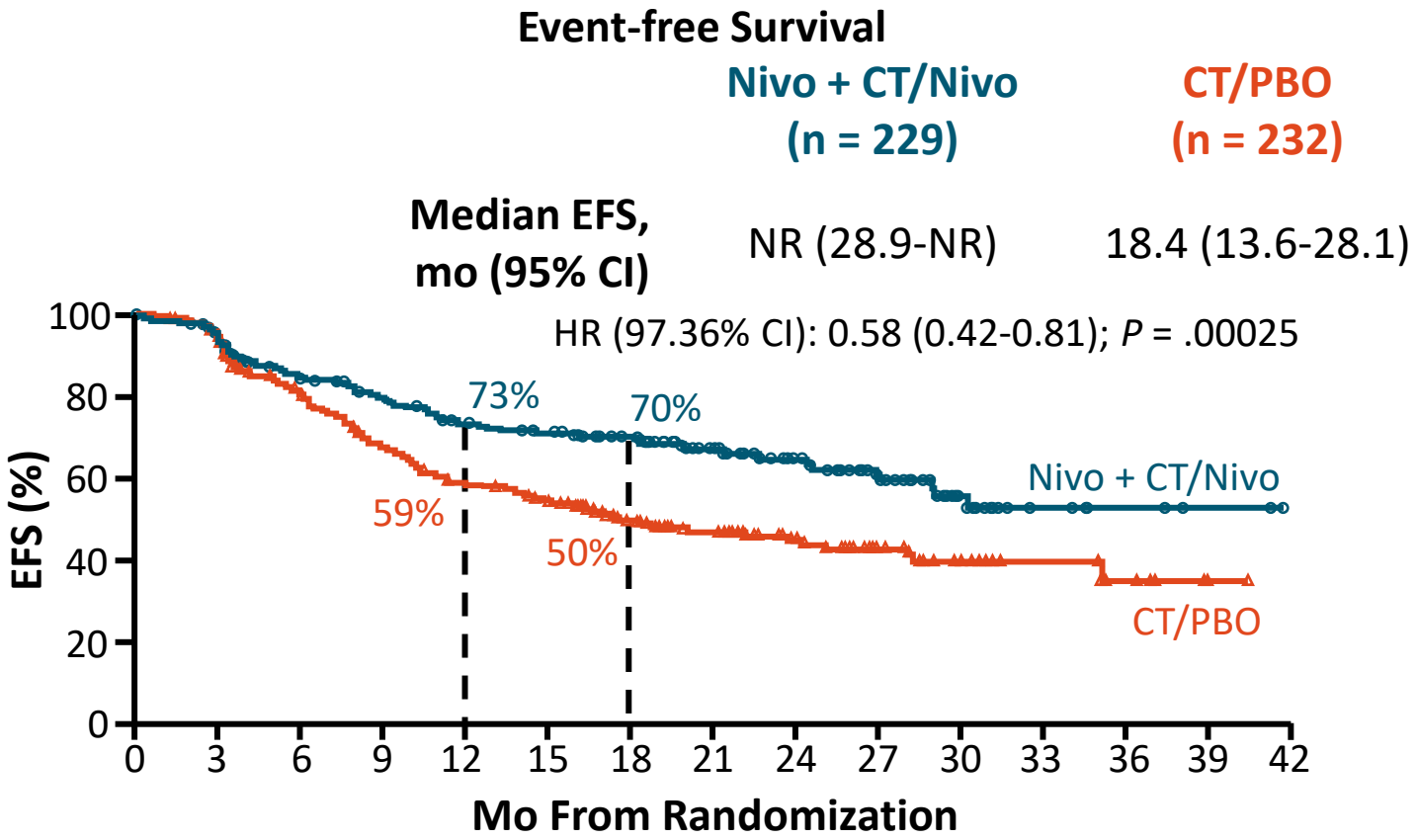
- EFS and pCR benefit with perioperative durvalumab was seen regardless of disease stage and PD-L1 expression

Heymach. NEJM. 2023;389:1672.

Slide credit: clinicaloptions.com

CheckMate 77T: Perioperative Nivolumab in Resectable NSCLC





- EFS benefit was across key subgroups including disease stage, nodal status, tumor histology, and PD-L1 expression
- MPR (35.4% vs 12.1%) rates were improved in the nivolumab arm compared with the chemotherapy arm

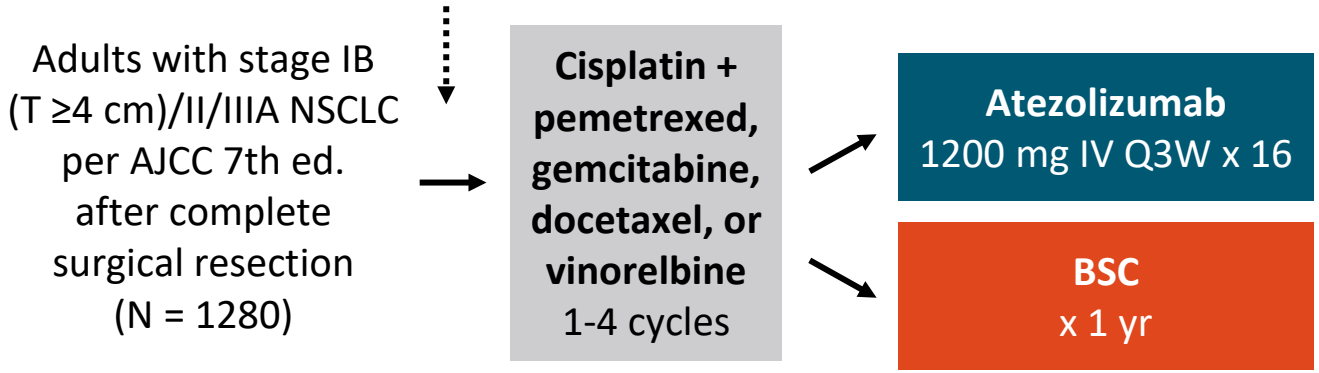
Cascone. ESMO 2023. Abstr LBA1.

Slide credit: clinicaloptions.com

Phase III Adjuvant Immunotherapy Trials

IMpower010[1,2]

Stratified by PD-L1 expression, sex, stage (IB vs II vs IIIA), and histology

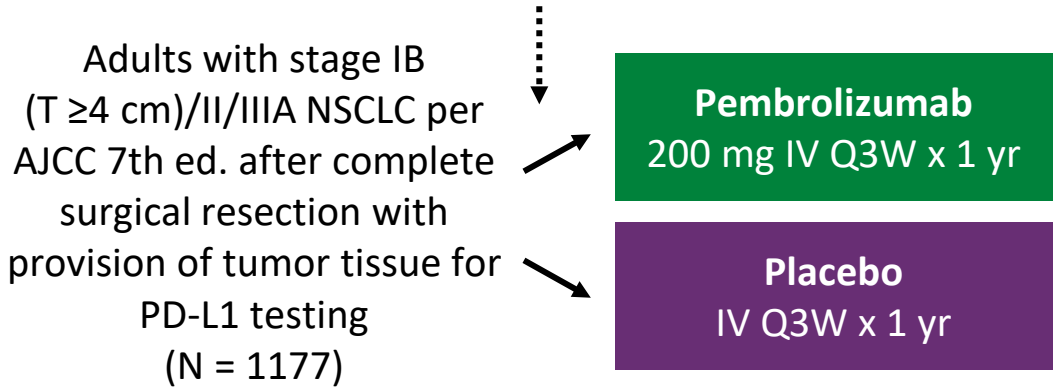


Chemotherapy mandatory

- **Primary endpoint:** DFS by investigator (hierarchical design) in PD-L1+ stage II-IIIA > all stage II-IIIA > ITT (stage IB-IIIA)

PEARLS/KEYNOTE-091[3]

Stratified by disease stage (IB vs II vs IIA), PD-L1 TPS (<1% vs 1%-49% vs ≥50%, and geographic region



Chemotherapy not mandatory

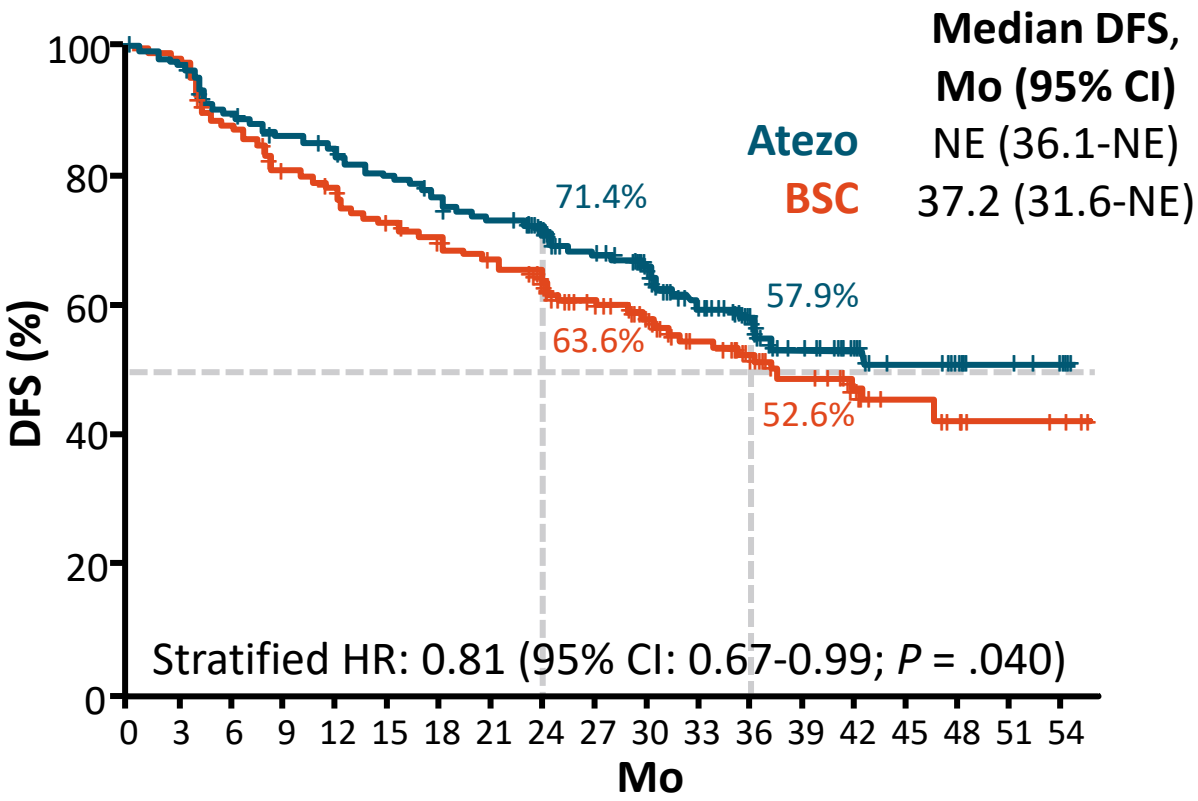
- **Primary endpoint:** DFS

Cross-trial comparisons have significant limitations. The information in this section is presented in order to generate discussion, not to make direct comparisons between study results.

1. Wakelee. ASCO 2021. Abstr 8500. 2. Felip. Lancet. 2021;398:1344. 3. Paz-Ares. ESMO Virtual 2022. Abstr VP3-2022.

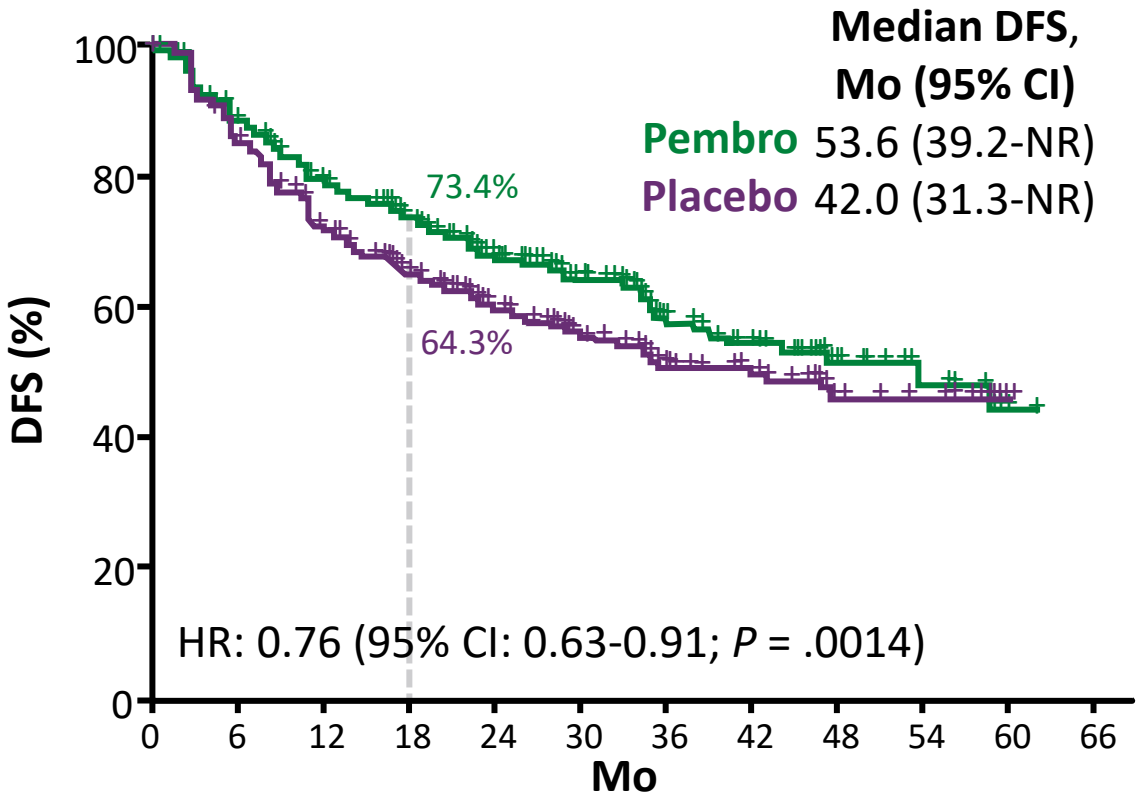
Adjuvant IO Trials: DFS in Overall Population (ITT)

IMpower010[1,2]



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

PEARLS/KEYNOTE-091[4,5]



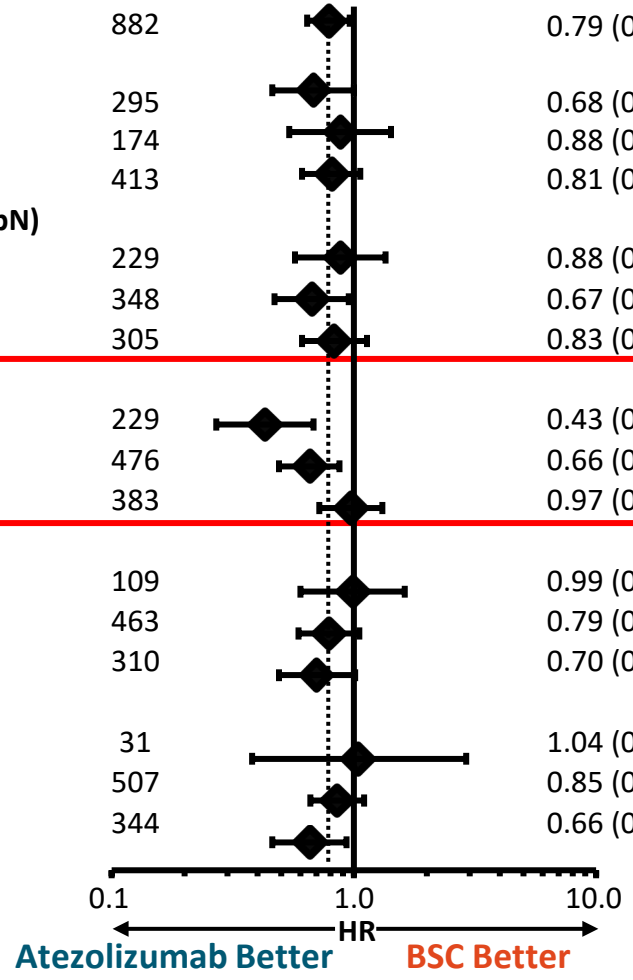
FDA-approved in January 2023 for **adjuvant treatment** following resection and platinum-based CT for adult patients with stage IB (T2a ≥4 cm), II, or IIIA NSCLC[6]

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

Adjuvant IO Trials: DFS by Subgroup

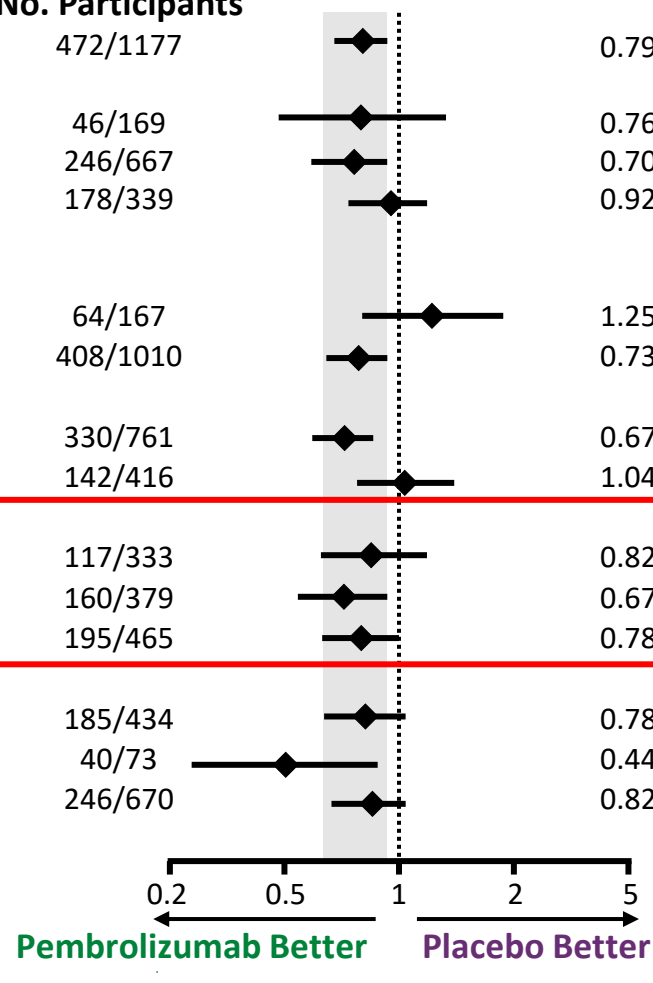
IMpower010: All Randomized Stage II-IIIA[1,2]

Subgroup	N	HR (95% CI)
All patients	882	0.79 (0.64-0.96)
Stage		
IIA	295	0.68 (0.46-1.00)
IIB	174	0.88 (0.54-1.42)
IIIA	413	0.81 (0.61-1.06)
Regional lymph node stage (pN)		
N0	229	0.88 (0.57-1.35)
N1	348	0.67 (0.47-0.95)
N2	305	0.83 (0.61-1.13)
SP263 PD-L1 status		
TC ≥50%	229	0.43 (0.27-0.68)
TC ≥1%	476	0.66 (0.49-0.87)
TC <1%	383	0.97 (0.72-1.31)
***EGFR* mutation status**		
Yes	109	0.99 (0.60-1.62)
No	463	0.79 (0.59-1.05)
Unknown	310	0.70 (0.49-1.01)
***ALK* rearrangement status**		
Yes	31	1.04 (0.38-2.90)
No	507	0.85 (0.66-1.10)
Unknown	344	0.66 (0.46-0.93)



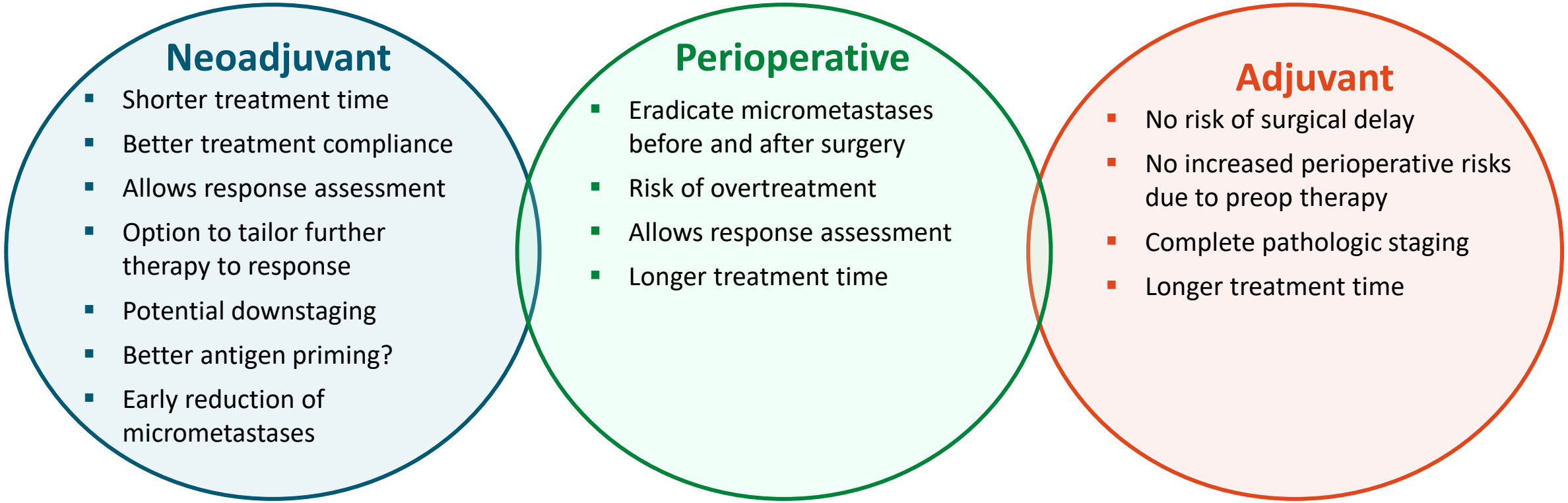
PEARLS/KEYNOTE-091: Overall Population[3,4]

Subgroup	No. Events/ No. Participants	HR (95% CI)
Overall	472/1177	0.79 (0.63-0.91)
Pathologic stage		
IB	46/169	0.76 (0.43-1.37)
II	246/667	0.70 (0.55-0.91)
IIIA	178/339	0.92 (0.69-1.24)
Received adjuvant chemotherapy		
No	64/167	1.25 (0.76-2.05)
Yes	408/1010	0.73 (0.60-0.89)
Histology		
Nonsquamous	330/761	0.67 (0.54-0.83)
Squamous	142/416	1.04 (0.75-1.45)
PD-L1 TPS		
≥50%	117/333	0.82 (0.57-1.18)
1%-49%	160/379	0.67 (0.48-0.92)
<1%	195/465	0.78 (0.58-1.03)
***EGFR* mutation**		
No	185/434	0.78 (0.59-1.06)
Yes	40/73	0.44 (0.23-0.84)
Unknown	246/670	0.82 (0.63-1.06)



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

How Is the Decision Made?

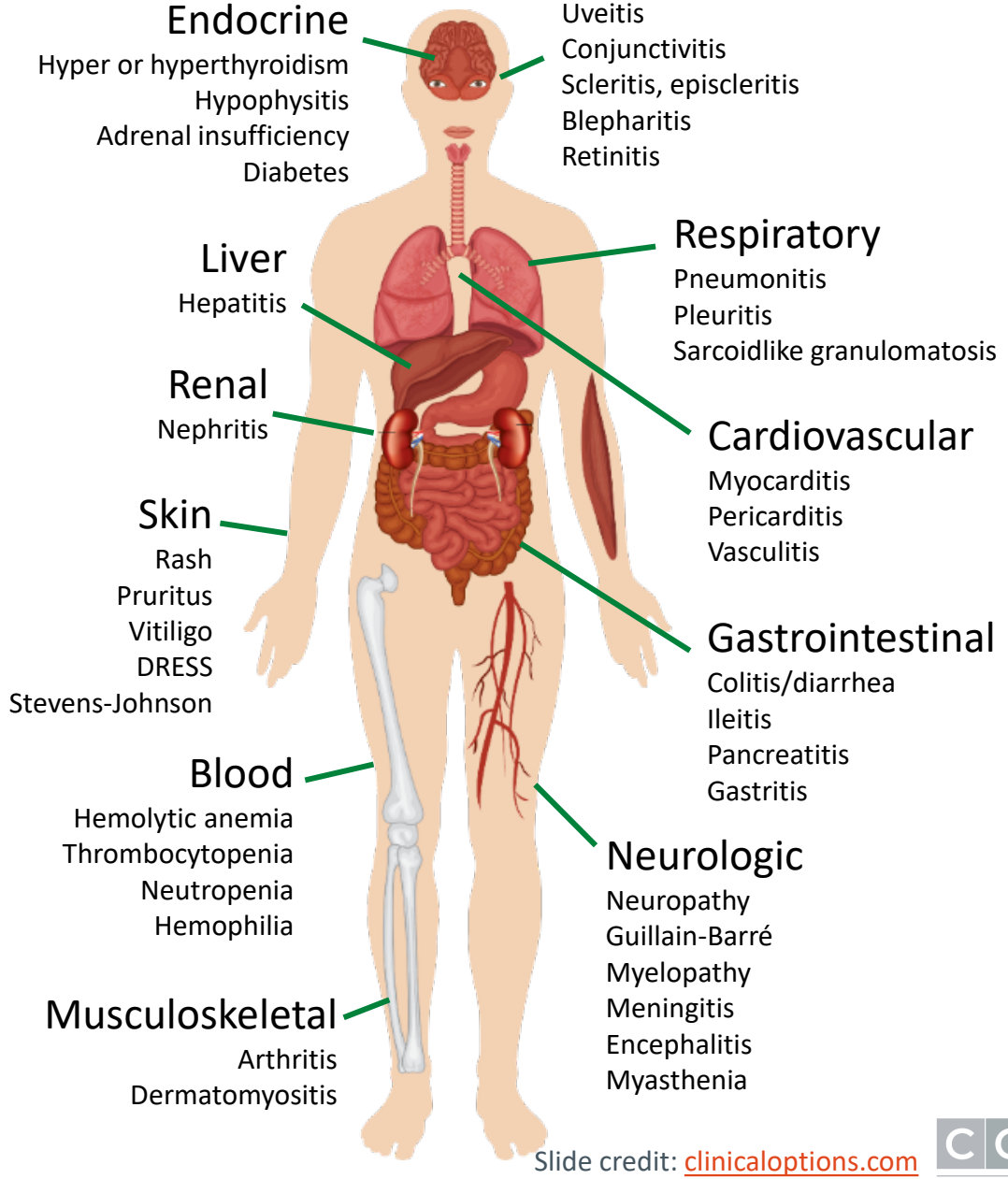


- Multidisciplinary discussion is critical and should be done early—prior to surgery but after mediastinal staging

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

Spectrum of irAEs

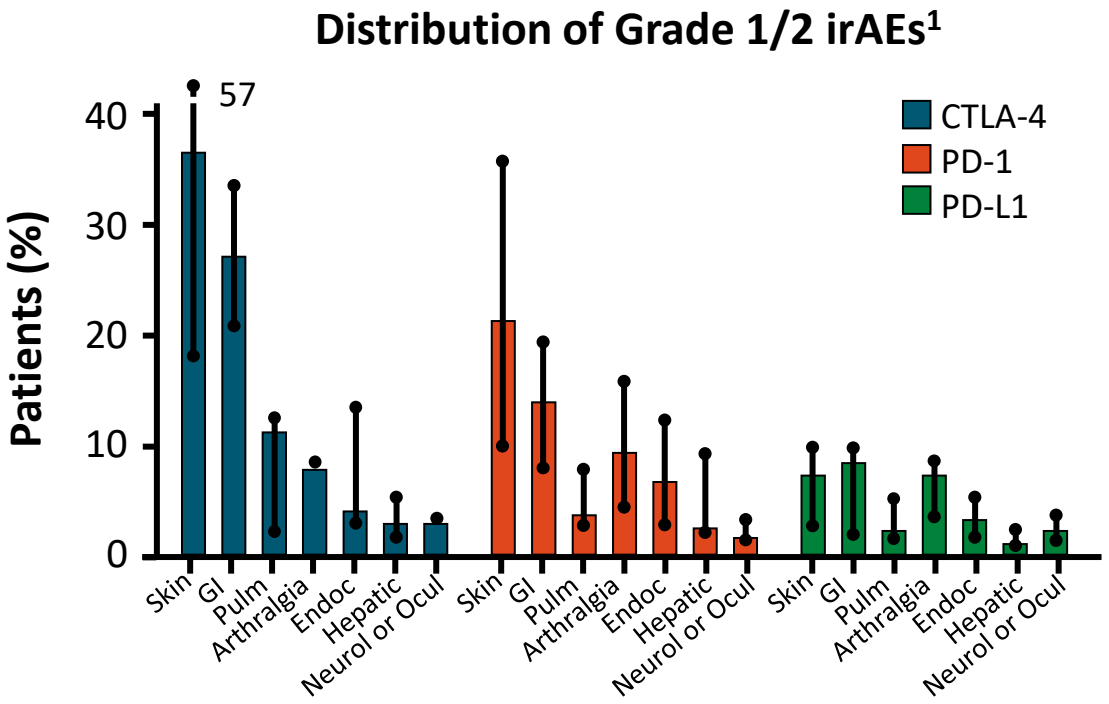
- irAEs can affect **any** organ of the body
- Onset varies
  - Usually 2 to 3 mo after starting tx
  - Up to 2 yr after tx completion
- Maintain high level of suspicion for irAEs when new symptoms develop
- If irAEs are suspected, conduct a complete workup, including lab tests, to rule out other causes

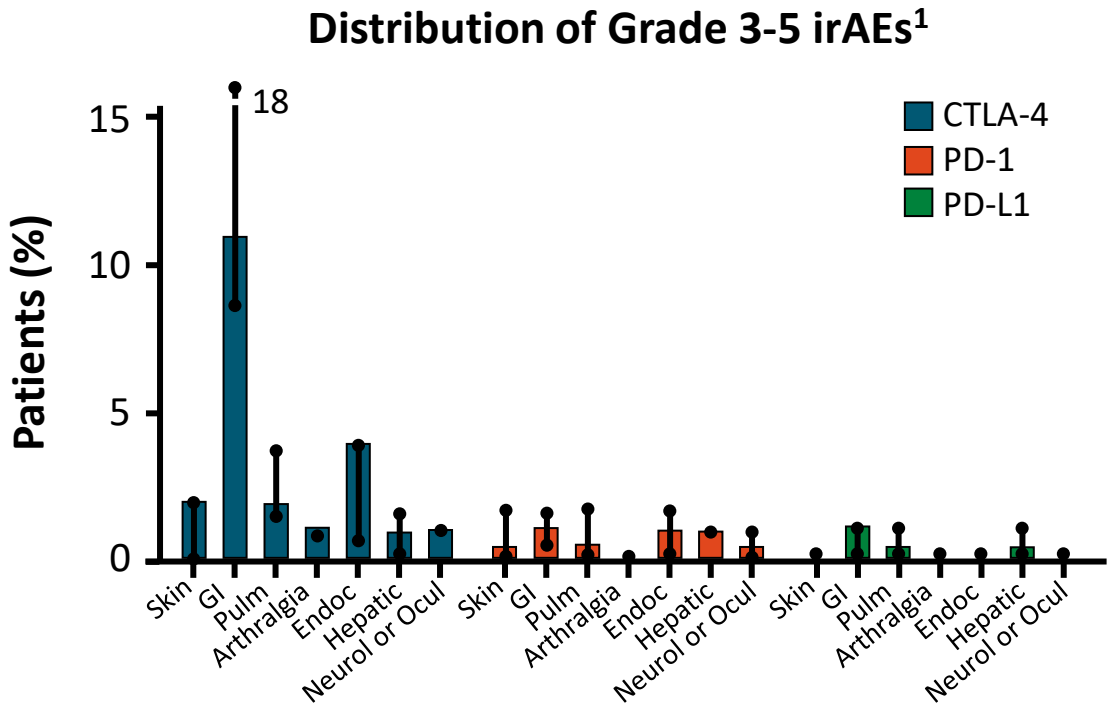


Brahmer. JCO. 2018;36:1714. Champiat. Ann Oncol. 2016;27:559. Michot. Eur J Cancer. 2016;54:139. Robert. ASCO 2017. Education session: checkpoint inhibitor immunotherapy. Steven. Rheumatology (Oxford). 2019;58:vii29. Winer. J Thorac Dis. 2018;10:S480. Zimmerman. Am Soc Clin Oncol Educ Book. 2018;38:682.

Slide credit: clinicaloptions.com

Frequency of irAEs With ICI Monotherapy*





*CTLA4 monotherapy is not used in NSCLC

- Incidence of irAEs varies among malignancies
  - Colitis more common in melanoma, pneumonitis more common in NSCLC[2]

1. Michot. Eur J Cancer. 2016;54:139. 2. Owen. ESMO 2018. Abstr 4304.

Slide credit: clinicaloptions.com

Patient and Caregiver Education and Counseling

- Provide overview of MoA
- Provide information booklet, wallet card
- Review recommendations for inactivated (nonlive) vaccinations (eg, COVID-19)

ons.org/clinical-practice-resources/immunotherapy-patient-wallet-card

- Ensure patient understands AEs associated with both ICI and CT during and after tx
  - Address any concerns about reporting symptoms
  - Review how to contact office to report symptoms
  - Review symptoms that patient needs to report urgently (eg, temp ≥100.5°F)
  - Counsel to report all symptoms!

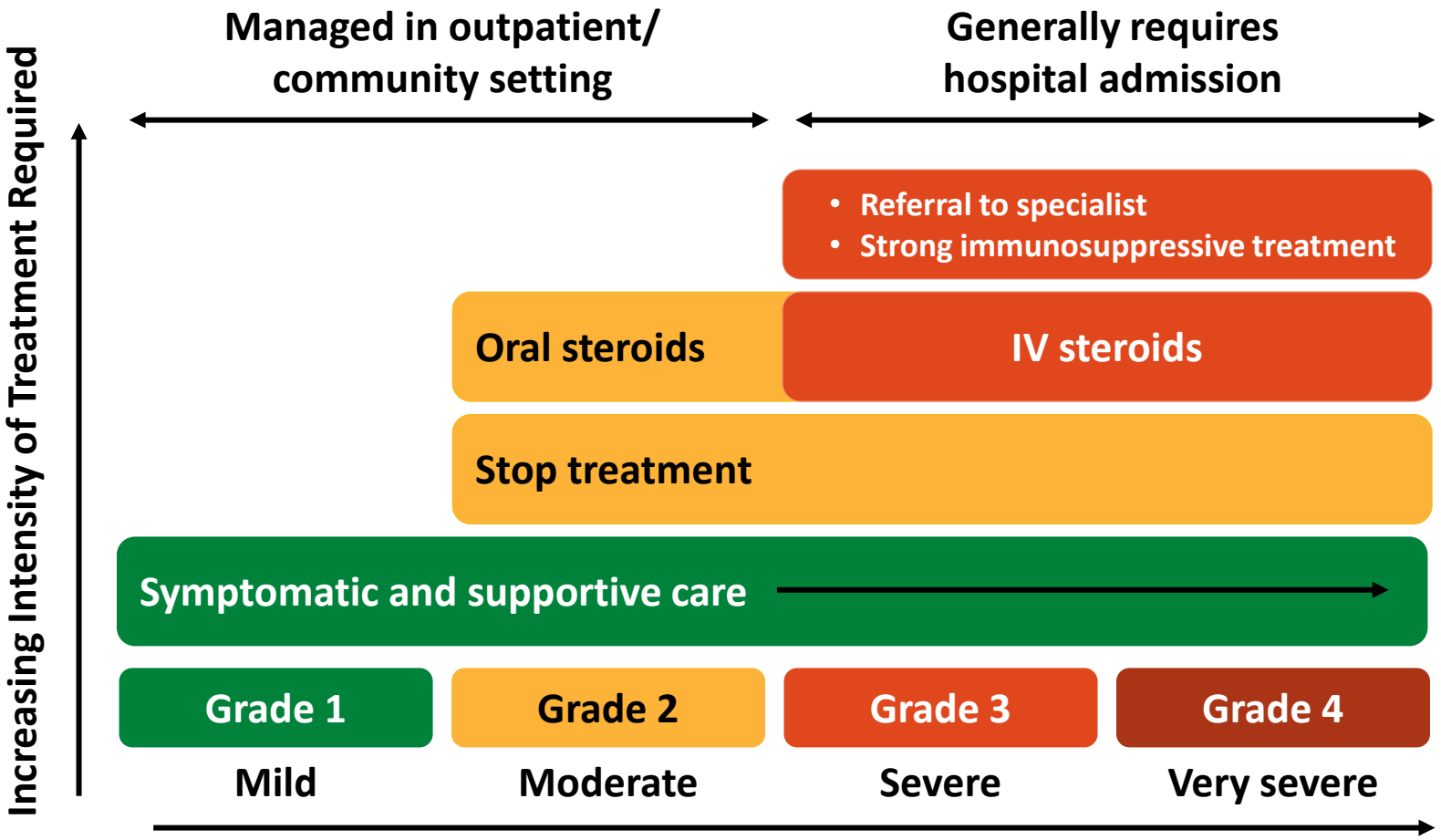
Patient Counseling Script

"If we catch the irAE early, there's a better chance we can reverse it and restart you on the ICI."

Aso. Asia Pac J Oncol Nurs. 2022;9:100076. Brahmer. J Immunother Cancer. 2021;9:e002435. Cheema. Curr Oncol. 2022;29:869. Wood. Clin J Oncol Nurs. 2019;23:271.

Slide credit: clinicaloptions.com

General Recommendations for Treatment of irAEs



- Steroids (PO/IV): 0.5-2 mg/ kg/d prednisone or equivalent; slow taper over 4-6 wk
- For some irAEs, ICI can be restarted after resolution (eg, rash)
- Endocrinopathies: ICI can generally be continued with management
- Multidisciplinary approach management is beneficial
  - Consult with specialists for severe irAEs

Haanen. Ann Oncol. 2022;33:1217. NCCN. Clinical practice guidelines in oncology: management of immunotherapy-related toxicities. v.2.2023. Vaddepally. Biomedicines. 2022;10:790.

General Recommendations for Management of AEs With Chemoimmunotherapy

- Counsel patients: "Report all your symptoms and let the provider figure out what's causing it"
  - Sometimes patients assume a symptom is just due to CT
- Management depends on figuring out cause of AE → **timing is critical!**
  - Employ a multidisciplinary approach for challenging cases

Parameter	CT	ICI
Typical timing/pattern	▪ Rapid onset after administration ▪ Cyclical onset/recovery	▪ Onset after several cycles ▪ Persists/worsens over time
General management strategies		
▪ Hold dose	**Yes**	**Yes**
▪ Reduce dose	**Yes**	**No**
▪ Switch to less toxic agent	**Yes**	**No**
▪ Steroids	**Rarely (depends on toxicity)**	**Yes***
▪ Permanently discontinue	**Yes (if severe)**	**Yes (if severe)**

*Steroid should be tapered slowly over 4-6 wk.

Hoffner. Cancer Treat Rev. 2020;85:101979. Madden. Clin J Oncol Nurs. 2017;21:30. Schneider. J Clin Oncol. 2021;39:4073.