DUTCH THORACIC GROUP

Neoadjuvant therapy in stage III NSCLC and the (changing) role of the surgeon

DTG-congress
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Declaration of interests K.J. Hartemink, MD, PhD

Affiliation / financial interest	Commercial company
Grants / Research support	KWF (ESLUNG study), NKI-AVL (UPLAN-I and -II study, ESLUNG-II study)
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Stock stakeholder	NA
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TOPICS

Staging

Landmark papers

Guidelines

Operability and resectability

(Neo)adjuvant ICI trials

Questions and challenges

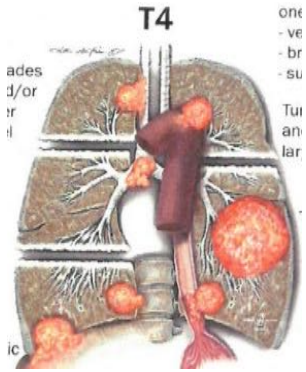
Conclusions

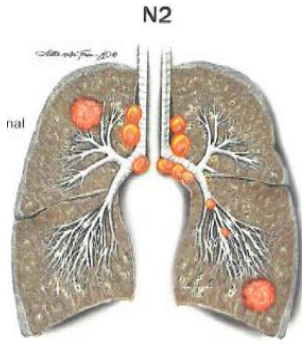
NSCLC STAGE III; A HETEROGENEOUS DISEASE

- Stage IIIA
  - T1a-2bN2
  - T3N1
  - T4N0
- Stage IIIB
  - T1a-T2bN3
  - T3-4N2
- Stage IIIC
  - T3-4N3

Stage			
Occult carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IA1	T1mi	N0	M0
	T1a	N0	M0
Stage IA2	T1b	N0	M0
Stage IA3	T1c	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
Stage IIB	T1a-c, T2a, b	N1	M0
	T3	N0	M0
Stage IIIA	T1a-c, T2a, b	N2	M0
	T3	N1	M0
	T4	N0, N1	M0
Stage IIIB	T1a-c, T2a, b	N3	M0
	T3, T4	N2	M0
Stage IIIC	T3, T4	N3	M0
Stage IV	Any T	Any N	M1
Stage IVA	Any T	Any N	M1a, M1b
Stage IVB	Any T	Any N	M1c

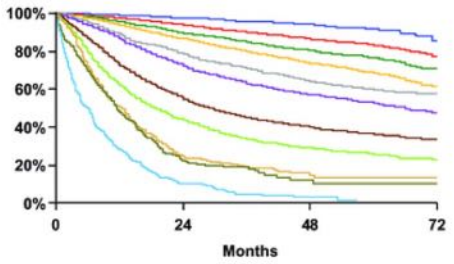
T3N1
T4N0
N2-3





NSCLC STAGE III, STAGING, PROGNOSIS AND TREATMENT

- Staging NSCLC provides information about prognosis
- However, in guidelines: choice of treatment is based on clinical staging
- Questions in stage III NSCLC
  - For this heterogeneous stage of disease; 1 single treatment (or combination of treatments) fits all subgroups?
  - What is the role of surgery in the treatment of stage III NSCLC?



Proposed	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%

Overall survival by clinical stage

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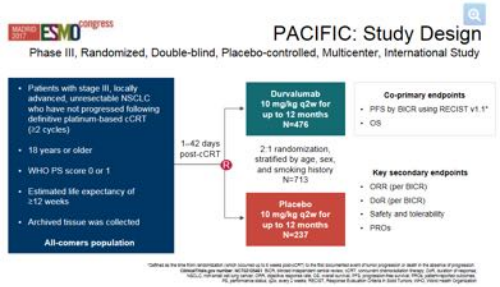
LANDMARK PAPERS 2007-2023

Van Meerbeeck, et al. J Natl Cancer Inst 2007
Eberhardt, et al. J Clin Oncol 2015

Albain, et al. Lancet 2009
Pless, et al. Lancet 2015

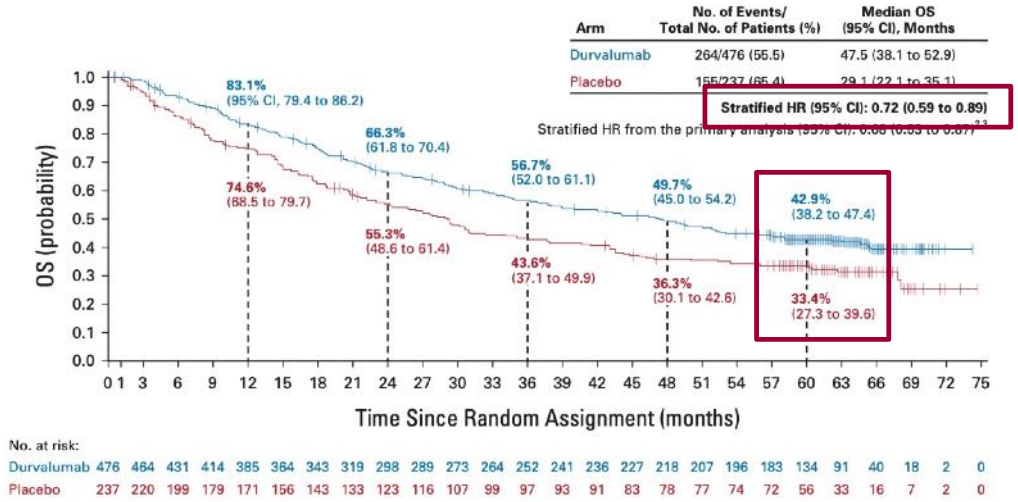
Auperin, et al. J Clin Oncol 2010
Köning, et al. ESMO open 2022

LANDMARK PAPERS; PACIFIC (5-YEAR OS)



Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

David R. Spigel, MD[1]; Corinne Faivre-Finn, MD, PhD[2]; Jhanelle E. Gay, MD[3]; David Vicente, MD[4]; David Planchard, MD, PhD[5]; Luis Paz-Ares, MD, PhD[6]; Johan F. Vansteenkiste, MD, PhD[7]; Marina C. Garassino, MD[8,9]; Rina Hui, PhD[10]; Xavier Quantin, MD, PhD[11]; Andreas Rimner, MD[12]; Yi-Long Wu, MD[13]; Mustafa Özgüroğlu, MD[14]; Ki H. Lee, MD[15]; Terufumi Kato, MD[16]; Maike de Wit, MD, PhD[17]; Takeaasu Kurata, MD[18]; Martin Reck, MD, PhD[19]; Byoung C. Cho, MD, PhD[20]; Suresh Senan, PhD[21]; Jarushka Naidoo, MBBCH, MHS[22]; Helen Mann, MSc[23]; Michael Newton, PharmD[24]; Piruntha Thiyagarajah, MD[25]; and Scott J. Antonia, MD, PhD[3]; on behalf of the PACIFIC Investigators



- HR for OS: 0.72
- ± 10% survival benefit after adjuvant durvalumab
- Note: 'Unresectable' tumors (% resectable?)

2007 EORTC | 2009 INT-0139 | 2010 Meta-analyse | 2015 ESPATUE | 2015/2022 SAKK | 2017/2018/2022 PACIFIC

Antonia, et al. N Engl J Med 2018
Spigel, et al. J Clin Oncol 2022

LANDMARK PAPERS; ADAURA (5-YEAR OS)


The NEW ENGLAND JOURNAL of MEDICINE

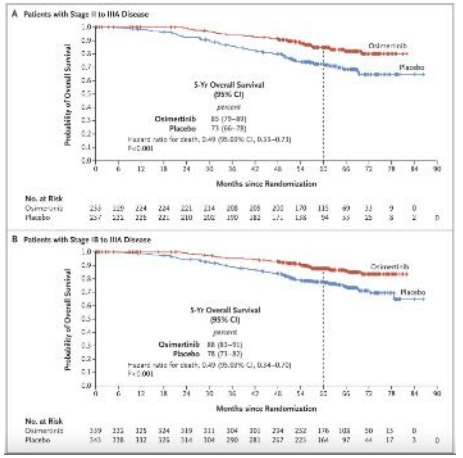
ESTABLISHED IN 1812 OCTOBER 29, 2020 VOL. 383 NO. 18

Osimertinib in Resected *EGFR*-Mutated Non–Small-Cell Lung Cancer

Yi-Long Wu, M.D., Masahiro Tsuboi, M.D., Jie He, M.D., Thomas John, Ph.D., Christian Grohe, M.D., Margarita Majem, M.D., Jonathan W. Goldman, M.D., Konstantin Laktionov, Ph.D., Sang-We Kim, M.D., Ph.D., Terufumi Kato, M.D., Huu-Vinh Vu, M.D., Ph.D., Shun Lu, M.D., Kye-Young Lee, M.D., Ph.D., Charuwan Akewanlop, M.D., Chong-Jen Yu, M.D., Ph.D., Filippo de Marinis, M.D., Laura Bonanno, M.D., Manuel Domine, M.D., Ph.D., Frances A. Shepherd, M.D., Lingmin Zeng, Ph.D., Rachel Hodge, M.Sc., Ajlan Atasoy, M.D., Yuri Rukazenkov, M.D., Ph.D., and Roy S. Herbst, M.D., Ph.D., for the ADAURA Investigators*

NSCLC, IB-IIIA, EGFR+, resection ± adjuvant chemotherapy + (*r*) osimertinib or placebo; improvement 2-yr DFS (primary endpoint)

OS



HR 0.49

HR 0.49

ORIGINAL ARTICLE

Overall Survival with Osimertinib in Resected EGFR-Mutated NSCLC

Masahiro Tsuboi, M.D., Roy S. Herbst, M.D., Ph.D., Thomas John, M.B., B.S., Ph.D., Terufumi Kato, M.D., Margarita Majem, M.D., Ph.D., Christian Grohé, M.D., Jie Wang, M.D., Ph.D., Jonathan W. Goldman, M.D., Shun Lu, M.D., Wu-Chou Su, M.D., Filippo de Marinis, M.D., Frances A. Shepherd, M.D., et al., for the ADAURA Investigators*

Improvement 5-yr OS; II-IIIA: 85 vs. 73% (HR 0.49), IB-IIIA: OS = 88 vs. 78% (HR 0.49) (secondary endpoints)

2007 EORTC

2009 INT-0139

2010 Meta-analyse

2015 ESPATUE

2015/2022 SAKK

2017/2018/2022 PACIFIC

2020/2023 ADAURA

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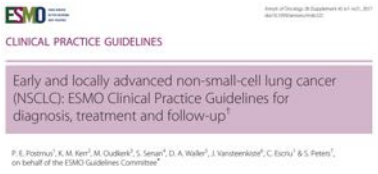
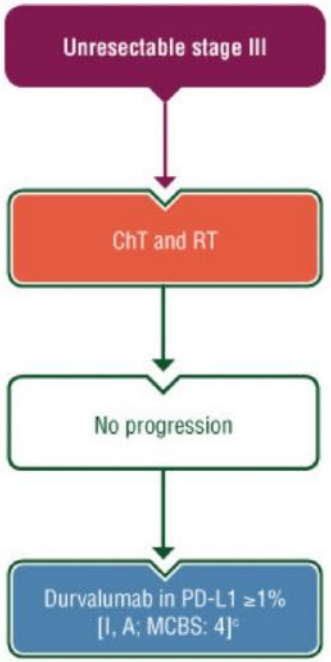
GUIDELINES; ESMO


ESMO
CLINICAL PRACTICE GUIDELINES
Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

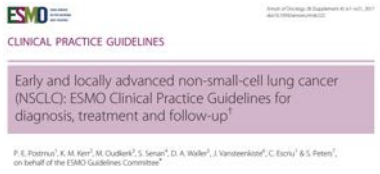
- Distinction resectable vs. unresectable LA-NSCLC (stage III)
- Definition <u>unresectable</u> stage III (as discussed in MDT):
  - complete resection (R0) (± induction treatment) is not possible (?)
- Treatment: cCRT (cisplatinum-based, 60-66 Gy)
- eUpdate (4-2020): adjuvant ICI (PACIFIC, i.e. durvalumab)



Recommendation

The consolidation administration of the immune checkpoint inhibitor durvalumab 1 to 42 days after the end of chemoradiotherapy has demonstrated a survival benefit in unresectable stage III NSCLC and is recommended in patients whose tumours express PD-L1 on ≥1% of tumour cells and whose disease has not progressed following platinum-based chemoradiotherapy (as per the EMA approved indication {[I, A;

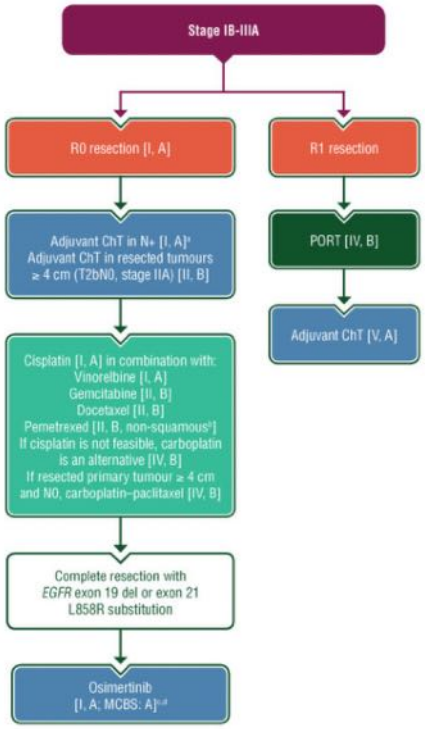
GUIDELINES; ESMO


ESMO
CLINICAL PRACTICE GUIDELINES
Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

- Definition <u>resectable</u> stage III (as discussed in MDT):
  - Stage III NSCLC, with a single station N2, nodal downstaging (?) after induction treatment, R0 resection deemed possible (no pneumonectomy)

- Treatment:
  - Resection + adjuvant chemotherapy
  - (neoadjuvant) cCRT + resection
  - eUpdate (9-2021): adjuvant osimertinib (IB-IIIA) (EGFR) (ADAURA)

Osimertinib is indicated for the <u>adjuvant</u> treatment after complete tumour resection in adult patients with stage IB-IIIA NSCLC whose tumours have *EGFR* exon 19 deletions or exon 21 L858R substitution mutations [I, A].



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‘OPERABLE’ NSCLC

- Multidisciplinary patient assessment (and treatment planning)

- Is the patient ‘operable’?
  - Performance status
  - Cardiac function
  - Lung function (spirometry, (bicycle) ergospirometry)
  - Comorbidity (…ies) and medication
  - Patient preferences

- What is the surgical approach; thoracotomy, sternotomy, VATS, robot?
- What is the extend of surgery required (for an R0 resection)?
- Is my patient fit for this kind of surgical approach?
- What kind of risks is the patient (and treating team) willing to take?
- Alternative treatment(s) possible?

‘RESECTABLE’ NSCLC

Postmus et al. Ann Oncol 2017
ESMO Guidelines Committee; eUpdate 2021

NCCN Guidelines, NSCLC Version 2.2024
Brandao et al. J Thorac Oncol 2023

‘RESECTABLE NSCLC’

No consensus between tumor board members

First multidisciplinary meeting (ERS, ETOP, ESP, ESTRO and IASLC), 3-2023, Copenhagen

Leids Universitair Medisch Centrum

Postmus, et al. Ann Oncol 2017
ESMO Guidelines Committee; eUpdate 2021

NCCN Guidelines, NSCLC Version 2.2024
Brandao, et al. J Thorac Oncol 2023

NETHERLANDS CANCER INSTITUTE

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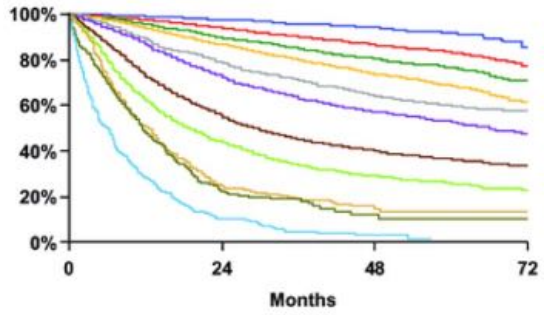
NSCLC STAGE III; WHAT IS THE PROBLEM AND WHAT DO WE NEED?



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GOALS IN TREATING STAGE III NSCLC

‘NEW’ MULTIMODALITY STRATEGIES, INCL. SURGERY

Many multimodality trials, introducing

- Immune Checkpoint Inhibition (ICI/IO)
- Chemotherapy + ICI
- Radiotherapy + ICI
- Chemoradiation + ICI
- Targeted therapy (EGFR-TKI, ALK, etc.)

In what order?

- Neoadjuvant
- Perioperative
- Adjuvant

Neoadjuvant/perioperative chemo-ICI

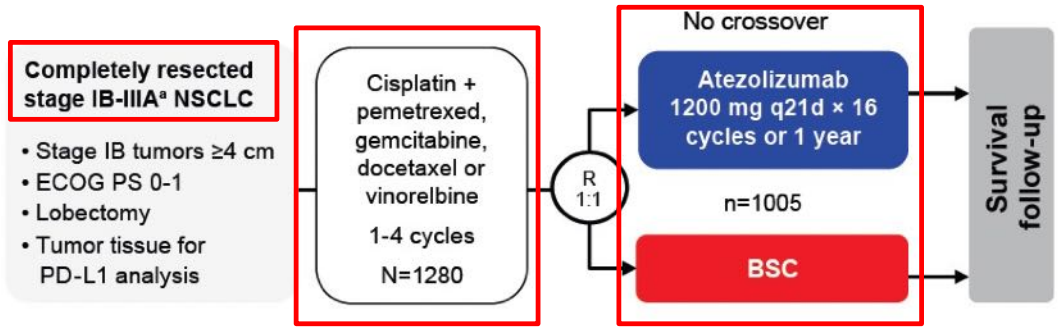
- CheckMate 816
- NADIM-II
- AEGEAN
- NEOTORCH
- CheckMate 77T
- KeyNote 671
- NEOSTAR
- NEOCOAST
- CANOPY-N
- RATIONALE 315
- IMpower 030
- …

Adjuvant (chemo-) ICI

- KeyNote 091
- IMpower 010
- BR21/NVALT 24
- ANVIL
- ACCIO
- …

ADJUVANT TREATMENT; IMPOWER-010

Adjuvant IO trial in resectable stage IB-IIIA NSCLC (with longest follow-up)



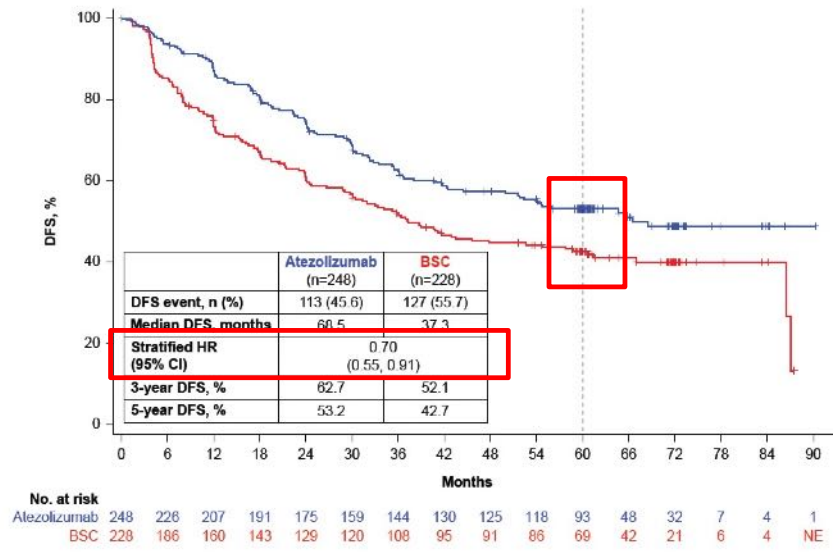
Stratification factors
• Sex | Disease stage | Histology | PD-L1 status

Primary endpoint
• Investigator-assessed DFS tested hierarchically

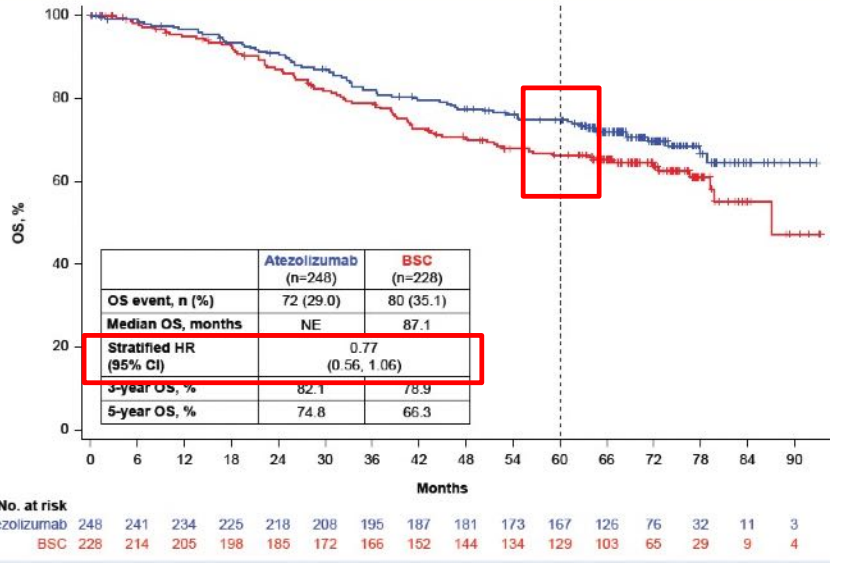
Key secondary endpoints
• OS in ITT | DFS in PD-L1 TC ≥50% stage II-IIIA | 3- and 5-year DFS

IMPOWER-010; 5-YEAR UPDATE

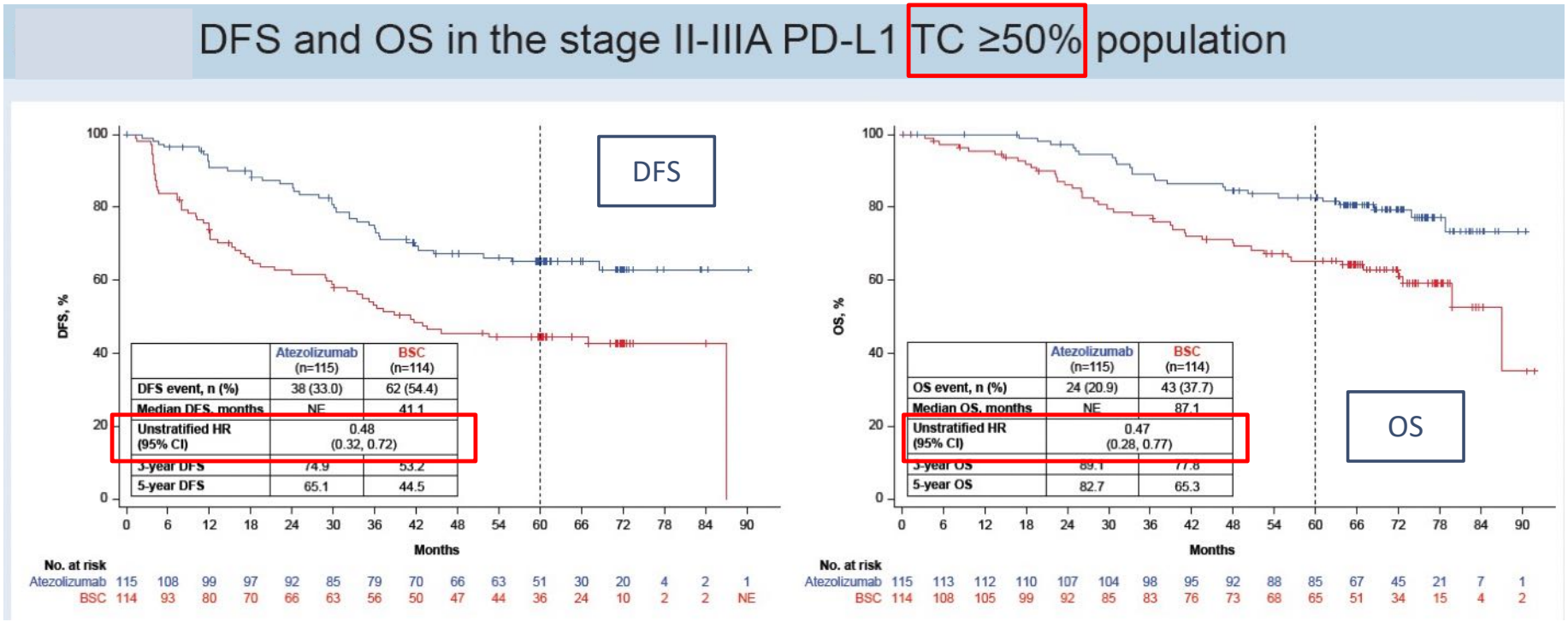
DFS in the stage II-IIIA PD-L1 TC ≥1% population



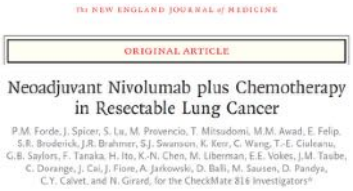
OS in the stage II-IIIA PD-L1 TC ≥1% population



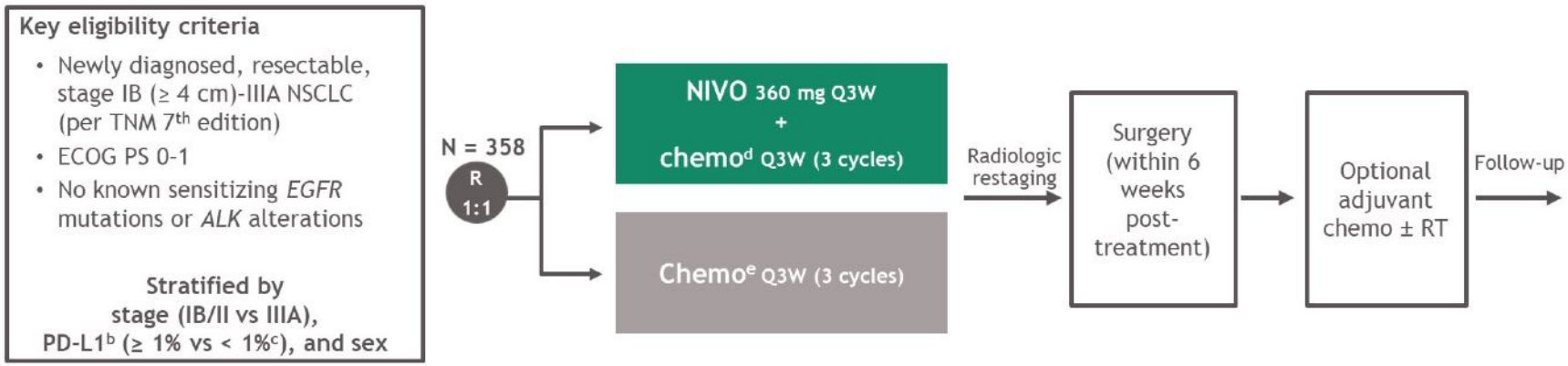
IMPOWER-010; 5-YEAR UPDATE



NEOADJUVANT TREATMENT; CHECKMATE 816

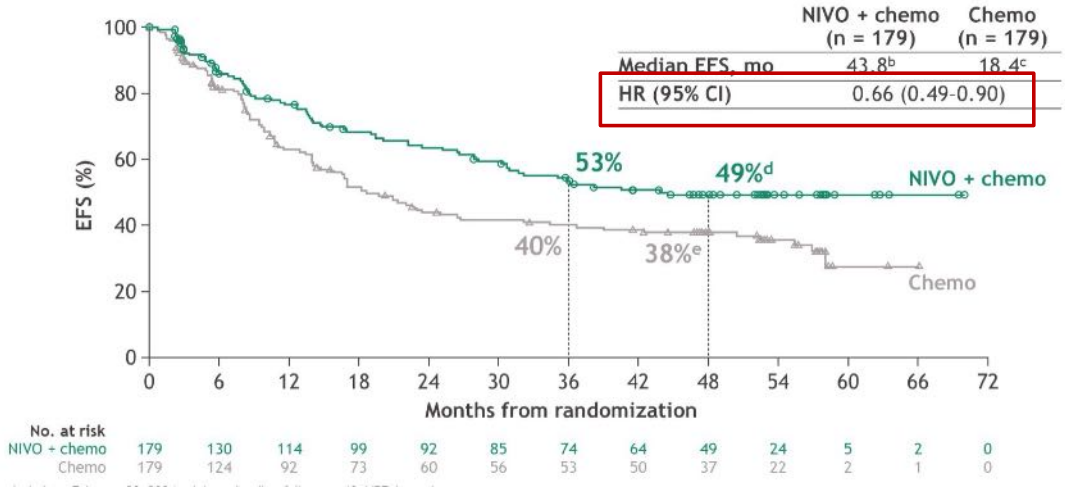


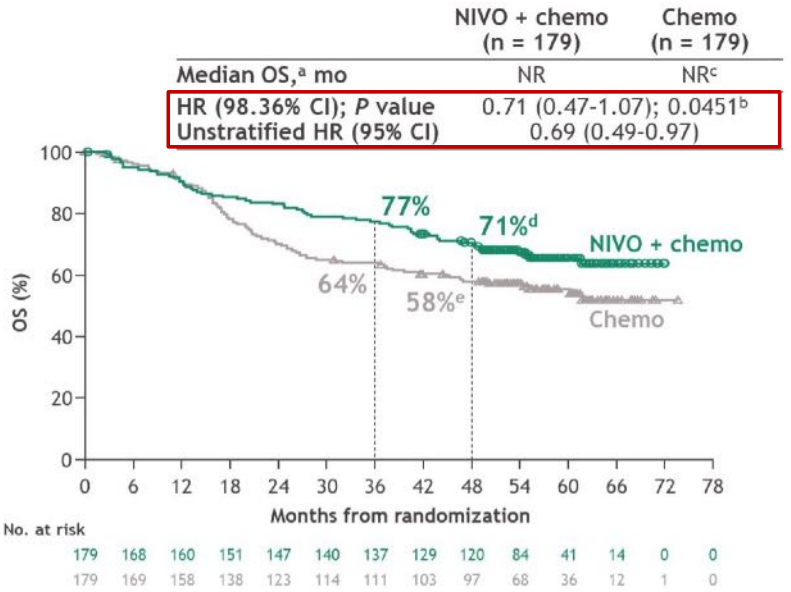
- (first phase III) RCT NSCLC IB-IIIA (N = 358, stage III = 64%) (*r*) (3x nivo/chemo or 3x chemo) + resection
- Endpoints: EFS (progression/recurrence/death), pCR



CHECKMATE 816; 4-YEAR UPDATE

- EFS benefit most in <u>stage IIIA</u> and <u>PD-L1 ≥1%</u>



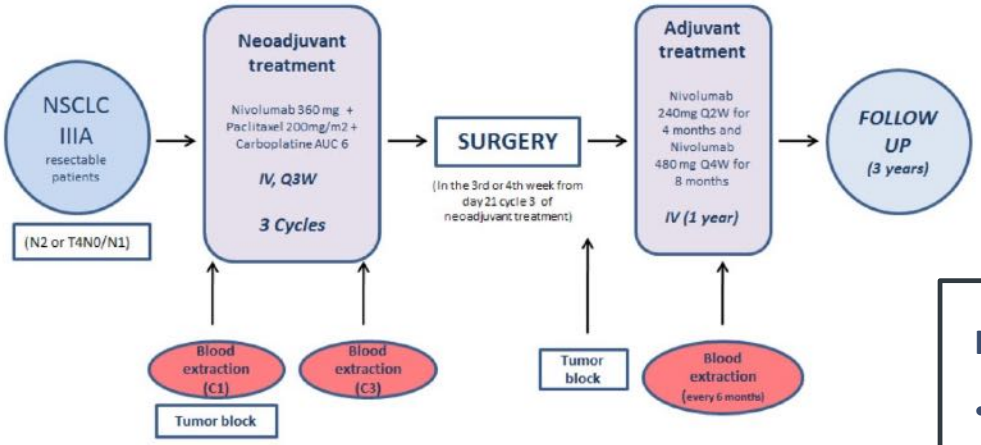


Forde, et al. N Engl J Med 2022
Spicer, et al. ASCO 2024

PERIOPERATIVE TREATMENT; NADIM-I

NADIM I study; (first) perioperative chemo-IO in stage III NSCLC (2019)

NADIM Patient baseline characteristics	N=46 (ITT)
Age (median, range)	63(41-77)
Co-morbidities, N (%)	43 (93,5)
N2	33 (89.2)
Multiple station	25 (75.8)



Initial results

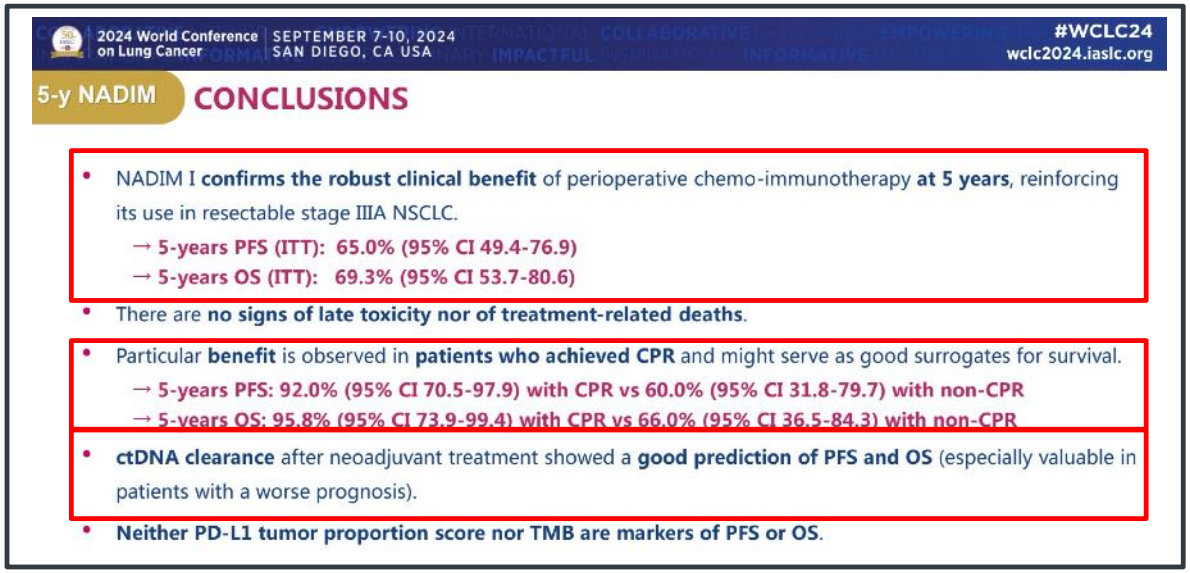
- PFS 77% (2-year)
- OS 82% (3-year)

Provencio et al. Lancet Oncol 2020
Provencio et al. J Clin Oncol 2022

NADIM-I; 5-YEAR UPDATE

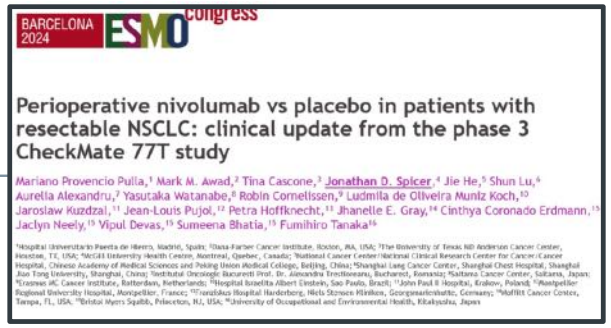
- Most benefit PFS/OS in pCR
- ctDNA clearance predicts PFS/OS

Courtesy Mariano Provencio



Provencio et al. Lancet Oncol 2020
Provencio et al. J Clin Oncol 2022

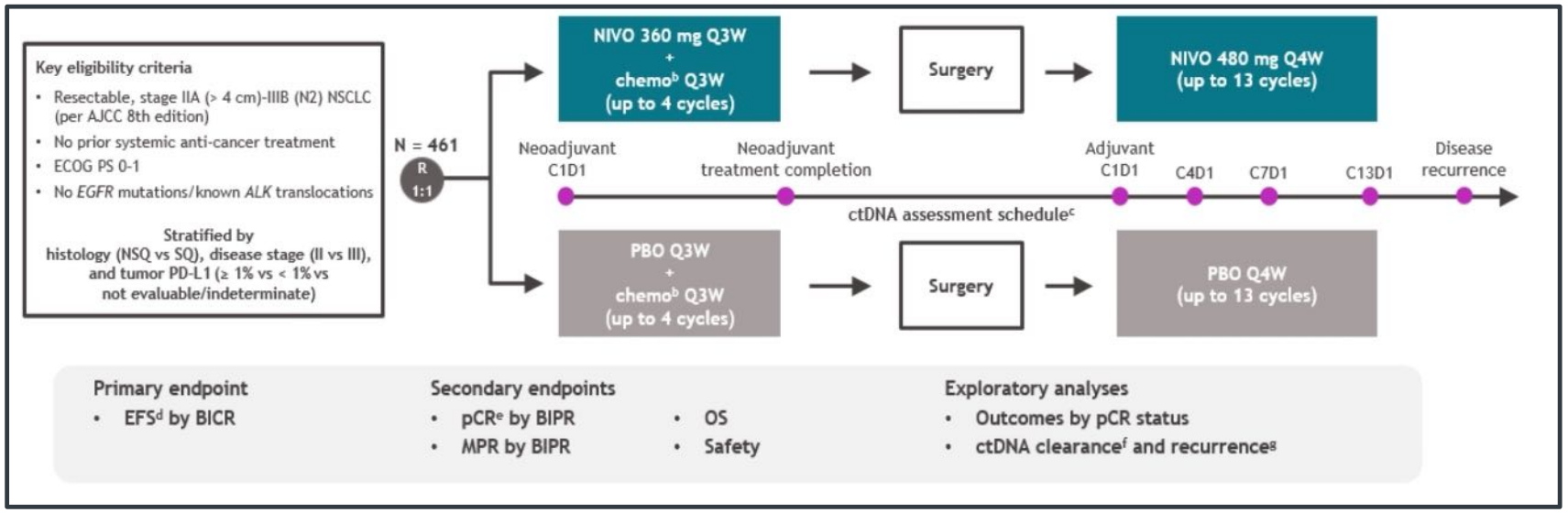
PERIOPERATIVE TREATMENT; CHECKMATE 77T


BARCELONA 2024 ESMO Congress

Perioperative nivolumab vs placebo in patients with resectable NSCLC: clinical update from the phase 3 CheckMate 77T study

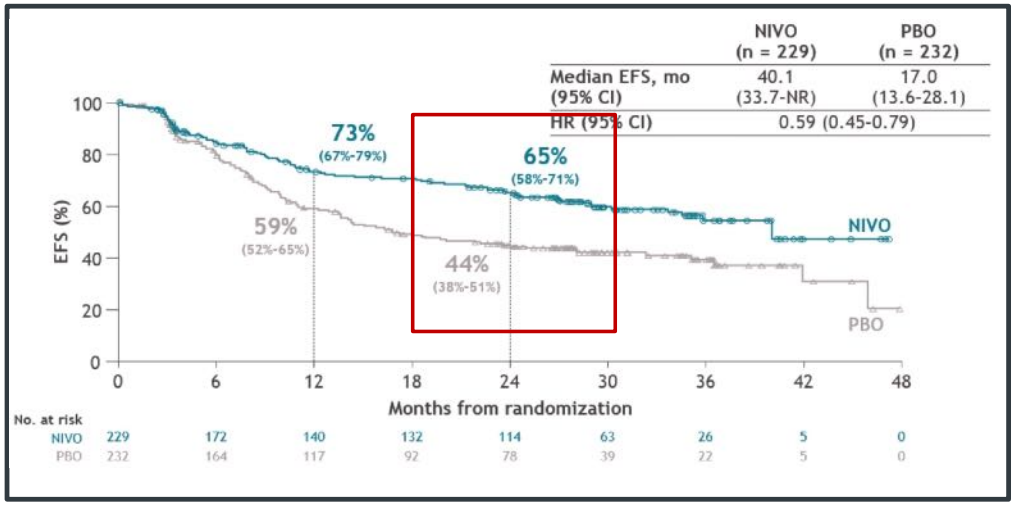
Mariano Provencio Pulla,[1] Mark M. Awad,[2] Tina Cascone,[3] Jonathan D. Spicer,[4] Jie He,[5] Shun Lu,[6] Aurelia Alexandru,[7] Yasutaka Watanabe,[8] Robin Cornelissen,[9] Ludmila de Oliveira Muniz Koch,[10] Jaroslaw Kuzdzal,[11] Jean-Louis Pujol,[12] Petra Hoffknecht,[13] Jhanelle E. Gray,[14] Cinthya Coronado Erdmann,[15] Jaclyn Neely,[15] Vipul Devas,[15] Sumeena Bhatia,[15] Fumihiro Tanaka[16]

Stage IIA-IIIB (N2) NSCLC
Endpoint: EFS (pCR, MPR, OS)
N=461

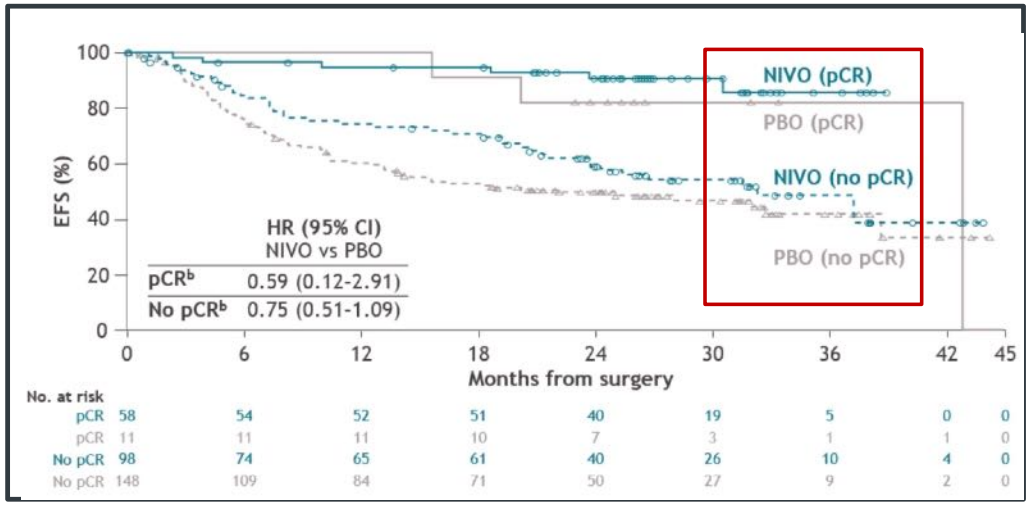


CHECKMATE 77T; CLINICAL OUTCOMES BY pCR

Courtesy Jonathan Spicer



EFS; HR 0.59 (0.45-0.79)

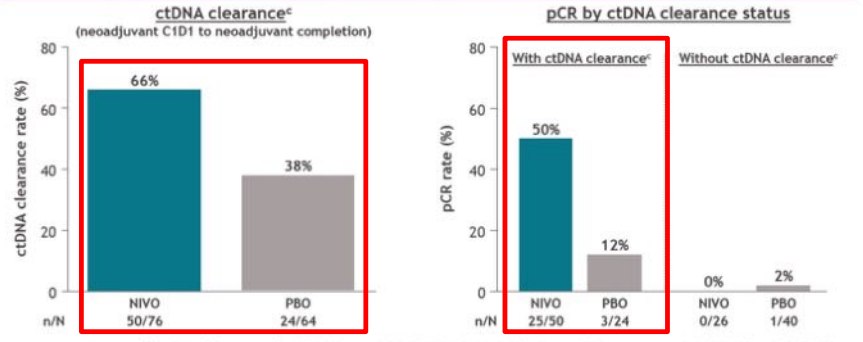


EFS (by pCR vs no pCR)

CHECKMATE 77T; CLINICAL OUTCOMES BY ctDNA

Courtesy Jonathan Spicer

ctDNA clearance during the neoadjuvant period[a,b]



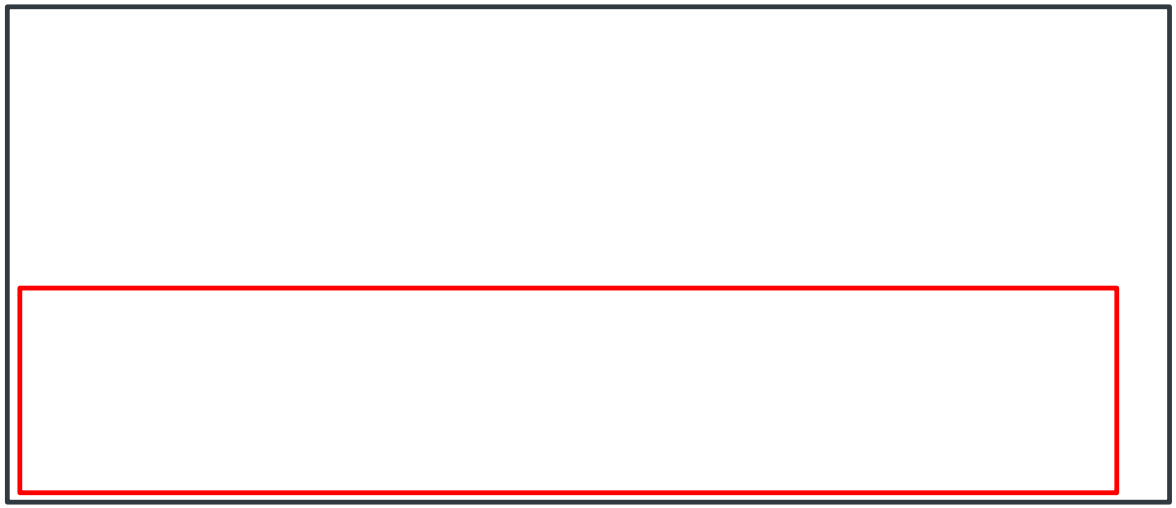
- Among patients with ctDNA clearance, the EFS HR was 0.38 (95% CI, 0.16-0.88); 2-year EFS rates were 81% (NIVO) vs 58% (PBO)
- Among patients without ctDNA clearance, the EFS HR was 0.74 (95% CI, 0.39-1.42); 2-year EFS rates were 50% (NIVO) vs 31% (PBO)

More often ctDNA clearance in nivolumab group (neoadjuvant)
With ctDNA clearance, more often pCR

Summary

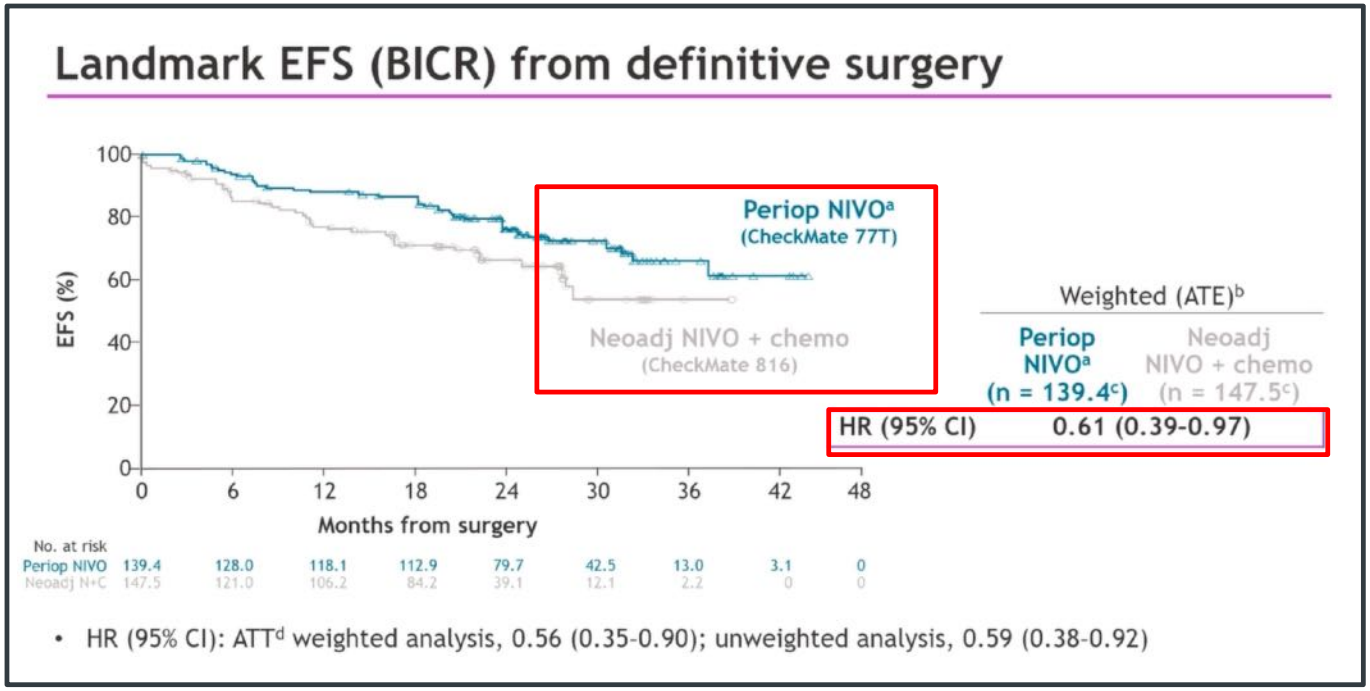
- In this updated analysis from CheckMate 77T, perioperative NIVO continued to show EFS benefit vs PBO in patients with resectable NSCLC (HR, 0.59)
  - Landmark EFS from definitive surgery favored NIVO, regardless of pCR status
- In an exploratory ctDNA analysis,
  - Neoadjuvant treatment with NIVO + chemo showed greater ctDNA clearance vs PBO + chemo, which was associated with pCR and EFS benefit
  - ctDNA recurrence appeared to be less frequent in patients who received adjuvant NIVO vs PBO, suggesting a potential benefit of adjuvant NIVO
- Perioperative NIVO had similar safety outcomes between patients with or without pCR; no new safety signals were observed
- Taken together, these efficacy and comprehensive ctDNA results further support perioperative NIVO as an efficacious treatment option for patients with resectable NSCLC

NEOADJUVANT/PERIOPERATIVE TREATMENT; CM816 VS. CM77T



Courtesy Patrick Forde

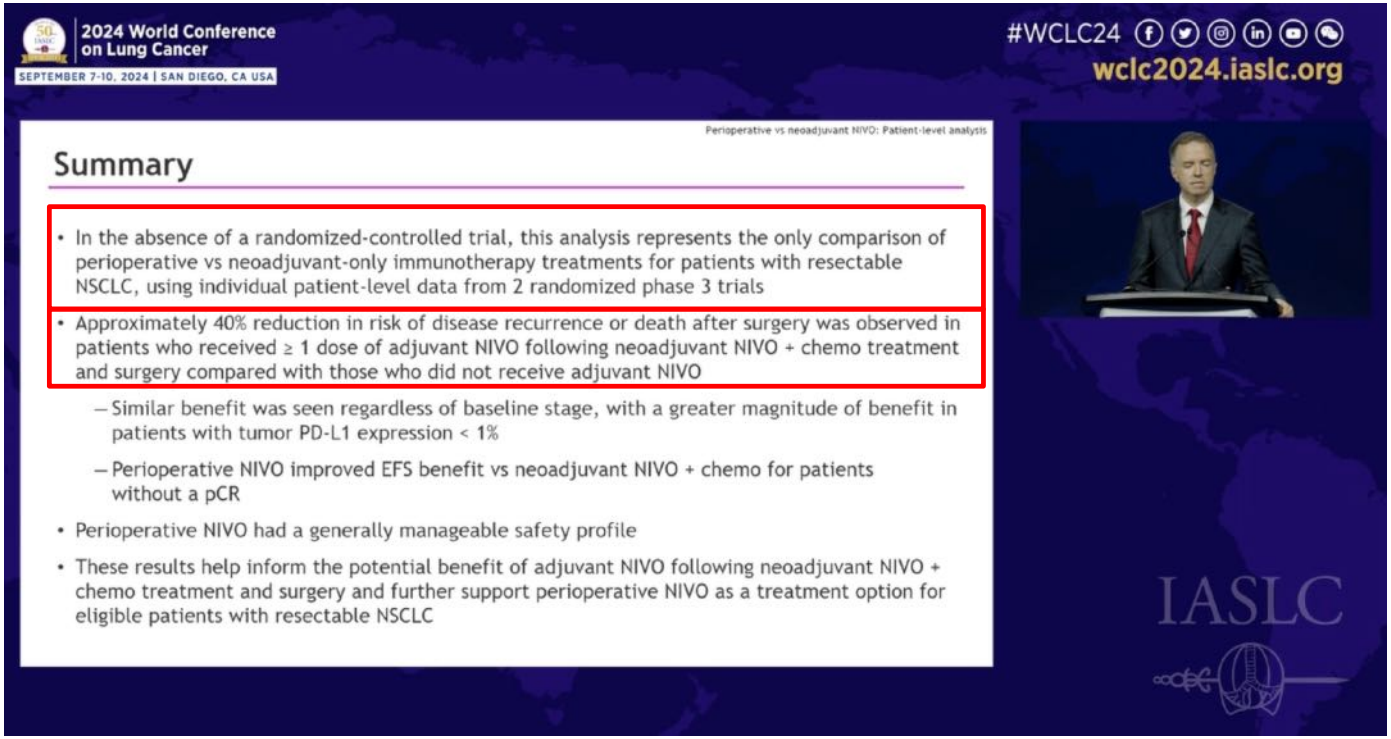
NEOADJUVANT/PERIOPERATIVE TREATMENT; CM816 VS. CM77T



- EFS benefit more when PD-L1<1%
- EFS benefit more when no pCR
- No relation with stage (IB-II vs. III)
- No difference in AE's

Courtesy Patrick Forde

NEOADJUVANT/PERIOPERATIVE TREATMENT; CM816 VS. CM77T



Courtesy Patrick Forde

PERIOPERATIVE TREATMENT; CANCELLATION OF SURGERY

After neoadjuvant treatment (trials including N2+); 78-93% has surgery

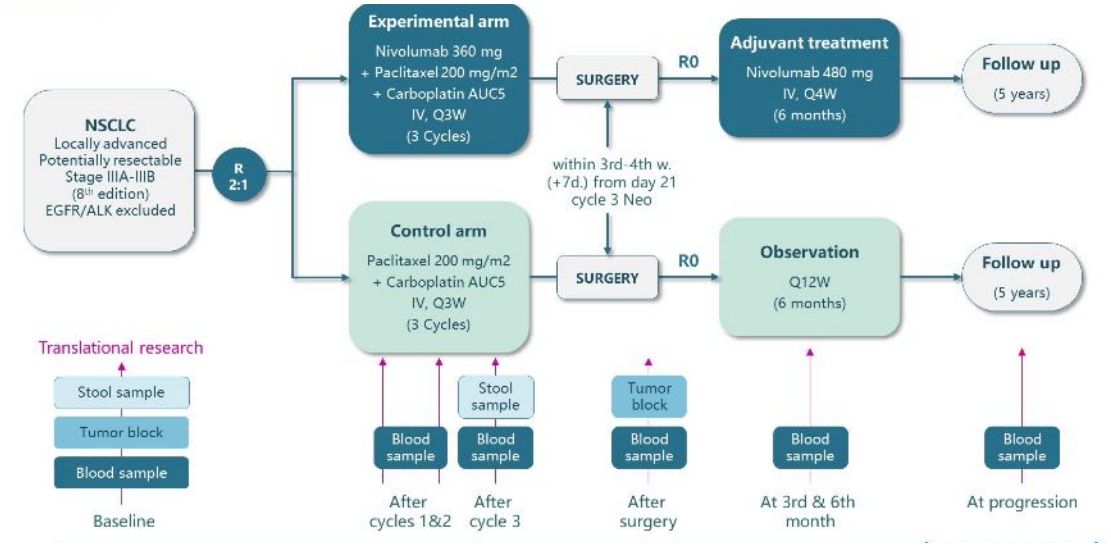
Cancellation of surgery does not seem to depend on N2 status (data not shown)

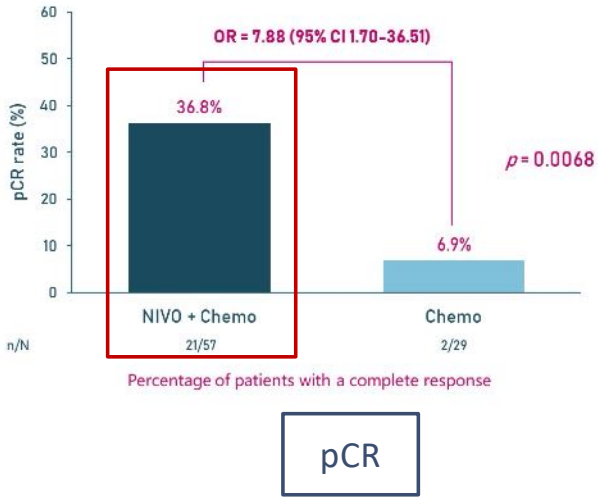
Trial Exp. Arm	Neo-adjuvant Compliance	Surgery
NADIM 2	94%	93 %
AEGEAN	86%	81 %
Neo-TORCH	NR	90 %
KEYNOTE-671	74.5%	82 %
CheckMate 77T	85%	78 %
RATIONALE 315	93.4% 34.5% 4 cycles	84%

Forde et al. N Engl J Med 2022
Cascone et al. N Engl J Med 2024

Opitz et al. ESMO 2024
Provencio et al. ASCO 2024

SURGERY FOR STAGE III-N2; NADIM-II AND CM77T



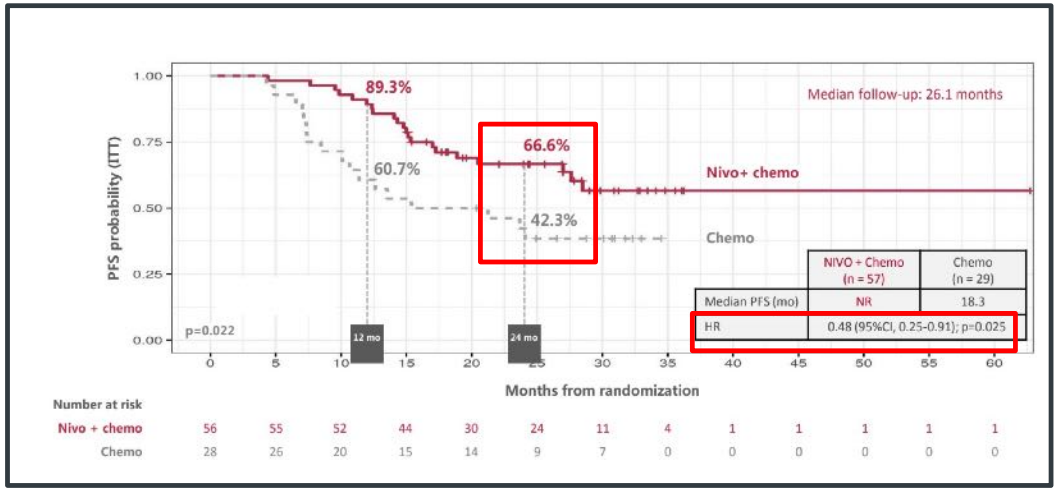


pCR

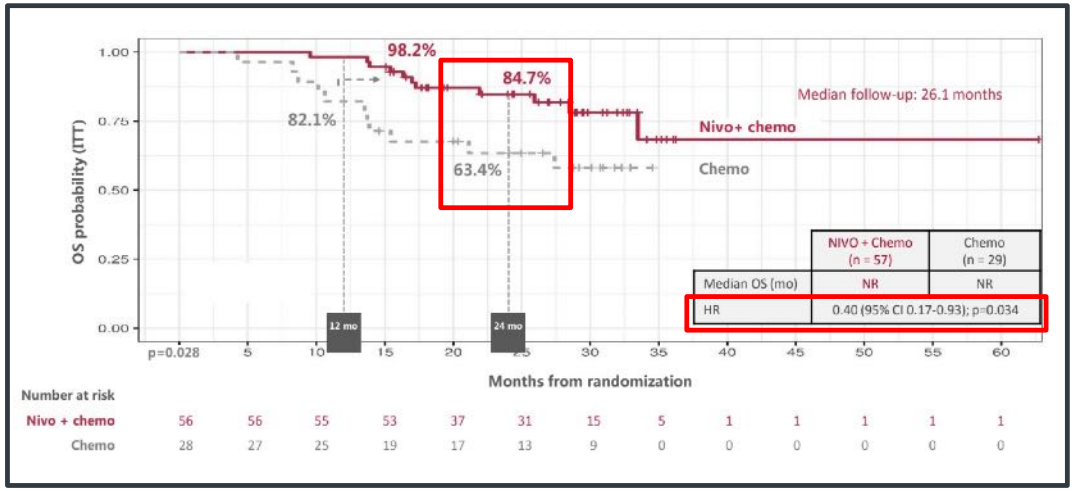
Provencio et al. J Clin Oncol 2022
Provencio et al. N Engl J Med 2023

Provencio et al. ASCO 2024
Provencio et al. WCLC 2024

SURGERY FOR STAGE III-N2; NADIM-II AND CM77T



PFS



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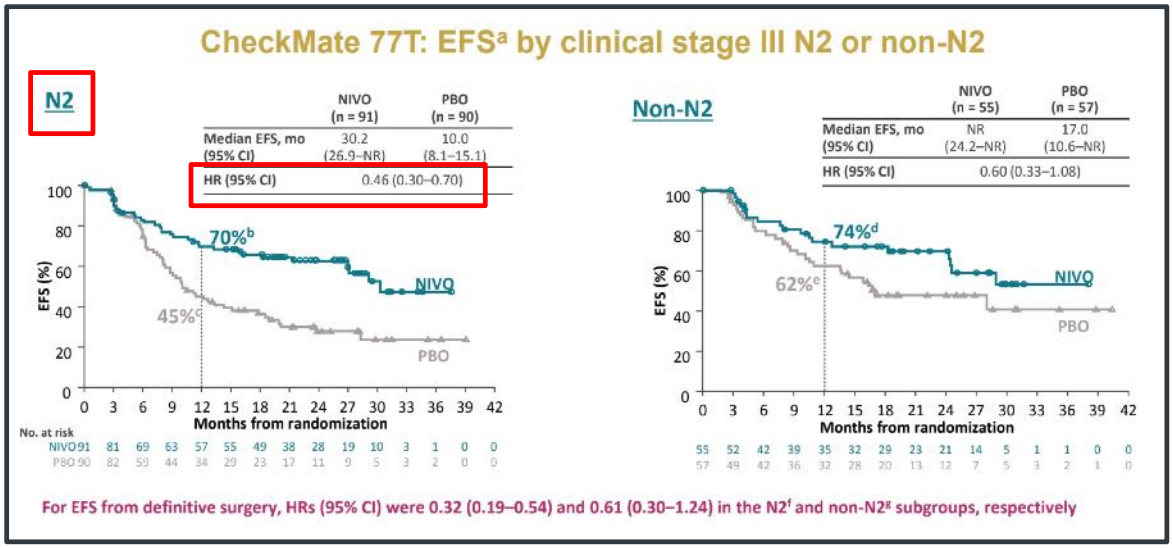
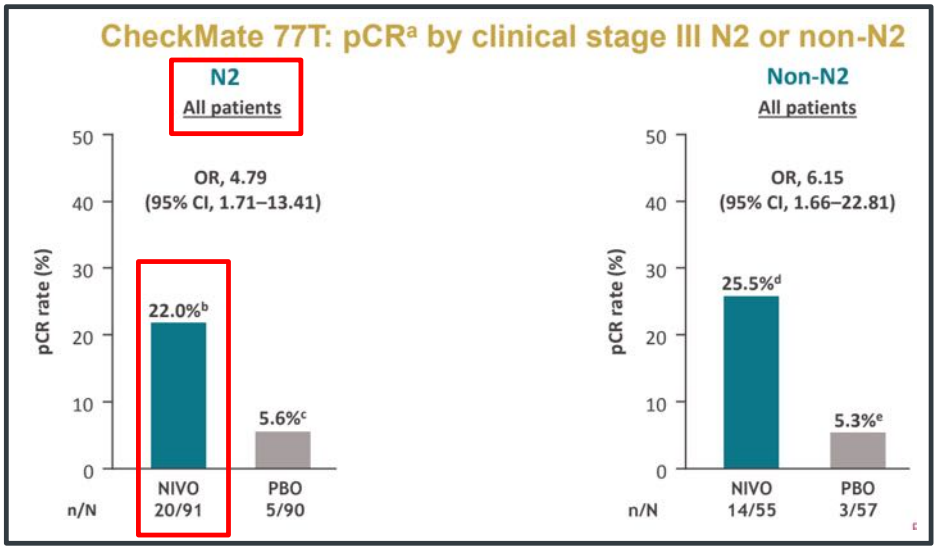
Provencio et al. J Clin Oncol 2022
Provencio et al. N Engl J Med 2023

Provencio et al. ASCO 2024
Provencio et al. WCLC 2024

SURGERY FOR STAGE III-N2; NADIM-II AND CM77T



EFS IN N2+ group (chemo-IO vs chemo), HR 0.46



pCR in N2+

Cascone et al. N Engl J Med 2024
Spicer et al. ESMO 2024

Provencio et al. WCLC 2024

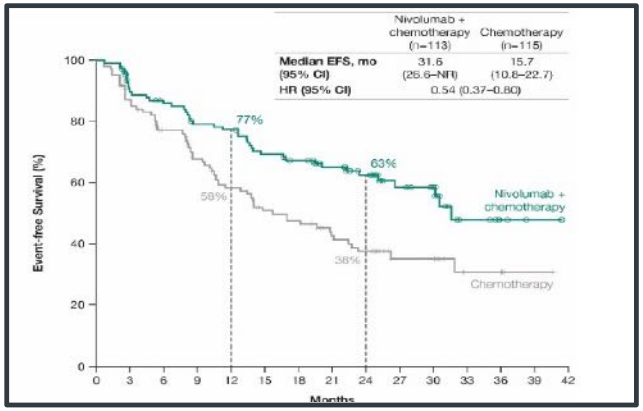
Trial	IMpower010[1]	KEYNOTE-091[2]	BR31[9]	CheckMate -816[3]	AEGEAN[4]	Neotorch[5]	KEYNOTE-671[6]	CheckMate -77T[7]	RATIONALE-315[8]
Timing	Adjuvant	Adjuvant	Adjuvant	Neoadjuvant	Perioperative	Perioperative	Perioperative	Perioperative	Perioperative
Size	1005	1177	1415 (477)	358	802	500	797	461	453
Agent I/O	Atezolizumab (PD-L1)	Pembrolizumab (PD-1)	Durvalumab (PD-L1)	Nivolumab (PD-1)	Durvalumab (PD-L1)	Toripalimab (PD-1)	Pembrolizumab (PD-1)	Nivolumab (PD-1)	Tislelizumab (PD-1)
No. cycles	16	18	12	3	16	17	13	16	12
Inclusion	Completely resected IB (>4cm)-IIIA (7^{th})	Completely resected IB (>4cm)-IIIA (7^{th})	Completely resected IB (>4cm)-IIIA (7^{th}) ESTS	Resectable IB (>4cm)-IIIA (7^{th})	Resectable II-IIIB (8^{th}) by lobectomy	Resectable II-IIIB (8^{th})	Resectable II-IIIB (8^{th})	Resectable II-IIIB (8^{th})	Resectable II-IIIA (8^{th})
Stage IB+II/III, %	59 / 41	72 / 28	71/39	36 / 64	29 / 71	20 / 80	30 / 70	35 / 65	41 / 59
Primary endpoint	DFS hierarchical	DFS, DFS in PD-L1 ≥50%	DFS in PD-L1 ≥25% & EGFR/ALK WT	pCR, EFS	pCR, EFS	MPR, EFS	EFS, OS	EFS	MPR, EFS
Chemotherapy	Cisplatin doublet	Platinum doublet encouraged	Platinum doublet if not ineligible	Platinum doublet	Platinum-based	Platinum-based	Cisplatin doublet	Platinum doublet	Platinum doublet
EGFR/ALK	Included (15%)	Included (7.4%)	Included	No documented mutation (WT Asia)	No documented mutation	WT	Included (7%)	No *EGFR*, no documented *ALK*	WT

1. Felipe E et al. *Lancet*. 2021;398:1344-1357. 2. O'Brien M et al. *Lancet Onc*. 2022;23:1274-1286. 3. Forde P et al. *N Engl J Med*. 2022;386:1973-1985.
4. Heymach J et al. AACR 2023. Abstract CT005. 5. Lu S et al. ASCO 2023. Abstract 8501. 6. Wakelee H et al. *N Engl J Med*. 2023;389:491-503. 7. Cascone T et al. ESMO 2023. Abstract LBA1. 8. Yue D et al. ELCC 2024. Abstract 1080. 9. Goss, ESMO 2024

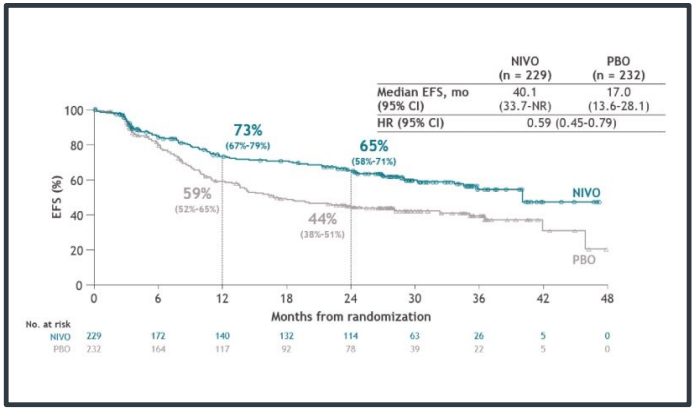
ICI; NEOADJUVANT VS. ADJUVANT

NEOADJUVANT VS. PERIOPERATIVE VS. ADJUVANT STRATEGY?

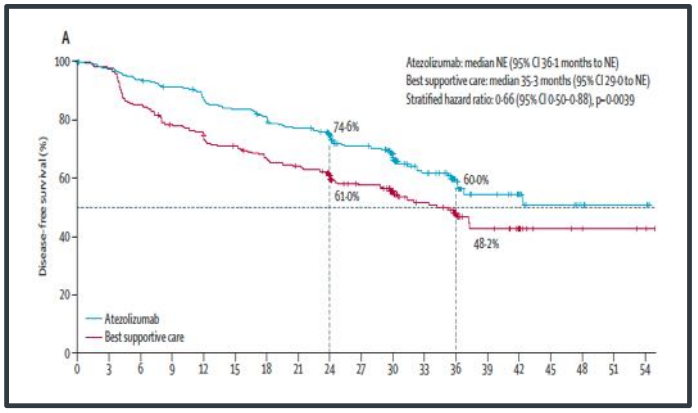
CheckMate 816



CheckMate 77T



IMpower 010



In resectable stage III NSCLC, there are no trials comparing neoadjuvant chemo-ICI vs. perioperative vs. adjuvant (chemo-) ICI

Forde, et al. N Engl J Med 2022
Felip, et al. Lancet 2021

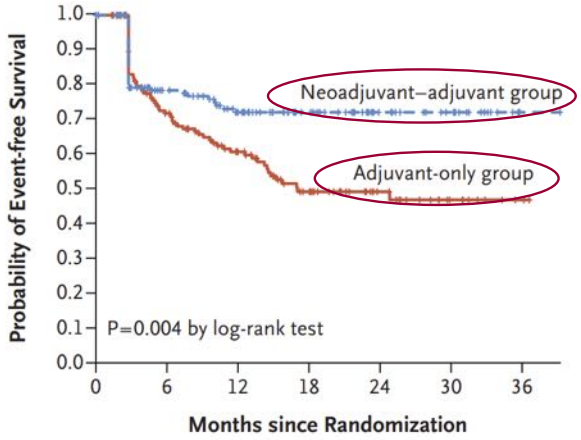
WE NEED TRIALS COMPARING DIFFERENT STRATEGIES

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Neoadjuvant–Adjuvant or Adjuvant-Only Pembrolizumab in Advanced Melanoma

S.P. Patel, M. Othus, Y. Chen, G.P. Wright, Jr., K.J. Yost, J.R. Hyngstrom, S. Hu-Lieskovan, C.D. Lao, L.A. Fecher, T.-G. Truong, J.L. Eisenstein, S. Chandra, J.A. Sosman, K.L. Kendra, R.C. Wu, C.E. Devoe, G.B. Deutsch, A. Hegde, M. Khalil, A. Mangla, A.M. Reese, M.I. Ross, A.S. Poklepovic, G.Q. Phan, A.A. Onitilo, D.G. Yasar, B.C. Powers, G.C. Doolittle, G.K. In, N. Kokot, G.T. Gibney, M.B. Atkins, M. Shaheen, J.A. Warneke, A. Ikeguchi, J.E. Najera, B. Chmielowski, J.G. Crompton, J.D. Floyd, E. Hsueh, K.A. Margolin, W.A. Chow, K.F. Grossmann, E. Dietrich, V.G. Prieto, M.C. Lowe, E.I. Buchbinder, J.M. Kirkwood, L. Korde, J. Moon, E. Sharon, V.K. Sondak, and A. Ribas



No. at Risk							
Neoadjuvant–adjuvant group	154	96	69	46	25	17	1
Adjuvant-only group	159	98	67	40	22	10	2

Courtesy Lizza Hendriks

TOPICS

Staging

Landmark papers

Guidelines

Operability and resectability

(Neo)adjuvant ICI trials

Questions and challenges

Conclusions

QUESTIONS AND CHALLENGES

- How to deal with borderline resectable stage III tumors?
- ICI; which agent, what dose, how many cycles, what combination (chemotherapy, radiotherapy, chemoradiation)?
- ICI neoadjuvant, perioperative or adjuvant?
- Which or what biomarker(s) will guide in treatment decision making?
- Role of targeted therapy (EGFR-TKI, ALK, etc.) in stage III NSCLC needs to be clarified
- Organ preserving (no surgery) treatment possible in stage III NSCLC (follow-up with ctDNA and radiology)? (data not shown)
- Role of salvage surgery after systemic treatment needs to be evaluated (data not shown)

TOPICS

Staging

Landmark papers

Guidelines

Operability and resectability

(Neo)adjuvant ICI trials

Questions and challenges

Conclusions

CONCLUSIONS; IN GENERAL

- Neoadjuvant (and/or adjuvant) (chemo-) ICI new standard in stage III NSCLC (no driver mutation)
  - Neoadjuvant chemo-ICI superior vs. chemo in resectable (stage III) NSCLC
    - At least for pCR, MPR, EFS
    - OS data are not yet mature
  - Adjuvant ICI seems beneficial for certain subgroups (stage II-III, PD-L1 ≥50%)
- Trials are needed to elucidate optimal strategy; neoadjuvant, perioperative or adjuvant treatment
- Biomarker studies (PD-L1, ctDNA (clearance), pCR, EGFR, ALK, etc.) are needed to guide treatment choice

CONCLUSIONS; SURGERY

- Definition about resectability varies between hospitals and surgical teams, in terms of experience and risk tolerance
- More and better criteria (e.g. anatomical and functional aspects) are needed for decision making about resectability
- Resectability should preferably be evaluated after neoadjuvant therapy (data not shown)
- Incorporating biological parameters and criteria
  - Avoid futile resections
  - Offer demanding resections to patients with favorable biology

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