Year in Review in Non-Targeted Lung Cancer: Locally Advanced and Metastatic NSCLC

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Agenda: NSCLC non-targeted therapy

- Locally Advanced
  - Durvalumab consolidation in unresectable stage III (PACIFIC 3-year OS)
- Metastatic: Combinations
  - Pembrolizumab + carboplatin/pemetrexed (KEYNOTE-189 update)
  - Nivolumab/ipilimumab (CheckMate 227 3-year OS)
  - Nivolumab/ipilimumab + 2 cycles chemo (CheckMate 9LA)
  - Durvalumab +/- tremelimumab (MYSTIC)
- Metastatic: Single agents
  - Pembrolizumab in PD-L1 ≥50% (KEYNOTE-024 5-year OS)
  - Atezolizumab (IMpower110)
  - Cemiplimab in PD-L1 ≥50% (EMPOWER-Lung 1)
- Metastatic: Special populations
  - Pembrolizumab in patients with brain metastases

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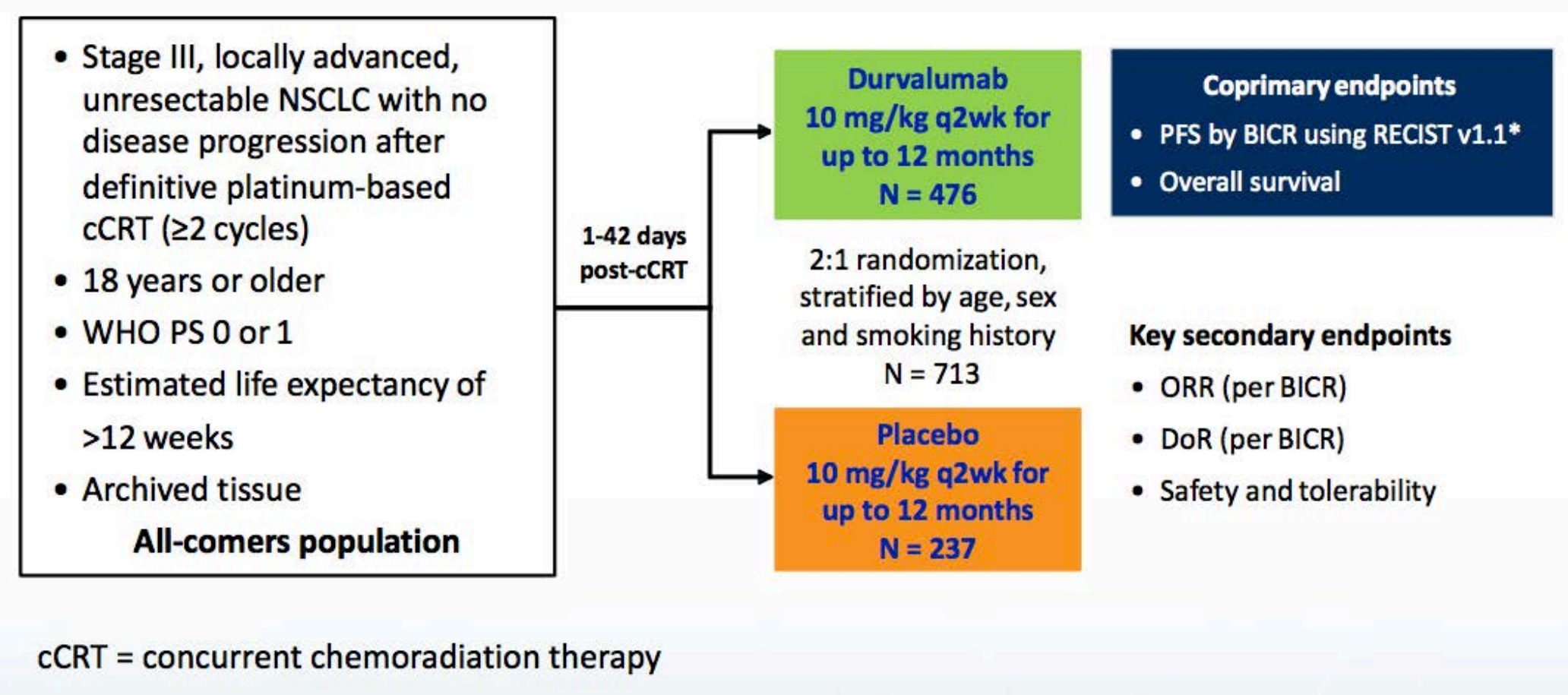
Locally advanced NSCLC

Courtesy of Matthew Gubens, MD, MS

Durvalumab consolidation in stage III (PACIFIC 3-year OS)



Gray JE et al. Three-year overall survival with durvalumab after chemoradiotherapy in Stage III NSCLC — Update from PACIFIC. J Thorac Oncol 2020;15(2):288-93.
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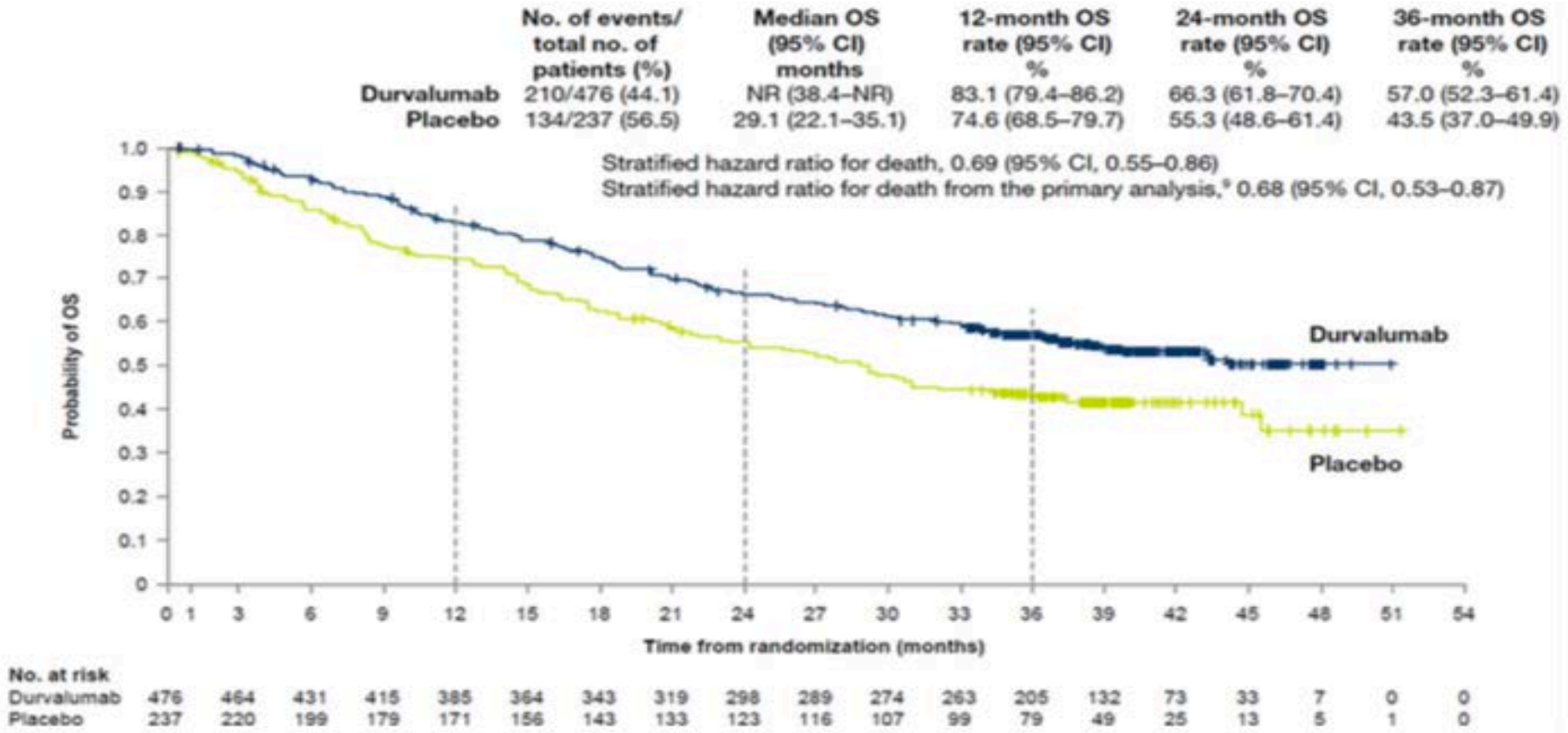
Durvalumab consolidation in stage III (PACIFIC 3-year OS)



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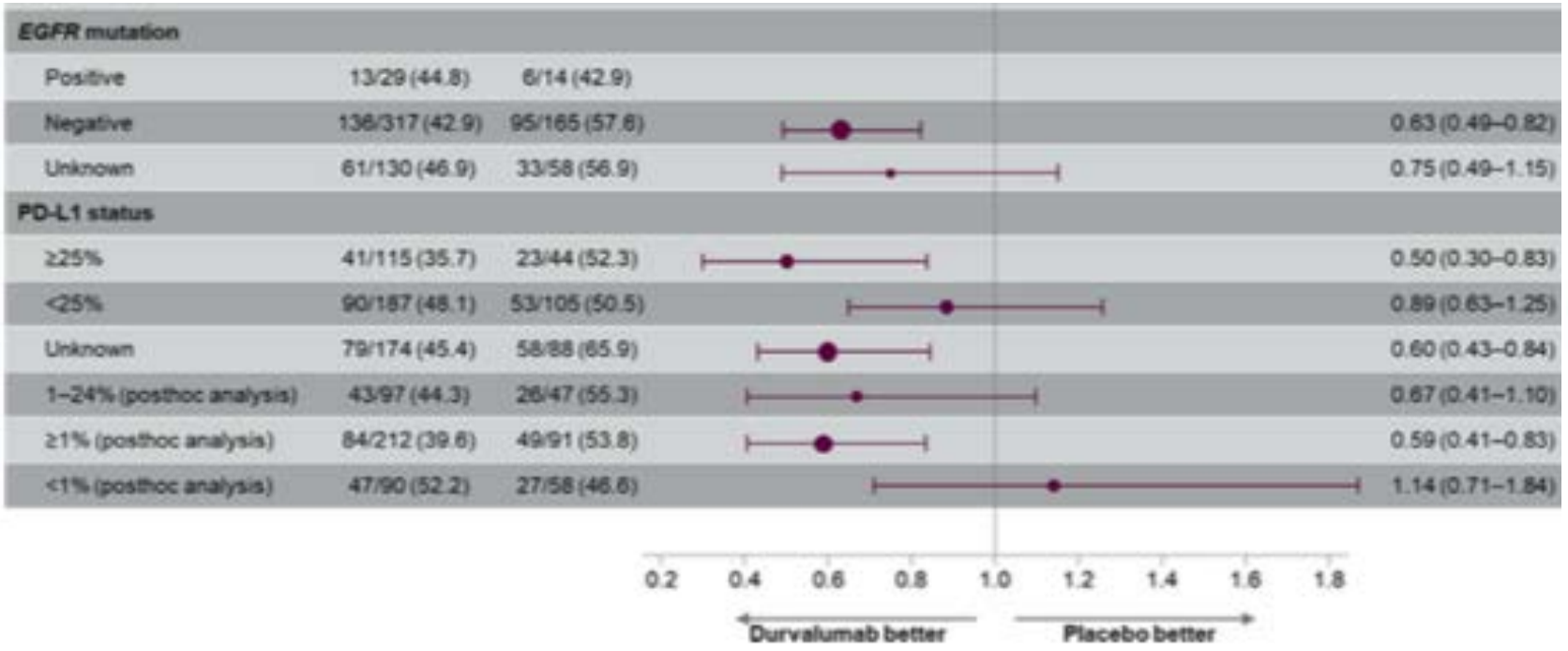
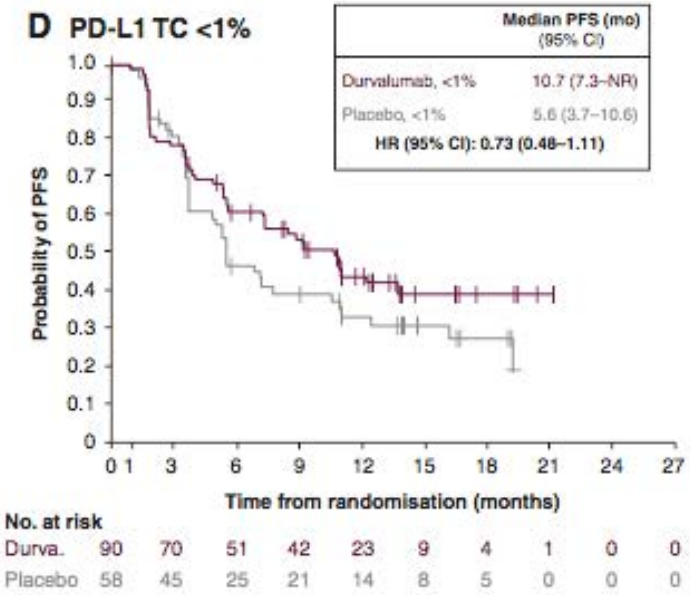
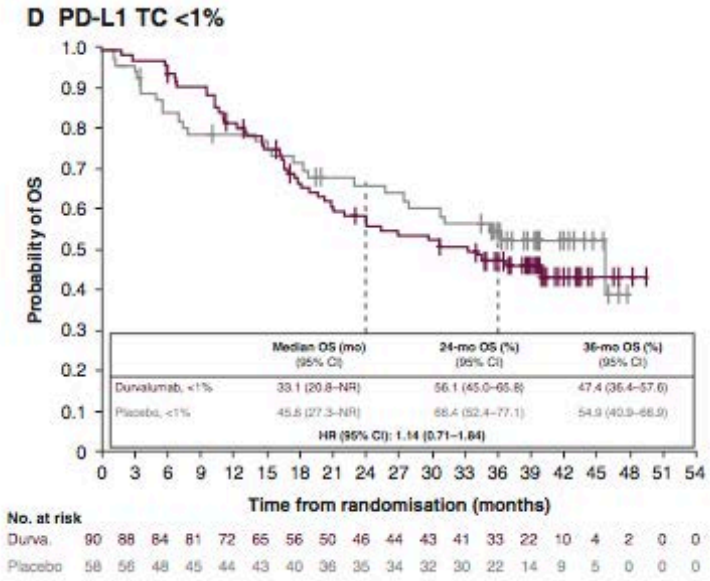
Durvalumab consolidation in stage III (PACIFIC 3-year OS)







PD-L1 <1%: a post-hoc analysis, small subgroup of 148 pts

- ?Pre-CRT samples, whereas hypothesis is that CRT may alter PD-L1
- ?37% samples unevaluable, perhaps not missing at random

Courtesy of Matthew Gubens, MD, MS

Durvalumab consolidation in stage III (PACIFIC 3-year OS: Conclusions)

- Impact on Patient Care and Treatment Algorithm
  - Confirms durvalumab consolidation as standard of care in unresectable stage III NSCLC after chemoradiation
  - In US, no PD-L1 requirement, but EU approved only for PD-L1 ≥1%
  - Await 5-year data and “cure” rate
  - Recent FDA approval for 4-week durvalumab dosing

- Implications for Future Research
  - Clinical trials for concurrent immunotherapy with chemoradiation
  - Role of immunotherapy in patients with targetable mutations (eg EGFR, ALK)
  - Biomarkers for benefit including PD-L1 and TMB

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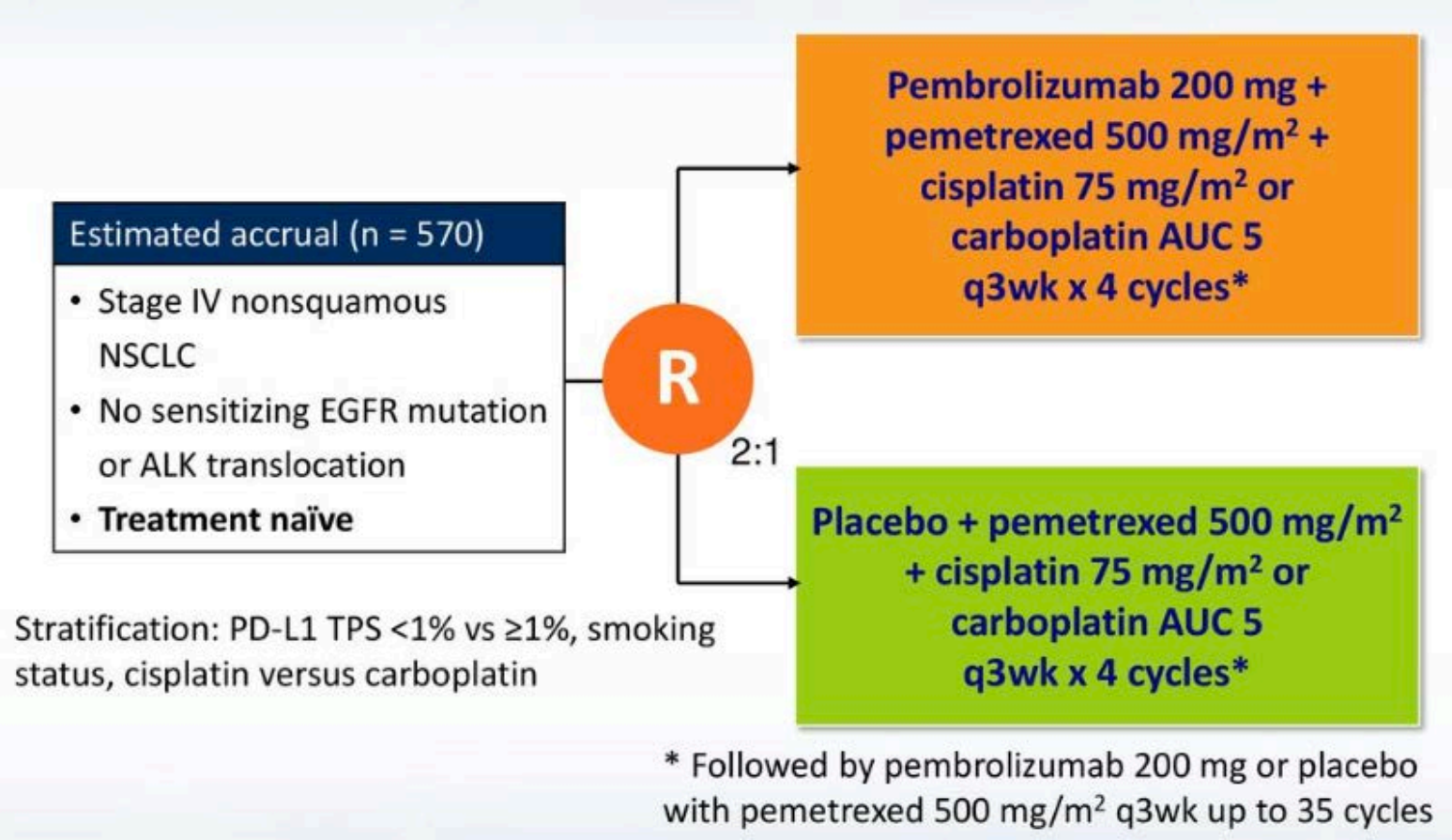
Courtesy of Matthew Gubens, MD, MS

Metastatic NSCLC: Combinations

Courtesy of Matthew Gubens, MD, MS

Pembrolizumab + carboplatin/pemetrexed (KEYNOTE-189 update)

- Median follow-up 23.1 mos



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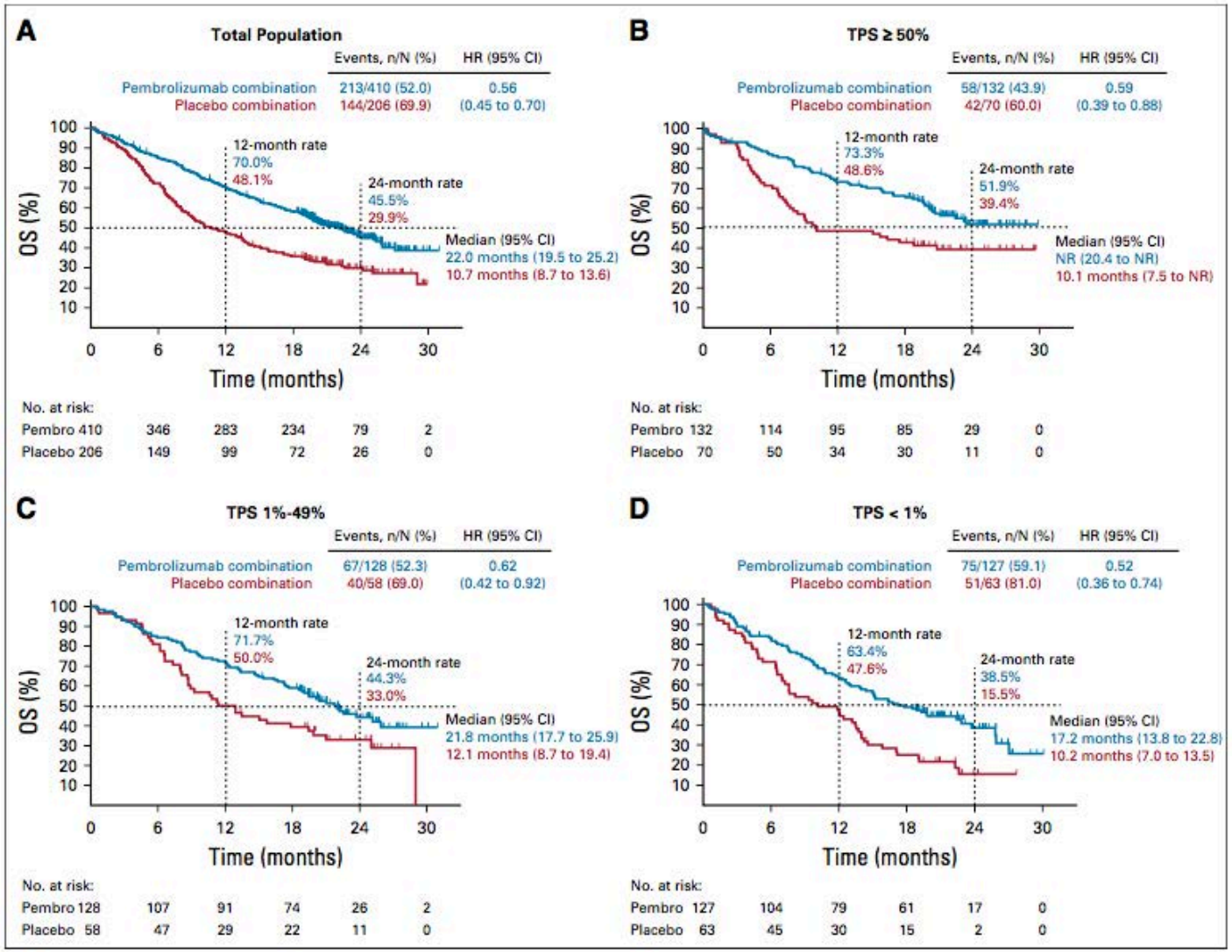
Pembrolizumab + carboplatin/pemetrexed (KEYNOTE-189 update)



Courtesy of Matthew Gubens, MD, MS

Pembrolizumab + carboplatin/pemetrexed (KEYNOTE-189 update)

- Liver metastases
  - OS with liver mets HR 0.62, OS without HR 0.58
- Brain metastases
  - OS with brain mets HR 0.41, OS without 0.59
- Though both show poorer OS overall as expected

- PFS2 analysis also shows clear benefit for pembro in first line

- Safety as expected
  - Grade 3-5 adverse events 72% with pembro, 67% without

Gadgeel S et al. Updated Analysis From KEYNOTE-189: Pembrolizumab or Placebo Plus Pemetrexed and Platinum for Previously Untreated Metastatic Nonsquamous Non-Small-Cell Lung Cancer. J Clin Oncol. 2020 May 10;38(14):1505-1517.

Courtesy of Matthew Gubens, MD, MS

Pembrolizumab + carboplatin/pemetrexed (KEYNOTE-189 update: Conclusions)

- Impact on Patient Care and Treatment Algorithm
  - Confirms pembrolizumab + carbo/pem as a standard of care in 1st line non-squamous NSCLC
  - OS benefit remains across all PD-L1 levels: ≥50%, 1-49%, <1%
  - OS benefit in liver and brain met patients

- Implications for Future Research
  - Which 1st line regimen for whom, especially high PD-L1?
  - INSIGNIA cooperative group trial
    - pembro → carbo/pem
    - pembro → carbo/pem/pembro
    - carbo/pem/pembro
  - Additions to chemo + PD-L1 inhibition, eg TIGIT
  - Immunorefractory disease

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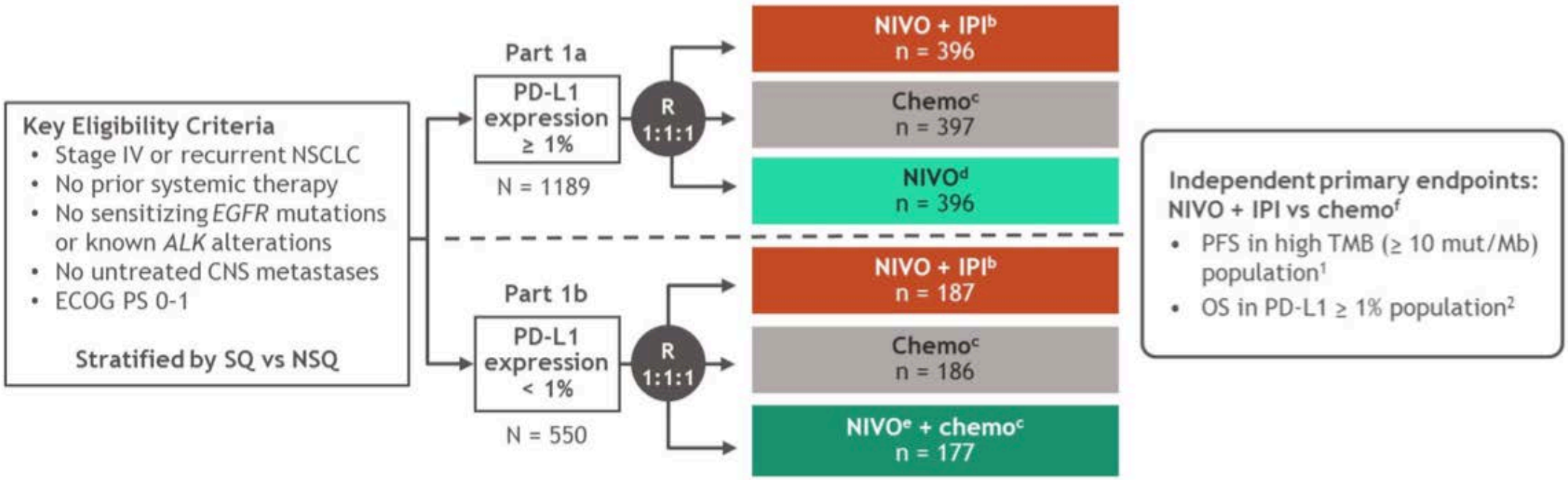
Nivolumab/ipilimumab (Checkmate 227 3-year OS)



Ramalingam SS et al. Nivolumab + ipilimumab versus platinum-doublet chemotherapy as first-line treatment for advanced non-small cell lung cancer: Three-year update from CheckMate 227 Part 1. ASCO 2020; Abstract 9500. Oral, HoD

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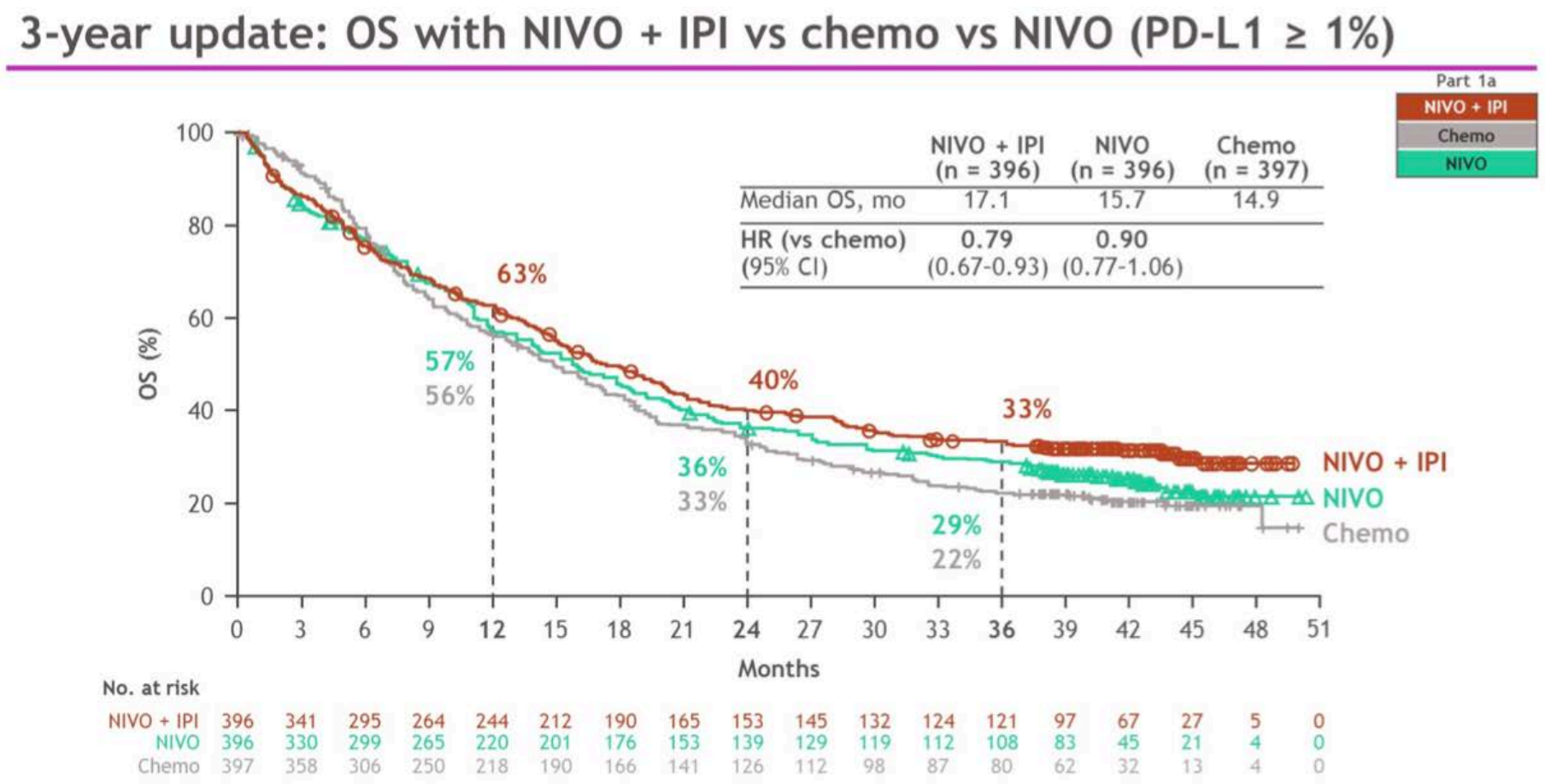

Landmark analysis

For patients with response (CR or PR) at 6 mos:
OS@1 year 90 vs 73%
OS@2 year 76 vs 51%
OS@3 year 70 vs 39%

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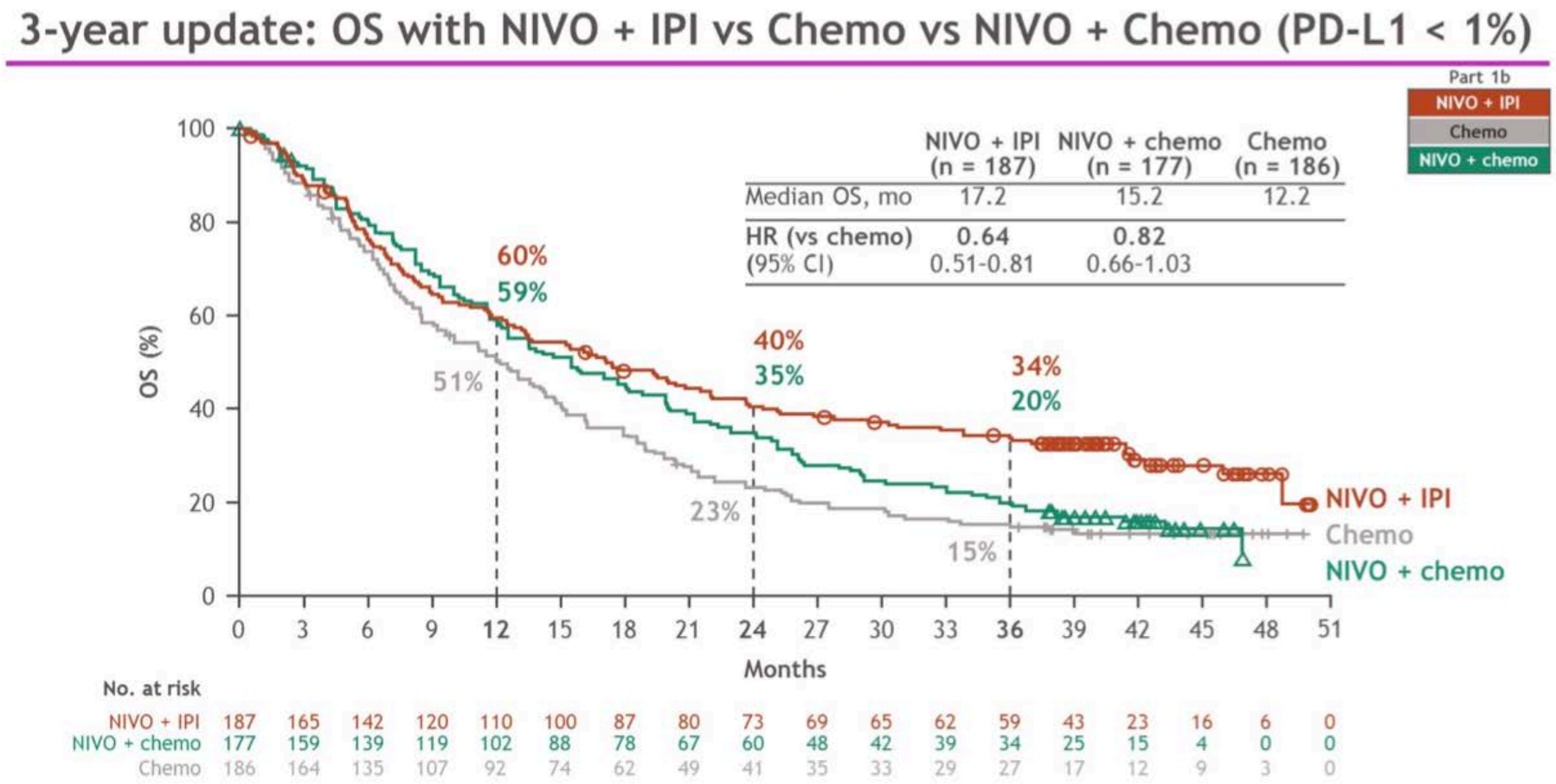

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Nivolumab/ipilimumab (Checkmate 227 3-year OS)

Safety summary: NIVO + IPI, chemo, NIVO, NIVO + chemo

TRAE,[a] %	All randomized (PD-L1 ≥ 1% and PD-L1 < 1%)				PD-L1 ≥ 1%		PD-L1 < 1%	
	NIVO + IPI (n = 576)		Chemo (n = 570)		NIVO (n = 391)		NIVO + chemo (n = 172)	
	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4
Any TRAE	77	33	82	36	66	20	92	56
TRAEs leading to discontinuation of any component of the regimen	18	12	9	5	12	7	14	8
Treatment-related deaths[b]	1		1		< 1		2	

- With a minimum safety follow-up of 36.3 months, safety was consistent with the previous reports[1,2]

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Nivolumab/ipilimumab (Checkmate 227 3-year OS: Conclusions)

- Impact on Patient Care and Treatment Algorithm
  - Nivolumab/ipilimumab now approved for PD-L1 ≥1%
  - Though PD-L1<1% results also robust
  - Safety profile acceptable
  - No predictive value for TMB

- Implications for Future Research
  - No head to head trials with chemo/immunotherapy combos planned
  - Patient selection?

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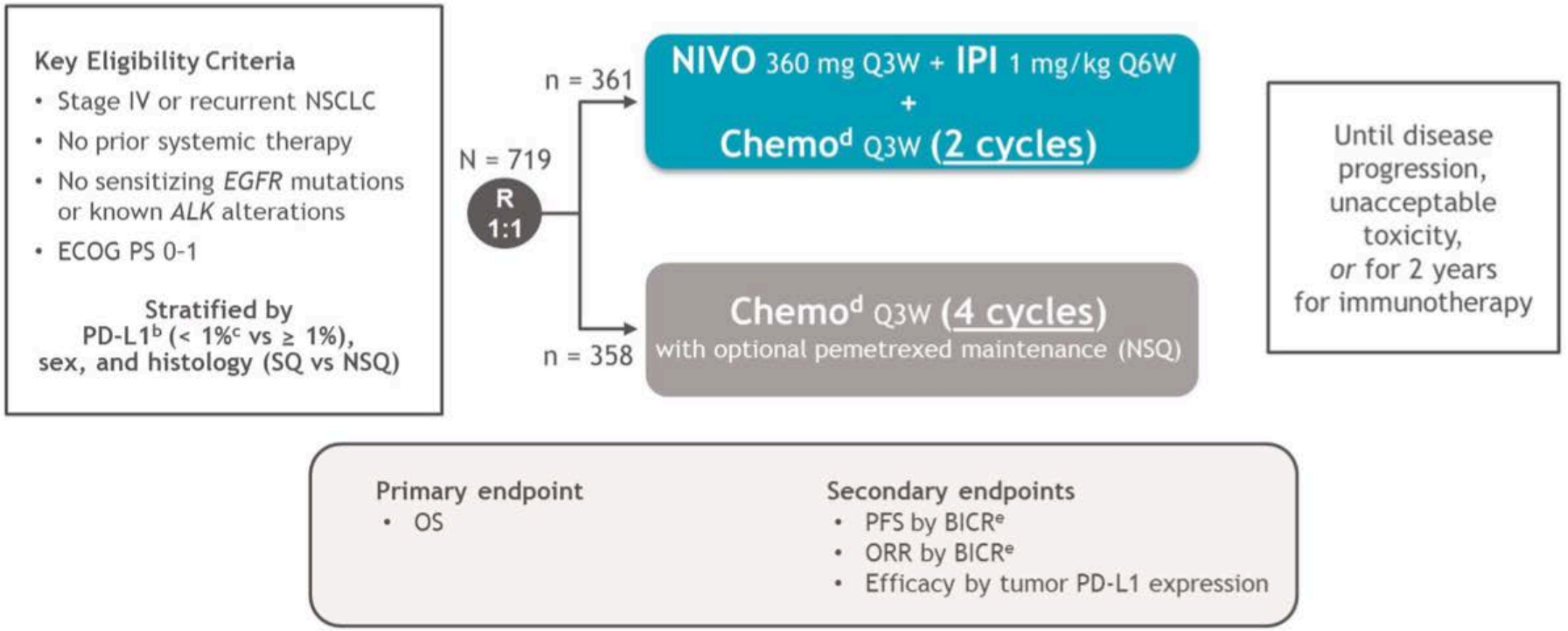
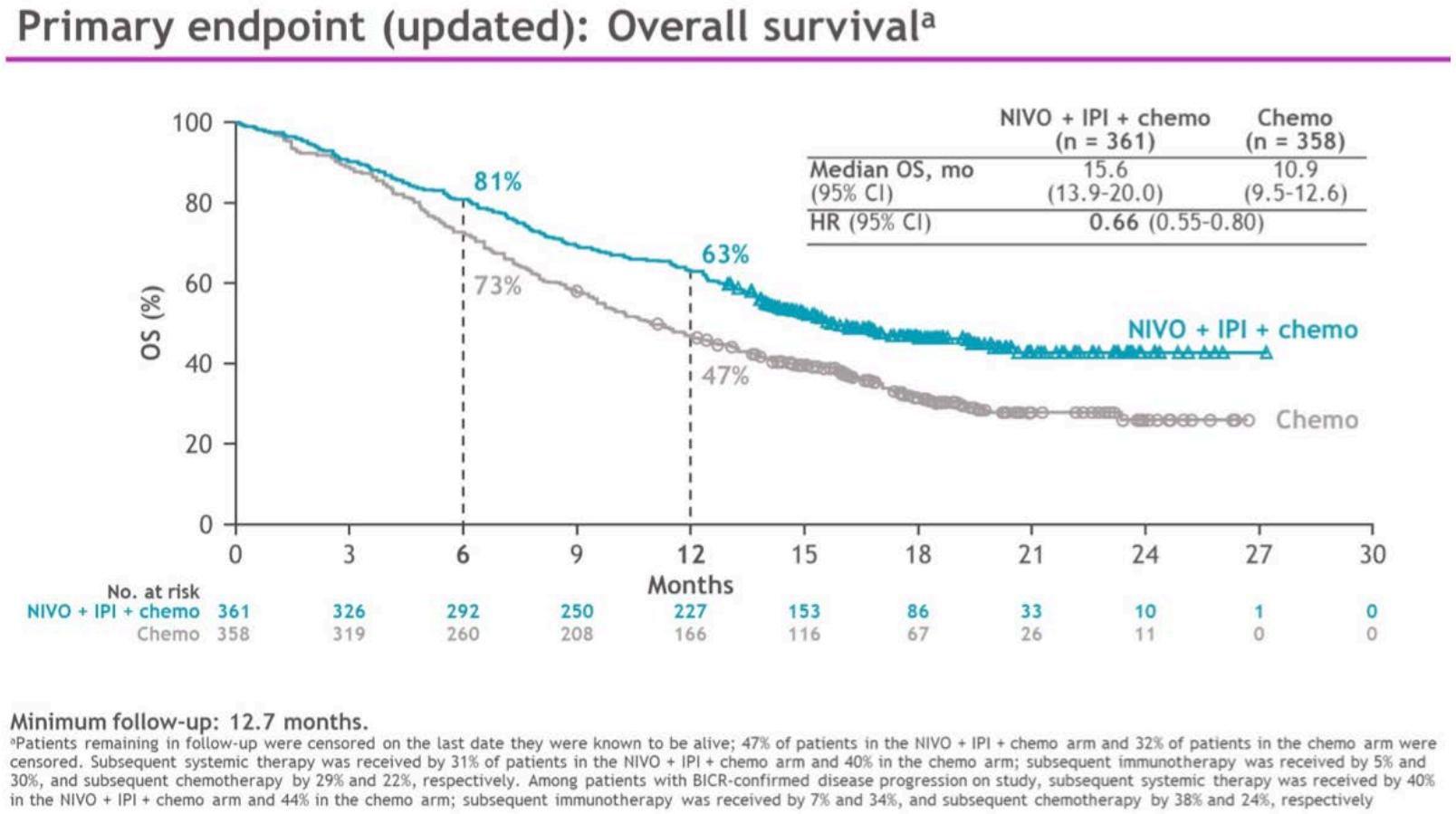
Nivolumab/ipilimumab + 2 cycles chemo (Checkmate 9LA)



Reck M et al. Nivolumab (NIVO) + ipilimumab (IPI) + 2 cycles of platinum-doublet chemotherapy (chemo) vs 4 cycles chemo as first-line (1L) treatment (tx) for stage IV/recurrent non-small cell lung cancer (NSCLC): CheckMate 9LA. Proc ASCO 2020; Abstract 9501. Oral, HoD

Courtesy of Matthew Gubens, MD, MS

Nivolumab/ipilimumab + 2 cycles chemo (Checkmate 9LA)



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Nivolumab/ipilimumab + 2 cycles chemo (Checkmate 9LA)

- By PD-L1 status
  - PD-L1 <1% OS HR 0.62 (0.45-0.85)
  - PD-L1 1-49% OS HR 0.61 (0.44-0.84)
  - PD-L1 ≥50% HR 0.66 (0.44-0.99)
- By histology
  - Non-squamous OS HR 0.69 (0.55-0.87)
  - Squamous OS HR 0.62 (0.45-0.86)
- Safety
  - Gr 3-4 TRAEs 47 vs 38%
  - Treatment discontinuation due to AEs 19 vs 7%

Reck M et al. Nivolumab (NIVO) + ipilimumab (IPI) + 2 cycles of platinum-doublet chemotherapy (chemo) vs 4 cycles chemo as first-line (1L) treatment (tx) for stage IV/recurrent non-small cell lung cancer (NSCLC): CheckMate 9LA. Proc ASCO 2020; Abstract 9501. Oral, HoD

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Nivolumab/ipilimumab + 2 cycles chemo (Checkmate 9LA: Conclusions)

- Impact on Patient Care and Treatment Algorithm
  - Nivolumab/ipilimumab + 2 cycles chemo now approved
  - Follow-up data less mature
  - HR not clearly superior, 0.66 vs 0.64 in CheckMate 227 (granted, cross-trial comparison)
  - But could be an option for rapidly growing/symptomatic/high burden disease

- Implications for Future Research
  - Doesn’t seem to be a path for other phase 3s for now

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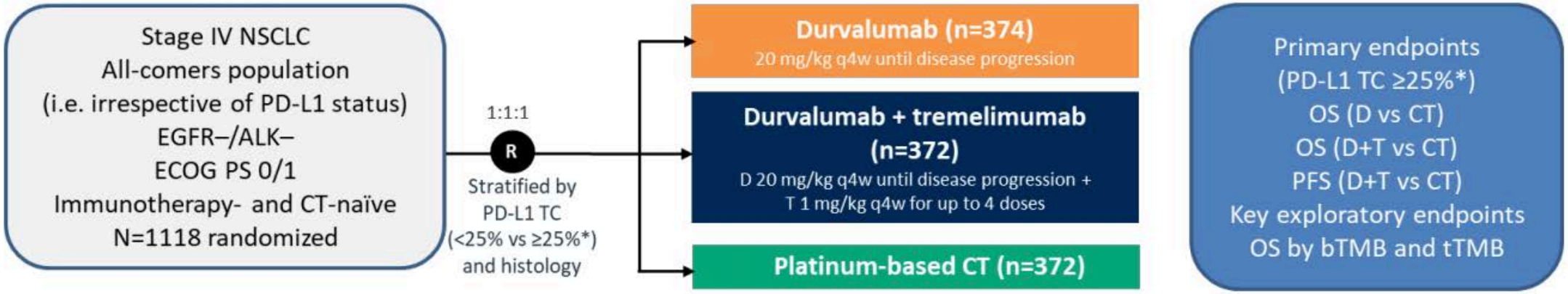
Courtesy of Matthew Gubens, MD, MS

Durvalumab +/- tremelimumab (MYSTIC)



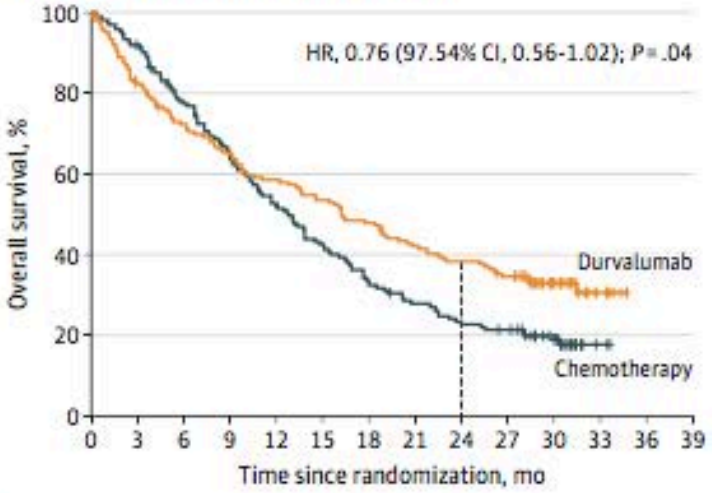
Rizvi NA et al; MYSTIC Investigators. Durvalumab With or Without Tremelimumab vs Standard Chemotherapy in First-line Treatment of Metastatic Non-Small Cell Lung Cancer: The MYSTIC Phase 3 Randomized Clinical Trial. JAMA Oncol. 2020 May 1;6(5):661-674.

Courtesy of Matthew Gubens, MD, MS

Durvalumab +/- tremelimumab (MYSTIC)

Figure 2. Overall Survival and Progression-free Survival Among Patients With Programmed Cell Death Ligand 1 TC ≥25%

A Overall survival for durvalumab vs chemotherapy

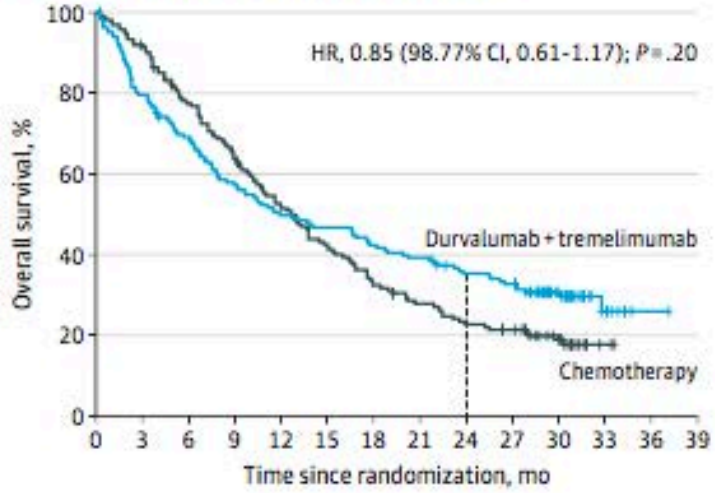


No. at risk

Durvalumab	163	134	116	104	93	85	76	66	60	53	25	6	0	0
Chemotherapy	162	147	123	101	83	67	53	43	35	32	20	2	0	0

Treatment group	Events/ patients, No.	OS, mo Median (95% CI)	24-mo OS, % (95% CI)
Durvalumab	108/163	16.3 (12.2-20.8)	38.3 (30.7-45.7)
Chemotherapy	128/162	12.9 (10.5-15.0)	22.7 (16.5-29.5)

B Overall survival for durvalumab + tremelimumab vs chemotherapy



No. at risk

Durvalumab + tremelimumab	163	130	111	92	80	75	68	63	54	50	30	6	1	0
Chemotherapy	162	147	123	101	83	67	53	43	35	32	20	2	0	0

Treatment group	Events/ patients, No.	OS, mo Median (95% CI)	24-mo OS, % (95% CI)
Durvalumab + tremelimumab	113/163	11.9 (9.0-17.7)	35.4 (28.1-42.8)
Chemotherapy	128/162	12.9 (10.5-15.0)	22.7 (16.5-29.5)

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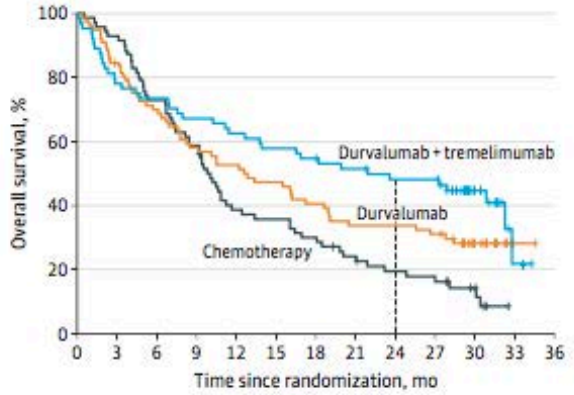
Courtesy of Matthew Gubens, MD, MS

Durvalumab +/- tremelimumab (MYSTIC)

Figure 3. Exploratory Analysis of Overall Survival and Progression-free Survival According to Blood Tumor Mutational Burden

A Overall survival in the population with bTMB ≥20 mut/Mb

Durvalumab vs chemotherapy: HR, 0.72 (95% CI, 0.50-1.05)
Durvalumab + tremelimumab vs chemotherapy: HR, 0.49 (95% CI, 0.32-0.74)
Durvalumab + tremelimumab vs durvalumab: HR, 0.74 (95% CI, 0.48-1.11)

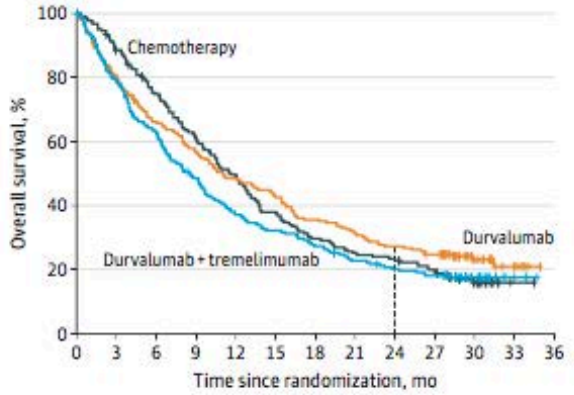


No. at risk													
Durvalumab	77	64	53	44	39	35	30	25	25	23	10	1	0
Durvalumab + tremelimumab	64	50	47	43	40	37	35	32	29	29	14	2	0
Chemotherapy	70	65	51	41	27	25	21	16	12	11	6	0	0

Treatment group	Events/ patients, No.	OS, mo Median (95% CI)	24-mo OS, % (95% CI)
Durvalumab	54/77	12.6 (7.8-18.6)	33.8 (23.4-44.5)
Durvalumab + tremelimumab	38/64	21.9 (11.4-32.8)	48.1 (35.5-59.7)
Chemotherapy	61/70	10.0 (8.1-11.7)	19.4 (11.0-29.5)

B Overall survival in the population with bTMB <20 mut/Mb

Durvalumab vs chemotherapy: HR, 0.93 (95% CI, 0.74-1.16)
Durvalumab + tremelimumab vs chemotherapy: HR, 1.16 (95% CI, 0.93-1.45)
Durvalumab + tremelimumab vs durvalumab: HR, 1.22 (95% CI, 0.98-1.52)



No. at risk													
Durvalumab	209	167	134	114	98	86	72	63	55	49	21	8	0
Durvalumab + tremelimumab	204	161	129	98	75	65	55	45	39	35	18	4	0
Chemotherapy	185	162	135	110	89	68	53	45	41	34	17	1	0

Treatment group	Events/ patients, No.	OS, mo Median (95% CI)	24-mo OS, % (95% CI)
Durvalumab	157/209	11.0 (8.9-14.9)	27.2 (21.2-33.4)
Durvalumab + tremelimumab	167/204	8.5 (6.7-9.8)	20.2 (14.9-26.0)
Chemotherapy	150/185	11.6 (9.6-13.1)	22.9 (17.0-29.2)

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Courtesy of Matthew Gubens, MD, MS

Durvalumab +/- tremelimumab (MYSTIC: Conclusions)

- Impact on Patient Care and Treatment Algorithm
  - Negative study by primary endpoint of OS for PD-L1 ≥25%
  - High TMB (≥20Muts/Mb) did show OS benefit, though exploratory
  - But only 41% of samples evaluable for TMB

- Implications for Future Research
  - Ongoing research into role of TMB in patient selection: CheckMate 227 had shown PFS improvement at TMB 10Muts/Mb, but this is the first robust OS study
  - Phase 3 PEARL study will specifically evaluate durvalumab vs chemo
  - Phase 3 POSEIDON has shown PFS improvement in durva vs chemo and durva/treme vs chemo, but OS results are pending

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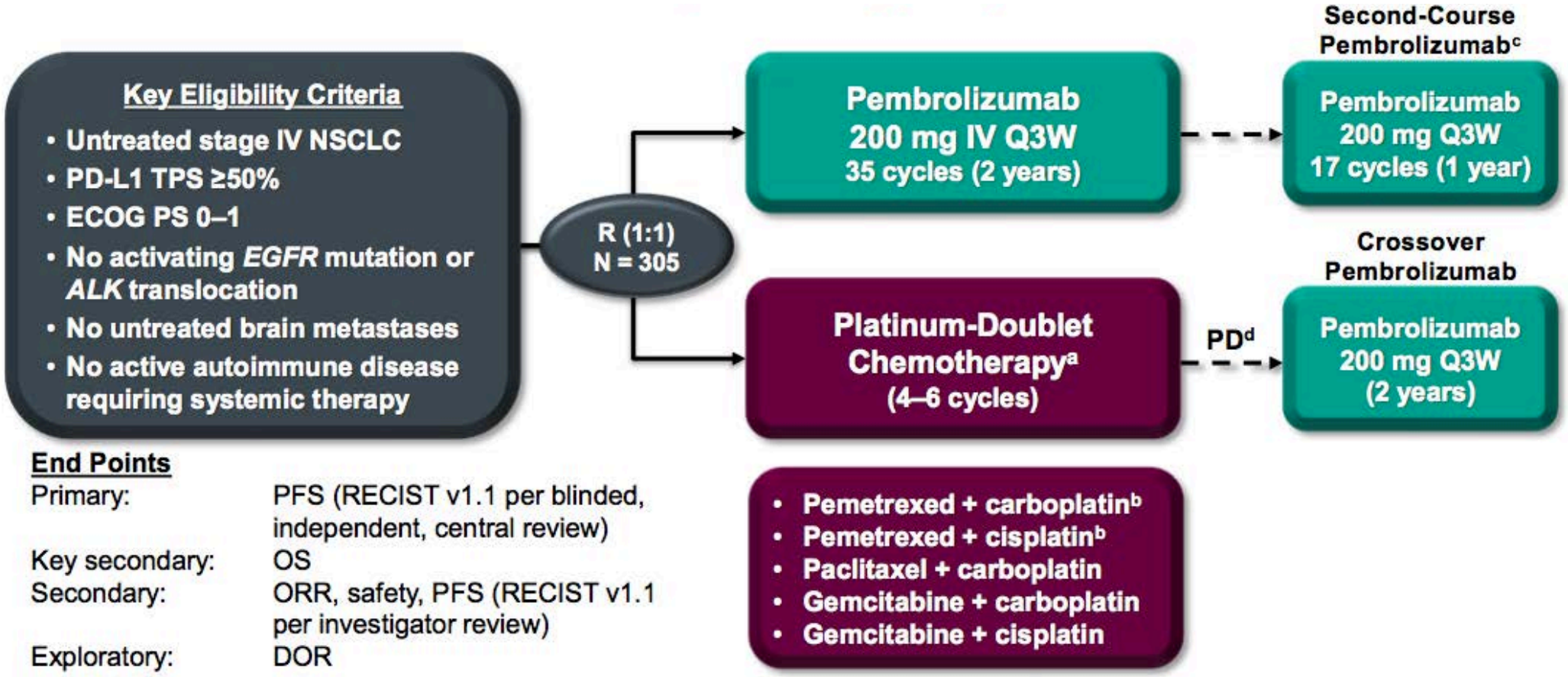
Courtesy of Matthew Gubens, MD, MS

Metastatic NSCLC: Single agents

Courtesy of Matthew Gubens, MD, MS

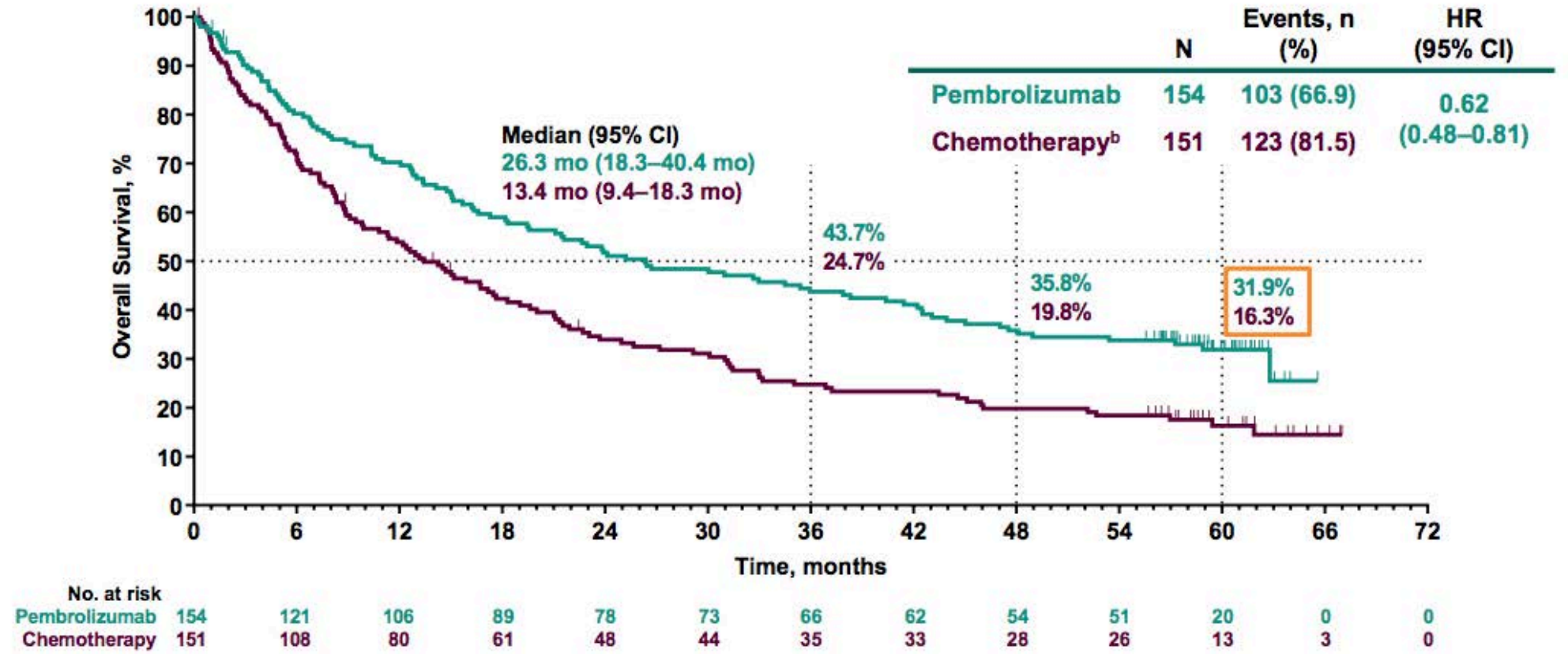
Pembrolizumab in PD-L1 ≥50% (KEYNOTE-024 5-year OS)



Brahmer J et al. KEYNOTE-024 5-year OS update: first-line (1L) pembrolizumab(pembro) vs platinum-based chemotherapy (chemo) in patients (pts) with metastatic NSCLC and PD-L1 tumor proportion score (TPS) ≥50%. ESMO 2020; Abstract LBA51. Oral

Courtesy of Matthew Gubens, MD, MS

Pembrolizumab in PD-L1 ≥50% (KEYNOTE-024 5-year OS)



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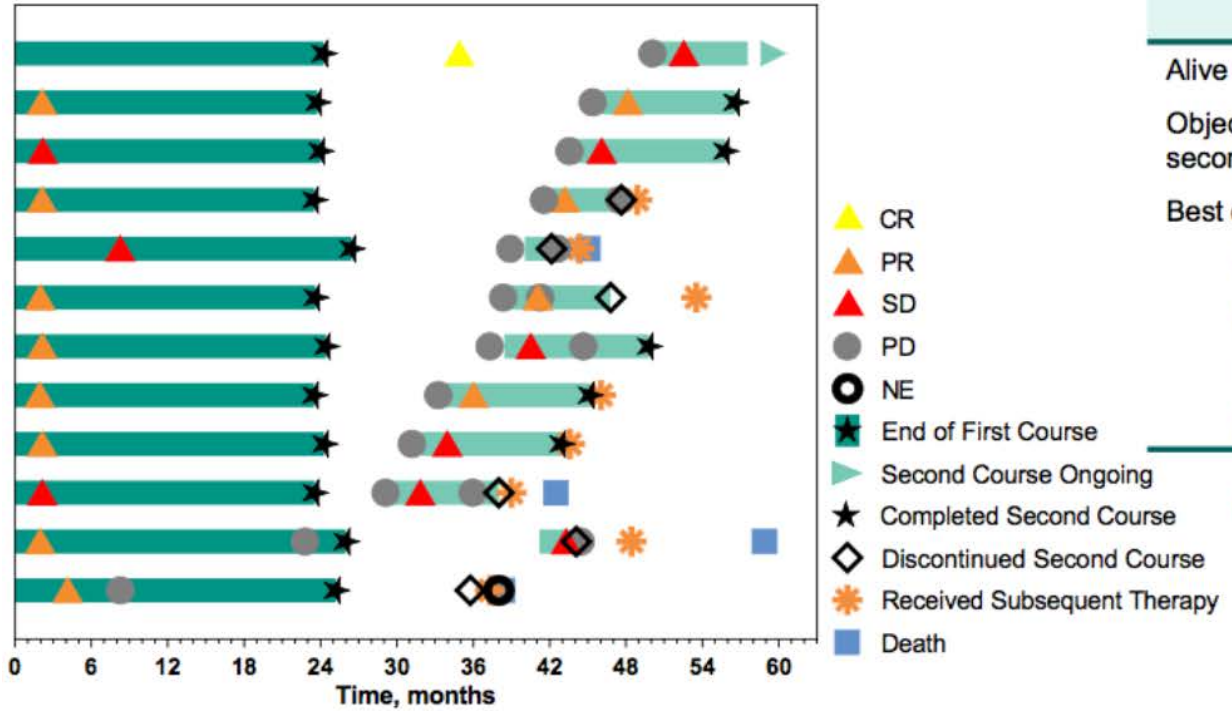
Pembrolizumab in PD-L1 ≥50% (KEYNOTE-024 5-year OS)

Treatment Duration and Time to Response

Second Course of Pembrolizumab



	N = 12
Alive at data cutoff, n (%)	8 (67)
Objective response during second course, n (%)	4 (33)
Best objective response, n (%)	
Complete response	0
Partial response	4 (33)
Stable disease	6 (50)
Progressive disease	1 (8)

- **At data cutoff, 5/12 patients (42%) were alive without PD per investigator assessment**
  - **3 (25%) did not receive subsequent therapy**

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Courtesy of Matthew Gubens, MD, MS

Pembrolizumab in PD-L1 ≥50% (KEYNOTE-024 5-year OS: Conclusions)

- Impact on Patient Care and Treatment Algorithm
  - Confirms pembrolizmab as a standard of care for PD-L1 ≥50%, with 5-year survival rate of 32% vs 16% in control arm
  - Second course of pembrolizumab if patient progresses after 2 years appears to be feasible and effective in most

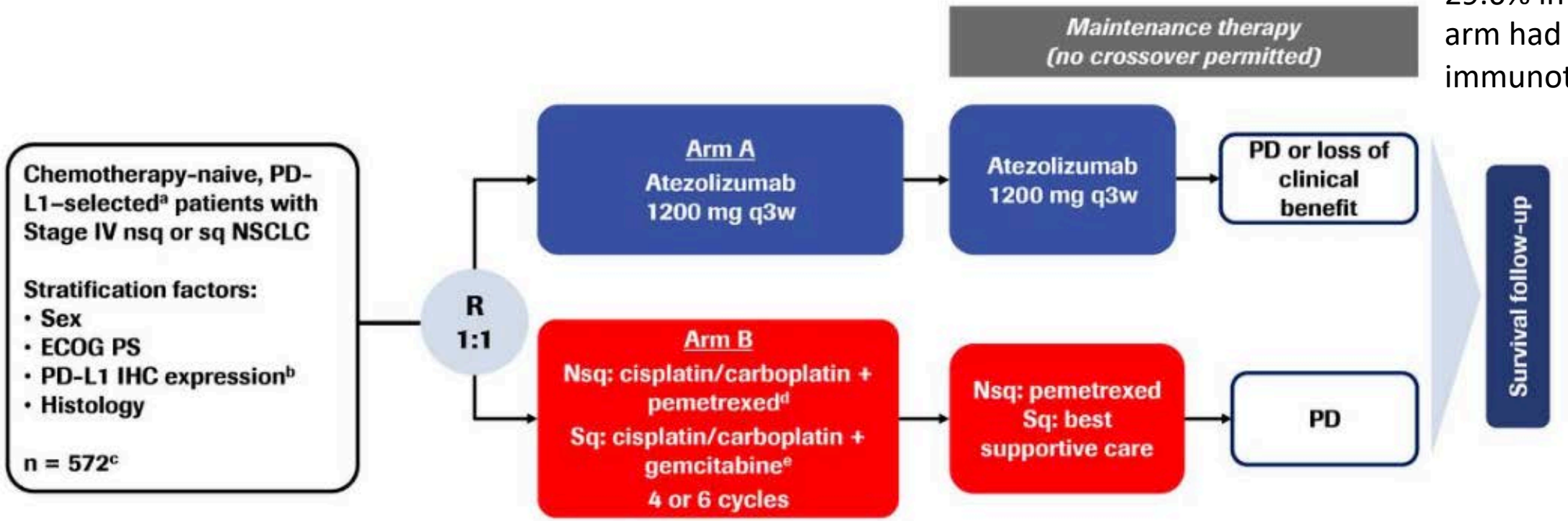
- Implications for Future Research
  - Important in this and other studies to evaluate benefit of second course treatment
    - KEYNOTE-010: Second course in 14 patients: 43% with PR, 36% with SD) (Herbst JCO 2020)
  - Biomarkers, duration of therapy?

Brahmer J et al. KEYNOTE-024 5-year OS update: first-line (1L) pembrolizumab(pembro) vs platinum-based chemotherapy (chemo) in patients (pts) with metastatic NSCLC and PD-L1 tumor proportion score (TPS) ≥50%. ESMO 2020; Abstract LBA51. Oral

Courtesy of Matthew Gubens, MD, MS

Atezolizumab (IMpower110)

29.6% in chemo arm had later immunotherapy



- Primary endpoint: OS in WT population[f]
- Key secondary endpoints: investigator-assessed PFS, ORR and DOR (per RECIST 1.1)

Herbst RS et al; IMpower110 investigators. Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. N Engl J Med. 2020 Oct 1;383(14):1328-1339.

Courtesy of Matthew Gubens, MD, MS

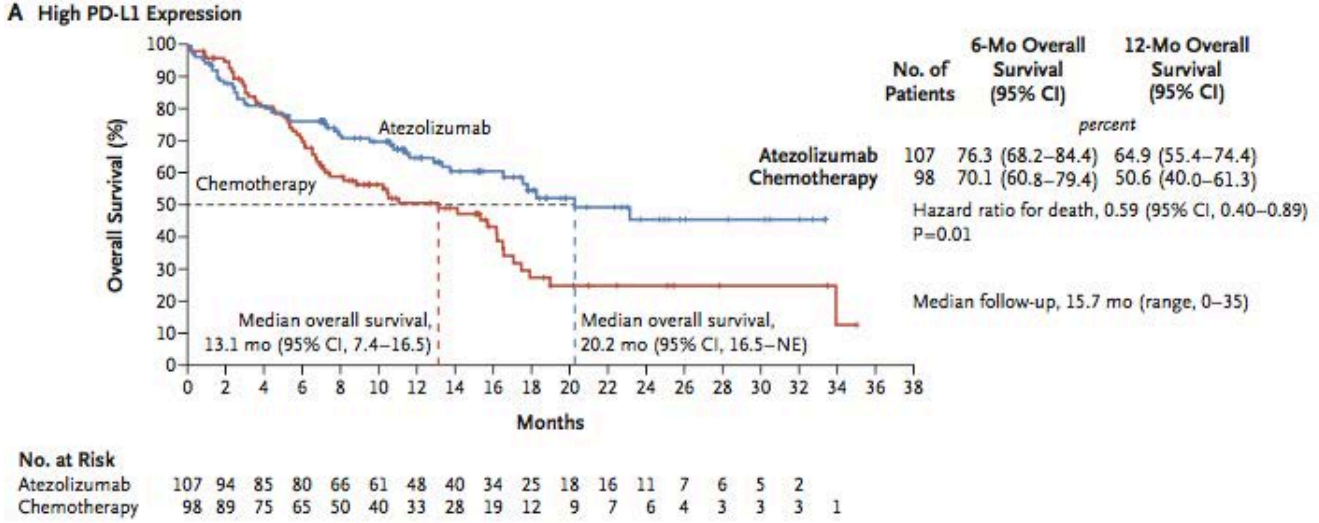
Atezolizumab (IMpower110)

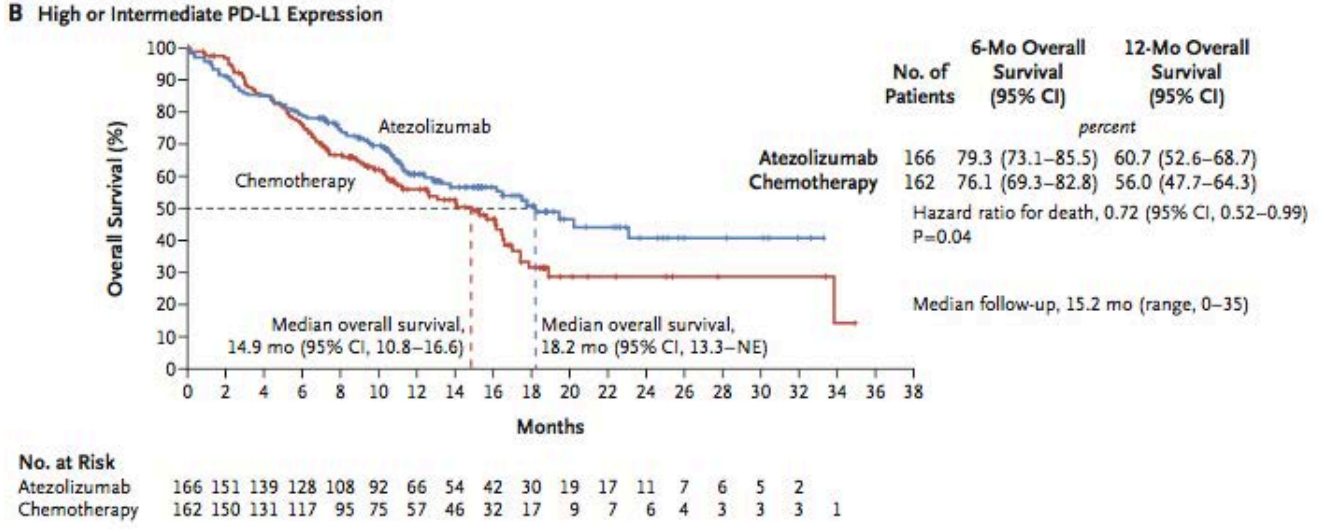
- Primary endpoints relate to evaluation by PD-L1 assay SP142
  - High: ≥50% of tumor cells or ≥10% tumor-infiltrating immune cells – 205 pts
  - Intermediate: ≥5% of tumor cells or tumor-infiltrating immune cells – 123 pts
  - Any: ≥1% of tumor cells or tumor-infiltrating immune cells – 554 pts
- Secondary endpoint related to 22C3
  - High: ≥50% of tumor cells
  - Any: ≥1% of tumor cells

Herbst RS et al; IMpower110 investigators. Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. N Engl J Med. 2020 Oct 1;383(14):1328-1339.

Courtesy of Matthew Gubens, MD, MS

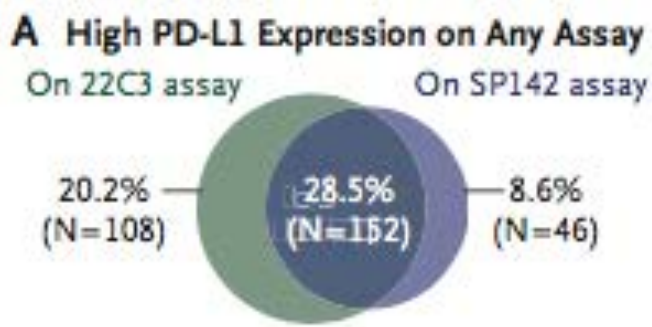
Atezolizumab (IMpower110)





HR for OS (SP142 assay)

- High: 0.59 (0.40-0.89)
- High or int: 0.72 (0.52-0.99)
- Any: 0.83 (0.65-1.07)



HR for OS (22C3 assay)

- High: 0.60 (0.42-0.86)

HR for OS (SP263 assay)

- High: 0.71 (0.50-1.00)

Courtesy of Matthew Gubens, MD, MS

Atezolizumab (IMpower110: Conclusions)

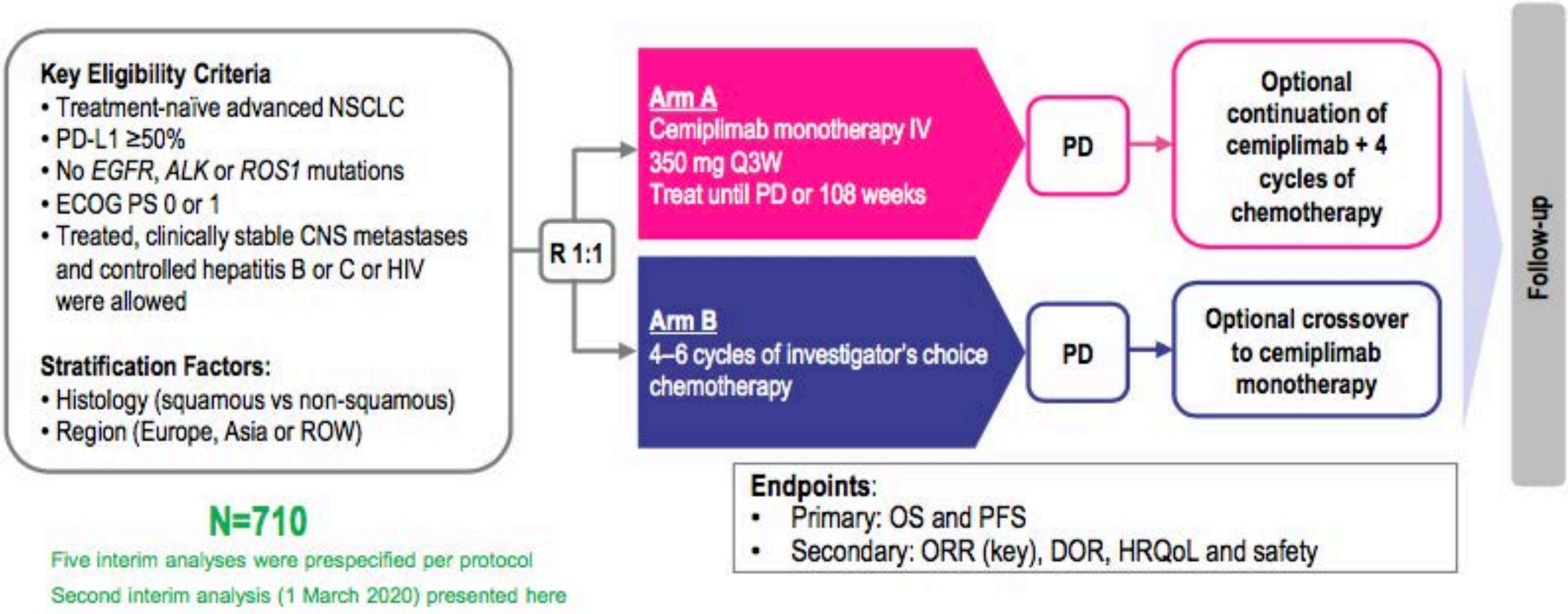
- Impact on Patient Care and Treatment Algorithm
  - Adds atezolizumab as a standard of care for high PD-L1 expression by the SP142 assay, either tumor cells or tumor-infiltrating immune cells
  - Exploratory analysis also suggests benefit in 22C3 high tumors
  - Might be practically limited by most labs choosing one PD-L1 assay
  - No crossover allowed on this trial, and only 29.6% of chemo arm patients had subsequent immunotherapy

- Implications for Future Research
  - First NSCLC approval including reference to PD-L1 staining on TILs

Herbst RS et al; IMpower110 investigators. Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. N Engl J Med. 2020 Oct 1;383(14):1328-1339.

Courtesy of Matthew Gubens, MD, MS

Cemiplimab in PD-L1 ≥50% (EMPOWER-Lung 1)

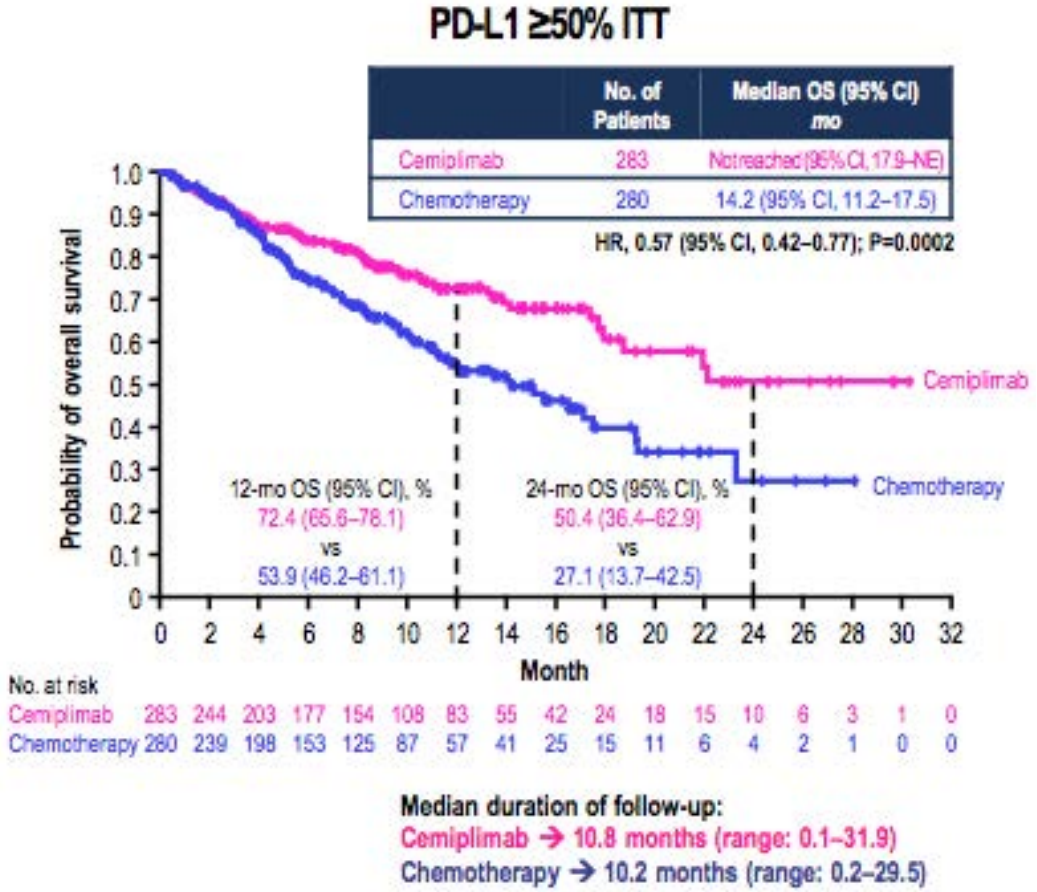


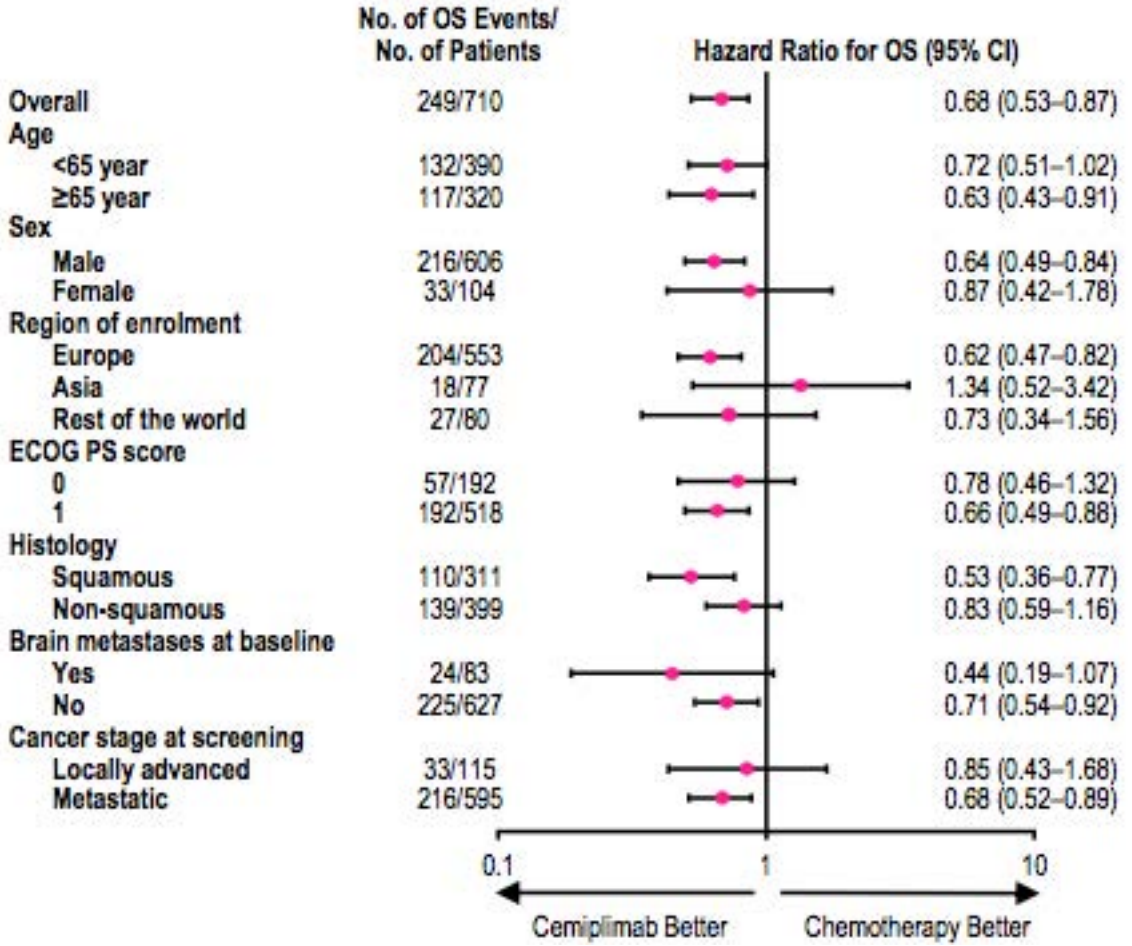
Sezer A et al. EMPOWER-Lung 1: Phase 3 first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%. ESMO 2020; Abstract LBA52. Oral

Courtesy of Matthew Gubens, MD, MS

Cemiplimab in PD-L1 ≥50% (EMPOWER-Lung 1)

74% crossover





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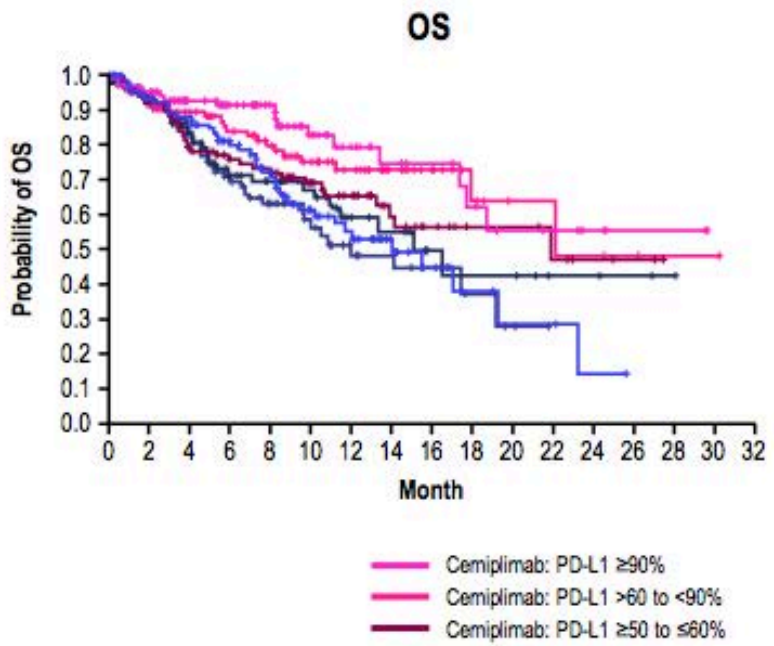
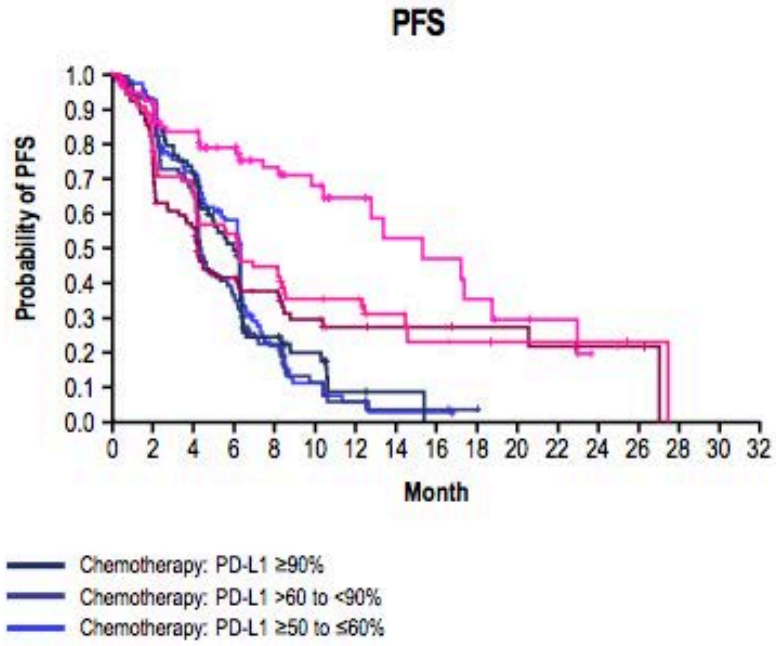
Courtesy of Matthew Gubens, MD, MS

Cemiplimab in PD-L1 ≥50% (EMPOWER-Lung 1)

PD-L1 levels	ORR, % (95% CI)
≥90%	45.9 (35.8–56.3) vs 18.1 (10.9–27.4)
>60 to <90%	39.3 (29.1–50.3) vs 20.0 (12.3–29.8)
≥50 to ≤60%	32.3 (23.1–42.6) vs 22.9 (15.0–32.6)
50% or unknown	26.0 (16.5–37.6) vs 21.6 (12.9–32.7)

Cemiplimab
vs
Chemotherapy





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Courtesy of Matthew Gubens, MD, MS

Cemiplimab in PD-L1 ≥50% (EMPOWER-Lung 1: Conclusions)

- Impact on Patient Care and Treatment Algorithm
  - Not yet approved in US, but could be another option in PD-L1 ≥50% disease
  - No clear advantage compared to pembro or atezo, though

- Implications for Future Research
  - Later to the 1st line field, but study useful with more crossover use of IO in 2nd line and beyond
  - Might be more important for future combos with in-house compounds

Sezer A et al. EMPOWER-Lung 1: Phase 3 first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%. ESMO 2020; Abstract LBA52. Oral

Courtesy of Matthew Gubens, MD, MS

Metastatic NSCLC: Special populations

Courtesy of Matthew Gubens, MD, MS

Pembrolizumab in patients with NSCLC and brain mets

- Phase 2 trial, open-label, single-institution
- Inclusion criteria
  - metastatic NSCLC
  - ≥1 brain metastasis 5-20mm not previously treated, or progressive after prior radiation
  - no neurologic symptoms or steroid requirement
- Cohort 1: PD-L1 ≥1%
- Cohort 2: PD-L1 <1% or inevaluable
- Primary endpoint: Brain metastasis response

Goldberg SB et al. Pembrolizumab for management of patients with NSCLC and brain metastases: long-term results and biomarker analysis from a non-randomised, open-label, phase 2 trial. Lancet Oncol. 2020 May;21(5):655-663.

Courtesy of Matthew Gubens, MD, MS

Pembrolizumab in patients with NSCLC and brain mets

- 42 patients accrued, median 8.3mo f/u
  - Line of therapy: 36% 1st line, 33% 2nd line, 31% 3rd+ line
  - No prior local CNS therapy: 50%
  - Histology: 86% adeno, 10% squam, 5% poorly diff carcinoma
  - Alterations: 33% KRAS, 14% EGFR, 2% ALK, 2% HER2, 2% MET exon 14

- Cohort 1 (PD-L1 ≥1%): 11/37 responders, 29.7%
  - Duration of CNS response 5.7 mos (IQR 4.0-17.7 mos)
  - Systemic response in 11/37 (29.7%), discordant in 6 (brain progression in 3, systemic progression in 3)
  - 1 year survival 40%, 2-year survival 34%

- Cohort 2 (PD-L1 <1% or inevaluable): 0/5 responders, 0%

Goldberg SB et al. Pembrolizumab for management of patients with NSCLC and brain metastases: long-term results and biomarker analysis from a non-randomised, open-label, phase 2 trial. Lancet Oncol. 2020 May;21(5):655-663.

Courtesy of Matthew Gubens, MD, MS

Pembrolizumab in patients with NSCLC and brain mets

- Biomarkers other than tumor PD-L1
  - Tumors with PD-L1 expression ≥1% in stromal/immune cells had longer OS, p=0.031
  - No significant effect by baseline TILs
  - Nanostring targeted mRNA immune profiling showed higher levels of pro-inflammatory genes than non-responders

Goldberg SB et al. Pembrolizumab for management of patients with NSCLC and brain metastases: long-term results and biomarker analysis from a non-randomised, open-label, phase 2 trial. Lancet Oncol. 2020 May;21(5):655-663.

Courtesy of Matthew Gubens, MD, MS

Pembrolizumab in patients with NSCLC and brain mets: Conclusions

- Impact on Patient Care and Treatment Algorithm
  - First study to proactively evaluate immunotherapy alone in patients with untreated or progressed brain mets, showing response
  - Will still be a case-by-case decision, as in targeted therapies
  - Close monitoring warranted if delaying radiation

- Implications for Future Research
  - Warrants further evaluation, perhaps in randomized studies, and in combination with other immune therapies, radiation, or chemotherapy

Goldberg SB et al. Pembrolizumab for management of patients with NSCLC and brain metastases: long-term results and biomarker analysis from a non-randomised, open-label, phase 2 trial. Lancet Oncol. 2020 May;21(5):655-663.

Courtesy of Matthew Gubens, MD, MS

Agenda: NSCLC non-targeted therapy (overall conclusions)

- Locally Advanced
  - Durvalumab consolidation in unresectable stage III (PACIFIC 3-year OS)
    - Persistent OS benefit, only SOC
- Metastatic: Combinations
  - Pembrolizumab + carboplatin/pemetrexed (KEYNOTE-189 update)
    - Persistent OS benefit across PD-L1 subgroups
  - Nivolumab/ipilimumab (CheckMate 227 3-year OS)
    - New option, ?pt selection
  - Nivolumab/ipilimumab + 2 cycles chemo (CheckMate 9LA)
    - New option, ?early follow-up
  - Durvalumab +/- tremelimumab (MYSTIC)
    - Negative, but TMB of interest
- Metastatic: Single agents
  - Pembrolizumab in PD-L1 ≥50% (KEYNOTE-024 5-year OS)
    - Persistent OS benefit
  - Atezolizumab (IMpower110)
    - New option, but needs SP142
  - Cemiplimab in PD-L1 ≥50% (EMPOWER-Lung 1)
    - Not yet approved, seems comparable
- Metastatic: Special populations
  - Pembrolizumab in patients with brain metastases
    - Effective in untreated brain mets

Courtesy of Matthew Gubens, MD, MS