KEYNOTE-189 5-Year Update: First-Line Pembrolizumab + Pemetrexed and Platinum vs Placebo + Pemetrexed and Platinum for Metastatic Nonsquamous NSCLC

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Disclosures

- Marina C. Garassino
  - Personal financial interests: AstraZeneca, MSD International GmbH, BMS, Boehringer Ingelheim Italia S.p.A, Celgene, Eli Lilly, Ignyta, Incyte, Inivata, MedImmune, Novartis, Pfizer, Roche, Takeda, Seattle Genetics, Mirati, Daiichi Sankyo, Regeneron, Merck & Co., Inc., Rahway, NJ, USA, Ose Immuno Therapeutics, Blueprint, Janssen, Sanofi
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Phase 3 KEYNOTE-189 Study (NCT02578680)

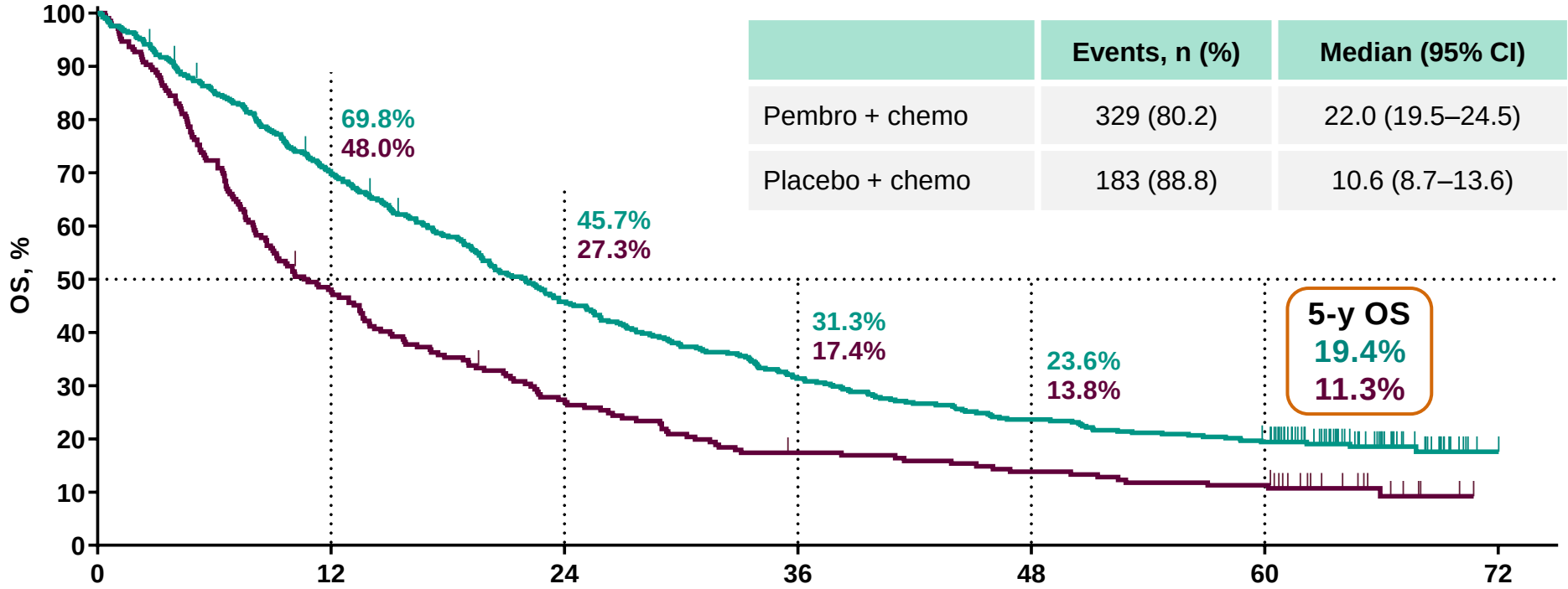
- Pembrolizumab + carboplatin/cisplatin and pemetrexed significantly improved OS and PFS vs placebo + carboplatin/cisplatin and pemetrexed in patients with previously untreated metastatic NSCLC without *EGFR/ALK* alterations[1]

	Primary analysis[1]	Protocol-specified final analysis[2]
Median follow-up (range), mo	10.5 (0.2–20.4)[a]	31.0 (26.5–38.8)[b]
OS HR (95% CI)	0.49 (0.38–0.64); *P* < 0.001	0.56 (0.46–0.69)
PFS HR (95% CI)	0.52 (0.43–0.64); *P* < 0.001	0.49 (0.41–0.59)

- **Current analysis:** 5-year efficacy and safety outcomes update
  - Median follow-up[b]: 64.6 (range, 60.1–72.4) months
  - Effective crossover rate**:** 57.3%
    - 118/206 patients crossed over from placebo + pemetrexed-platinum to anti–PD-(L)1 therapy on (n = 84) or off (n = 34)[c] study

[a]Defined as time from randomization to date of death or data cutoff.
[b]Defined as time from randomization to data cutoff.
[c]Some patients received >1 subsequent anti–PD-(L)1 therapy.
1. Gandhi L, et al. *N Engl J Med*. 2018;387(22):2078-2092. 2. Rodríguez-Abreu D, et al. *Ann Oncol*. 2021;32(7):881-895.

OS: ITT Population



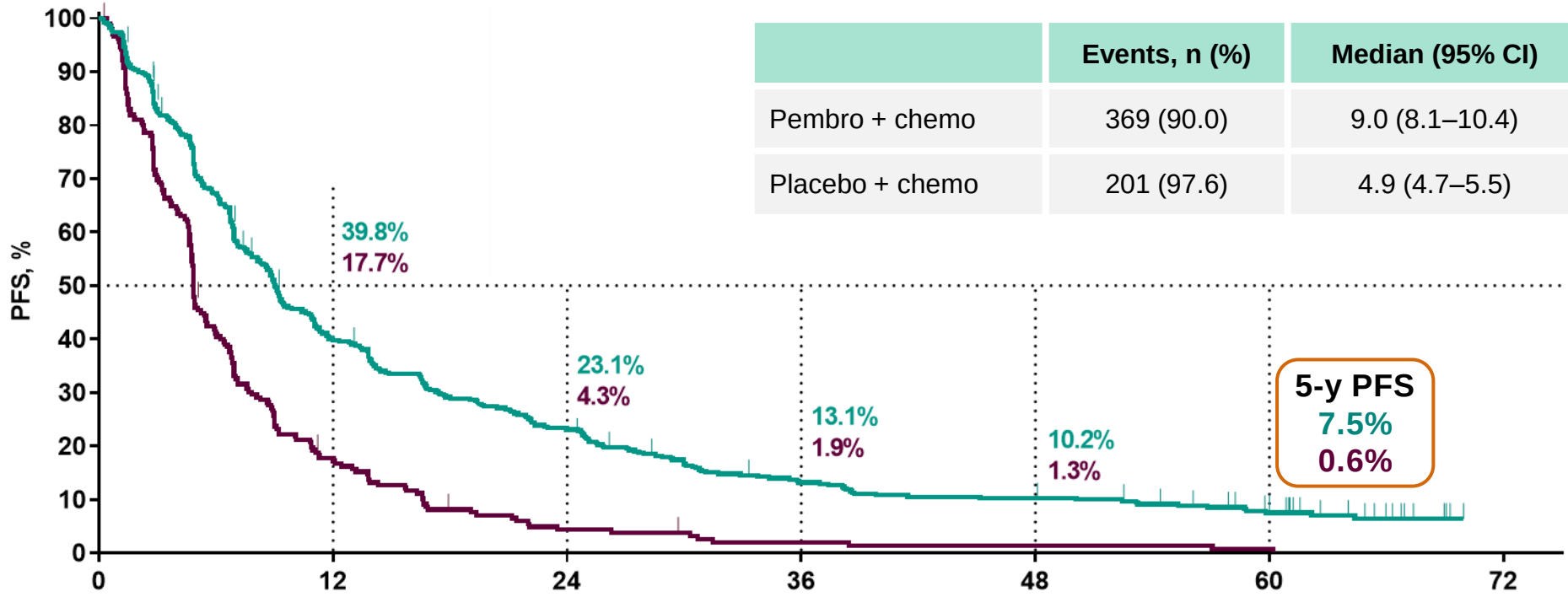
	Events, n (%)	Median (95% CI)	HR (95% CI)
Pembro + chemo	329 (80.2)	22.0 (19.5–24.5)	0.60 (0.50–0.72)
Placebo + chemo	183 (88.8)	10.6 (8.7–13.6)	

No. at risk							
Pembro + chemo	410	283	184	126	95	77	0
Placebo + chemo	206	98	55	34	27	22	0

	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 132)	Placebo + chemo (n = 70)	Pembro + chemo (n = 128)	Placebo + chemo (n = 58)	Pembro + chemo (n = 127)	Placebo + chemo (n = 63)
OS HR (95% CI)	0.68 (0.49–0.96)		0.65 (0.46–0.90)		0.55 (0.39–0.76)	
5-y OS rate,[a] %	29.6	21.4	19.8	7.7	9.6	5.3

[a]Kaplan-Meier estimate. Data cutoff date: March 8, 2022.

PFS[a]: ITT Population



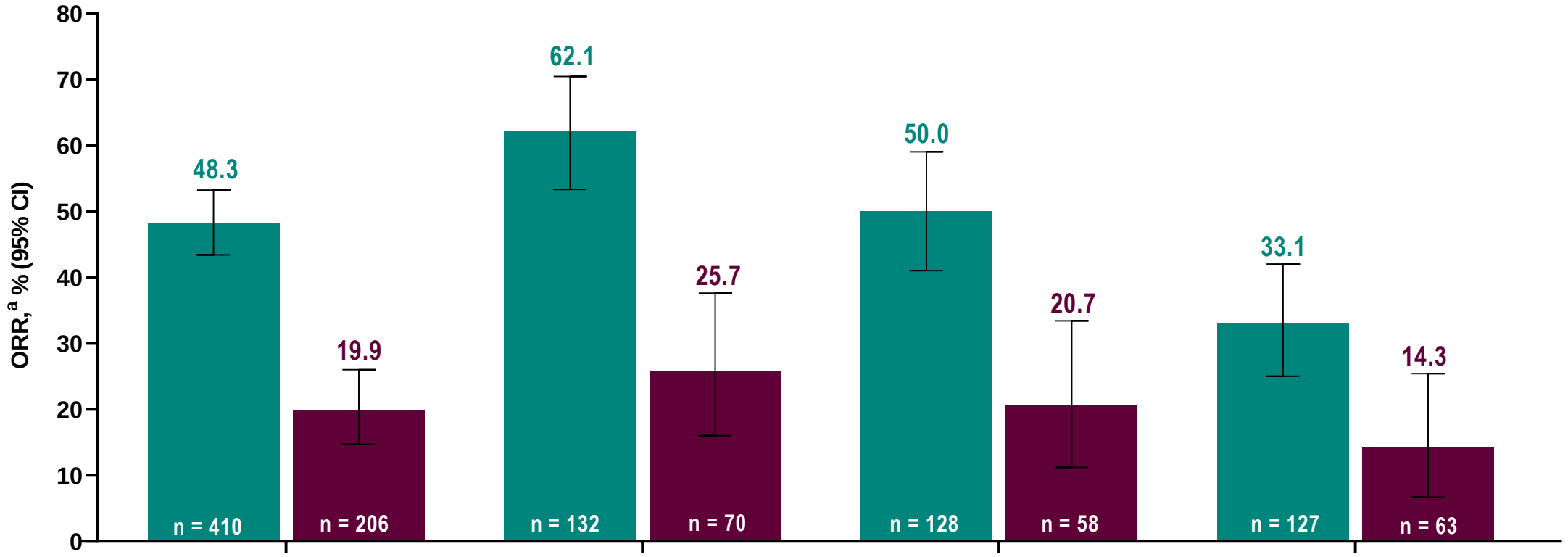
	Events, n (%)	Median (95% CI)	HR (95% CI)
Pembro + chemo	369 (90.0)	9.0 (8.1–10.4)	**0.50 (0.42–0.60)**
Placebo + chemo	201 (97.6)	4.9 (4.7–5.5)	

No. at risk							
Pembro + chemo	410	158	91	49	37	21	0
Placebo + chemo	206	35	8	3	2	1	0

	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 132)	Placebo + chemo (n = 70)	Pembro + chemo (n = 128)	Placebo + chemo (n = 58)	Pembro + chemo (n = 127)	Placebo + chemo (n = 63)
PFS HR (95% CI)	0.35 (0.25–0.49)		0.57 (0.41–0.80)		0.67 (0.49–0.92)	
5-y PFS rate,[b] %	12.8	0	6.5	1.9	2.4	0

[a]Per RECIST version 1.1 by BICR. [b]Kaplan-Meier estimate. Data cutoff date: March 8, 2022.

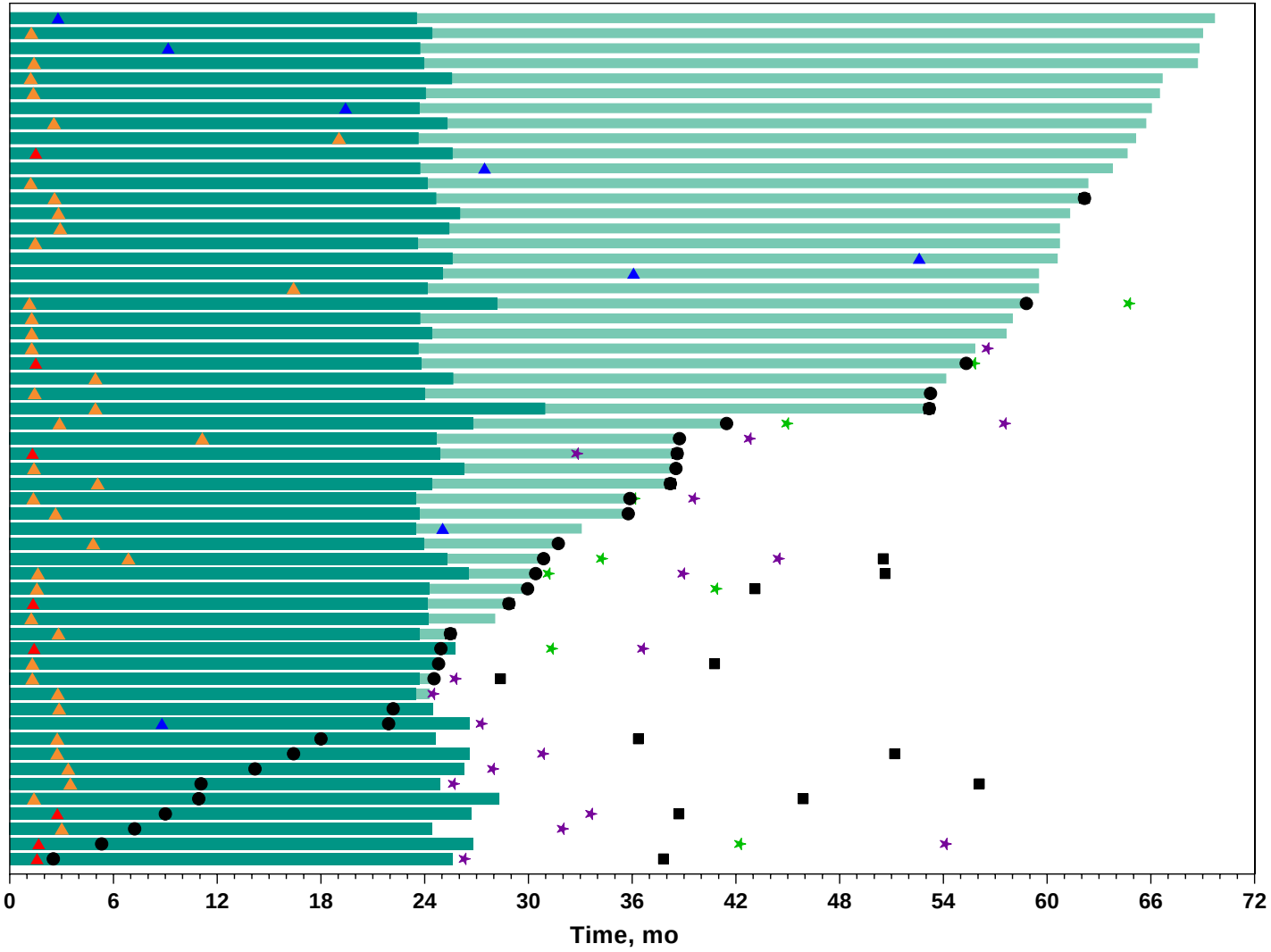
Tumor Response



	ITT		PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo	Placebo + chemo	Pembro + chemo	Placebo + chemo	Pembro + chemo	Placebo + chemo	Pembro + chemo	Placebo + chemo
DOR[b] Median (range), mo	12.7 (1.1+ to 68.3+)	7.1 (2.4 to 31.5)	15.3 (1.2+ to 68.3+)	7.1 (3.4 to 31.5)	13.6 (2.1+ to 67.6+)	7.6 (2.4 to 31.0+)	10.8 (1.1+ to 59.4+)	7.8 (4.1 to 28.3+)

[a]Per RECIST version 1.1 by BICR. [b]Kaplan-Meier estimate. Data cutoff date: March 8, 2022.

Outcomes in Patients Who Completed 35 Cycles of Pembrolizumab



	n = 57
ORR (95% CI),[a] %	86.0 (74.2–93.7)
Best overall response, n (%)	
CR	8 (14.0)
PR	41 (71.9)
Median DOR (range),[b] mo	57.7 (4.2 to 68.3+)
3-y OS rate after completing 35 cycles[c]	71.9%
Alive without PD or subsequent therapy, n (%)	23 (40.4)

[a]Per RECIST version 1.1 by BICR. [b]Kaplan-Meier estimate. [c]Approximately 5 years after randomization. Data cutoff date: March 8, 2022.

Safety: All Treated Patients

Adverse event, n (%)	All treated patients		Completed 35 cycles of pembro n = 57
	Pembro + chemo n = 405	Placebo + chemo n = 202	
Any AE	404 (99.8)	200 (99.0)	57 (100)
Grade 3–5	295 (72.8)	136 (67.3)	38 (66.7)
Led to discontinuation of any treatment component	145 (35.8)	35 (17.3)	19 (33.3)
Led to death[a]	29 (7.2)	14 (6.9)	0
Treatment-related AE	377 (93.1)	183 (90.6)	56 (98.2)
Grade 3–5	212 (52.3)	85 (42.1)	27 (47.4)
Immune-mediated AEs and infusion reactions[b]	113 (27.9)	27 (13.4)	23 (40.4)
Grade 3–5	52 (12.8)	9 (4.5)	7 (12.3)

[a]All deaths were previously reported in Rodríguez-Abreu D, et al. *Ann Oncol*. 2021;32(7):881-895.
[b]Events considered regardless of attribution to treatment or immune relatedness by the investigator.
Data cutoff date: March 8, 2022.

Conclusions

- With ≥5 years follow-up, pembrolizumab + pemetrexed-platinum maintained an OS and PFS benefit vs placebo + pemetrexed-platinum in patients with previously untreated metastatic nonsquamous NSCLC, regardless of PD-L1 expression in the subgroups analyzed
  - Benefits were observed despite an effective crossover rate of 57% from placebo + chemo group to subsequent anti–PD-(L)1 therapy during/outside study
- Consistent with previous reports,[1,2] toxicity was manageable
- Patients who completed 35 cycles (≈2 years) of pembrolizumab experienced durable responses and 72% were alive 3 years after completion of 35 cycles (~5 years from randomization)
- These results continue to support the combination of first-line pembrolizumab + pemetrexed-platinum as a standard of care in patients with metastatic nonsquamous NSCLC without *EGFR*/*ALK* alterations

1. Rodríguez-Abreu D, et al. *Ann Oncol*. 2021;32(7):881-895. 2. Gadgeel S, et al. *J Clin Oncol*. 2020;38:1505-1517.

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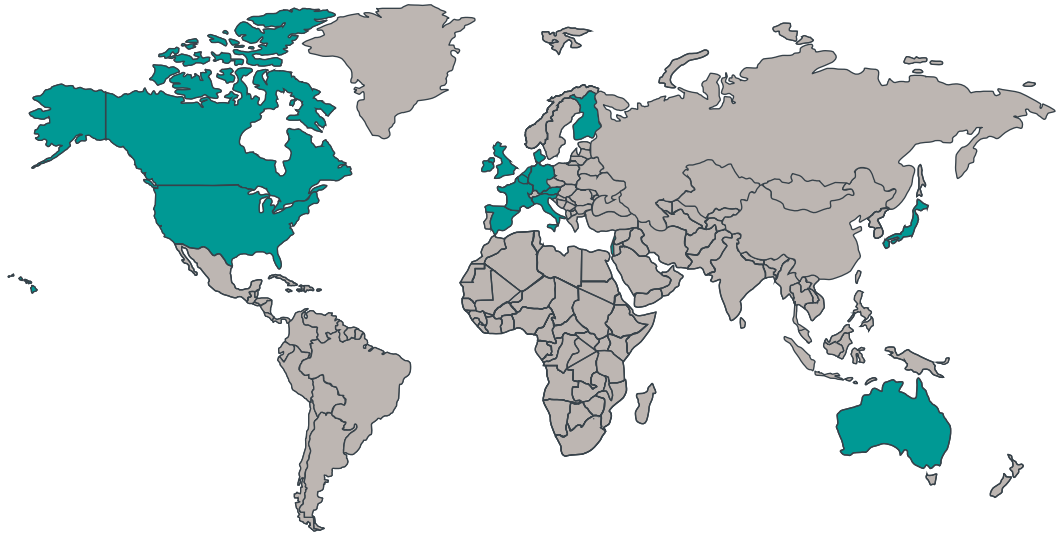

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