

Pembrolizumab Plus Chemotherapy for Metastatic Non-Small-Cell Lung Cancer: 8-Year Follow-Up From KEYNOTE-189 and KEYNOTE-407

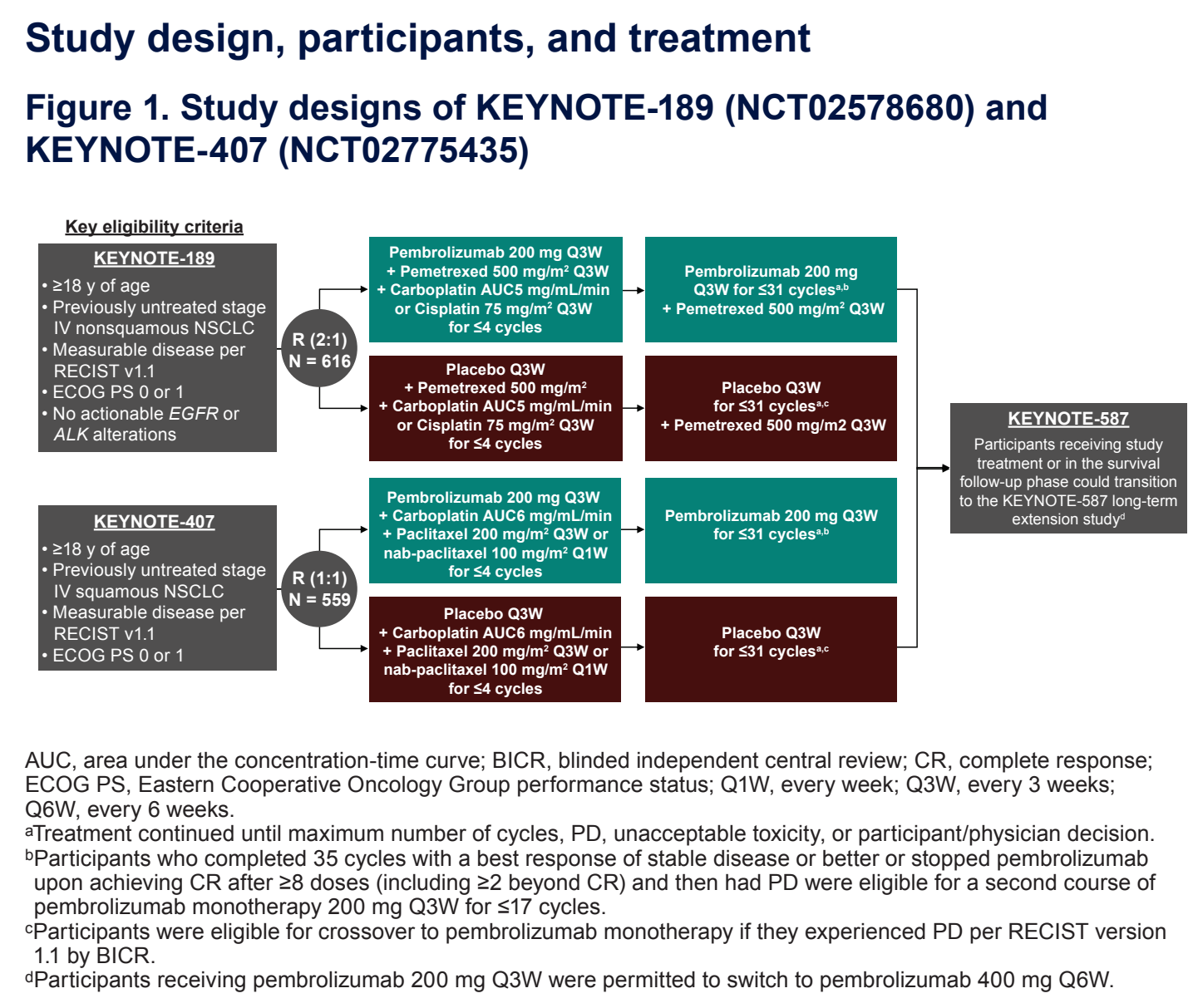
Background

- First-line pembrolizumab plus chemotherapy significantly improved overall survival (OS) vs chemotherapy alone in participants with metastatic nonsquamous NSCLC in the phase 3 KEYNOTE-189 study (HR, 0.49; 95% CI, 0.38–0.64; $P < 0.001$) and in those with metastatic squamous NSCLC in the phase 3 KEYNOTE-407 study (HR, 0.64; 95% CI, 0.49–0.85; $P < 0.001$).^{1,2}
- Survival benefits with pembrolizumab plus chemotherapy vs chemotherapy alone were maintained after 5 years of follow-up^{3,4}
 - In KEYNOTE-189, 5-year OS was 19.4% vs 11.3% (HR, 0.60; 95% CI, 0.50–0.72)³
 - In KEYNOTE-407, 5-year OS was 18.4% vs 9.7% (HR, 0.71; 95% CI, 0.59–0.85)⁴
- At the closure of these 2 studies, surviving participants had the option to transition to the KEYNOTE-587 extension study (NCT03486873) for long-term follow-up
- We report survival with a median follow-up of ≥8 years in participants from the KEYNOTE-189 and KEYNOTE-407 studies, including those who consented to transition to KEYNOTE-587

Objectives

- Primary**
- OS, defined as time from randomization in KEYNOTE-189 or KEYNOTE-407 to death from any cause
- Secondary**
- Modified progression-free survival (modified PFS; censored at last known alive date), defined as time from randomization to first documented occurrence of PD per RECIST version 1.1 by investigator assessment or death from any cause
- Post hoc**
- Lung cancer–specific survival (LCSS), defined as time from randomization in KEYNOTE-189 or KEYNOTE-407 to death from malignant neoplasm progression or lung cancer–specific death

Methods



Statistical analysis

- Efficacy was assessed in all randomized participants
- OS, modified PFS, and LCSS were estimated using the Kaplan-Meier method, with HRs and 95% CIs assessed using an unstratified Cox proportional hazard model with the Efron method of tie handling

- For all endpoints, participants who did not transition to KEYNOTE-587 were censored at the last known alive date or database cutoff date in KEYNOTE-189 and KEYNOTE-407; participants who transitioned to KEYNOTE-587 and did not have an event were censored at the last known alive date or database cutoff date in KEYNOTE-587

Results

- Participants**
- Across studies, 1175 participants were randomized to pembrolizumab plus chemotherapy (n = 688) or chemotherapy (n = 487), and 105 participants transitioned to KEYNOTE-587
 - KEYNOTE-189: 44/410 participants in the pembrolizumab plus chemotherapy arm and 12/206 in the chemotherapy arm transitioned
 - KEYNOTE-407: 34/278 participants in the pembrolizumab plus chemotherapy arm and 15/281 in the chemotherapy arm transitioned
 - Median (range) time from randomization to data cutoff (November 10, 2025) was 9.1 (8.7–9.6) years for KEYNOTE-189 and 8.5 (7.9–9.1) years for KEYNOTE-407

Table 1. Participant demographics and baseline characteristics of participants who transitioned to KEYNOTE-587 by parent study

	KEYNOTE-189		KEYNOTE-407	
	Pembro + Chemo n = 44	Chemo n = 12	Pembro + Chemo n = 34	Chemo n = 15
Age, median (range), y	65.0 (42–80)	60.0 (49–75)	64.5 (40–78)	68.0 (45–83)
Female	23 (52.3)	8 (66.7)	7 (20.6)	1 (6.7)
Geographic region				
East Asia	1 (2.3)	0	4 (11.8)	2 (13.3)
Other	43 (97.7)	12 (100)	30 (88.2)	13 (86.7)
ECOG PS 0	29 (65.9)	8 (66.7)	13 (38.2)	10 (66.7)
Current or former smoker	40 (90.9)	11 (91.7)	32 (94.1)	15 (100)
PD-L1 TPS ^a				
<1%	4 (9.1)	0	11 (32.4)	7 (46.7)
≥1%	39 (88.6)	12 (100)	21 (61.8)	8 (53.3)
1%–49%	9 (20.5)	2 (16.7)	9 (26.5)	6 (40.0)
≥50%	30 (68.2)	10 (83.3)	12 (35.3)	2 (13.3)
Unknown	1 (2.3)	0	2 (5.9)	0
Brain metastases	9 (20.5)	3 (25.0)	1 (2.9)	0
Prior therapy				
(Neo)adjuvant therapy	4 (9.1)	3 (25.0)	0	1 (6.7)
Radiation	7 (15.9)	2 (16.7)	2 (5.9)	2 (13.3)
Thoracic radiation	3 (6.8)	1 (8.3)	1 (2.9)	2 (13.3)

Data are n (%) unless otherwise specified.
Chemo, chemotherapy; pembro, pembrolizumab; TPS, tumor proportion score.
^aPD-L1 expression was measured using PD-L1 IHC 22C3 pharmDx (Agilent Technologies, Carpinteria, CA).

- References**
- Gandhi L, et al. *N Engl J Med*. 2018;378(22):2078-2092.
 - Paz-Ares L, et al. *N Engl J Med*. 2018;379(21):2040-2051.
 - Garassino MC, et al. *J Clin Oncol*. 2023;41(11):1992-1998.
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Disclosures

Marina C. Garassino¹: has received consulting fees from AstraZeneca, Abion, MSD, International GmbH, Bayer, BMS, Boehringer Ingelheim Italia S.p.A, Celgene, Eli Lilly, Incyte, Novartis, Pfizer, Roche, Takeda, Seattle Genetics, Mirati, Daiichi Sankyo, Regeneron, MSD, Blueprint, Janssen, Sanofi, AbbVie, BeiGene, Oncoshift, Medscape, Gilead, IO Biotech, and Revolution Medicines; payment or honoraria for lectures from AstraZeneca, MSD, Daiichi Sankyo, Gilead, Eli Lilly, and Regeneron; and support for attending meetings or travel from AstraZeneca.

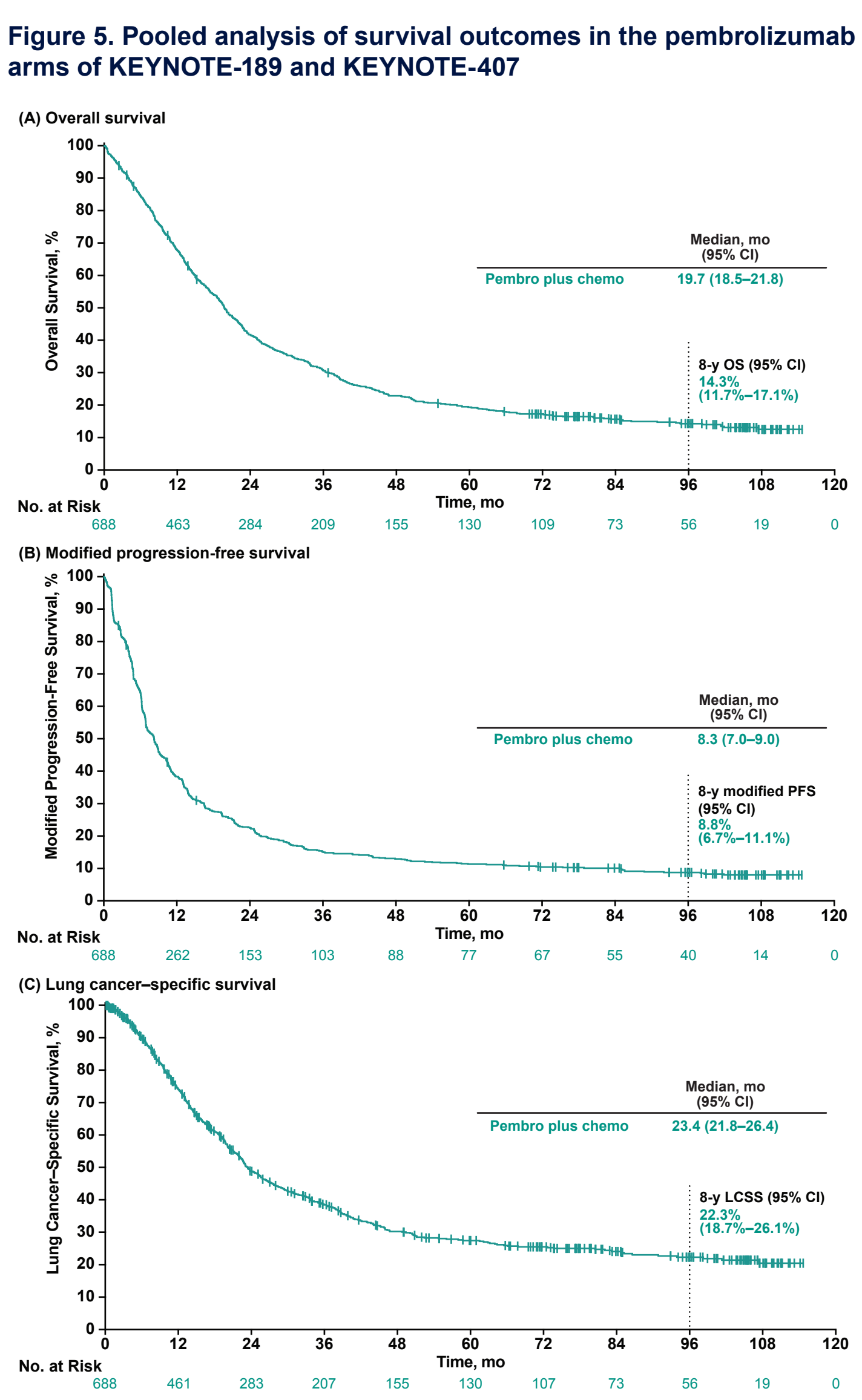
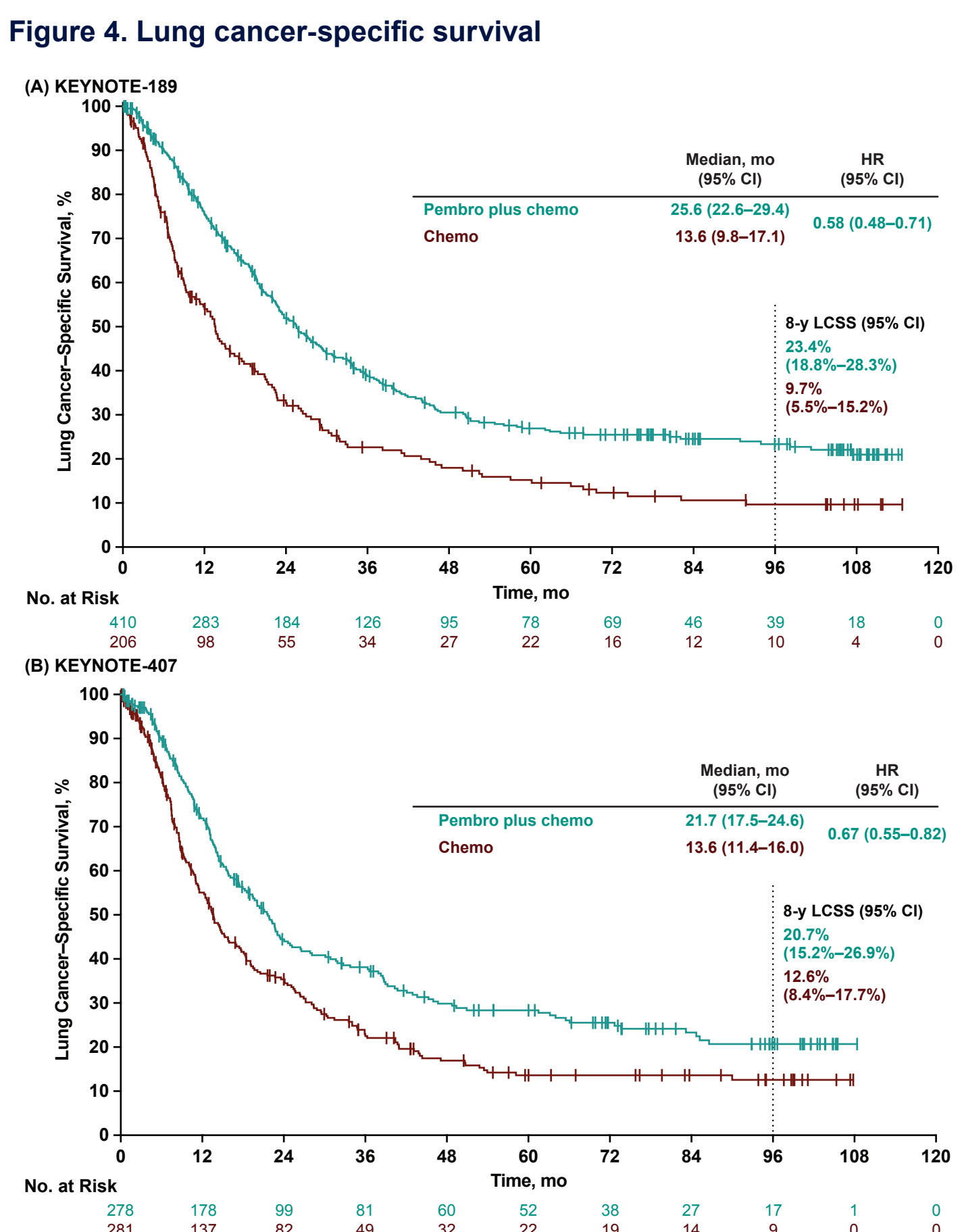
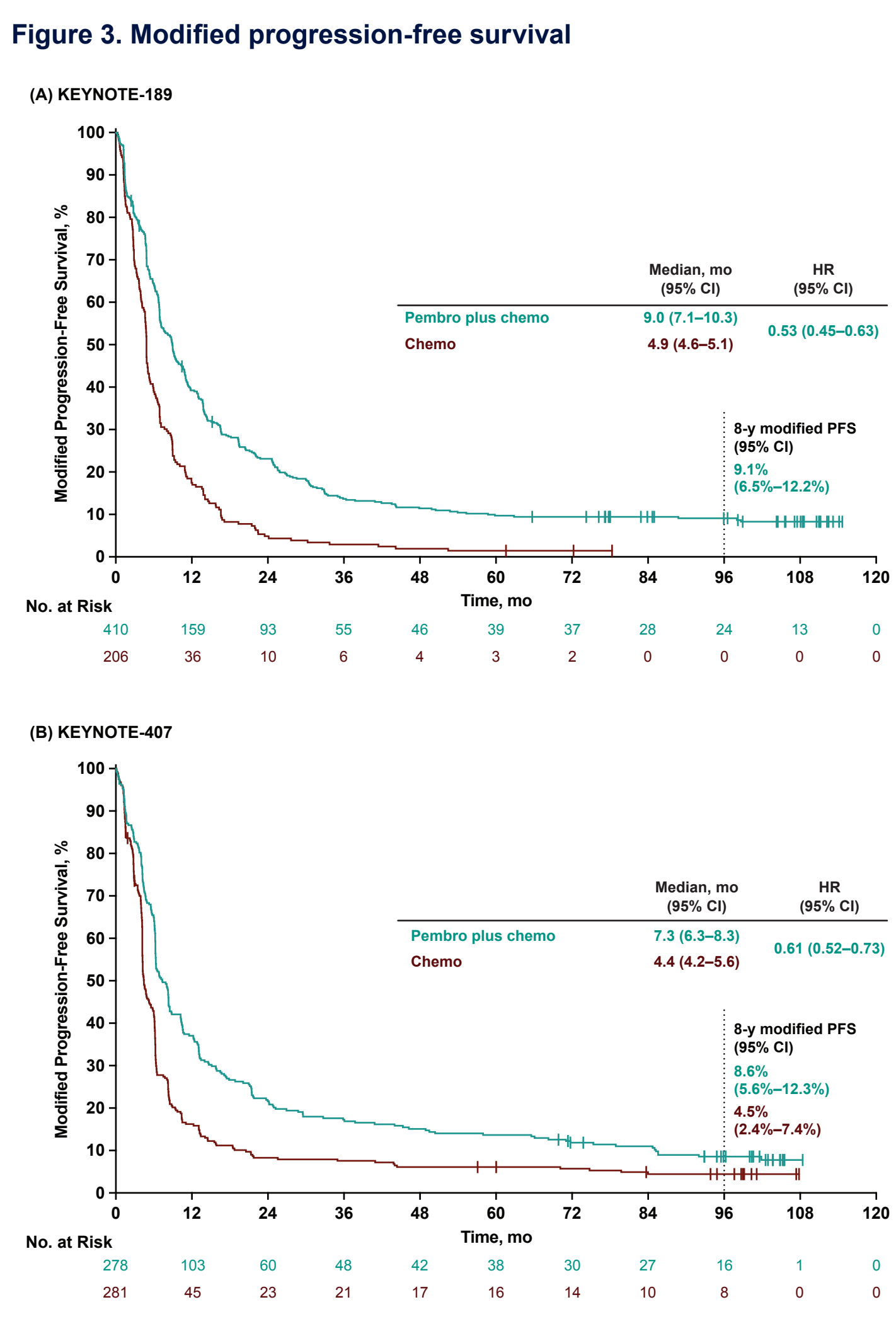
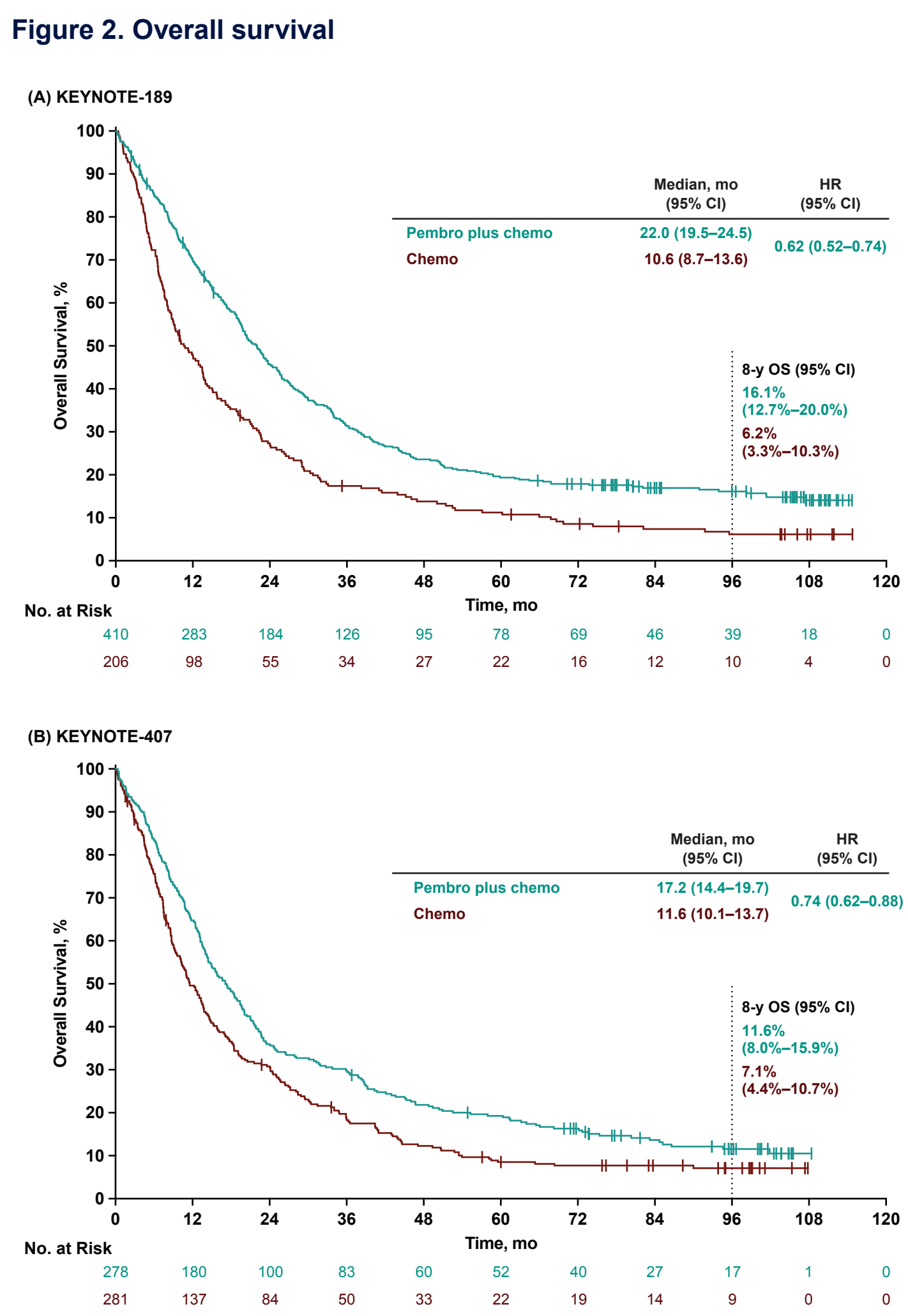


Table 2. Causes of death in all participants

	KEYNOTE-189		KEYNOTE-407	
	Pembro + Chemo n = 410	Chemo n = 206	Pembro + Chemo n = 278	Chemo n = 281
All-cause deaths	341 (83.2)	190 (92.2)	243 (87.4)	255 (90.7)
All-cause deaths in parent study	334 (81.5)	188 (91.3)	231 (83.1)	254 (90.4)
All-cause deaths in KEYNOTE-587	7 (1.7)	2 (1.0)	12 (4.3)	1 (0.4)
Lung cancer–specific deaths ^a	273 (66.6)	161 (78.2)	182 (65.5)	211 (75.1)
Lung cancer–specific deaths in parent study	267 (65.1)	160 (77.7)	175 (62.9)	210 (74.7)
Lung cancer–specific deaths in KEYNOTE-587	6 (1.5)	1 (0.5)	7 (2.5)	1 (0.4)
Other cause of death	39 (9.5)	20 (9.7)	40 (14.4)	31 (11.0)
Unknown cause of death	29 (7.1)	9 (4.4)	21 (7.6)	13 (4.6)

Data are n (%).
^aIncludes deaths from malignant lung neoplasm, malignant neoplasm progression, metastatic neoplasm, NSCLC, or PD.

Conclusions

- After a median follow-up of ≥8 years, pembrolizumab plus chemotherapy continued to demonstrate durable survival benefits vs chemotherapy alone in participants with previously untreated, metastatic, nonsquamous or squamous NSCLC
- Long-term OS benefits were supported by favorable modified PFS and LCSS results with pembrolizumab plus chemotherapy vs chemotherapy alone, suggesting sustained disease-related benefits
- All-cause deaths and lung cancer–specific deaths were limited in KEYNOTE-587
- This analysis confirms the clinically meaningful, long-term survival benefits of first-line pembrolizumab plus chemotherapy, supporting its continued use as a standard of care for patients with metastatic NSCLC

Poster presented

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Poster slides

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