Table: 973MO

	ITT N = 616	TPS ≥50% n = 202	TPS 1%–49% n = 186	TPS <1% n = 190
OS HR (95% CI)[a]	0.60 (0.50–0.72)	0.68 (0.49–0.96)	0.65 (0.46–0.90)	0.55 (0.39–0.76)
5-y OS rate[a],%	19.4 vs 11.3	29.6 vs 21.4	19.8 vs 7.7	9.6 vs 5.3
PFS HR (95%CI)[a,b]	0.50 (0.42–0.60)	0.35 (0.25–0.49)	0.57 (0.41–0.80)	0.67 (0.49–0.92)
ORR[b], %	48.3 vs 19.9	62.1 vs 25.7	50.0 vs 20.7	33.1 vs 14.3
Median DOR[a,b] mo (range)	12.7 (1.1+ to 68.3+) vs 7.1 (2.4 to 31.5)	15.3 (1.2+ to 68.3+) vs 7.1 (3.4 to 31.5)	13.6 (2.1+ to 67.6+) vs 7.6 (2.4 to 31.0+)	10.8 (1.1+ to 59.4+) vs 7.8 (4.1 to 28.3+)

+, no PD at last follow up; DOR, duration of response. Data are for pembro + pem-platinum vs pbo + pem-platinum.
[a]K-M estimate. [b]Per RECIST v1.1 by blinded independent central review.

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974MO 5-year update from KEYNOTE-407: Pembrolizumab plus chemotherapy in squamous non-small cell lung cancer (NSCLC)

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Background: Pembrolizumab (pembro) + platinum-based chemotherapy (chemo) significantly prolonged OS and PFS compared with placebo + chemo in patients (pts) with previously untreated, metastatic squamous NSCLC in the phase III KEYNOTE-407 study (NCT02775435). We report the 5-y outcomes in the ITT population and in pts who completed 35 cycles of pembro (~2 y).

Methods: Eligible pts were randomized 1:1 to receive pembro 200 mg or placebo + carboplatin and paclitaxel/nab-paclitaxel Q3W for 4 cycles, followed by pembro or placebo up to 35 cycles. Eligible pts in the placebo + chemo group were allowed to crossover on-study to up to 35 cycles of open-label pembro monotherapy upon unblinding after verification of PD by BICR. Primary endpoints were OS and PFS per RECIST v1.1 by BICR.

Results: Pts were randomized to pembro + chemo (n = 278) or placebo + chemo (n = 281). As of Feb 23, 2022, median time from randomization to data cutoff was 56.9 (range, 49.9–66.2) mo; 117 pts crossed over from the placebo + chemo group to receive pembro monotherapy, and an additional 26 pts received subsequent anti–PD-(L)1 therapy; the effective crossover rate was 51.1%. Median OS in the ITT population was 17.2 mo for the pembro + chemo group and 11.6 mo for the placebo + chemo group; HR, 0.71 (95% CI, 0.59–0.85). Respective 5-y OS rates were 18.4% and 9.7%. Additional efficacy outcomes are described in the table. Grade 3–5 AEs occurred in 74.8% and 70.0% of pts in the pembro + chemo and placebo + chemo groups, respectively. Among 55 pts who completed 35 cycles of pembro, ORR was 90.9%, and 3-y OS rate after completion of 35 cycles (~5 y after randomization) was 69.5%.

Conclusions: After 5 y of follow-up, pembro + chemo continued to demonstrate prolonged OS and PFS vs chemo alone without increased toxicity. Most pts who completed 35 cycles had objective responses and were alive at data cutoff. These long-term data support use of pembro + chemo as a standard first-line treatment option for metastatic squamous NSCLC.

Table: 974MO

ITT population	Pembrolizumab + chemotherapy n = 278	Placebo + chemotherapy n = 281
Median OS (95% CI), mo	17.2 (14.4–19.7)	11.6 (10.1–13.7)
OS HR (95% CI)	0.71 (0.59–0.85)	
5-year OS rate, %	18.4	9.7
Median PFS (95% CI), mo	8.0 (6.3–8.5)	5.1 (4.3–6.0)
PFS HR (95% CI)	0.62 (0.52–0.74)	
5-year PFS rate, %	10.8	3.5
ORR (95% CI), %	62.2 (56.2–68.0)	38.8 (33.1–44.8)
Median DOR (range), mo	9.0 (1.3+ to 61.5+)	4.9 (1.3+ to 58.6+)
−DOR ≥4 y; %	21.6	16.0

+ indicates no PD by time of last assessment.

Clinical trial identification: NCT02775435.

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975P Trastuzumab deruxtecan in patients (pts) with HER2-overexpressing (HER2-OE) metastatic non-small cell lung cancer (NSCLC): Results from the DESTINY-Lung01 trial

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Background: DESTINY-Lung01 (NCT03505710) is a multicenter, phase II study evaluating the safety and efficacy of T-DXd (HER2 antibody-drug conjugate) in pts with HER2-OE or *HER2*-mutated unresectable and/or metastatic NSCLC. We report the results of T-DXd in pts with HER2-OE NSCLC.

Methods: Pts with pretreated metastatic NSCLC with HER2 immunohistochemistry (IHC) 3+ or 2+ (without known *HER2* mutation) received T-DXd 6.4 mg/kg (cohort 1) or 5.4 mg/kg (cohort 1a) every 3 weeks. Primary endpoint was confirmed objective response rate (ORR) by independent central review (ICR). Additional endpoints were disease control rate (DCR), duration of response (DOR), progression-free survival (PFS), overall survival (OS), and evaluation of safety.

Results: As of Dec 3, 2021, 49 and 41 pts were enrolled in cohorts 1 and 1a. Central nervous system metastases at baseline were present in 17 (34.7%; cohort 1) and 12 (29.3%; cohort 1a) pts. Median number of prior treatment regimens was 3 (range, 1-8 [cohort 1] and 1-5 [cohort 1a]); median treatment duration was 4.1 months (mo) (range, 0.7-27.8) and 5.5 mo (range, 0.7-16.5) in cohorts 1 and 1a, respectively. ORR by ICR was 26.5% and 34.1% (table), median PFS was 5.7 mo and 6.7 mo, and median OS was 12.4 mo and 11.2 mo in cohorts 1 and 1a, respectively. All pts had at least 1 treatment-emergent adverse event (TEAE) and the most common were nausea (59.2% and 73.2%), decreased appetite (44.9.% and 46.3%), and fatigue (32.7% and 51.2%); grade (G) ≥3 TEAEs occurred in 81.6% and 51.2% of pts (drug-related, 53.1% and 22.0%) in cohorts 1 and 1a, respectively. Independently adjudicated drug-related interstitial lung disease (ILD) (any G) occurred in 20.4% (2 G1, 5 G2, 3 G5; cohort 1) and 4.9% (1 G1, 1 G5; cohort 1a) of pts.

Table: 975P Efficacy and safety of T-DXd in pts with HER2-OE NSCLC

	Cohort 1 (6.4 mg/kg) N = 49	Cohort 1a (5.4 mg/kg) N = 41
Efficacy		
ORR by ICR, % (95% CI)	26.5 (15.0-41.1)	34.1 (20.1-50.6)
Complete response	0	4.9
Partial response	26.5	29.3
Stable disease	42.9	43.9
Progressive disease	22.4	9.8
Non-evaluable	8.2	12.2
ORR for HER2 IHC 3+/IHC 2+, % (n/N)	20.0 (2/10)/ 28.2 (11/39)	52.9 (9/17)/ 20.8 (5/24)
DCR, % (95% CI)	69.4 (54.6-81.8)	78.0 (62.4-89.4)
DOR, median (95% CI), mo	5.8 (4.3-NE)	6.2 (4.2-9.8)
Safety, %		
Drug-related TEAE	89.8	92.7
TEAE associated with drug discontinuation/dose reduction	26.5/36.7	17.1/17.1
TEAE associated with drug interruption	49.0	24.4
ILD, any G/G≥3	20.4/6.1	4.9/2.4

Conclusions: Both T-DXd doses had encouraging and consistent antitumor activity in heavily pretreated pts with HER2-OE NSCLC. T-DXd 5.4 mg/kg was associated with a better safety profile vs the 6.4-mg/kg dose.