

2217R0 Updated results from the phase 1b/2 KEYNOTE-365 cohort I: Pembrolizumab (pembro) + carboplatin and etoposide chemotherapy (chemo) or chemo alone for neuroendocrine prostate cancer (NEPC)

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Background

No standard of care based on a randomized study has been established for patients with NEPC. Preliminary data from cohort I of KEYNOTE-365 (NCT02861573) showed that the addition of pembro to chemo was associated with promising antitumor activity vs chemo alone in participants (pts) with NEPC. We present updated results with additional pt accrual.

Methods

Adults with central pathological confirmation of treatment (tx)-emergent or de novo metastatic NEPC (small cell carcinoma, large cell neuroendocrine carcinoma, or mixed) with or without prior androgen deprivation therapy were randomized 1:1, or 3:1 after a protocol amendment, to 4-6 cycles of chemo (carboplatin AUC 5 Q3W + etoposide 100 mg/m² on d1-3 Q3W) with or without pembro 200 mg Q3W for ≤35 cycles. Primary end points included ORR per RECIST v1.1 by blinded independent central review (BICR) and safety. DOR and rPFS per PCWG3-modified RECIST v1.1 by BICR and OS were secondary end points. Efficacy by PD-L1 status was assessed post hoc. No formal hypothesis testing was performed.

Results

As of Nov 19, 2025, 70 pts received ≥1 dose of study tx (pembro + chemo n = 40; chemo n = 30). Most pts had tx-emergent (73%) NEPC and PD-L1–negative tumors (CPS <1; 56%). Median follow-up was 15.4 mo (range 0.8-43.5). Pembro + chemo showed favorable ORR, rPFS, and OS vs chemo (table). Median DOR was 5.9 mo (range 2.0+ to 10.2+) with pembro + chemo vs 4.5 mo (2.8+ to 6.2) with chemo. Efficacy favored pembro + chemo vs chemo across PD-L1 subgroups, particularly in CPS ≥1 tumors; however, sample sizes were small and point estimates had wide CIs (table). Grade 3-5 tx-related AEs occurred in 63% of pts with pembro + chemo vs 80% with chemo (grade 5, 0% vs 3%).

Conclusions

Pembro + chemo was associated with promising efficacy outcomes, including OS, vs chemo alone in pts with NEPC. The safety profile was consistent with the known profiles of each agent. Table: 2217R0

	Total population Pembro + chemon = 40	PD-L1 CPS ≥1 Chemon = 30	PD-L1 CPS <1 Pembro + chemon = 15	Chemon = 12	Pembro + chemon = 23	Chemon = 16
ORR (n/N; 95% CI) ^a , %	28 (10/36; 14-45)	15 (4/27; 4-34)	40 (6/15; 16-68)	18 (2/11; 2-52)	15 (3/20; 3-38)	13 (2/15; 2-40)
Median rPFS (95% CI), mo	5.1 (4.1-6.3)	4.0 (2.1-5.0)	6.0 (3.9-NR)	3.8 (0.4-5.0)	5.1 (4.0-6.3)	4.1 (1.9-7.0)
HR (95% CI)	0.66 (0.36-1.21)	0.40 (0.16-1.01)	0.87 (0.38-1.97)			
Median OS (95% CI), mo	10.2 (8.0-11.4)	7.1 (4.0-8.2)	11.0 (8.7-11.9)	4.8 (1.9-8.6)	8.1 (6.6-13.0)	7.1 (3.6-9.9)
HR (95% CI)	0.33 (0.17-0.63)	0.16 (0.05-0.49)	0.49 (0.21-1.11)			

CPS, combined positive score.^aN is the number of pts with RECIST-measurable disease.

Clinical trial identification

NCT02861573.

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Disclosure

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