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Final protocol-prespecified analysis of the phase 3 KEYNOTE-564 trial of adjuvant pembrolizumab versus placebo in clear cell renal cell carcinoma (ccRCC)

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Background

Adjuvant pembrolizumab is standard of care for patients with ccRCC at increased risk of recurrence post-surgery based on significantly improved disease-free survival (DFS) and overall survival (OS) vs placebo in the primary results of the KEYNOTE-564 trial (NCT03142334). We present updated data from the final protocol-prespecified analysis of KEYNOTE-564.

Methods

Adults who were at high risk for ccRCC recurrence after nephrectomy, with or without metastasectomy, were randomly assigned 1:1 to adjuvant pembrolizumab or placebo 200 mg IV every 3 weeks (≤17 cycles). The primary end point was DFS by investigator assessment (met at first interim analysis [IA1]). OS was a key secondary end point (met at IA2).

Results

Overall, 994 participants (pts) were randomly assigned to pembrolizumab (n = 496) or placebo (n = 498). Median study follow-up (data cutoff, February 4, 2026) was 85.9 months (range, 76.6-103.2). There were 197 DFS events in the pembrolizumab arm and 264 in the placebo arm. Median DFS was not reached (NR) vs 68.3 months (HR 0.68; 95% CI 0.56-0.82); 7-yr DFS rates were 57.2% vs 44.6%, respectively. There were 86 OS events in the pembrolizumab arm and 118 in the placebo arm. Median OS was NR in both arms (HR 0.70; 95% CI 0.53-0.92); 7-yr OS rates were 82.3% vs 76.6%. Outcomes by protocol-defined risk subgroups and sarcomatoid features are shown in the table. No new serious treatment-related AEs were reported.Table: 3589R0

	Protocol-defined risk subgroup	Sarcomatoid feature									
	Intermediate-high	High	M1 NED	Presence	Absence						
	Pembrolizumab n = 422	Placebo n = 433	Pembrolizumab n = 40	Placebo n = 37	Pembrolizumab n = 29	Placebo n = 28	Pembrolizumab n = 52	Placebo n = 59	Pembrolizumab n = 414	Placebo n = 415	
DFS											
Number of events	157	214	22	29	17	21	23	39	158	209	
Median	NR	76.7	22.4	13.7	55.3	11.5	86.4	33.4	NR	75.3	

	Protocol-defined risk subgroup	Sarcomatoid feature									
	Intermediate-high Pembrolizumab n = 422	High Placebo n = 433	M1 NED Pembrolizumab n = 40	Presence Placebo n = 37	Absence Pembrolizumab n = 29	Placebo n = 28	Pembrolizumab n = 52	Placebo n = 59	Pembrolizumab n = 414	Placebo n = 415	
HR (95% CI)	0.71 (0.58-0.87)	0.54 (0.31-0.94)	0.50 (0.26-0.96)	0.55 (0.33-0.92)	0.71 (0.57-0.87)						
OS											
Number of events	64	95	15	14	6	9	13	15	66	93	
Median	NR	NR	NR	91.1	NR	NR	NR	NR	NR	NR	
HR (95% CI)	0.66 (0.48-0.91)	0.92 (0.44-1.90)	0.54 (0.19-1.53)	0.93 (0.44-1.94)	0.68 (0.50-0.93)						

Conclusions

At the final planned analysis of KEYNOTE-564, DFS and OS benefits with adjuvant pembrolizumab remained consistent with earlier reports from the study for the total and key subgroup populations. Results continue to support adjuvant pembrolizumab as standard treatment for patients with an increased risk of ccRCC recurrence.

Clinical trial identification

NCT03142334.

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