1715P: Interim analysis results from a phase II study of adjuvant penpulimab in very high-risk clear cell renal cell carcinoma

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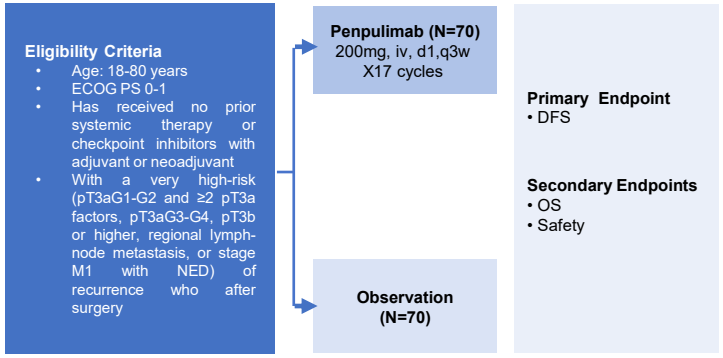
Background

- The Keynote-564 study showed that adjuvant pembrolizumab improved disease-free survival (DFS) in high-risk clear cell renal cell carcinoma (ccRCC) patients. However, subgroup analysis showed that not all patients benefited.
- Hence, we aim to explore the efficacy and safety of penpulimab after nephrectomy in ccRCC with a very high-risk of recurrence (ChiCTR2200062189).

Methods

- In this prospective, standard of care-controlled, phase Ⅱ trial, eligible ccRCC patients were aged 18-80 years with a very high-risk (pT3aG1-G2 and ≥2 pT3a factors, pT3aG3-G4, pT3b or higher, regional lymph-node metastasis, or stage M1 with NED) of recurrence who after surgery, without prior systemic therapy or immunotherapy, and ECOG PS of 0 or 1 (Figure 1).
- Patients received penpulimab 200 mg intravenously on day 1 every 3 weeks until progression, intolerable toxicities, or completion of 17 cycles, or observation after surgery.
- Primary endpoint was DFS. Secondary endpoints included overall survival (OS) and safety.

Figure 1. Study Design



- Data Cut-off date : August 2024

Results

Baseline characteristics

- Between July 2022 and March 2024, 63 patients were enrolled to receive penpulimab (n=31) or observation (n=32). Most patients in the penpulimab group had M1 NED status (19.4%) than the control group (3.1%). The group of individuals who were treated with penpulimab had a higher risk than the control group (P=0.040). Baseline characteristics were shown in Table 1.

Efficacy

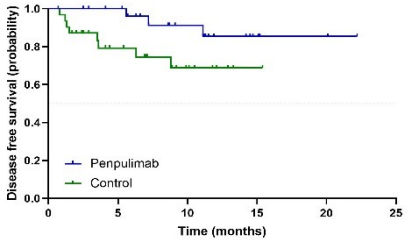
- At data cutoff of August 5, 2024, median follow-up for the penpulimab and control groups were 11.2m (95% CI: 9.426-12.974) and 6.4m (95% CI: 3.192-9.608), respectively. During follow-up, 3 and 8 patients had recurrence or distant metastases respectively. mDFS was not reached in the two groups (HR 0.286, 95% CI 0.075-1.089；P=0.067). The 12-month DFS rate in the penpulimab and control group were 85.5% and 68.9%, respectively. There was a beneficial trend in the penpulimab group (Figure 2).

Table 1: Baseline characteristics

	Penpulimab (N=31)	Control (N=32)
Age, years		
Median (range)	61 (41-75)	60 (42-83)
<65	21 (67.7%)	19 (59.4%)
Sex		
Male	21 (67.7%)	23 (71.9%)
Female	10 (32.3%)	9 (28.1%)
ECOG PS		
0	28 (90.3%)	28 (87.5%)
1	3 (9.7%)	4 (12.5%)
Type of nephrectomy		
Partial	4 (12.9%)	3 (9.4%)
Radical	27 (87.1%)	29 (90.6%)
Primary tumor stage		
T1	2 (6.5%)	2 (6.3%)
T2	0 (0.0%)	0 (0.0%)
T3	25 (80.6%)	28 (87.5%)
T4	4 (12.9%)	2 (6.3%)
Tumor nuclear grade		
1	0 (0%)	0 (0%)
2	5 (16.1%)	6 (18.7%)
3	22 (71.0%)	18 (56.3%)
4	4 (12.9%)	8 (25.0%)
Lumph node stage		
N0	29 (93.5%)	29 (90.6%)
N1	2 (6.5%)	3 (9.4%)
Metastatic stage		
M0	25 (80.6%)	31 (97.8%)
M1 with no evidence of disease	6 (19.4%)	1 (3.2%)
Disease risk category		
M0 intermediate-high	23 (74.2%)	26 (81.3%)
M0 high	2 (6.5%)	5 (15.6%)
M1 with no evidence of disease	6 (19.4%)	1 (3.1%)
Sarcomatoid features		
Present	2 (6.5%)	7 (21.9%)
Absent	25 (80.6%)	25 (78.1%)
Unknown	4 (12.9%)	0 (0%)

Results

Figure 2. Kaplan-Meier curves for DFS



Safety

- As shown in table 2, In the penpulimab group, the TEAE was 100%, and any grade TRAE was 74.19% (23/31), mainly Grade 1-2, without Grade 3 and only 1 case of Grade 4, which was immune-related myositis. Most common TEAEs were proteinuria (38.71%), rash (35.48%), increased blood creatine (22.58%) and increased alanine aminotransferase (19.35%). No treatment-related death was observed.

Table 2. Treatment-emergent adverse events (TEAEs) of any grade (N=31)

TEAEs	Penpulimab N (%, ≥10%)		
	Any Grade	Grade 1-2	Grade 3-4
Proteinuria	12 (38.71)	12 (38.71)	0
Rash	11 (35.48)	11 (35.48)	0
Increased blood creatine	7 (22.58)	7 (22.58)	0
Increased alanine aminotransferase	6 (19.35)	6 (19.35)	0
Fatigue	4 (12.90)	4 (12.90)	0
Increased γ-glutamyltransferase	4 (12.90)	4 (12.90)	0
Increased urea	4 (12.90)	4 (12.90)	0
Increased aspartate aminotransferase	4 (12.90)	4 (12.90)	0
Increased creatine kinase	4 (12.90)	4 (12.90)	0
Cold-like symptoms	4 (12.90)	4 (12.90)	0
Urinary system infection	4 (12.90)	4 (12.90)	0

Conclusions

- Adjuvant penpulimab demonstrated promising antitumor activity and manageable safety profile in ccRCC with a very high-risk of recurrence.
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