KN046 in Patients with ≥2L R/M Thymic Carcinoma: A Prospective, Single-arm, Multi-center, Phase 2 Study

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BACKGROUND

- Thymic carcinoma (TC)is a rare but highly aggressive cancer, with no standard treatment for patients who progress after platinum-containing chemotherapy.
- Mechanism of action of KN046 (Figure 1)：
  - ✓ Blocking CTLA-4 with B7 and PD-L1 with PD-1.
  - ✓ Limited peripheral distribution reduces treatment-associated on-target off-tumor toxicity.
  - ✓ IgG1 Fc domain, CTLA-4 blocking-mediated Treg cells deletion.
- Here we reported the results from KN046-205, a phase II study to evaluate the efficacy and safety of KN046 in the population who progressed after front line chemotherapy.

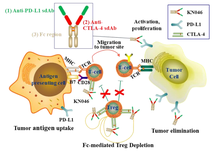

Figure 1 Structure of KN046

METHODS

- Study design is shown in Figure 2.
- Eligible pts received KN046 5 mg/kg Q2W.
- Tumor response was evaluated Q8W per RECIST v1.1.
- PD-L1 expression on immune cells was measured using 22C3 PharmDx assay.
- The cut-off date was Aug 30, 2023.

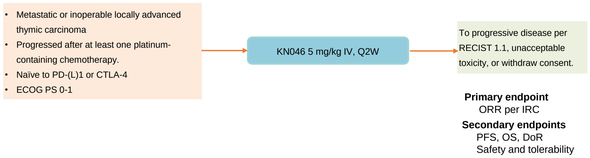

Figure 2 Study Design

RESULTS

- From December 2020 to December 2022, 48 subjects were enrolled, the median age was 58, gender distribution was 25:23, and most patients were stage IV B.
- The median follow-up was 21.5 months (IQR: 16.7, 24.8). The ORR, DoR, and PFS were assessed by investigators. The ORR, PFS, and OS was evaluated based on the evaluable (EAS) population.

Table 1 Demographics & Baseline Characteristics

		N(%)
Number of Patients (n)		48
Age		
	Median	58
	Range	33-70
Sex		
	Male	25 (52%)
	Female	23 (48%)
ECOG PS		
	0	10 (21%)
	1	38 (79%)
Stage		
	IV A	2 (4%)
	IV B	46 (96%)
PD-L1 Status		
	UNK	6 (13%)
	TPS < 1%	25 (52%)
	TPS ≥ 1%	17 (35%)

Table 2 Objective Response Rate in EAS per IRC

	TPS < 1% or UK (N=29)	TPS ≥ 1% (N=16)	Total (N=45)
Best Overall Response			
Complete Response (CR)	0	1 (6.3%)	1
Partial Response (PR)	4 (13.8%)	2 (12.5%)	6 (13.3%)
Stable Disease (SD)	14 (48.3%)	6 (37.5%)	20 (44.4%)
Progressive Disease (PD)	10 (34.5%)	5 (31.3%)	15 (33.3%)
Not Evaluable (NE)	1 (3.4%)	2 (12.5%)	3 (6.7%)
Objective Response Rate (ORR)	13.8%	18.8%	15.6%
95% CI	3.9%, 31.7%	4.1%, 45.7%	6.5%, 29.5%
Disease Control Rate (DCR)	62.1%	56.3%	60.0%
95% CI	42.3%, 79.3%	29.9%, 80.3%	44.3%, 74.3%
Clinical Benefit Rate (CBR)	27.6%	37.5%	31.1%
95% CI	15.2%, 64.6%	12.2%, 73.8%	18.2%, 46.7%
Duration of Response (DoR)	——	——	14.7 months
95% CI	——	——	1.9, NE

- The median PFS was already mature, with 3.9 (95% CI, 1.3 - 11.3) months. Among the TPS ≥1% pts, the median PFS was 5.7 (95%CI, 1.8 - NE) months.
- The median OS is immature. the 12-months and 24-months OS rate was 92.4% (95%CI: 78.3%, 93.5%) and 72.1% (95%CI: 53.8%, 84.4%), respectively, which was numerically higher than historical data reported in the literature.

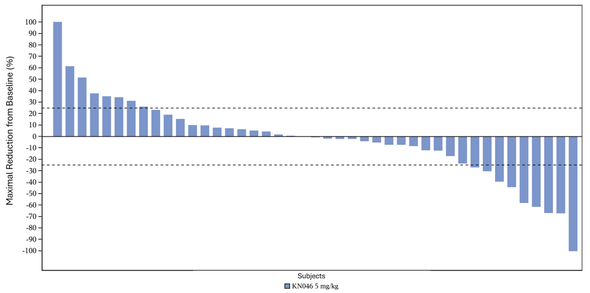

Figure 3 Waterfall Plot of EAS per IRC

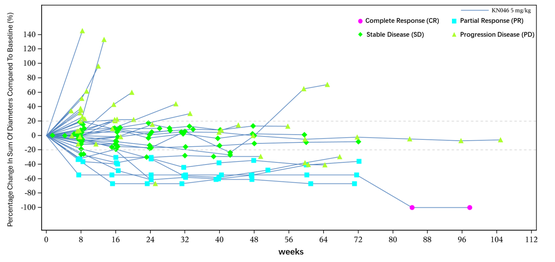

Figure 5 Spider Plot of EAS per IRC

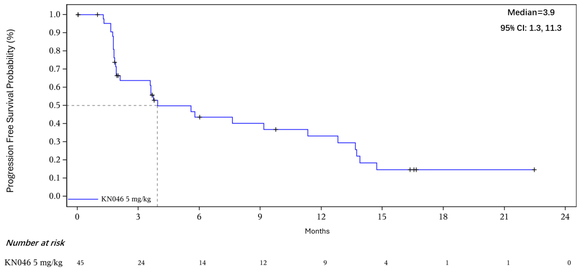

Figure 5 Kaplan - Meier Curve for Progression Free Survival per IRC

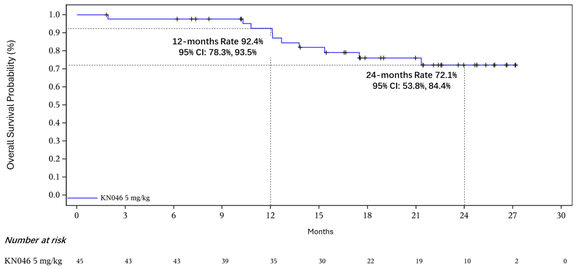

Figure 6 Kaplan - Meier Curve for Overall Survival

- Patients tolerated well to combination therapy. The incidence of grade ≥ 3 TRAE was 39.6%, with no TEAE leading to death.

Table 3 Safety Summary (N=27)

	KN046 5 mg/kg (N=48) n (%)	
	Grade ≥ 3	Any Grade
TEAE	21 (43.8%)	47 (97.9%)
TEAE associated with KN046	19 (39.6%)	46 (95.8%)
Infusion-related AE	11 (68.8%)	7 (63.6%)
Immune-related AE	10 (20.8%)	32 (66.7%)
Serious Adverse Event（SAE）	11 (22.9%)	19 (39.6%)
SAE associated with KN046	11 (22.9%)	16 (33.3%)
TEAE leading to discontinuation	5 (10.4%)	8 (16.7%)
TRAE leading to discontinuation	5 (10.4%)	7 (14.6%)
TEAE leading to death	0	0

Table 4 The Most Commonly Reported (≥10%) Adverse Events

Preferred Term (≥10%)	KN046 5 mg/kg (N=48) n (%)	
	Grade ≥3	All grades
Subjects with any study drug related TEAE	19 (39.6%)	46 (95.8%)
Rash	2 (4.2%)	18 (37.5%)
Aspartate aminotransferase increased	1 (2.1%)	15 (31.3%)
Alanine aminotransferase increased	1 (2.1%)	13 (27.1%)
Anemia	0	11 (22.9%)
Fatigue	0	11 (22.9%)
Fever	0	8 (16.7%)
Hypothyroidism	0	8 (16.7%)
Infusion-related Reaction	2 (4.2%)	8 (16.7%)
Amylase increased	0	6 (12.5%)
Lymphocyte count decreased	2 (2.1%)	6 (12.5%)
C-reactive protein increased	2 (2.1%)	5 (10.4%)
White blood cell decreased	0	5 (10.4%)
Hypertriglyceridemia	0	5 (10.4%)
Hyperthyroidism	0	5 (10.4%)

CONCLUSIONS

- KN046 demonstrated promising antitumor activity and acceptable toxicity in thymic carcinoma patients who have received at least one line of chemotherapy.
- By the cut-off date, the mOS is not mature and there is still more than half of pts alive, demonstrating an encouraging signal in survival benefit..

CONFLICT OF INTEREST

The authors has no conflicts of interest.

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