The preliminary efficacy and safety data of KN046（bispecific anti-PD-L1/CTLA4）in patients failed on prior immune checkpoint inhibitors therapy

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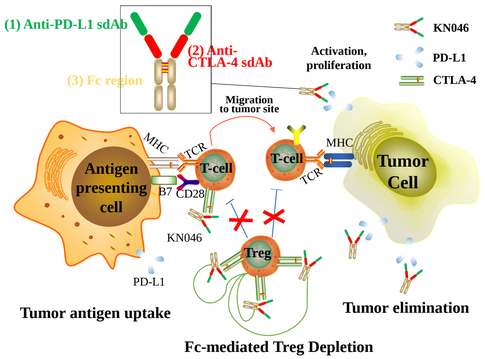
Background:

KN046 is a novel bispecific antibody that blocks both PD-L1 and CTLA-4 by interaction with PD1 and CD80/CD86, respectively. KN046-CHN-001 is an open-label, dose escalation and expansion phase Ia/Ib clinical trial in China. Here we reported safety, tolerability and preliminary efficacy in patients failed on prior immune checkpoint inhibiters (ICIs) treatment.



Mechanism of action of KN046

- Blocking CTLA-4 with B7 restores T effector cell function in lymph nodes and deletes Treg (inhibitory T cell) in tumor microenvironment
- Blocking PD-L1 with PD-1 restore T cell effector function at tumor site
- Binds PD-L1 more strongly than CTLA-4, which enables KN046 targeting tumor microenvironment with PD-L1 high expression
- Limited peripheral distribution reduces treatment-associated on-target off-tumor toxicity
- With wide type of IgG1 Fc domain, CTLA-4 blocking-mediated Treg cells deletion was retained via Fc effector function

Methods:

Patients were enrolled and received intravenous KN046 treatment across four dose levels including 3.0 mg/kg and 5.0 mg/kg Q2W; and 5.0 mg/kg (n=4), 300.0 mg flat dose (n=2) Q3W. Treatment-emergent adverse events (TEAEs) and Immune related AEs (irAEs) were assessed by CTCAE v5.0. Efficacy evaluation was performed by RECIST 1.1 every 6 weeks.

Trial design

- Dose escalation (mTPI-2)
- Dose expansion

Eligibility

- Men/Women ≥ 18 y/o
- ECOG 0 or 1
- Advanced/metastatic solid tumors
- Refractory/intolerant to standard of care
- Treatment by previous immune checkpoint inhibitors (ICIs) allowed

	1.0 mg/kg Q2W	3.0 mg/kg Q2W	5.0 mg/kg Q2W	5.0 mg/kg Q3W	300 mg Q3W	Prior ICIs Total, n
	n = 1	n = 30	n = 44	n = 6	n = 6	
Dose escalation, N	3	3	3	3		
Prior ICIs, n	*0*	*1*	*2*	*1*		*4*
Dose expansion, N	27	41	3	3		
Prior ICIs, n	*3*	*19*	*2*	*1*		*25*
						29

Note: Yellow Color represents patients previously treated by immune checkpoint inhibitors from each dose cohort and hereby reported in this presentation

Results:

- As of Jan 22, 2020, Twenty-nine patients have progressed on prior ICIs therapy. Among 29 patients, 19 were nasopharyngeal cancer (NPC) and 9 were non-small cell lung cancer (NSCLC). The median duration of the exposure of KN046 was 12 weeks (range 2 to 40).

KN046
showed a favorable safety profile and promising clinical benefit in advanced solid tumor patients

- Patients enrolled are those who failed on prior immune checkpoint inhibitors therapy
- Grade ≥3 KN046 related TRAEs were experienced in 2 out of 29 patients (6.9%)
- Median progression free survival was 2.69 months （95%CI 1.3, 5.5）
- Median overall survival was not reached
- Objective responses rate was 12.0%

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Clinical trial information: NCT03733951

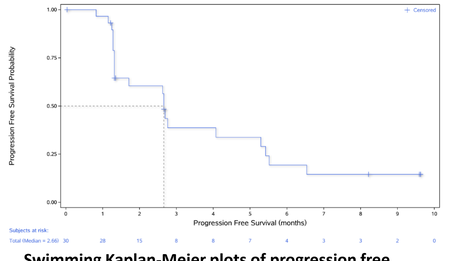
Patient demographics, disease characteristics

Parameters	Total (N = 29)
Gender，n (%)	
Male	22 (75.9%)
Female	7 (24.1%)
Age（years）	
Mean（SD）	49.3 (12.5)
Median (Min, Max)	50.0 (32, 74)
ECOG, n (%)	
0	17 (58.6%)
1	12 (41.4%)
Tumor Type	
NSCLC	9 (31.0%)
NPC	19 (65.5%)
Melanoma	1 (3.4%)
Lines of Chemotherapy	
> Line 2	21 (72.4%)
Types of ICIs	
Anti-PD-1	25 (86.2%)
Anti-OX40	3 (10.3%)
Anti-CD137	1 (3.4)

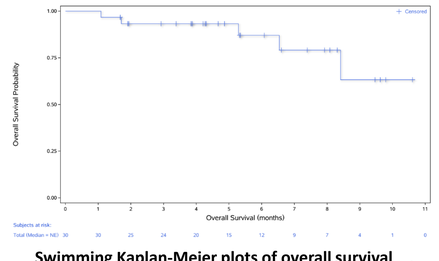
KN046 related TEAE (> 5%, or Grade ≥ 3)

Preferred Term (CTCAE v5.0)	Grade ≥ 3 (N = 29)	Total (N = 29)
Subjects with at least 1 KN046 related TEAE	2 (6.9%)	26 (89.7%)
Pruritus	0	8 (27.6%)
Rash	0	8 (27.6%)
Asthenia	0	6 (20.7%)
Fatigue	0	6 (20.7%)
Pyrexia	0	5 (17.2%)
Infusion related reaction	1 (3.4%)	4 (13.8%)
Alanine aminotransferase increased	0	3 (10.3%)
White blood cell count increased	0	3 (10.3%)
Aspartate aminotransferase increased	0	2 (6.9%)
Dizziness	0	2 (6.9%)
Neutrophil count increased	0	2 (6.9%)
Vomiting	0	2 (6.9%)
Anaemia	1 (3.4%)	1 (3.4%)

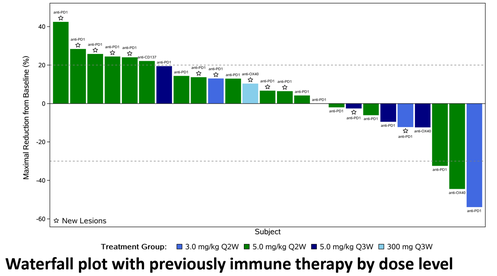
- Twenty-six (89.7%) patients experienced TRAEs and 6.9% were of grade ≥ 3. No TRAE leading to discontinuation nor death. Objective responses were observed in 3 patients (12.0%, 25 evaluable) , disease control rate was 52.0% (10 stable disease). Median progression free survival was 2.69 (95%CI 1.3, 5.5) months. Median overall survival was not reached.



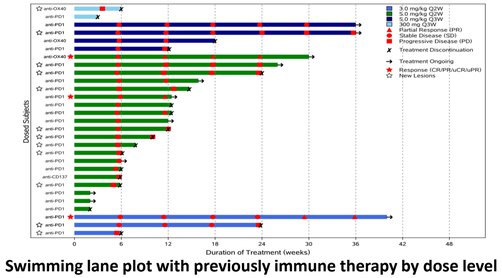
Swimming Kaplan-Meier plots of progression free survival with preciously immune therapy (safety analysis set)



Swimming Kaplan-Meier plots of overall survival with preciously immune therapy (safety analysis set)



Waterfall plot with previously immune therapy by dose level



Swimming lane plot with previously immune therapy by dose level