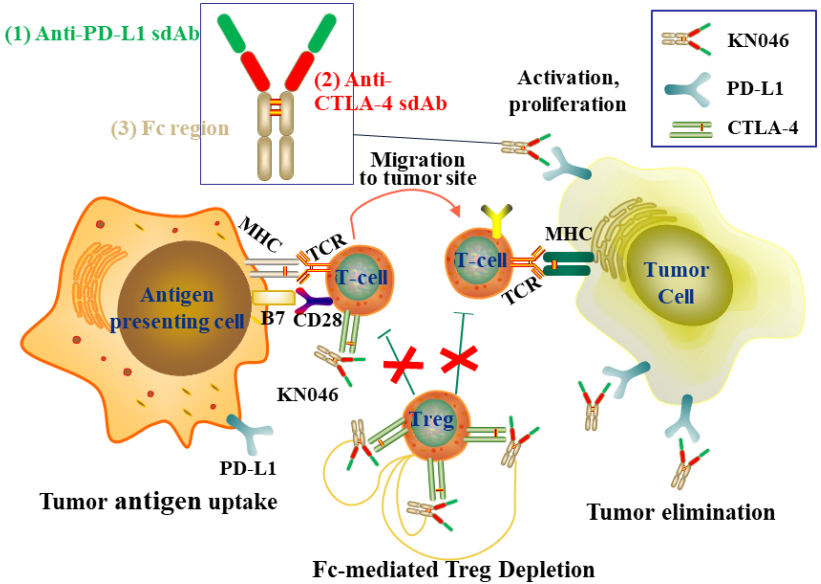
Preliminary safety, efficacy results of KN046 (bispecific anti-PD-L1/CTLA4) in subjects with rare thoracic tumors

Gary Richardson
Cabrini
Australia

DISCLOSURES

Commercial Interest	Relationship(s)

Background and Study Design



Mechanism of action of KN046

- ☑ 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.

Trial KN046-AUS-001

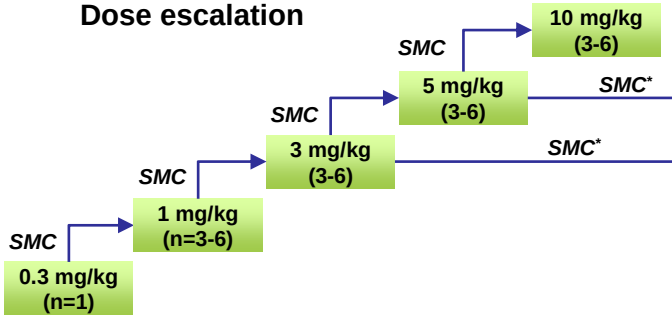
Eligibility

- Men/Women ≥ 18 y/o
- ECOG 0 or 1
- Advanced/metastatic solid tumors
- Refractory/intolerant to standard of care
- Starting at DL3, must have at least 1 measurable lesion

Trial design

- Dose escalation
- Dose expansion

Dose escalation



Note: * Cohort expansion will be proposed to enroll approximately 30 subjects based on available safety, pharmacokinetics and preliminary efficacy data and the agreement between sponsor and SMC.

Demographics

Patient characteristics

Parameters	Total (N =54)
Gender, n (%)	
Male	20 (37.0%)
Female	34 (63.0%)
Age (years)	
Mean (SD)	58.7 (14.1)
Median (Min, Max)	59.0 (26, 80)
ECOG, n (%)	
0	29 (53.7%)
1	25 (46.3%)
Primary Tumor Type	
Breast	8 (14.8%)
Pancreas	7 (13.0%)
Ovary	6 (11.1%)
Thymus	4 (7.4%)
Pleural	1 (1.9%)
Others	28 (52%)
Primary prior Therapies	
Surgery	48 (88.9%)
Chemotherapy	45 (83.3%)
Systemic Therapies	49 (90.7%)
Immunotherapy	6 (11.1%)

Safety

KN046 related TEAE (Grade 3/4)

Preferred Term	n (%) (N = 54)
Subjects Who Had a KN046 Related CTCAE Grade 3/4 TEAE	18 (33.3%)
Immune-mediated enterocolitis	2 (3.7%)
Autoimmune myositis	2 (3.7%)
Hepatic function abnormal	2 (3.7%)
Abdominal pain lower, Chronic gastritis, Colitis, Gastrooesophageal reflux disease, Arthralgia, Autoimmune arthritis, Polyarthritis, Autoimmune hepatitis, Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood lactate dehydrogenase increased, Decubitus ulcer, Pruritus, Rash erythematous, Adrenal insufficiency, Fatigue, Infusion related reaction, Insomnia, Renal impairment and Pneumonitis	1 (1.9%)

irAEs (Grade 3/4)

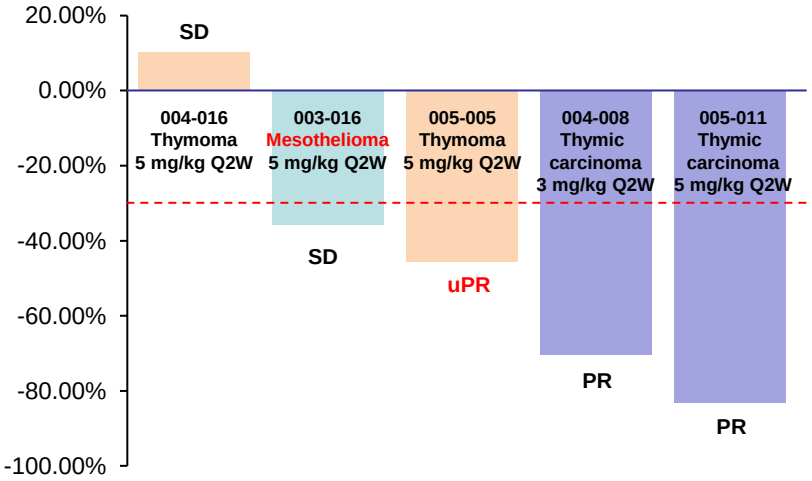
Preferred Term	n (%) (N = 54)
Subjects Who Had a CTCAE Grade 3/4 irAE	13 (24.1%)
Autoimmune myositis	2 (3.7%)
Hepatic function abnormal	2 (3.7%)
Arthralgia, Autoimmune arthritis, Polyarthritis, Chronic gastritis, Colitis, Gastrooesophageal reflux disease, Immune-mediated enterocolitis, Autoimmune hepatitis, Alanine aminotransferase increased, Blood lactate dehydrogenase increased, Adrenal insufficiency, Fatigue, Renal impairment and Rash erythematous	1 (1.9%)

KN046 is safe and highly effective in rare thoracic tumors

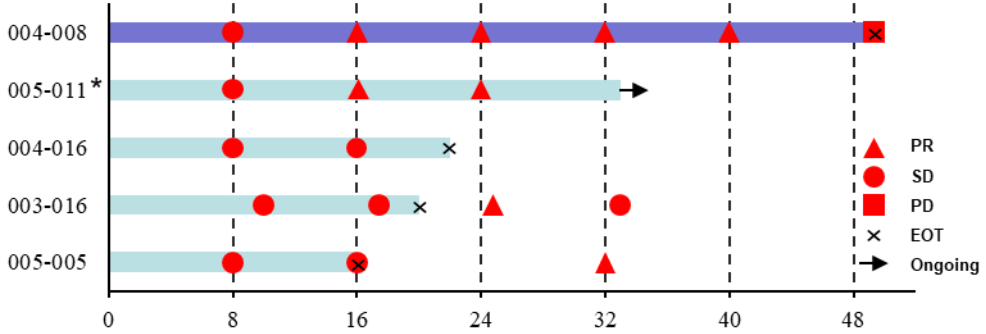
- 5 subjects including 2 thymic carcinoma (stage IV), 2 thymoma (stage IV) and 1 pleural mesothelioma (sarcomatoid variant, stage ⅢB).
- Median duration of treatment was 22.7 (range: 16-48) weeks.
- Most of TRAEs were Grade 1 or 2. Grade 3 TRAEs occurred in 1 subject, were autoimmune hepatitis, alanine aminotransferase increased and autoimmune myositis. No Grade 4 or above TRAE reported.
- 14 irAEs occurred in 3 subjects, three Grade 3 irAE occurred in 1 subject, were autoimmune hepatitis, alanine aminotransferase increased and autoimmune myositis. No Grade 4 or above irAE reported.

KN046 is safe and highly effective in rare thoracic tumors

Waterfall plot

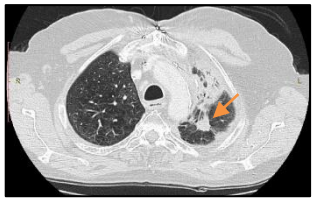


Swimming plot

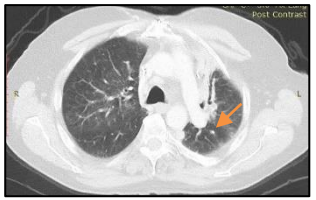


Response observed in 3 subjects thymic epithelial tumors (005-005, 004-008 and 005-011), 2 confirmed PRs and 1 unconfirmed PR
ORR: 75% (3/4)
DCR: 100% (4/4)

Baseline



24 weeks



Thymic carcinoma, target lesion almost disappear at 24 weeks

Summary

Single agent KN046 has an acceptable safety profile and in line with other immune checkpoint inhibitors in patients with rare thoracic cancers, and had demonstrated preliminary but promising efficacy.

- ☑ Grade 3 TRAE observed in 1 of 5 subjects, no Grade 4 or above TRAE reported.
- ☑ Grade 3 irAE observed in 1 of 5 subjects, no Grade 4 or above irAE reported.
- ☑ In thymic epithelial tumor, objective response observed in 3 subjects, 2 PR, 1 uPR and 1 SD. Disease control rate is 100%.
- ☑ Follow on study in thymic carcinoma is planned.