AK104 (PD-1/CTLA-4 Bispecific) Combined with Chemotherapy as First-line Therapy for Advanced Gastric (G) or Gastroesophageal Junction (GEJ) Cancer: Updated Results from a Phase Ib/II Study

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PRESENTED AT: Gastrointestinal Cancers Symposium

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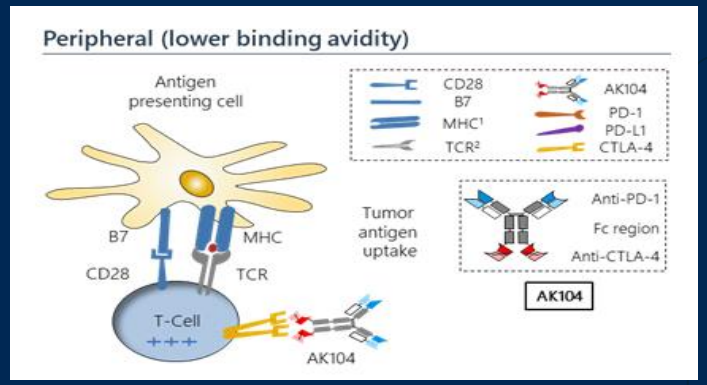
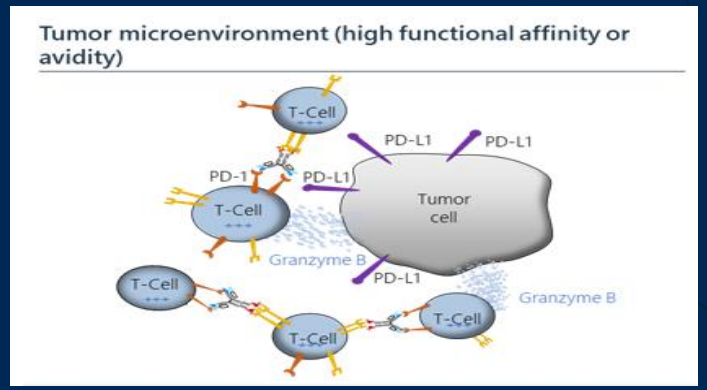
#GI21

Study Profiles

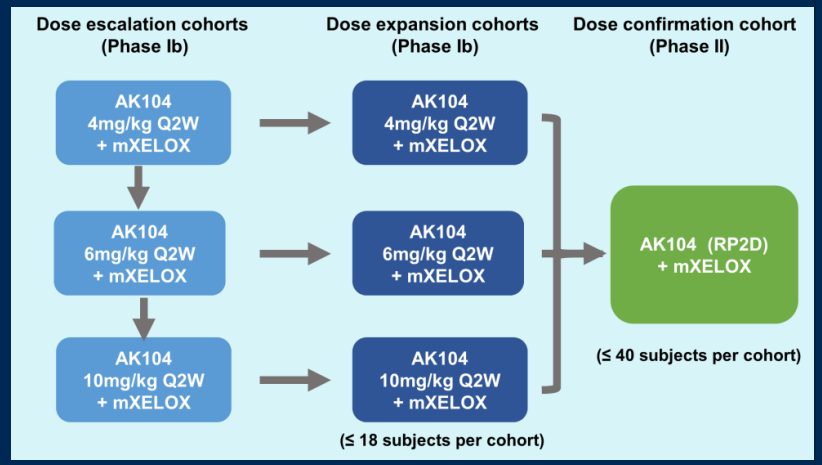
- AK104, a PD-1/CTLA-4 bispecific antibody, is designed as a novel tetrameric form. It could preferentially binds to tumor-infiltrating lymphocytes (TILs) co-expressing PD-1 and CTLA-4 with higher avidity in the tumor micro-environment than peripheral sites.
- This Phase Ib/II study evaluated the safety and efficacy of AK104 and mXELOX in the first-line setting of G/GEJ cancer cohorts (NCT03852251).

AK104





Study Design



mXELOX:

- Oxaliplatin 85 mg/m^2 day1 every 2 weeks up to 12 cycles
- Capecitabine 1000 mg/m^2 PO twice daily day 1-10 every 2 weeks up to 12 cycles, followed by maintenance therapy

Baseline Characteristics and AK104 Exposure

	Total (N=54)
Age, median (range)	62.8 (29, 75)
Gender, n (%)	
Male	37 (68.5)
Female	17 (31.5)
ECOG PS, n (%)	
0	22 (40.7)
1	32 (59.3)
Diagnosis, n (%)	
Gastric Adenocarcinoma	44 (81.5)
GEJ Adenocarcinoma	10 (18.5)
Surgery History, n (%)	11 (20.4)
Metastatic Sites, n (%)	
Liver	23 (42.6)
Lung	4 (7.4)
Number of AK104 Dose , median (range)	5 (1,24)

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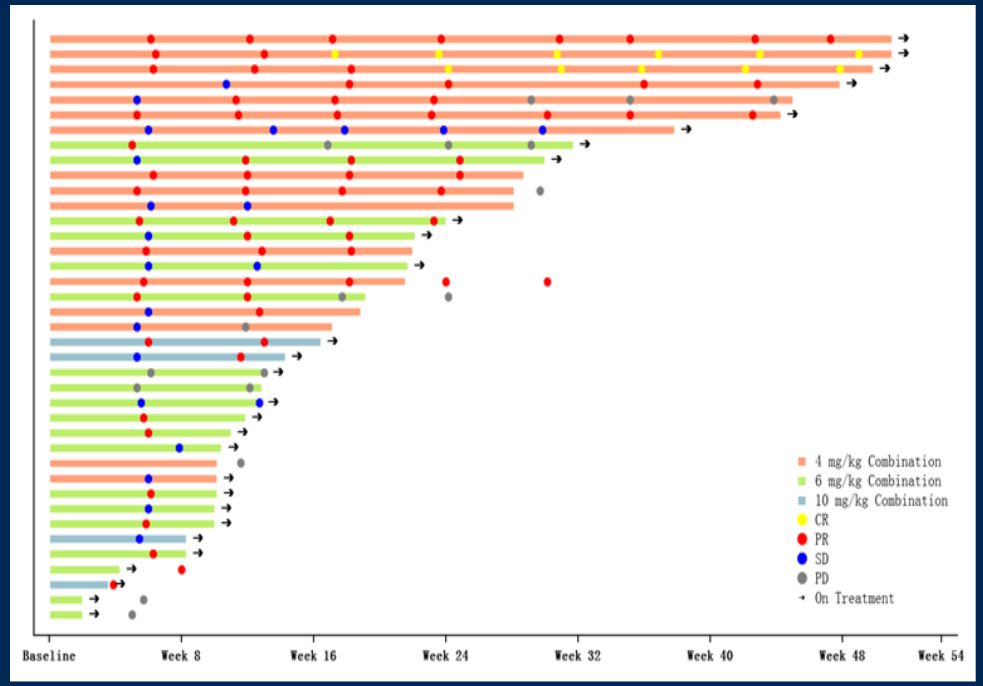
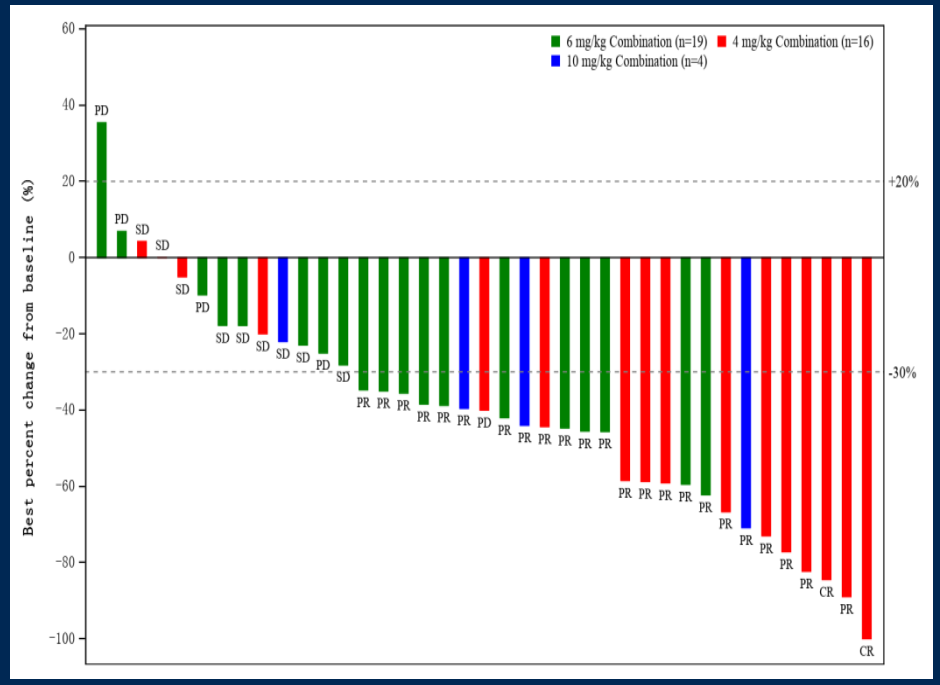
Clinical benefits

- As of 20 Nov, 2020, 54 patients (pts) have received AK104 at doses of 4 mg/kg (n = 18) , 6 mg/kg (n = 32) and 10 mg/kg (n = 4) + mXELOX.
- Of 39 pts evaluable for antitumor activity, ORR was 64.1% (95% CI 47.2, 78.8) including 2 CRs and 23 PRs; DCR was 87.2% (95% CI 72.6, 95.7).
  - At a median follow-up of 8.0 mons for the 4mg/kg cohort, median DoR was not rearched (range 2.89+, 9.49+) , 6-mons PFS rate was 76.5% (95%CI 48.8, 90.4).
  - At dose level of 10mg/kg, 3 out of 4 pts achieved PRs, 1 pt had target lesion reduction of 22%.
- Response was seen regardless of PD-L1 status. PD-L1 negative was defined by combined positive score (CPS)＜1 with PD-L1 IHC Dako 22C3 pharmDx staining.
  - Of 19 pts with PD-L1 status evaluable for efficacy, ORR for pts with PD-L1 negative was 57.1% (8/14).

Time on treatment and Tumor Response by Weeks (N=39)



Maximum Percentage Change in Target Lesion Size (N=39)



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Safety Overview

AEs Summary

AEs	Total (N=54)
	Any Grade
Any treatment-related AE (TRAE)	45 (83.3)
≥Grade 3 TRAE	21 (38.9)
Any immune-related AE (irAE)	17 (31.5)
≥Grade 3 irAE	4 (7.4)
Any treatment-related SAE	13 (24.1)
≥Grade 3 treatment-related SAE	8 (14.8)
TRAE leading to discontinuation	1 (1.9)

- Treatment related indicates either AK104 or mXELOX related
- No TRAE leading to death; No DLT.
- ≥ Grade 3 irAE included immune-mediated hepatitis (n=1), hyponatraemia (n=1), amylase increased (n=1), colitis (n=1).
- TRAE leading to discontinuation was infusion related reaction.

TRAEs with Incidence ≥ 10%

TRAEs, by PT, n(%)	Total (N=54)	
	Any Grade	Grade 3-4
Patients with at least one TRAE	45 (83.3)	21 (38.9)
Neutrophil count decreased	20 (37.0)	7 (13.0)
White blood cell count decreased	18 (33.3)	4 (7.4)
Platelet count decreased	16 (29.6)	2 (3.7)
Nausea	12 (22.2)	1 (1.9)
Anaemia	11 (20.4)	2 (3.7)
Vomiting	11 (20.4)	1 (1.9)
Alanine aminotransferase increased	7 (13.0)	1 (1.9)
Pyrexia	7 (13.0)	1 (1.9)
Asthenia	6 (11.1)	1 (1.9)
Aspartate aminotransferase increased	6 (11.1)	1 (1.9)
Rash	6 (11.1)	0 (0.0)
Infusion related reaction	6 (11.1)	0 (0.0)

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Conclusions

- AK104 up to 10 mg/kg Q2W combined with mXELOX in first-line GC or GEJ patients is acceptable safe and well-tolerated.
- AK104 showed encouraging anti-tumor activities across a range of different dose levels (4, 6, 10mg/kg Q2W combination regimens), regardless of PD-L1 status.
- AK104 demonstrated the durable response and improved progression-free survival.
- Enrollment is currently ongoing for 10 mg/kg cohort. Phase III study for the first-line GC or GEJ treatment is planning.

Acknowledgements
- With thanks to patients and caregivers.
- With thanks to invesitgators, coordinators and research staff.

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