Abstract #4031: A phase Ib/II, multicenter, open-label study of AK104, a PD-1/CTLA-4 bispecific antibody, combined with chemotherapy (chemo) as first-line therapy for advanced gastric (G) or gastroesophageal junction (GEJ) cancer: 2-year update data

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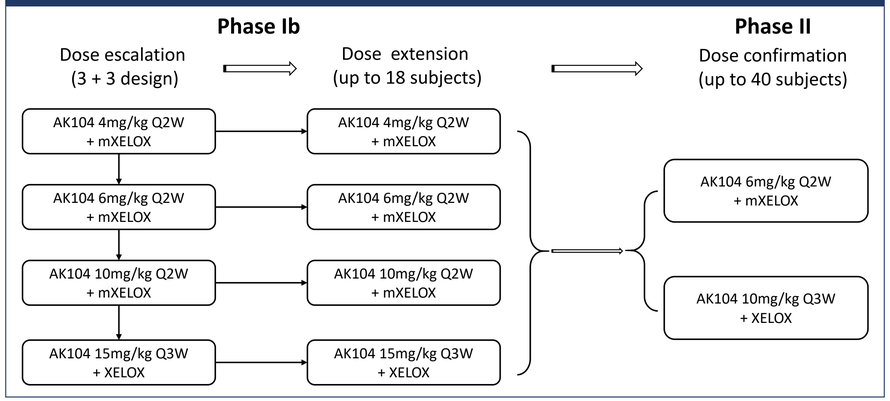
Background:

- Gastric cancer ranks fifth of the most common cancers and occupies the fourth leading cause of cancer mortality worldwide[1].
- Nivolumab combined with fluoropyrimidine platinum-based chemotherapy prolonged the survival in patients with unresectable advanced or metastatic gastric/gastroesophageal (G/GEJ) junction adenocarcinoma, whereas the improvement in overall survival (OS) was still limited and only patients with PD-L1 combined positive score (CPS)≥5 clinically were benefited[2].
- Combination of CTLA-4 and PD-1 blockade has consistently demonstrated the increase of the response rates and survival rates of the patients (pts) compared to monotherapy in various tumors[3].
- This phase Ib/II (AK104-201) study evaluated the efficacy and safety of AK104, a PD-1/CTLA-4 bispecific antibody, combined with XELOX or modified XELOX (mXELOX) in the first-line setting of G/GEJ cancer treatment.

Methods:

- Patients with unresectable advanced G/GEJ adenocarcinoma and no prior systemic therapy, regardless of PD-L1 status, were enrolled, excluding known HER2-positive pts.
- Enrolled patients received AK104 (4 mg/kg, 6 mg/kg or 10 mg/kg Q2W, 10 mg/kg or 15mg/kg Q3W) + chemo (mXELOX Q2W or XELOX Q3W).
- The primary endpoint was safety and the objective response rate (ORR) based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1).

Figure 1. Study design



Results:

- 98 pts were enrolled with only 4 pts in 10 mg/kg Q3W, the safety and efficacy of the regimen of 10mg/kg Q3W will be reported in the phase III study and not be reported here.
- Data cut-off date was October 31st, 2022, with a median follow-up of 24.0 months.
- 88 patients had at least one post-baseline tumor evaluation. The ORR was 68.2% (60/88), disease control rate (DCR) was 92.0% (81/88).
- The median PFS was 9.20 months (95%CI, 6.67 to 10.48). The median OS was 17.41 months (95%CI, 12.35 to 29.77). In pts with PD-L1 CPS≥5 and CPS＜5, the median OS was 20.24 months and 17.28 months, respectively (Table 2).
- Treatment-related adverse events (TRAEs) occurred in 97.9% of pts. The most frequent were platelet count decreased (62.8%), white blood cell count decreased (61.7%), neutrophil count decreased (59.6%), anemia (51.1%), aspartate aminotransferase increased (33.0%), nausea (30.9%), and vomiting (30.9%).

Conclusions: AK104 combined with mXELOX/XELOX showed promising activity and manageable safety in previously untreated pts with advanced G/GEJ adenocarcinoma.

A phase III study of AK104 combined with chemo as first-line therapy for G/GEJ adenocarcinoma is underway (NCT05008783).

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Table 1. Baseline Characteristics

	4mg/kg Q2W N=18	6mg/kg Q2W N=40	10mg/kg Q2W N=18	15mg/kg Q3W N=18	Total N=94
Median age (range), years	65.9 (29, 75)	62.8 (41, 74)	59.9 (30, 73)	62.5 (29, 70)	62.7 (29, 75)
Male, n(%)	13 (72.2)	28 (70.0)	15 (83.3)	10 (55.6)	66 (70.2)
ECOG PS 1, n(%)	12 (66.7)	26 (65.0)	10 (55.6)	11 (61.1)	59 (62.8)
GEJ Adenocarcinoma, n(%)	4 (22.2)	5 (12.5)	3 (16.7)	0 (0.0)	12 (12.8)
Gastric Adenocarcinoma, n(%)	14 (77.8)	35 (87.5)	15 (83.3)	18 (100.0)	82 (87.2)
Metastatic disease, n(%)	15 (83.3)	34 (85.0)	18 (100.0)	17 (94.4)	84 (89.4)
Previous surgery	2 (11.1)	8 (20.0)	3 (16.7)	4 (22.2)	17 (18.1)
CPS≥5 (2 missing)	4 (22.2)	7 (17.9)	1 (5.9)	2 (11.1)	14 (15.2)
Median duration of Follow-up (range),months	32.1 (0.5, 33.3)	22.3 (2.7, 30.6)	20.3 (5.5, 26.1)	16.7 (0.8, 20.3)	24.0 (0.5, 33.3)

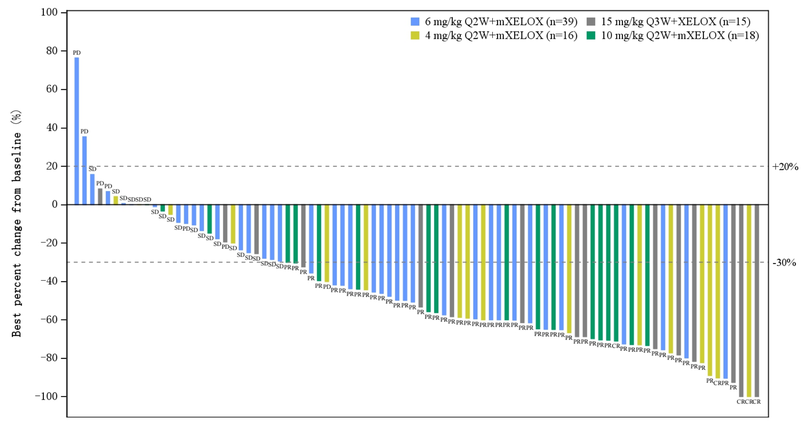
Table 2. OS and PFS based on RECIST 1.1 by CPS (22C3)

	CPS ≥ 1 N = 42	CPS < 1 N = 50	CPS ≥ 5 N = 14	CPS < 5 N = 78	Total N=94
Median PFS (months), (95% CI)	9.20 (5.72, 13.90)	8.18 (5.55, 11.27)	NR (3.65, NE)	7.23 (5.88, 10.48)	9.20 (6.67, 10.48)
6-month PFS Rate (%), (95% CI)	60.4 (43.0, 74.0)	64.5 (48.0, 76.9)	65.0 (31.0, 85.4)	61.9 (49.2, 72.3)	63.0 (51.4, 72.5)
Median OS (months), (95% CI)	17.48 (11.01, 20.40)	17.64 (11.63, NE)	20.24 (4.67, NE)	17.28 (11.86, NE)	17.41 (12.35, 29.77)
12-month OS Rate (%), (95% CI)	58.4 (41.8, 71.8)	64.6 (48.9, 76.6)	64.3 (34.3, 83.3)	61.1 (48.8, 71.3)	61.4 (50.4, 70.7)

Table 3. Safety

	4mg/kg Q2W N=18	6mg/kg Q2W N=40	10mg/kg Q2W N=18	15mg/kg Q3W N=18	Total N=94
TRAEs	18 (100.0)	38 (95.0)	18 (100.0)	18 (100.0)	92 (97.9)
≥Grade3 TRAEs	14 (77.8)	25 (62.5)	13 (72.2)	14 (77.8)	66 (70.2)
TRSAEs	7 (38.9)	15 (37.5)	10 (55.6)	12 (66.7)	44 (46.8)
TRAEs leading to interruption	18 (100.0)	31 (77.5)	15 (83.3)	16 (88.9)	80 (85.1)
TRAEs leading to discontinuation	7 (38.9)	8 (20.0)	4 (22.2)	6 (33.3)	25 (26.6)
AK104-related TRAEs leading to Death	1 (5.6)	1 (2.5)	0 (0.0)	1 (5.6)	3 (3.2)
Infusion-related AEs	8 (44.4)	9 (22.5)	8 (44.4)	5 (27.8)	30 (31.9)
≥Grade 3 Infusion-related AEs	1 (5.6)	1 (2.5)	1 (5.6)	0 (0.0)	3 (3.2)

Figure 2. Tumor Respnse -Waterfall Plot



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