A Phase II, Multicenter, Open-label Study (COMPASSION-26) of Cadonilimab, a PD-1/CTLA-4 Bispecific Antibody, Combined with Chemotherapy as First-line Therapy for Advanced Pancreatic Ductal Adenocarcinoma (PDAC)

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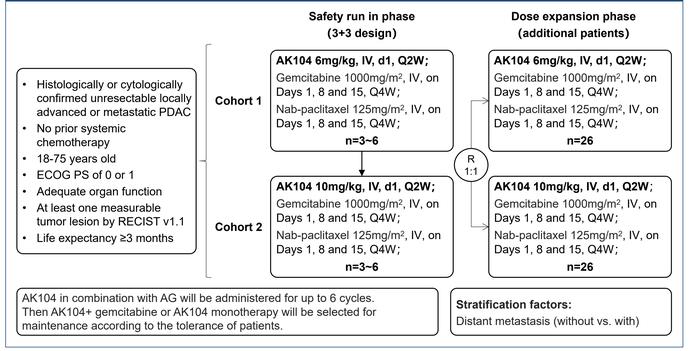
Abstract #CT145

Background/Methods:

- Pancreatic ductal adenocarcinoma (PDAC) is a highly lethal malignancy, with approximately 80% of patients presenting with unresectable locally advanced or metastatic disease at diagnosis[1]. Prognosis for advanced PDAC remains poor, with limited treatment options.
- Cadonilimab (AK104), a PD-1/CTLA-4 bispecific antibody, has shown convincing efficacy with favorable safety profile in Phase 3 trials in gastric cancer and cervical cancer[2-3].
- COMPASSION-26 (NCT05859750) was an open-label, randomized, multicenter Phase 2 study that evaluated the efficacy and safety of cadonilimab plus chemotherapy as the first-line treatment in patients with advanced PDAC.
- Eligible patients were 18 to 75 years of age with ECOG PS 0-1, had unresectable advanced or metastatic PDAC without prior systemic therapy, and had at least one measurable or evaluable lesion per the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.
- Patients received cadonilimab (6 mg/kg or 10 mg/kg, Q2W) + AG (gemcitabine combined with nab-paclitaxel, Q4W). The primary endpoints were safety and objective response rate (ORR). Pharmacokinetics, Progression-free survival (PFS) and overall survival (OS) were all secondary endpoints.

Figure 1. Study design



Key Results:

- As of 20 Oct 2025, 59 patients were enrolled (median age 63.1 years, 61.0% male, 74.6% ECOG PS 1, 59.3% with distant metastasis). The median follow-up time was 24.7 months (range: 3.0+, 27.4).
- 56 patients (95%) had at least one post-baseline tumor evaluation. The ORR and disease control rate (DCR) were 33.9% (19/56) and 96.4% (54/56), respectively, with similar results observed between patients with locally advanced and metastatic disease. Longer DoR and survival was observed in the patients with locally advanced diseases. The median DoR was 7.46 months (95%CI: 4.07, NE) vs 4.80 months (95%CI: 1.87, 11.01).
- The median PFS was 11.1 months (95%CI: 8.7, 15.9) vs 7.2 months (95%CI: 5.5, 7.7). The median OS was 23.4 months (95%CI: 14.9, NE) vs 10.5 months (95%CI: 8.5, 12.8).
- Treatment-related adverse events (TRAEs) occurred in 100.0% of patients, and the most frequent were neutrophil count decreased (96.6%), anemia (89.8%), white blood cell count decreased (84.7%), platelet count decreased (76.3%), rash (52.5%), alanine aminotransferase increased (49.2%), aspartate aminotransferase increased (47.5%), alopecia (45.8%), lymphocyte count decreased (35.6%), pyrexia (35.6%), asthenia (32.2%), and pruritus (32.2%). No new safety signals were identified.

Table 1. Baseline Characteristics

	AK104 6mg/kg (N=31)	AK104 10mg/kg (N=28)	Locally advanced (N = 24)	Metastatic (N = 35)	Total (N=59)
Age, median (range)	59.0 (44, 75)	66.6 (40, 75)	59.4 (40, 71)	66.8 (49, 75)	63.1 (40, 75)
<65, n(%)	22 (71.0)	12 (42.9)	18 (75.0)	16 (45.7)	34 (57.6)
≥65, n(%)	9 (29.0)	16 (57.1)	6 (25.0)	19 (54.3)	25 (42.4)
Sex, n(%)					
Male	21 (67.7)	15 (53.6)	12 (50.0)	24 (68.6)	36 (61.0)
Female	10 (32.3)	13 (46.4)	12 (50.0)	11 (31.4)	23 (39.0)
Baseline ECOG PS, n(%)					
0	7 (22.6)	8 (28.6)	8 (33.3)	7 (20.0)	15 (25.4)
1	24 (77.4)	20 (71.4)	16 (66.7)	28 (80.0)	44 (74.6)
Pancreatic tumor location, n (%)					
Head	12 (38.7)	15 (53.6)	13 (54.2)	14 (40.0)	27 (45.8)
Body	14 (45.2)	4 (14.3)	10 (41.7)	8 (22.9)	18 (30.5)
Tail	8 (25.8)	10 (35.7)	3 (12.5)	15 (42.9)	18 (30.5)
Recurrent Disease, n(%)	0	3 (10.7)	0	3 (8.6)	3 (5.1)
Metastatic Disease, n(%)	18 (58.1)	17 (60.7)	/	/	35 (59.3)
Site of metastases, n(%)					
Liver	13 (41.9)	12 (42.9)	/	25 (71.4)	25 (42.4)
Lung	3 (9.7)	4 (14.3)	/	7 (20.0)	7 (11.9)

Table 2. Summary of Efficacy Dose and Disease Status

	AK104 6mg/kg (N=31)	AK104 10mg/kg (N=28)	Locally advanced (N = 24)	Metastatic (N = 35)	Total (N=59)
Duration of Follow-up, months	24.8	24.0	24.7	24.1	24.7
PFS events, n(%)	18 (58.1)	17 (60.7)	11 (45.8)	24 (68.6)	35 (59.3)
Median PFS, months (95% CI)	8.5 (6.3, 15.9)	7.5 (5.6, 11.1)	11.1 (8.7, 15.9)	7.2 (5.5, 7.7)	8.5 (7.2, 10.4)
6-month PFS Rate, % (95% CI)	76.8 (55.2, 88.9)	60.7 (37.8, 77.4)	89.9 (65.3, 97.4)	54.2 (34.2, 70.5)	69.2 (54.0, 80.2)
OS events, n(%)	20 (64.5)	24 (85.7)	14 (58.3)	30 (85.7)	44 (74.6)
Median OS, months (95% CI)	13.6 (10.5, NE)	14.3 (10.4, 17.7)	23.4 (14.9, NE)	10.5 (8.5, 12.8)	13.8 (11.5, 17.7)
12-month OS Rate, % (95% CI)	58.1 (39.0, 73.1)	64.3 (43.8, 78.9)	91.7 (70.6, 97.8)	40.0 (24.0, 55.5)	61.0 (47.4, 72.1)
24-month OS Rate, % (95% CI)	38.7 (22.0, 55.1)	14.3 (4.5, 29.5)	44.1 (23.5, 62.8)	14.3 (5.2, 27.7)	26.2 (15.6, 38.1)
Subsequent systemic anticancer therapy, %	10 (32.3)	12 (42.9)	8 (33.3)	14 (40.0)	22 (37.3)

Table 3. Summary of Adverse Events

	AK104 6mg/kg (N=31)	AK104 10mg/kg (N=28)	Locally advanced (N = 24)	Metastatic (N = 35)	Total (N=59)
TEAEs	31 (100)	28 (100)	24 (100)	35 (100)	59 (100)
≥Grade3 TEAEs	26 (83.9)	27 (96.4)	22 (91.7)	31 (88.6)	53 (89.8)
TRAEs	31 (100)	28 (100)	24 (100)	35 (100)	59 (100)
≥Grade3 TRAEs	26 (83.9)	26 (92.9)	22 (91.7)	30 (85.7)	52 (88.1)
Serious TEAEs	15 (48.4)	13 (46.4)	11 (45.8)	17 (48.6)	28 (47.5)
Serious TRAEs	11 (35.5)	9 (32.1)	9 (37.5)	11 (31.4)	20 (33.9)
TEAEs leading to interruption	25 (80.6)	19 (67.9)	19 (79.2)	25 (71.4)	44 (74.6)
TEAEs leading to discontinuation	3 (9.7)	4 (14.3)	5 (20.8)	2 (5.7)	7 (11.9)
TEAEs leading to Death	1 (3.2)	1 (3.6)	0	2 (5.7)	2 (3.4)
AK104-related TEAEs leading to Death	1 (3.2)	0	0	1 (2.9)	1 (1.7)
Infusion-related AEs	5 (16.1)	4 (14.3)	4 (16.7)	5 (14.3)	9 (15.3)
≥Grade 3 Infusion-related AEs	0	0	0	0	0

Table 4. TRAEs occurring in ≥ 20% of patients

	AK104 6mg/kg (N=31)	AK104 10mg/kg (N=28)	Locally advanced (N = 24)	Metastatic (N = 35)	Total (N=59)
Neutrophil count decreased	31 (100)	26 (92.9)	24 (100)	33 (94.3)	57 (96.6)
Anaemia	29 (93.5)	24 (85.7)	23 (95.8)	30 (85.7)	53 (89.8)
White blood cell count decreased	24 (77.4)	26 (92.9)	20 (83.3)	30 (85.7)	50 (84.7)
Platelet count decreased	23 (74.2)	22 (78.6)	18 (75.0)	27 (77.1)	45 (76.3)
Rash	18 (58.1)	13 (46.4)	16 (66.7)	15 (42.9)	31 (52.5)
Alanine aminotransferase increased	17 (54.8)	12 (42.9)	12 (50.0)	17 (48.6)	29 (49.2)
Aspartate aminotransferase increased	14 (45.2)	14 (50.0)	11 (45.8)	17 (48.6)	28 (47.5)
Alopecia	12 (38.7)	15 (53.6)	10 (41.7)	17 (48.6)	27 (45.8)
Lymphocyte count decreased	12 (38.7)	9 (32.1)	15 (62.5)	6 (17.1)	21 (35.6)
Pyrexia	10 (32.3)	11 (39.3)	9 (37.5)	12 (34.3)	21 (35.6)
Asthenia	11 (35.5)	8 (28.6)	10 (41.7)	9 (25.7)	19 (32.2)
Pruritus	10 (32.3)	9 (32.1)	4 (16.7)	15 (42.9)	19 (32.2)
Vomiting	8 (25.8)	9 (32.1)	7 (29.2)	10 (28.6)	17 (28.8)
Hypoalbuminaemia	7 (22.6)	9 (32.1)	5 (20.8)	11 (31.4)	16 (27.1)
Hypoaesthesia	8 (25.8)	8 (28.6)	6 (25.0)	10 (28.6)	16 (27.1)
Peripheral sensory neuropathy	7 (22.6)	7 (25.0)	6 (25.0)	8 (22.9)	14 (23.7)
Diarrhoea	5 (16.1)	8 (28.6)	7 (29.2)	6 (17.1)	13 (22.0)
Nausea	9 (29.0)	4 (14.3)	3 (12.5)	10 (28.6)	13 (22.0)
Blood alkaline phosphatase increased	9 (29.0)	4 (14.3)	5 (20.8)	8 (22.9)	13 (22.0)
Blood bilirubin increased	7 (22.6)	5 (17.9)	6 (25.0)	6 (17.1)	12 (20.3)
C-reactive protein increased	8 (25.8)	4 (14.3)	7 (29.2)	5 (14.3)	12 (20.3)
Gamma-glutamyltransferase increased	9 (29.0)	3 (10.7)	6 (25.0)	6 (17.1)	12 (20.3)
Leukopenia	8 (25.8)	4 (14.3)	8 (33.3)	4 (11.4)	12 (20.3)
Oedema peripheral	8 (25.8)	4 (14.3)	3 (12.5)	9 (25.7)	12 (20.3)

Figure 2. Best Response by Disease Status

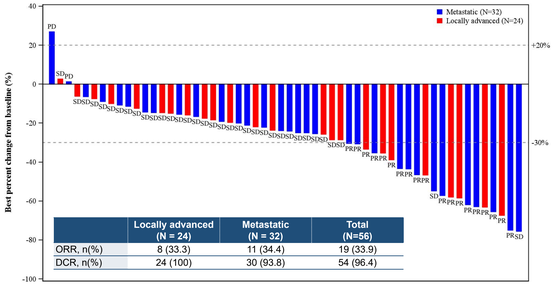


Figure 3. Progression-Free Survival by Disease Status

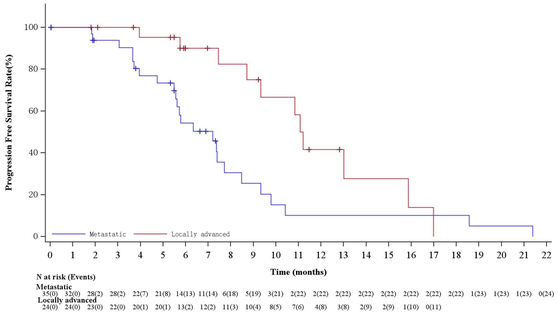
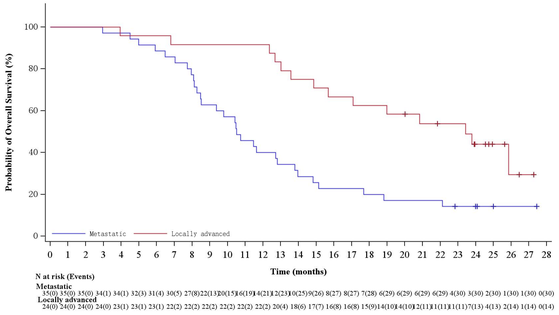


Figure 4. Overall Survival by Disease Status



Conclusions:

- Historical data for AG demonstrated an ORR of 23% with median PFS of 5.5 months and median OS of 8.5 months in patients with metastatic PDAC[4] , and an ORR of 30% with median PFS of 9.3 months and median OS of 14.16 months for patients with locally advanced disease[5].
- Results from COMPASSION-26 demonstrate the addition of cadonilimab to AG was safe and tolerable, with no new safety signals or significant added toxicity to AG.
- Efficacy outcomes appeared broadly similar between the two dose groups.
- Compared to standard chemotherapy, the combination of cadonilimab and AG as first-line therapy demonstrated encouraging preliminary antitumor activity in patients with PDAC, especially in those with locally advanced disease.

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- All authors contributed to and approved the presentation

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