Abstract No. 604

Preliminary Activity and Safety Results of KRAS G12C Inhibitor Glecirasib (JAB-21822) in Patients with Pancreatic Cancer and Other Solid Tumors

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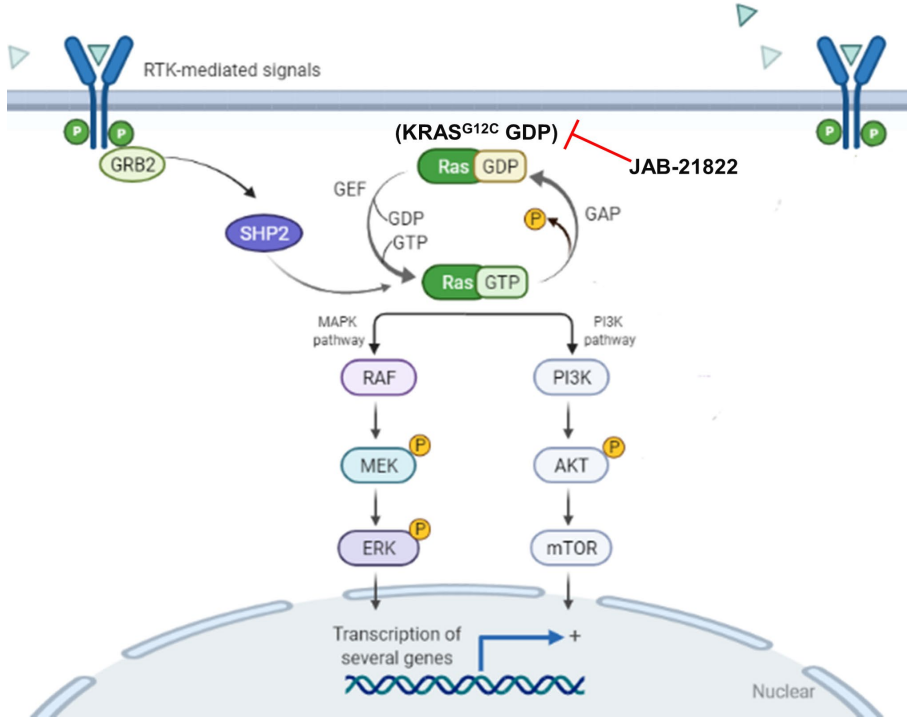
Declaration of Interests

- I am involved in research collaborations with Jacobio for study JAB-21822-1002.
- I do not hold any stocks or shares in Jacobio Pharmaceuticals Co., Ltd.

Background

- KRAS G12C mutation is a well-recognized oncogenic driver in solid tumors, with a mutation frequency of 1-3% in PDAC, 3.26% in appendix cancer, 3.14% in small bowel cancer, 1.45% in endometrial cancer, 1.2% in BTC, 0.8% in cervical cancer, 0.6% in GC, and 0.4% in OC.[1,2,3,4]
- Patients with KRAS G12C mutations are associated with a worse prognosis than patients without this mutation; however, there has not been any approved targeted therapy for patients with KRAS G12C mutated solid tumors except for NSCLC.
- Glecirasib is a highly selective covalent oral inhibitor of KRAS G12C which has shown promising efficacy in patients with NSCLC and CRC.[5,6]
- Here we report the pooled data in PDAC and other tumors from two clinical trials (JAB-21822-1001 and JAB-21822-1002) of glecirasib.



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5. 2022 ASCO Abstract #3089
6. 2023 JCA-AACR

Study Design of JAB-21822-1001&1002

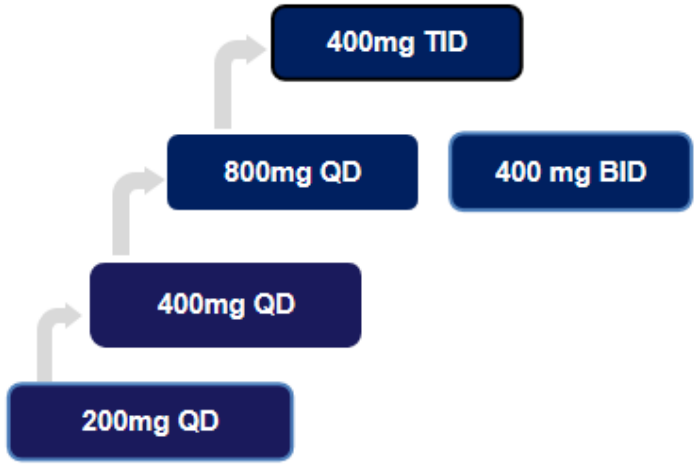
JAB-21822-1002 (NCT05009329) China Only

JAB-21822-1001 (NCT05002270) US, Israel and EU

Phase I (Dose escalation)

Key inclusion criteria:

- Locally advanced or metastasic solid tumors
- Progressed on or after standard treatment
- KRAS p.G12C mutated
- No active CNS metastasis



Primary endpoint:
- Safety and tolerability, DLT

Secondary endpoints:
- PK, ORR, DOR, DCR, TTR, PFS, OS

Phase IIa (Dose expansion)

NSCLC (400mg/800mg QD)

CRC (800mg QD)

Pancreatic cancer and other solid tumors (800mg QD)
N~52

Primary endpoint:
- ORR

Secondary endpoints:
- Safety and tolerability, PK, DOR, DCR, TTR, PFS, OS

Demographics and Baseline Characteristics

	PDAC(N=31)	Other tumors (N=21)	Total(N=52)
Age (Years)			
Median (Min-Max)	63.0 (35-83)	62.0 (34-85)	62.5 (34-85)
Gender, n (%)			
Male	18 (58.1%)	12 (57.1%)	30 (57.7%)
Female	13 (41.9%)	9 (42.9%)	22 (42.3%)
Race, n (%)			
Asian	29 (93.5%)	16 (76.2%)	45 (86.5%)
White	2 (6.5%)	5 (23.8%)	7 (13.5%)
ECOG PS, n (%))			
0	7 (22.6%)	4 (19.0%)	11 (21.2%)
1	24 (77.4%)	17 (81.0%)	41 (78.8%)
Prior lines of Therapy, n (%)			
0	0	2 (9.5%)	2 (3.8%)
1	18 (58.1%)	8 (38.1%)	26 (50.0%)
≥ 2	13(41.9%)	11 (52.4%)	24 (46.1%)
Tumor Type, n (%)			
PDAC			31 (59.6%)
Biliary tract cancer			8 (15.4%)
Gastric cancer			3 (5.8%)
Small bowel			3 (5.8%)
Appendiceal cancer			2 (3.8%)
Cervical cancer			1 (1.9%)
Head and Neck cancer			1 (1.9%)
Ovarian cancer			1 (1.9%)
Synovial sarcoma			1 (1.9%)
Mediastinal tumor			1 (1.9%)

Data cutoff date: 2023-12-06

Overall Response for all solid tumors

	Total(N=50*)
Overall Response (ORR)	**28 (56.0%)**
Complete Response (CR)	0
Partial Response (PR)	28 (56.0%)
Stable Disease (SD)	17 (34.0%)
Progressive Disease (PD)	4 (8.0%)
Not Evaluable (NE)	1 (2.0%)
Disease Control Rate (DCR)	45 (90.0%)
Confirmed Overall Response (Confirmed ORR)	**24 (48.0%)**
Complete Response (CR)	0
Partial Response (PR)	24 (48.0%)
Stable Disease (SD)	21 (42.0%)
Progressive Disease (PD)	4 (8.0%)
Not Evaluable (NE)	1 (2.0%)
Confirmed Disease Control Rate (DCR)	45 (90.0%)

*Two patients out of the 52 patients was not included in the efficacy evaluable population: one patient with BTC died prior to the first post treatment tumor assessment; the other patient with head and neck cancer with no result of post treatment tumor assessment data entered.

Data cutoff date: 2023-12-06

Response by Tumor Type

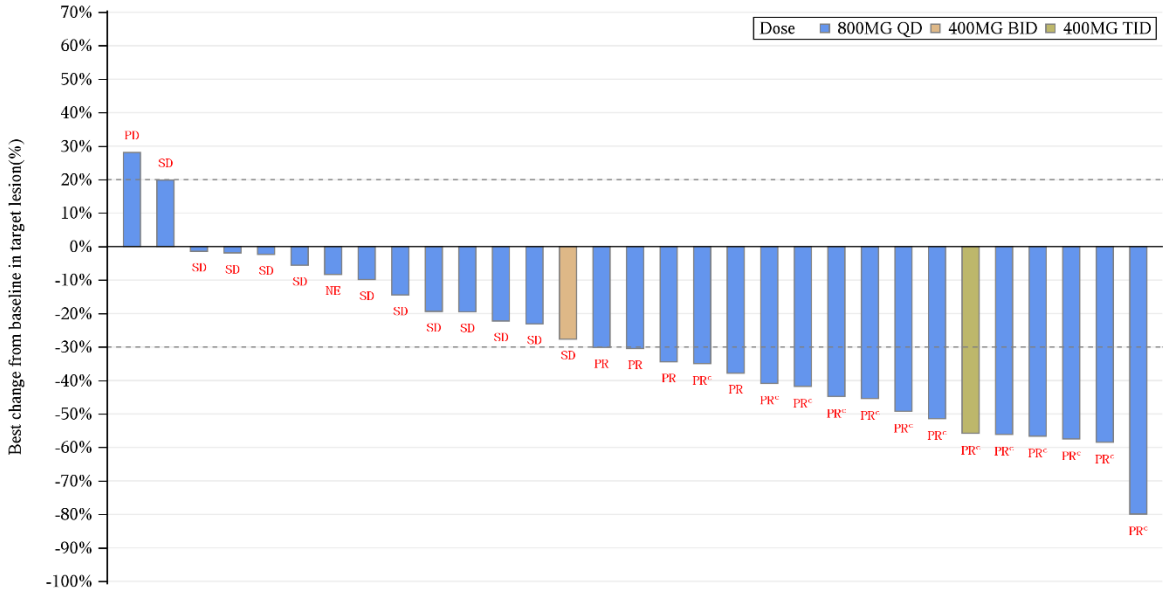
Tumor Type	N	ORR, n(%)	Confirmed ORR, n(%)	DCR, n(%)
PDAC[1]	31	17 (54.8%)	13 (41.9%)	29 (93.5%)
Other Tumors	19	11 (57.9%)	11 (57.9%)	16 (84.2%)
- BTC[2]	7	5 (71.4%)	5 (71.4%)	7 (100%)
- GC[3]	3	2 (66.7%)	2 (66.7%)	3 (100%)
- Small Bowel	3	3 (100%)	3 (100%)	3 (100%)

1. PDAC, pancreatic ductal adenocarcinoma
2. BTC, biliary tract cancer
3. GC, colorectal cancer

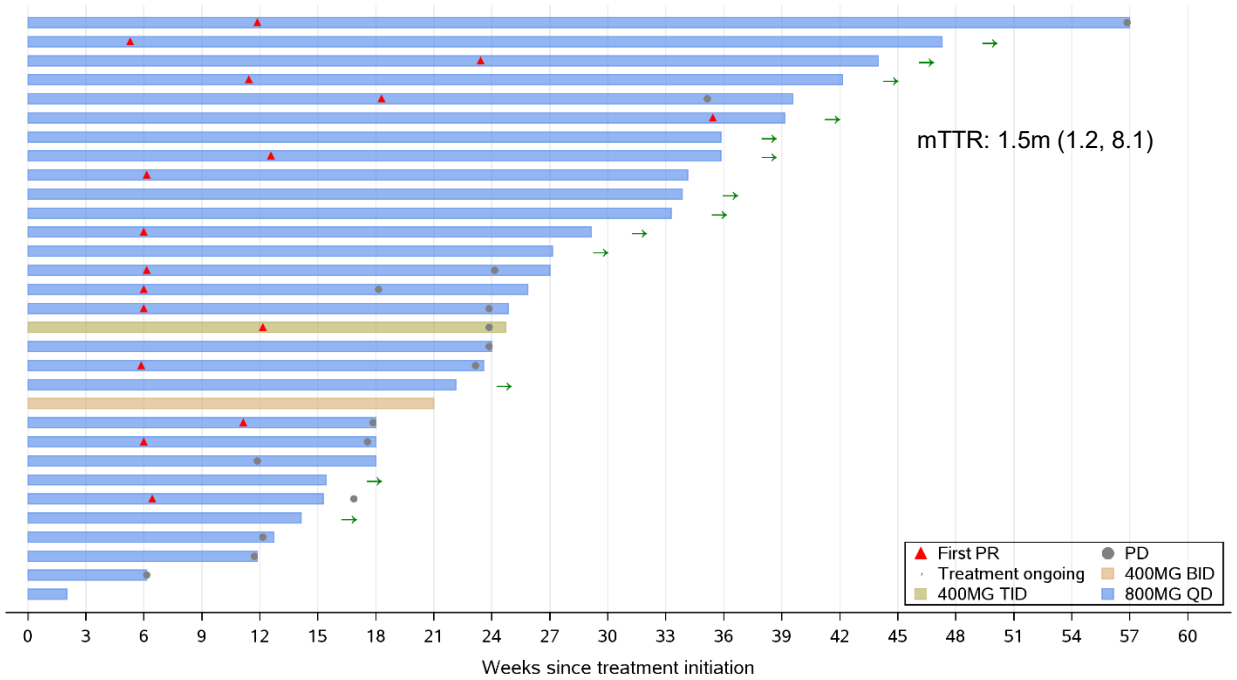
Data cutoff date: 2023-12-06

Efficacy of Glecirasib in PDAC

Best Tumor Change from Baseline



Duration of Treatment

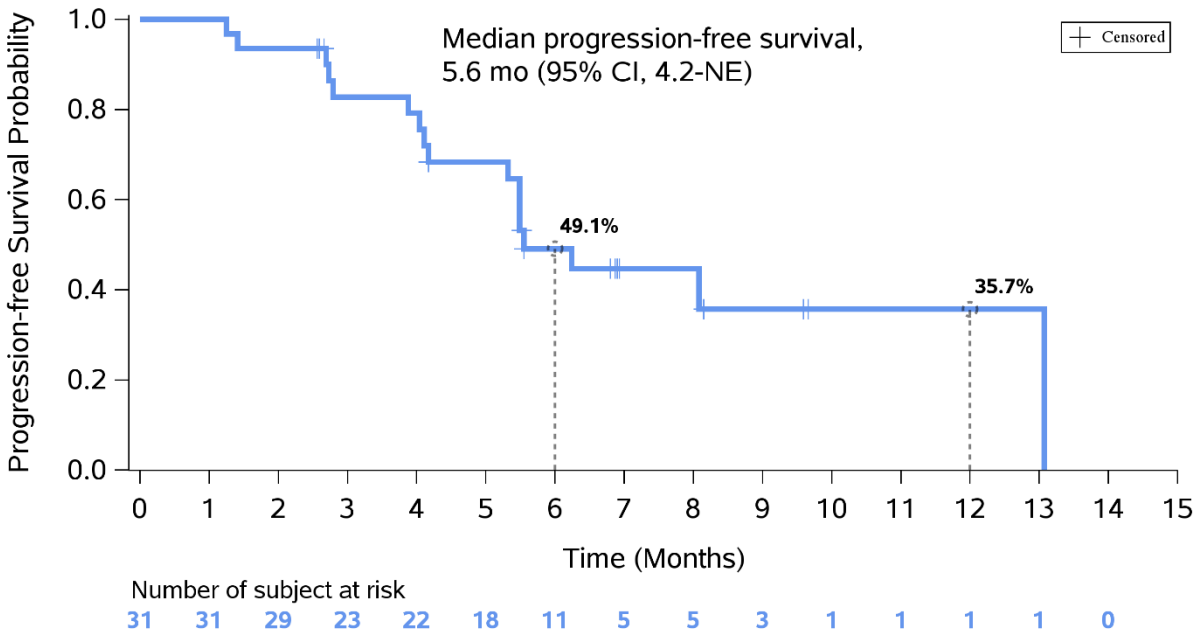


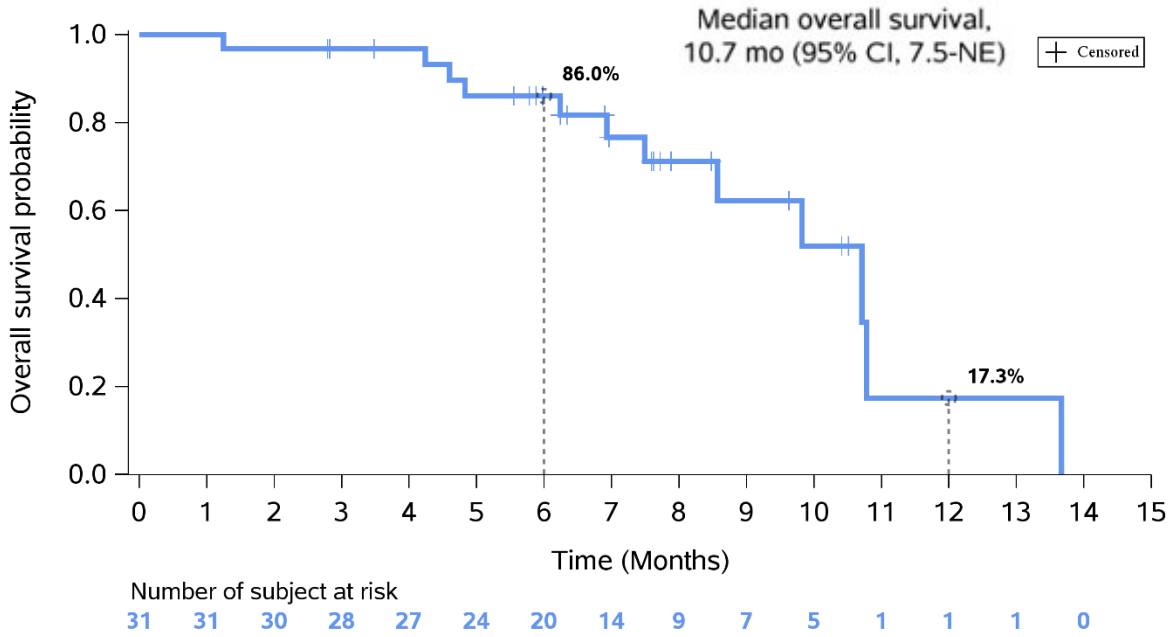
- cORR for PDAC is 41.9%, DCR is 93.5%
- 22.6%(7/31) of patients with PDAC experiencing tumor regression >50%

- 41.9% (13/31) of patients with PDAC still on study treatment at the time of data cutoff

Data cutoff date: 2023-12-06

PFS and OS in PDAC



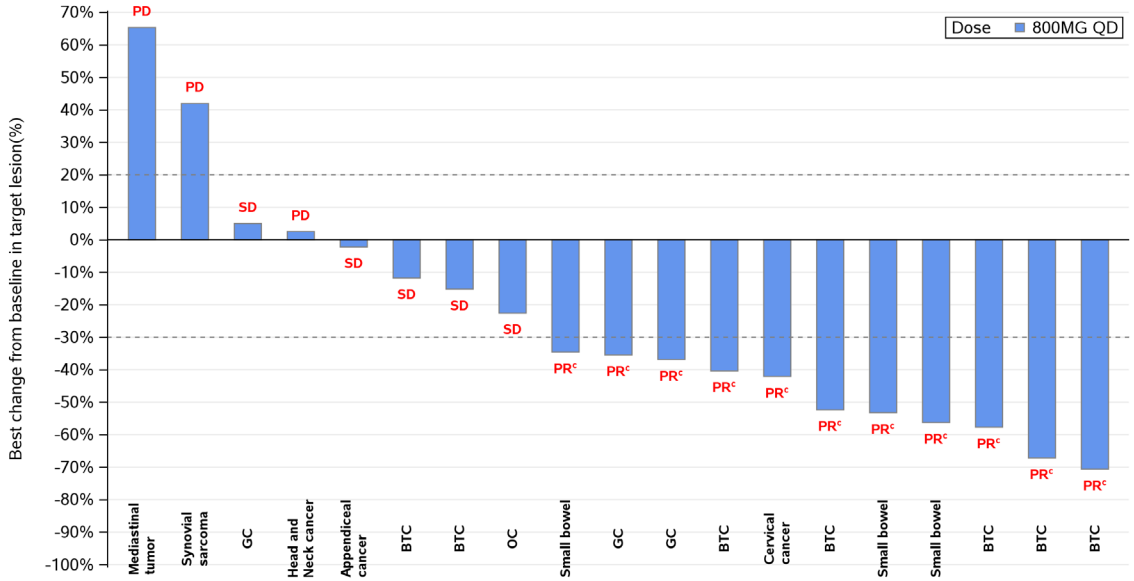


- **Glecirsib monotherapy yielded a mPFS of 5.6 months and a mOS of 10.7 months in PDAC.**

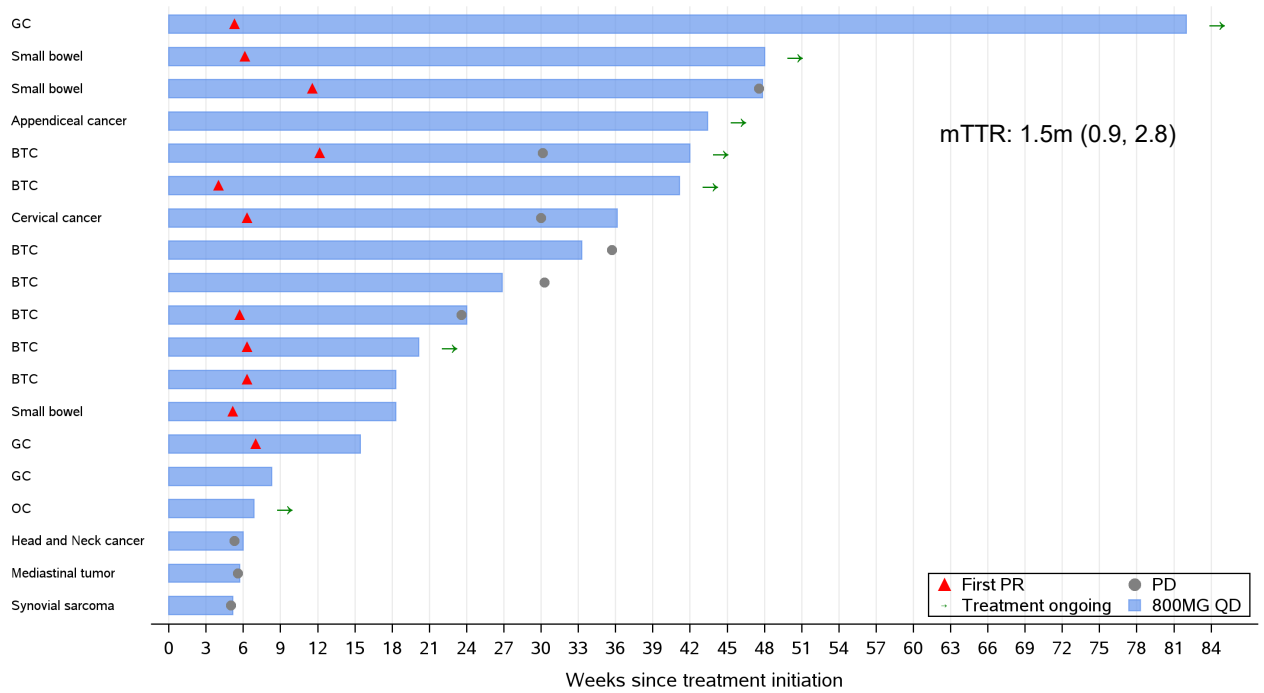
Data cutoff date: 2023-12-06

Efficacy of Glecirasib in Other Tumors

Best Tumor Change from Baseline



Duration of Treatment

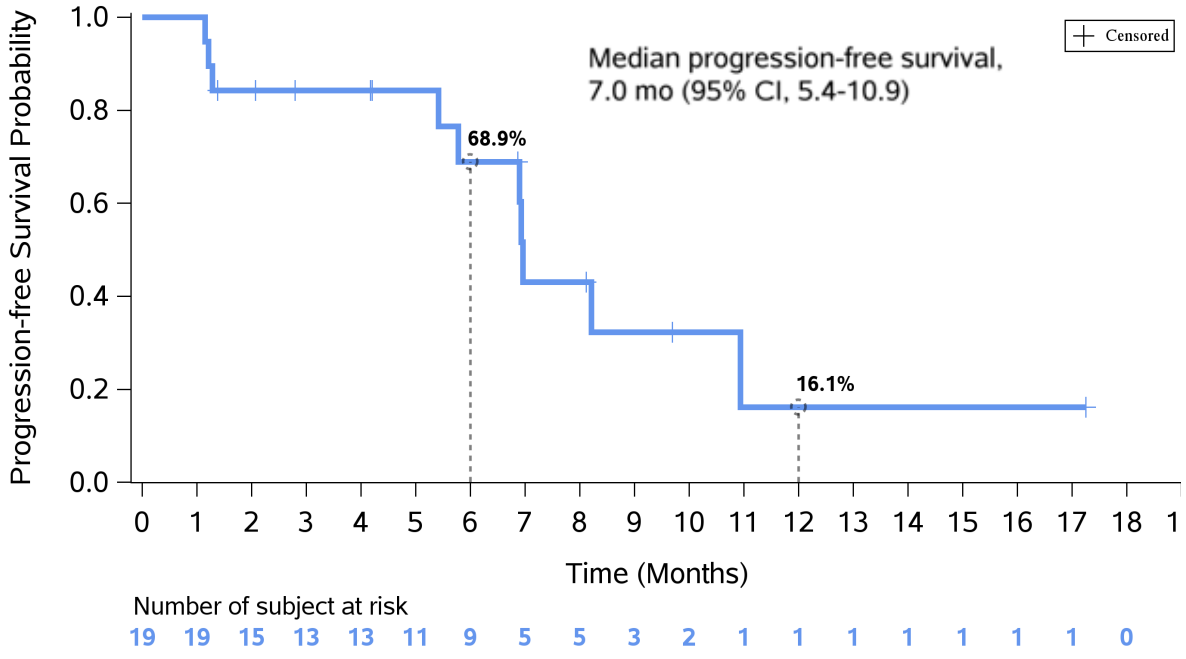


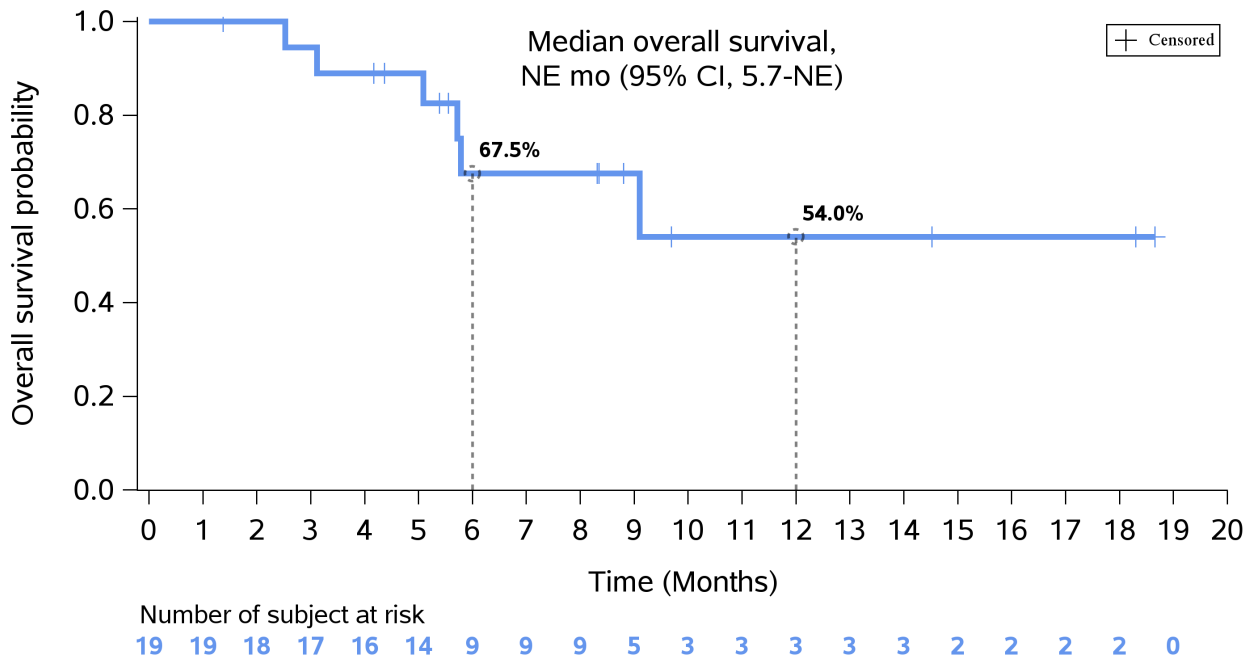
- cORR for other tumors is 57.9%, DCR is 84.2%
- 31.6%(6/19) of patients with other tumors experiencing tumor regression >50%

- 36.8% (7/19) of patients with other tumors still on study treatment at the time of data cutoff.

Data cutoff date: 2023-12-06

PFS and OS in Other Tumors





- **Glecirasib monotherapy yielded a mPFS of 7.0 months in other tumor types.**
- **Median OS not reach (12-month OS rate:58.2%).**

Data cutoff date: 2023-12-06

Treatment Related Adverse Events (≥10%)

	Total(N=52)	
Preferred Term	**Any grade**	**≥3 Grade**
Number of Patients with At Least One TRAE	48 (92.3%)	13 (25.0%)
Anemia	30 (57.7%)	3 (5.8%)
Blood bilirubin increased	26 (50.0%)	1 (1.9%)
Bilirubin conjugated increased	19 (36.5%)	1 (1.9%)
Asthenia	12 (23.1%)	1 (1.9%)
Aspartate aminotransferase increased	9 (17.3%)	1 (1.9%)
White blood cell count decreased	9 (17.3%)	1 (1.9%)
Blood bilirubin unconjugated increased	8 (15.4%)	0
Hypertriglyceridamia	7 (13.5%)	2 (3.8%)
Alanine aminotransferase increased	7 (13.5%)	1 (1.9%)
Nausea	6 (11.5%)	0
Diarrhea	6 (11.5%)	0

- TEAEs occurred in most patients (98.1%), and most of them are drug related (92.3%);
- TRAEs were mostly grade 1/2;
- TRAEs of ≥G3 occurred in 25.0% patients;
- Serious TRAEs accounted for only 5.8%;
- Low rate (9.6%) of dose reduction due to a TRAE;
- No TRAE leading to drug discontinuation or death;
- Most frequent TRAEs were anemia, blood bilirubin increased, bilirubin conjugated increased, and asthenia.

Data cutoff date: 2023-12-06

Conclusions

- Glecirasib monotherapy has demonstrated promising clinical activity in previously treated patients with KRAS G12C mutated PDAC and other tumor types.
  - PDAC: cORR 41.9%, DCR 93.5%, mPFS 5.6m, mOS 10.7m
  - Other tumors: cORR 57.9%, DCR 84.2%, mPFS 7.0m, mOS NR (12-month OS rate: 58.2%)
    - BTC: cORR 71.4%, DCR 100%,
    - GC: cORR 66.7%, DCR 100%
    - Small bowel: cORR 100%, DCR 100%
- Glecirasib monotherapy is well tolerated and with a favorable safety profile.
- The impressive clinical activities of glecirasib observed in PDAC and other tumor types warrant further expedited development for above mentioned tumor types with significant unmet medical needs.
- A pivotal clinical study in KRAS G12C mutated PDAC is currently enrolling in China (NCT06008288, CTR20232444).

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- This study was sponsored by Jacobio Pharmaceutical Co., Ltd.
- All authors have contributed to and approved this presentation.

Abbreviations

- KRAS, kirsten rat sarcoma viral oncogene homolog
- PDAC, pancreatic ductal adenocarcinoma
- BTC, biliary tract cancer
- GC, colorectal cancer
- CI, confidence interval
- CRC, colorectal cancer
- DCR, disease control rate
- DOR, duration of response
- OC, ovarian cancer
- NE, not evaluable
- NSCLC, non-small cell lung cancer
- ORR, objective response rate
- OS, overall survival
- PD, progressive disease
- PFS, progression-free survival
- PR, partial response
- TRAE, treatment-related adverse event
- TTR, time to response