D-1553 (Garsorasib) in patients with KRAS G12C mutated advanced pancreatic cancer (PCa)

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BACKGROUND

- KRAS mutations are found in approximately 90% of PCa, of which 1-2% are KRAS G12C.[1]
- Garsorasib is a novel oral and potent KRAS G12C inhibitor.
- Garsorasib has shown clinical activity in patients (pts) with KRAS G12C mutated non-small cell lung cancer and colorectal cancer. [2,3]
- Here, we report preliminary data of garsorasib in KRAS G12C mutated advanced PCa.

METHODS

Figure 1. Study Design

Key Eligibility

- Refractory to or intolerant of standard therapy.
- KRAS G12C identified by molecular testing.

Endpoints

- Safety;
- PK parameters;
- ORR, DCR, and PFS.

Phase Ia *		Phase II
Garsorasib Single Agent (150 ~ 1600 mg/day)	RP2D →	Arm B: Solid tumor Garsorasib Single Agent (600 mg BID)

* For detailed study design of phase Ia, refer to the presentation of this study published at AACR Annual Meeting 2022.

Abbreviation

ORR: Objective Response Rate; DCR: Disease Control Rate, PFS: Progression-Free Survival; RP2D: Recommended Phase 2 dose

References

1. Luo J. Semin Oncol. 2021 Feb;48(1):10-18.
2. Li Z, et al. J Thorac Oncol. 2023 Jul;18(7):940-951.
3. Ruan D, et al. ASCO 2023, #3563.

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RESULTS

Baseline Characteristics

- As of July 07, 2023, 14 KRAS G12C inhibitor naïve PCa pts (including 10 pts from this study, and 4 pts from another garsorasib study with similar inclusion/exclusion criteria and the treatment as this study) were enrolled and their baseline characteristics are summarized in **Table 1**.
- At data cutoff, 7 (50.0%) pts remained on treatment, and median follow-up was 9.51 (range: 1.45, 13.14) months.

Table 1. Baseline Characteristics

	Total (n=14)
Median age, years (range)	67.5 (48, 78)
Sex, female, n (%)	6 (42.9)
Race, n (%)	
Asian	11 (78.6)
White	3 (21.4)
ECOG PS, n (%)	
0/1	8/6 (57.1/42.9)
Stage at baseline, n (%)	
IV	14 (100)
Prior lines of systemic anticancer therapy	
Median (Min, Max)	1.5 (0, 4)
≥ 2	7 (50.0)
≥ 3	3 (21.4)

Safety

- Treatment-related adverse events (TRAE) are summarized in **Tables 2** and **3**. Grade 3 TRAE included ALT increased, AST increased, diarrhoea, and blood ALP increased.

Table 2. Overview of TRAEs

TRAE, n (%)	Total (n=14)
TRAE, any grade	9 (64.3)
Grade 1-2	6 (42.9)
Grade 3	3 (21.4)
Grade 4/5	0
Any TRAE Leading to	
Drug Interruption	3 (21.4)
Drug Reduction	3 (21.4)
Drug Discontinuation	0
Death	0

Safety

Table 3. Incidence of TRAEs

TRAEs (frequency ≥ 10%)	Total (n=14)	
	Any grade	Grade 3
ALT increased	6 (42.9)	2 (14.3)
AST increased	5 (35.7)	2 (14.3)
Diarrhoea	4 (28.6)	1 (7.1)
Blood bilirubin increased	2 (14.3)	0
Decreased appetite	2 (14.3)	0
Vomiting	2 (14.3)	0

Efficacy

Figure 2. Best Tumor Response and Tumor Burden Change

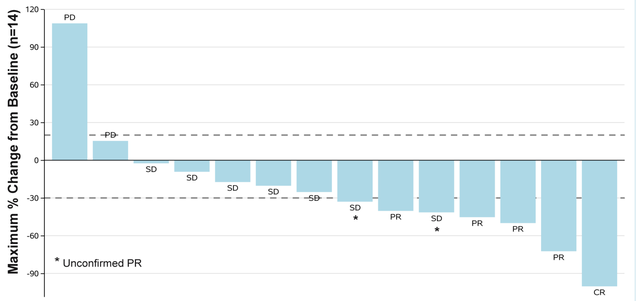
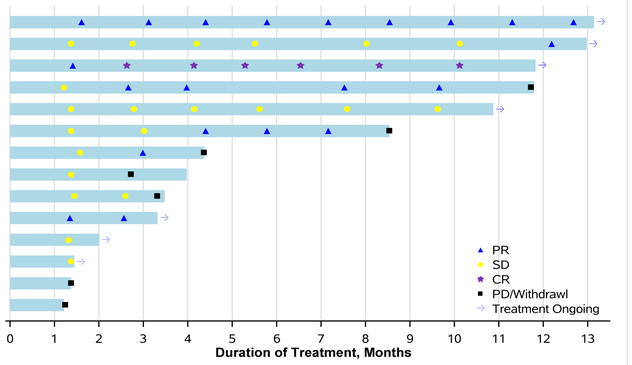


Figure 3. Duration of Treatment and Tumor Response

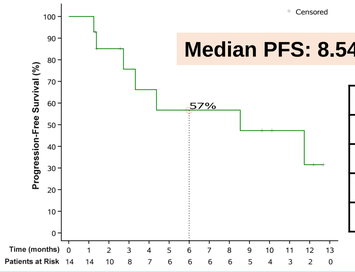


Efficacy

Table 4. Efficacy Outcomes

	Total (n=14)
Best overall response, n %)	
CR	1 (7.1)
PR	4 (28.6)
SD	7 (50.0)
PD	2 (14.3)
Confirmed ORR, n (%)	**5 (35.7)**
95%CI	(12.8, 64.9)
DCR, n (%)	**12 (85.7)**
95%CI	(57.2, 98.2)

Figure 4. Progression-Free Survival



Median PFS: 8.54 (95%CI, 2.73, NA) months

PFS rate, % (95% CI)	
At 3 months	75.7 (41.3, 91.6)
At 6 months	56.7 (24.6, 79.5)
At 9 months	47.3 (17.8, 72.3)
At 12 months	31.5 (6.2, 62.0)

CONCLUSIONS

- Garsorasib monotherapy is well tolerated in Pca pts.
- Garsorasib monotherapy showed promising activity in advanced PCa harboring KRAS G12C mutation.
  - **Confirmed ORR: 35.7%, DCR: 85.7%;**
  - **Median PFS: 8.54 (95%CI, 2.73, NA) months;**
  - Additionally, another PCa pt who was previously treated with KRAS G12C inhibitor and not included in this analysis had also achieved PR after garsorasib treatment.
- Clinical trial registry number: NCT04585035, NCT05383898