

A Phase 1a/1b Trial of Faridoxorubicin (AVA6000), a Fibroblast Activation Protein (FAP)-Released and Tumor Microenvironment (TME)-targeted Doxorubicin Peptide Drug Conjugate in Patients with Salivary Gland Cancers

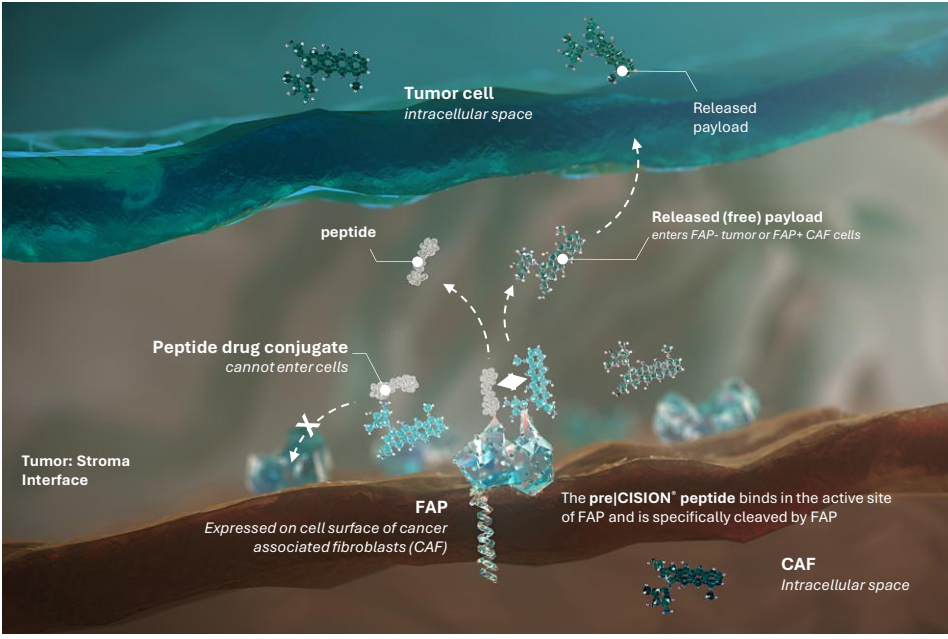
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BACKGROUND

pre[CISION][®] peptide drug conjugates comprise a dipeptide moiety (D-Ala-Pro) bound to an active payload by a linker that is specifically cleaved by FAP, a protease selectively overexpressed in the tumor microenvironment (TME) of many solid tumors on cancer-associated fibroblasts (including SGC)

The pre[CISION][®] dipeptide prevents cellular entry of the conjugate unless cleaved by FAP, enabling targeted delivery of released payload directly to the tumor-stroma interface

This targeted release mechanism has been validated in both preclinical animal models and clinical biopsy data, demonstrating that the payload is predominantly activated and released in the FAP-rich tumor environment



- Doxorubicin is an effective anthracycline, however, its clinical utility is significantly limited by dose-dependent, cumulative cardiotoxicity and bone marrow toxicity

- Encouraging safety and preliminary efficacy data from the Phase 1 trial with faridoxorubicin have been presented previously (Lahu et al AACR 2025, Tap et al, ESMO 2025) and initial efficacy in patients with salivary gland cancers (SGC) has been observed

- Benchmark efficacy in metastatic SGC was reviewed recently (Kanno et al. 2025). Median PFS among studies of cytotoxic chemotherapy was ~6.7 months (range 6.5-9 months) and median PFS among studies of targeted therapies was ~6 months (range 2.1-17.5 months)

Patient Population and Trial Methods

The Faridoxorubicin (AVA6000) Phase 1a dose escalation enrolled patients with a diagnosis of cancers frequently noted as FAP-positive, including salivary gland cancer (SGC). AVA6000 is administered i.v. Q3W or Q2W

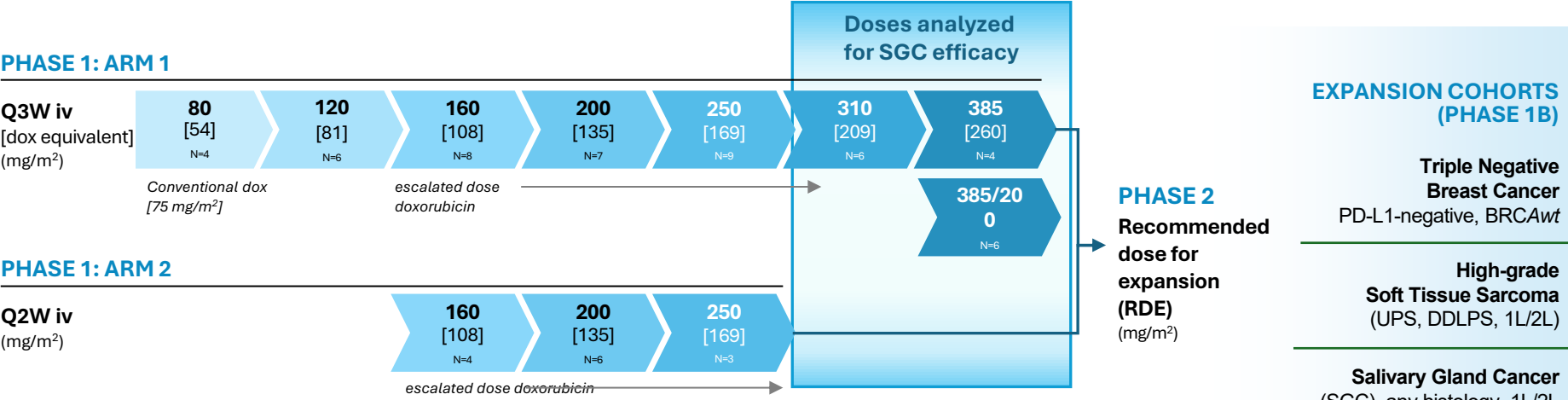
Specific indications were selected for Phase 1b expansion including salivary gland cancer. FAP expression was tested retrospectively

A total of N=120 patients have been treated across Phase 1a and 1b. Of these, n=51 patients have the diagnosis of SGC.

The data cutoff for safety and efficacy presented is 05 October 2026

- Trial analyzed for safety (primary endpoint) and efficacy.** Across Ph 1a and 1b, n=51 pts with SGC were enrolled. Endpoints include safety, PK and preliminary efficacy. Efficacy in patients with SGC was assessed in pts treated at the dose of 310 mg/m² and above, excluding pts with rare histologies and ECOG<1 (n=32)
- Prior therapy with any anthracycline was limited to total cumulative dose of less than 350 mg/m².** The lifetime cumulative maximum exposure was lifted in an amendment based on favorable cardiac safety data
- Prior reports of PK** in the trial (Lahu, et al 2025) demonstrate similar profiles comparing the 310 mg/m² and 385 mg/m² dose levels
- On-treatment biopsies were obtained at 24 hours after the dose was administered.** Biopsy samples and plasma samples were obtained at the same time to assess the tumor:plasma ratio of doxorubicin
- Longitudinal FAPI-PET imaging** was conducted at a single center to assess overall FAP expression over time

Fig. 1. Faridoxorubicin Phase 1 Design



Patient sets treated with SGC in this trial:

- Patients with SGC (n=51) treated across Phase 1a and 1b, all doses, any histology
- SGC Efficacy set:** patients eligible for pivotal trial (n=32) with exclusion for dose <310mg/m², rare SGC histologies and lower ECOG score
- The **SGC Efficacy set** includes patients with Adenoid Cystic Carcinoma (ACC, n=23), subsets of Salivary ductal cancer, Acinic Cell Carcinoma and Mucoctaneous carcinoma (n=9), all treated with dose ≥310mg/m²

Table 1. Baseline characteristics

	Phase 1a all dose levels N=63	Phase 1a / 1b all dose levels N=120	SGC Efficacy Set ≥310 mg/m ² Q3W n=32
Age, median (range)	60 (30-81)	61.5 (25-81)	59.5 (32-81)
Sex, m/f, n (%)	36 / 27 (57/43)	60 / 60 (50/50)	17 / 15 (53/47)
ECOG, 0/1, n (%)	25 / 38 (40/60)	60 / 60 (50/50)	22 / 10 (69/31)
Race			
White, n (%)	51 (81)	95 (79)	24 (75)
Asian, n (%)	6 (10)	12 (10)	4 (12.5)
Black or African American, n (%)	2 (3)	8 (7)	4 (12.5)
Not reported/unknown, n (%)	4 (6)	5 (4)	0
Ethnicity			
Hispanic/Latino, n (%)	0	2 (2)	1 (3)
Non-Hispanic, non-Latino, n (%)	59 (94)	113 (94)	29 (91)
Not reported/unknown, n (%)	4 (6)	5 (4)	2 (6)

Data cutoff 05 Oct 2026

Table 2. Diagnosis and prior cancer therapy

	Phase 1a / 1b all dose levels N=120	SGC Efficacy Set ≥310 mg/m ² Q3W n=32
Cancer diagnosis		
Salivary gland cancer, n (%)	51 (42.5)	32 (100)
Soft tissue sarcoma, n (%)	24 (20)	0
Other, n (%)	45 (37.5)	0
Prior systemic therapy		
Number of prior regimens, median (range)	1 (0-8)	1 (0-2)
Patients with no prior systemic therapy, n (%)	32 (27)	11 (34)

Concentrations of released doxorubicin in tumor biopsies (ng/g) and matched plasma samples (ng/mL) collected 24 hours (±6hr) after the first or second dose of faridoxorubicin.	
Symbol color indicates faridoxorubicin dose levels (80–385 mg/m ²), and lines connect matched tumor and plasma measurements.	

SAFETY

Table 3. Most Frequent Grade 3-4 AE in >1 pts

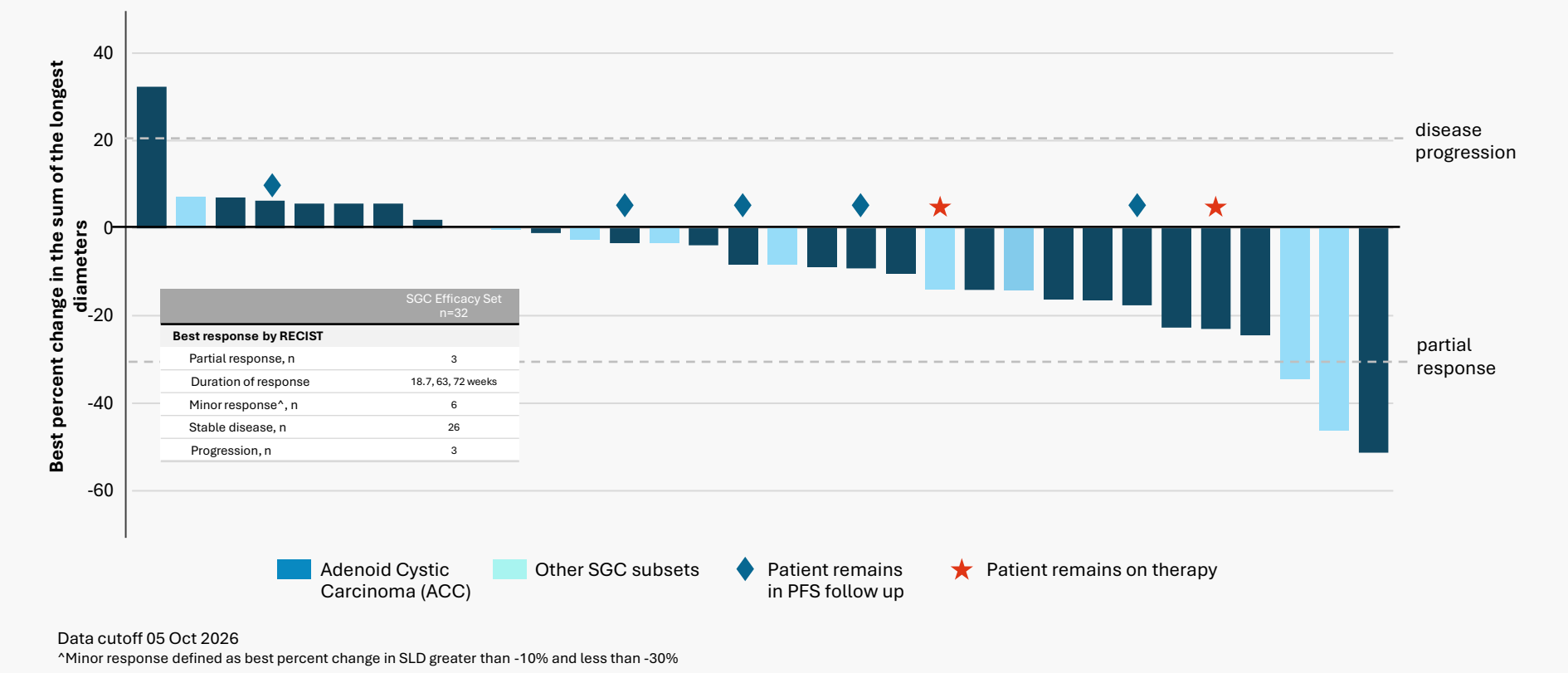
Adverse event	Phase 1a all dose levels N=63	Phase 1b 250 mg/m ² / 310 mg/m ² Q3W n=57	Phase 1a and 1b all dose levels N=120	Conventional doxorubicin 75 mg/m ² Q3W N=251*
Neutropenia, including low ANC, n (%)	13 (20.6)	15 (26.3)	28 (23.3)	122 (49)
Leukopenia, including low WBC, n (%)	6 (9.5)	10 (17.5)	16 (13.3)	59 (23.7)
Lymphopenia, including low LYMPH, n (%)	4 (6.3)	4 (7)	8 (6.7)	7 (2.8)
Anemia, including low Hg, n (%)	4 (6.3)	3 (5.3)	7 (5.8)	31 (12.4)
Fatigue, n (%)	2 (3.2)	5 (8.8)	7 (5.8)	12 (4.8)
Thrombocytopenia, including low plt, n (%)	3 (4.8)	2 (3.5)	5 (4.2)	21 (8.4)

Data cutoff 05 Oct 2026.

*Tap WD et al.; ANNOUNCE Investigators. JAMA. 2020;323(13):1266-1276.

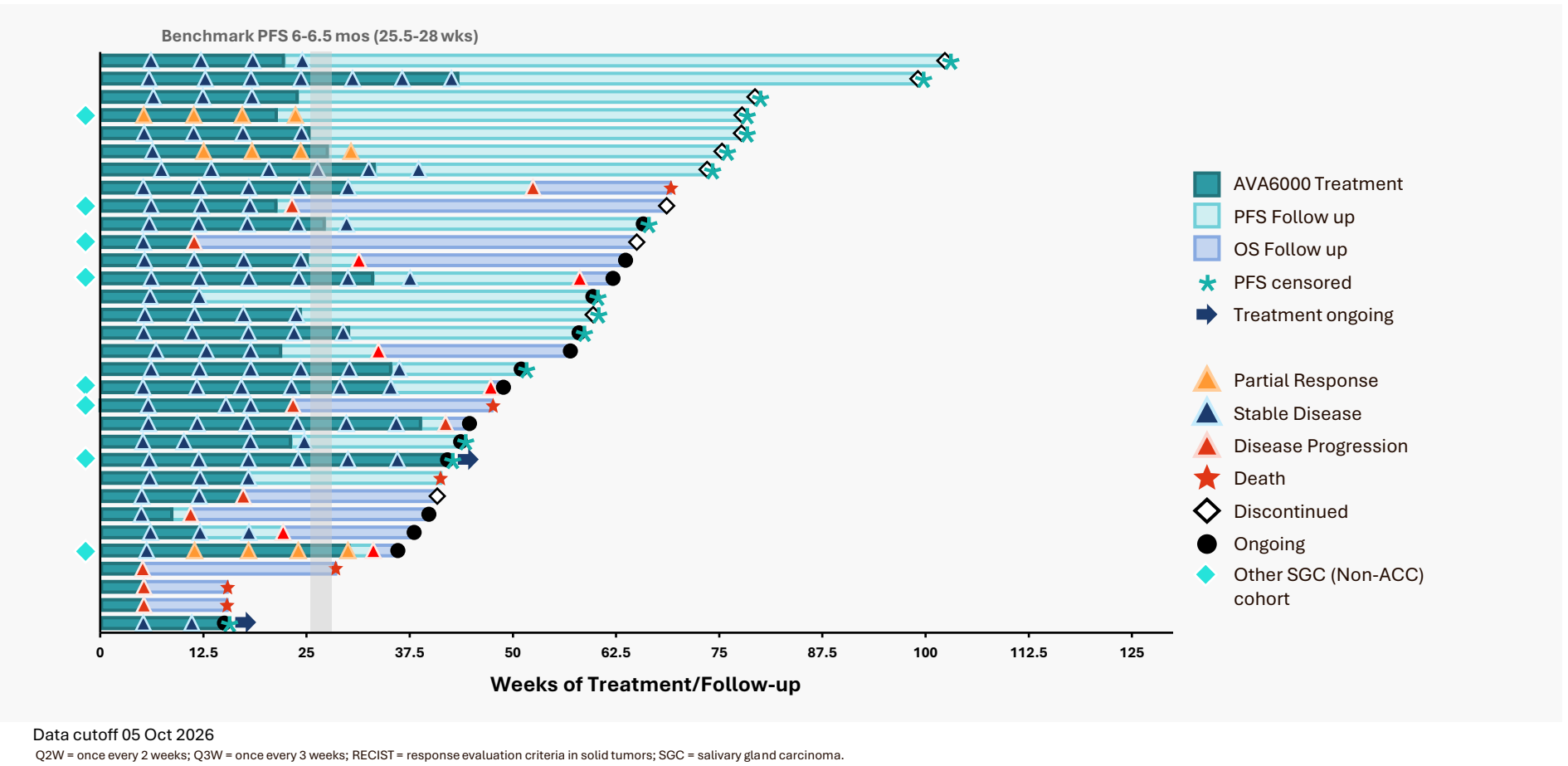
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Fig. 2. Best Overall Response Waterfall Plot in the SGC Efficacy Subset (n=32)



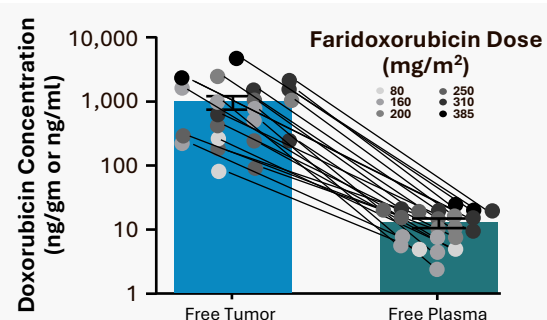
Swimmer Plot of Weeks on Study by Status, with RECIST Responses Efficacy Analysis Set – Subset of Salivary Gland Cancer (n=32)

Fig. 3. Swimmer Plot (SGC Efficacy Subset, n=32)



Doxorubicin Concentration is Observed in Tumor Biopsies in a Dose-Responsive Manner at all FAP Levels

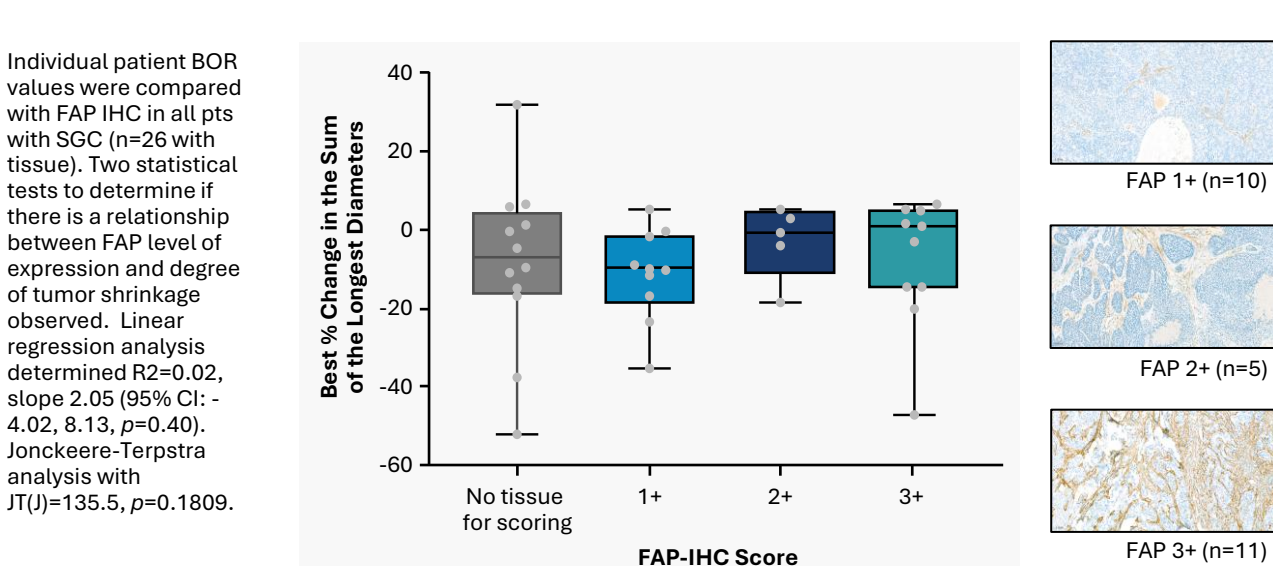
Fig. 4. Tumor concentration of released doxorubicin 24 hours after Dose 1 in SGC



Concentrations of released doxorubicin in tumor biopsies (ng/g) and matched plasma samples (ng/mL) collected 24 hours (±6hr) after the first or second dose of faridoxorubicin. Symbol color indicates faridoxorubicin dose levels (80–385 mg/m²), and lines connect matched tumor and plasma measurements.

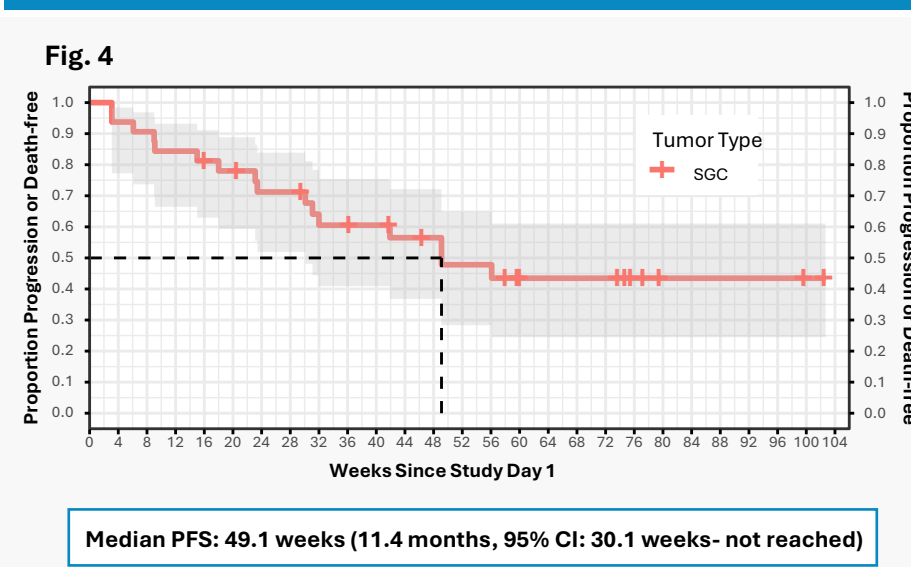
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Fig. 5. Best Overall Response (BOR) vs. FAP-IHC Status in Pts with SGC



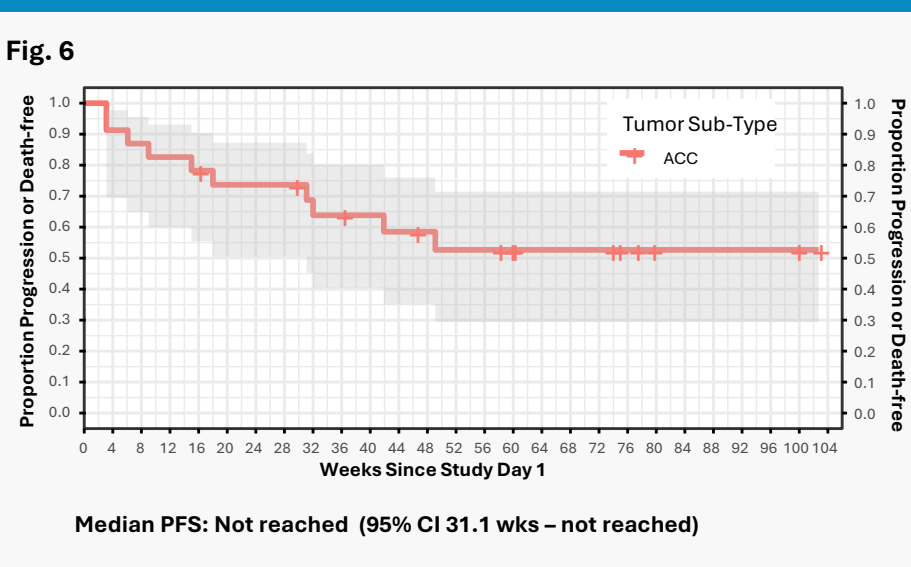
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PFS in the SGC Efficacy Subset (n=32)



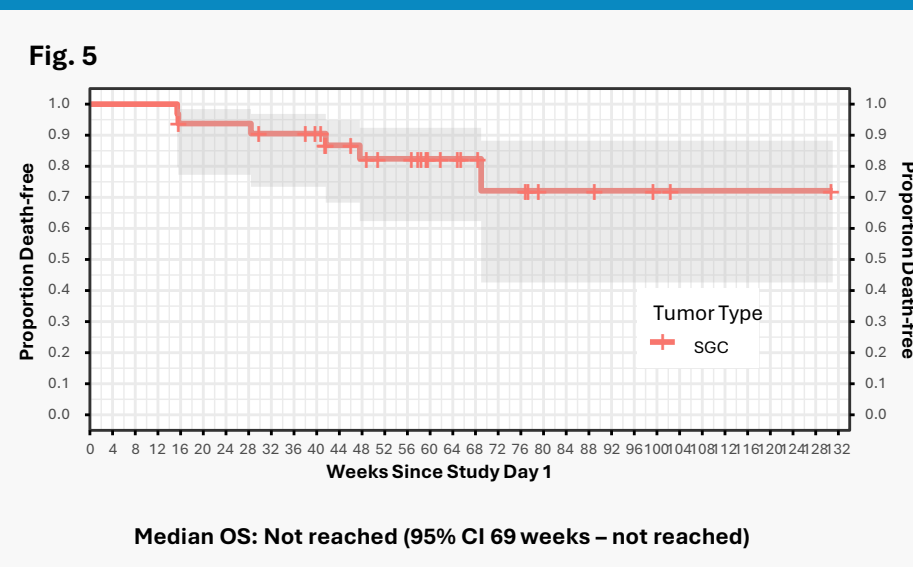
Data cutoff 05 OCT 2026

PFS in the ACC Efficacy Subset (n=23)



Data cutoff 05 OCT 2026

OS in the SGC Efficacy Subset (n=32)



OS in the ACC Efficacy Subset (n=23)

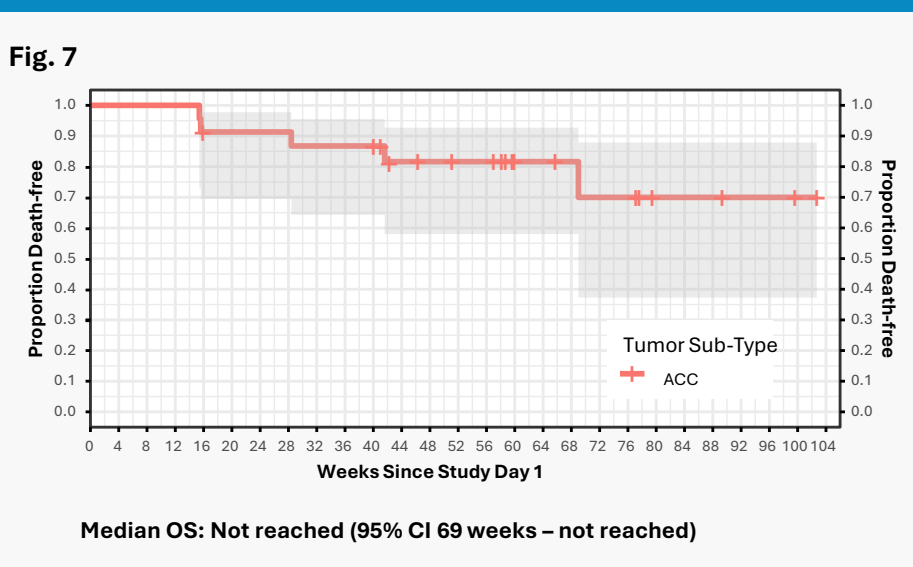


Fig 8: FAP Expression via FAPI-PET Imaging Persists Over Time Despite Deep Responses

Fig. 8A: Correlation of FAP expression by IHC v. FAPI-PET at Baseline

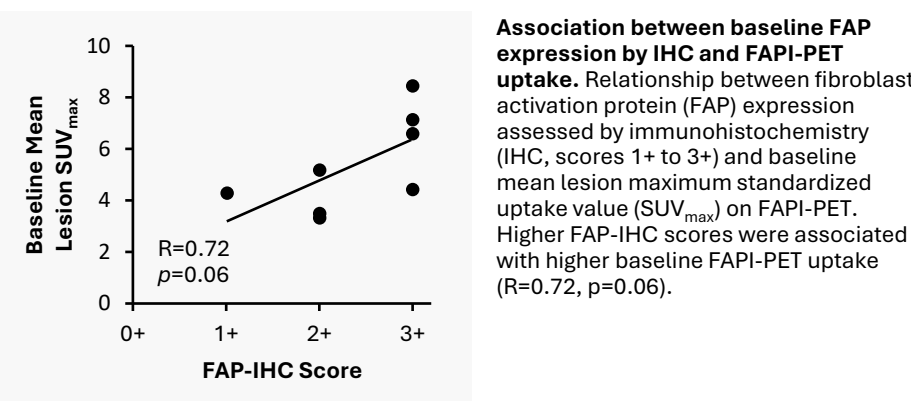


Fig. 8B: FAPI-PET signal over time in responders and non-responders

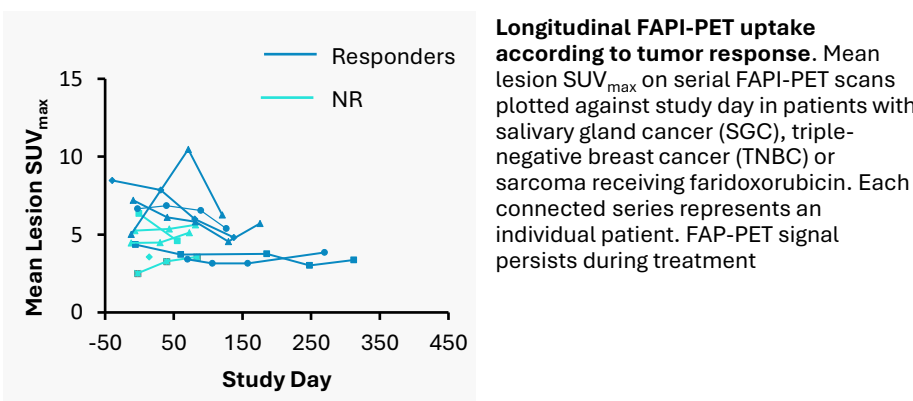
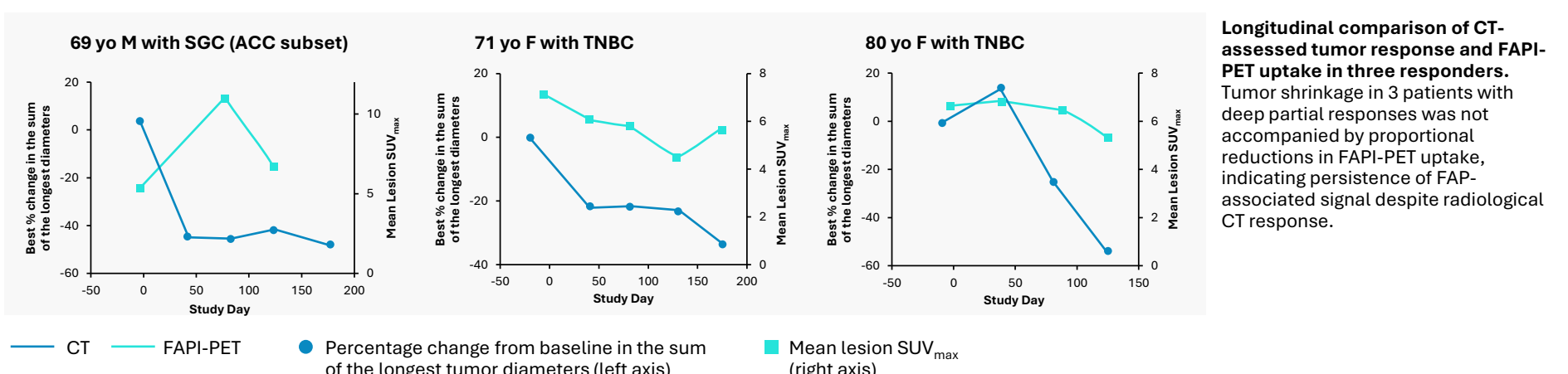
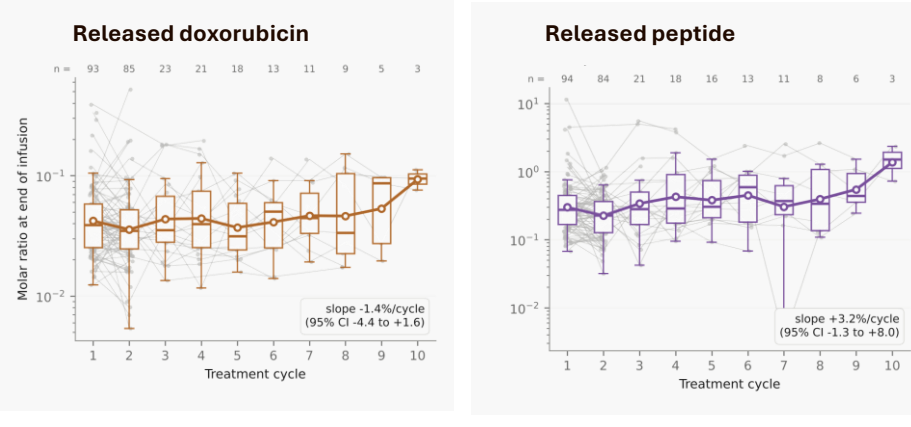


Fig. 8C: CT Assessment v. FAPI-PET assessments over time in 3 responders demonstrate persistent FAP expression despite tumor shrinkage



PK: Stable and Persistent Release of Doxorubicin and Peptide is Observed to at Least 10 Cycles

Fig. 11: Stable Release Over 10 Cycles

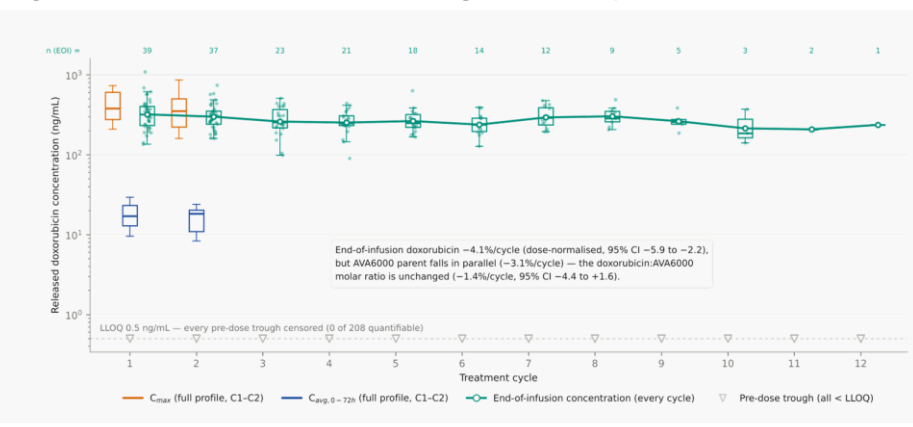


Metabolite-to-parent molar ratio at end of infusion is maintain

Grey = individual patients | colour = geometric mean | box = median and IQR. Log scale = Mixed-effect slope onto ratio, patient as random intercept.

PK: Release of Doxorubicin by Faridoxorubicin Cleavage Persists to 12 Cycles

Fig. 12: Persistent AVA6000 cleavage over 12 cycles



Doxorubicin release persists to Cycle 12 with no between-cycle accumulation (310 mg/m²)

End-of-infusion concentration is the only metric measured at every cycle and is directly comparable across them. Troughs are shown at shown at the LLQ because none were quantifiable.

CONCLUSIONS

- Faridoxorubicin (AVA6000) is safe and well-tolerated in patients with SGC and results in prolonged median PFS of 11.4 months (95% CI: 7 mos-not reached), exceeding benchmarks in the 1L and 2L setting by nearly two-fold across both cytotoxic chemotherapy and targeted therapy (median 6-6.7 months). Median OS in this population has not been reached.

- Multiple partial (n=3) and minor responses (n=6) observed in the SGC population with a range of duration (18.7-72 weeks)

- Biopsy data demonstrate a significant concentration of tumor to plasma of released doxorubicin of 100:1, resulting in tumor reductions even at low levels of FAP expression (1+)

- FAPI-PET imaging and FAP IHC data indicate that FAP expression in tumors does not diminish over time during treatment with faridoxorubicin

- Plasma PK studies out to 12 cycles of therapy indicate that cleavage of faridoxorubicin to peptide and doxorubicin by FAP is stable over time, indicating persistent FAP activity in tumors

References

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