FPA150 (B7-H4 antibody) Phase 1 Update in Advanced Solid Tumors: Monotherapy and in Combination with Pembrolizumab

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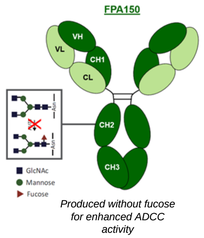
BACKGROUND

B7-H4:

- Transmembrane protein of the B7 family of T cell checkpoint ligands
- Shares significant homology with PD-L1 and PD-L2
- Expressed in 50-70% of breast and gynecologic malignancies



Produced without fucose for enhanced ADCC activity

FPA150
Fully human IgG1k monoclonal antibody
High affinity binding to B7-H4 IgV ectodomain • Fully cross-reactive with rodent and cyno B7-H4
T cell checkpoint blockade activity • FPA150 selected for its ability to relieve suppression of T cell activation by B7-H4
ADCC activity • FPA150 redirects FcγRIIIa+ effector cells (NK cells and macrophages) to eliminate B7-H4-expressing tumor cells • FPA150 is afucosylated and demonstrates higher affinity binding to FcγRIIIa and enhanced ADCC activity

FPA150 Demonstrates Dose-Dependent Antitumor Activity *In Vivo* and Elicits Complete Tumor Regressions in Combination with PD-1 Blockade

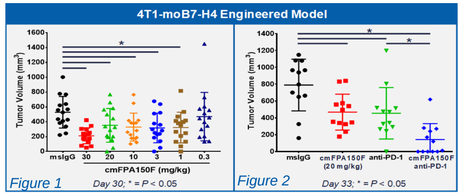


Figure 1 Day 30; * = $P < 0.05$ *Figure 2* Day 33; * = $P < 0.05$

- cmFPA150F is FPA150 engineered onto a msIgG2a Fc and is fucosylated
- Monotherapy demonstrates anti-tumor activity at ≥1 mg/kg in the engineered 4T1- and B16-moB7-H4/B7-H3 models (Figure 1)
- Results in complete tumor regressions at doses as low as 0.3 mg/kg in combination with anti-PD-1 blockade (Figure 2)

OBJECTIVES

Phase 1b Monotherapy FPA150 Expansion Objectives

Primary:

- Safety and tolerability of FPA150 as monotherapy in patients with B7-H4+ ovarian, breast and endometrial cancer

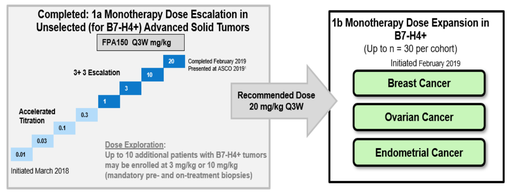
Phase 1a Combo FPA150 + Pembrolizumab Safety Lead-in Objectives

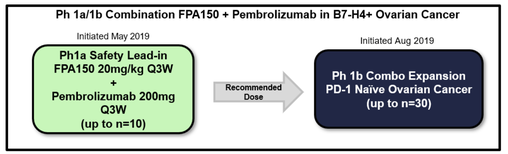
Primary:

- Safety and tolerability of FPA150 in combination with pembro in patients with B7-H4+ ovarian cancer
- Determine the MTD and/or RD of FPA150 in combination with pembro in patients with B7-H4+ ovarian cancer

METHODS

Study Schema: Phase 1a/1b Study of FPA150 ± Pembrolizumab in Advanced Solid Tumors





Data included in this presentation

DEMOGRAPHICS

Phase 1b Monotherapy FPA150 and Phase 1a Combination: Baseline Demographics and Prior Therapy

Characteristics	Phase 1b Mono FPA150 Ovarian, Endometrial, Breast Cancer (N=42)	Phase 1a Combo FPA150 + Pembro Ovarian Cancer (N=4)
Age, median (range)	62.5 (32-83)	59 years (55-67)
Female, n (%)	42 (100)	4 (100%)
ECOG	n (%)	n (%)
0	15 (35.7)	2 (50)
1	27 (64.3)	2 (50)
Prior anti-cancer treatments median (range)*	6 (2-16)*	6.5 (3-9)
Disease stage at study entry Stage IIIb/IV	34 (91.9)**	3 (75%)
Primary site of cancer	n (%)	n (%)
Ovary	15 (35.7)	4 (100)
Uterus	10 (23.8)	NA
Breast	17 (40.4)	NA

Data Cut Date 09 August 2019

*n=41
**n=37

RESULTS

Safety Summary

Safety Summary	Phase 1b Mono FPA150 Ovarian, Endometrial, Breast Cancer (N=42)	
	Most Common (>5%) Adverse Events N (%)	
	Preferred Term	All Grade	Grade 3
Treatment Emergent AEs	**Total # of Patients**	**28 (66.7%)**	**8 (19.0%)***
	Nausea	5 (11.9%)	0
	Vomiting	4 (9.5%)	0
	Abdominal pain	3 (7.1%)	2 (4.8%)
	Fever	3 (7.1%)	1 (2.4%)
	Constipation	3 (7.1%)	0
	Candida infection	3 (7.1%)	0
	Fatigue	3 (7.1%)	0
	Infusion-reaction	3 (7.1%)	0
	Flushing	3 (7.1%)	0
Treatment-Related AEs	**Total # of Patients**	**15 (35.7)**	**1 (2.4%)***
	Fatigue	3 (7.1%)	**0**
	Infusion reactions	3 (7.1%)	**0**

Data Cut Date 09 August 2019 *one patient had >G3 event (G4 hyponatremia and G5 sepsis) **pyrexia

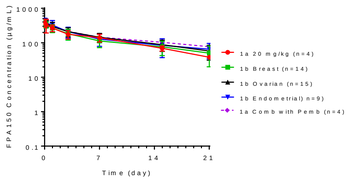
Safety: Phase 1b Monotherapy FPA150 (N=42)

- One patient had a Grade 4 event (hyponatremia) and a Grade 5 event (death due to sepsis). Neither event was treatment related.
- No patient discontinued FPA150 due to treatment-related toxicity
- 9 SAEs in 7 patients:
  - No SAE was treatment related
  - One event each of the following: sepsis (G5), hyponatremia (G4), CNS metastases (G3), gastro-esophageal reflux (G3), hematemesis (G3), nausea (G3), abdominal pain (G3), gastric obstruction (G3), dyspnea (G2)

Safety: Phase 1a Combination FPA150 + Pembro (N=4)

- No dose-limiting toxicities identified
- No ≥Grade 4 events
- No patient discontinued FPA150 due to treatment-related toxicity
- 3 SAEs in 2 patients:
  - No SAE was treatment related
  - One patient with small bowel obstruction (G3) and one with colitis (G2) and small bowel obstruction (G3)

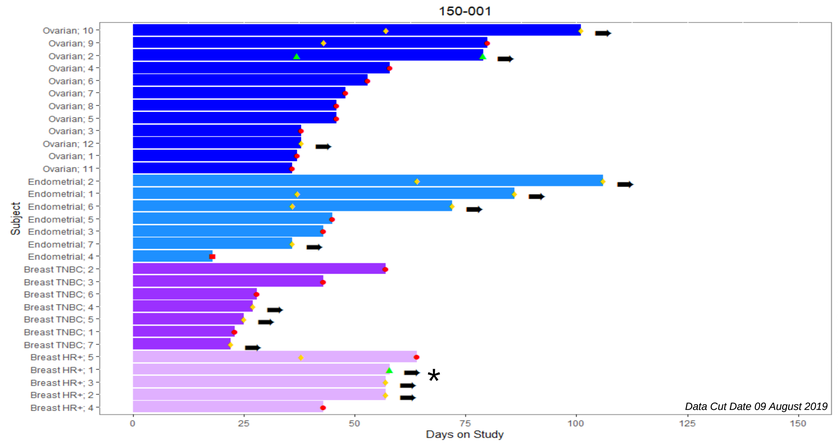
Serum concentration of FPA150 at 20mg/kg versus time profile is similar across tumor types and with/without pembrolizumab



Individual (symbol) and group mean (solid line) FPA150 serum concentration-time profile following first dose

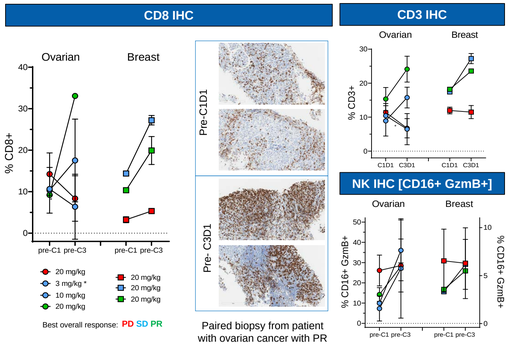
Observed trough concentration at the RD of 20mg/kg estimated to achieve ≥95% receptor saturation for both B7-H4 and FcγIIIa based on affinities

Phase 1b Monotherapy FPA150: Days on Study and Response by Tumor Type



*A partial response, based on target lesions, was reported at the first CT assessment, however, after the data cut of 09 Aug, the CT scan was reassessed a progression based on the identification of new lesions

Increased tumor infiltration of CD8+, CD3+ T cells and NK (CD16+GzmB+) cells observed in responding or stable tumors after treatment with monotherapy FPA150



Paired biopsy from patient with ovarian cancer with PR

Paired IHC analysis from biopsies obtained at baseline (pre-C1D1) and on treatment (pre-C3D1) with FPA150 (all available data as of 7/31/19)

CONCLUSIONS

- **Preliminary results provide the first clinical validation of B7H4 as a potential target**
- **Pharmacodynamic findings showing increased T and NK cell infiltration in tumors with SD and PR support immune-mediated MoA and the ongoing clinical evaluation of FPA150 in combination with an anti-PD1 antibody**
- **Highest clinical potential is likely to be in combination with anti-PD1 and standard of care therapy**
- **Phase 1b Monotherapy FPA150 in breast, ovarian and endometrial cancer**
  - RD of 20mg/kg is well tolerated
  - 2 confirmed PRs in ovarian cancer (one in dose escalation[1] and one at RD of 20mg/kg Q3W)
  - 11 patients with SD remain on therapy as of 9 August 2019
- **Phase 1a Combination FPA150 + Pembrolizumab in ovarian cancer**
  - Combination is well tolerated in the first 4 patients treated with FPA150 at 20mg/kg + pembro 200mg IV Q3W
  - Initiated enrollment in Phase 1b Combination Expansion cohort in August 2019
- **Lack of off-target toxicity suggests B7H4 may also be a potential target for anti-drug conjugates**

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Zev Wainberg has consulting agreements with Five Prime, Merck, Lily, Bayer, EMD Serono and research funding from BMS, Merck and Five Prime

1 Sachdev et al ASCO 2019