Phase 2 Clinical Trial of First-in-Class Fascin Inhibitor NP-G2-044 as Monotherapy and in Combination Therapy with anti-PD-1 Immunotherapy in Patients with Advanced Solid Tumor Malignancies

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Abstract # 3112

BACKGROUND:

Fascin is the main actin cross-linker in filopodia and its elevated levels are correlated with increased risk of cancer metastasis, disease progression and mortality. Pre-clinical evidence shows that deletion of the fascin gene delays tumor development, slows tumor growth, reduces metastatic colonization and increases overall survival. NP-G2-044 is a first-in-class fascin inhibitor that blocks tumor metastasis, inhibits cancer growth and increases antigen uptake by intra-tumoral dendritic cells. In a previously presented phase 1 clinical trial, the drug was well tolerated and demonstrated signals of anti-tumor and anti-metastatic activity.

METHODS:

Open-label study to establish recommended phase 2 dose (RP2D) of NP-G2-044 as both monotherapy (MT) and in combination therapy (CT) with anti-PD-1 immunotherapy (IO) followed by expansion cohorts.

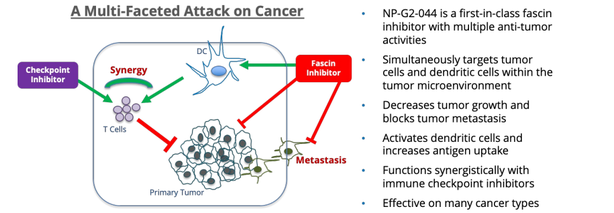
RESULTS:

MT-RP2D of 2100mg QD was selected based on a 16-patient comparative review of PK, safety, and efficacy between two highest doses previously identified in phase 1. No DLTs or drug-related SAEs were observed among MT-RP2D patients. As of the data cutoff date of November 30, 2023, the median PFS for 13 treatment-refractory GYN patients receiving the MT-RP2D was 20 weeks and more than 70% of these patients did not develop new metastases while on study. One patient (treatment-refractory ovarian cancer) was on study for over 26 months. Most common TEAEs observed for MT were diarrhea, fatigue and nausea. CT-RP2D of 1600 mg QD was selected. Among 33 enrolled CT patients evaluated to the data cutoff date of April 30, 2024, 87% of the enrolled pts had progressed on prior anti-PD(L)1. No DLTs were observed. SD or PR was observed in ~58% of CT patients including two confirmed RECIST PR (~50% reduction in tumor bulk) for a patient with cutaneous squamous cell cancer, and a patient with endometrial cancer (both had progressed on prior anti-PD(L)-1 therapies). Most common TEAEs observed for CT were diarrhea, transaminitis and nausea.

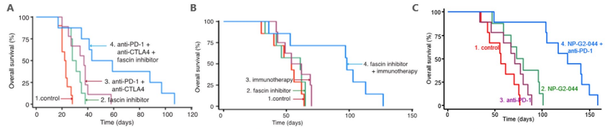
CONCLUSIONS:

The first-in-class fascin inhibitor, NP-G2-044, is safe and well tolerated administered both as MT and in CT with IO. Signals of anti-tumor and anti-metastatic activity were observed with both mono and combination therapy. A phase 2B/3 randomized clinical trial evaluating NP-G2-044 in combination with chemo in patients with platinum-resistant ovarian cancer (PROC) is in development. Additionally, a phase 2B study to further evaluate NP-G2-044 in combination with anti-PD-1 therapy in specific cancer indications is planned.

Background and Pre-Clinical Data



- NP-G2-044 is a first-in-class fascin inhibitor with multiple anti-tumor activities
- Simultaneously targets tumor cells and dendritic cells within the tumor microenvironment
- Decreases tumor growth and blocks tumor metastasis
- Activates dendritic cells and increases antigen uptake
- Functions synergistically with immune checkpoint inhibitors
- Effective on many cancer types



Lung cancer (LLC tumor cells with C57BL/6 mice)

Log rank test
2 vs. 1: 34%, p=0.002
3 vs. 1: 57%, p<0.001
4 vs. 1: 127%, p<0.001

Pancreatic cancer (Pan02 tumor cells with C57BL/6 mice)

Log rank test
2 vs. 1: 13%, p=0.33
3 vs. 1: 7%, p=0.18
4 vs. 1: 81%, p<0.001

Ovarian Cancer (ID8 cells with C57BL/6 mice)

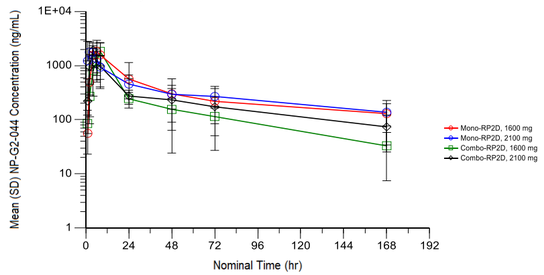
Log rank test
2 vs 1: 37%, p=0.02
3 vs 1: 37%, p=0.02
4 vs 1: 127%, p< 0.001

Methods and Study Design

- Open-label study designed to establish recommended phase 2 dose (RP2D) of NP-G2-044 administered as both monotherapy (MT) and in combination therapy (CT) with anti-PD-1 immunotherapy (IO).
- Efficacy assessed by RECIST 1.1 and iRECIST (CT patients only).
- Following MT-RP2D identification, additional treatment-refractory gynecologic (GYN) malignancies treated at the MT-RP2D.
- CT-RP2D established by a 3+3 design followed by expansion cohort in patients experiencing stable disease (SD) or progressive disease (PD) on prior anti-PD(L)-1 therapy.

Pharmacokinetics

- No statistical difference in PK parameters between monotherapy and IO combination therapy.



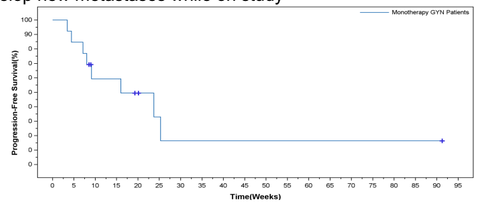
Safety

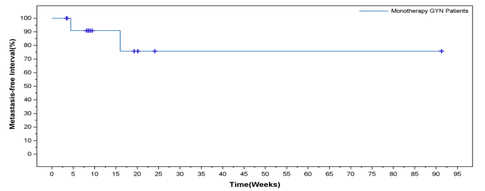
- No DLTs or drug-related SAEs observed among MT-RP2D
- No DLTs observed among CT-RP2D pts

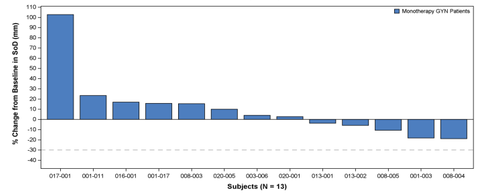
	Monotherapy in Treatment-Refractory GYN Cancers (N=15) n (%)	Combination Therapy with anti-PD-1 in Solid Tumors (N=33) n (%)
Subjects with any Study Drug Related TEAEs	14 (93.3%)	18 (56.3)
Subjects with Study Drug Related Grade 3/4/5 TEAEs	4 (26.7)	6 (18.8)
Subjects with any Serious AEs (SAEs)	7 (46.7)	10 (31.3)
Subjects with any Study Drug Related Serious AEs (SAEs)	0 (0.0)	2 (6.3)
Subjects with any TEAEs Leading to Study Drug Dose Reduction	1 (6.7)	1 (3.1)
Subjects with any TEAEs Leading to Study Drug Discontinuation	5 (33.3)	3 (9.4)
Subjects with any TEAEs Leading to Death	1 (6.7)	0 (0.0)
Any TEAEs with >/= 20% Occurrence	Diarrhea, Fatigue, Nausea, Vomiting, Abdominal pain, Decreased appetite, Dyspnoea, Weight decreased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Back pain, Headache, Hypokalaemia, Insomnia, Palpitations.	Diarrhea, Alanine aminotransferase increased, Aspartate aminotransferase increased, Nausea, Fatigue.

Anti-Tumor Efficacy - Monotherapy

- 13 treatment-refractory GYN ca. patients (10 with metastatic ovarian ca.)
- 85% (n=13) with stable disease after starting NP-G2-044
- Median PFS was 20 weeks and more than 70% of these patients did not develop new metastases while on study

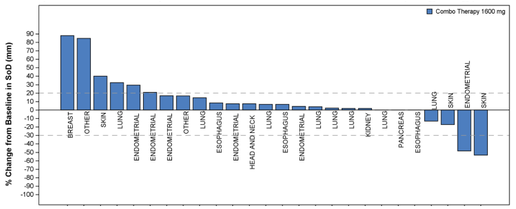


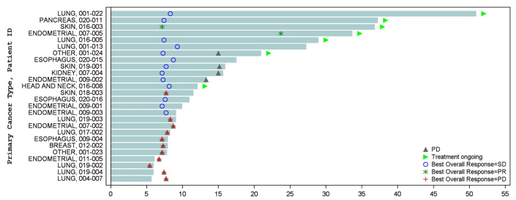


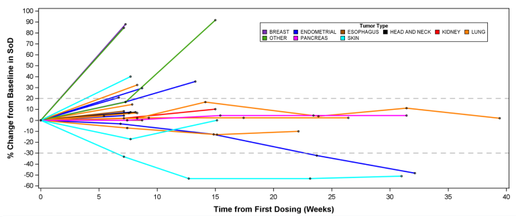


Anti-Tumor Efficacy - IO Combo Therapy

- 87% of the enrolled pts progressed on prior anti-PD(L)1 treatment
- 58% (n=26) derived clinical benefit (SD or PR) with addition of NP-G2-044
- 2 patients with confirmed PR (one cutaneous SCC, one endometrial ca.)
- One pancreatic ca. pt. on treatment for >9 months (ongoing)







Summary and Next Steps

- NP-G2-044 is the first fascin inhibitor used in clinical studies.
- Anti-tumor activity achieved through tandem ability to block tumor metastasis, inhibit tumor growth, and activate dendritic cells in the TME.
- Phase 1 and 2 clinical trials demonstrate favorable tolerability with both monotherapy and in combination with anti-PD-1 therapy.
- NP-G2-044 prolongs PFS and MFI for treatment-refractory GYN cancers as monotherapy.
- Durable RECIST 1.1 responses observed among PD-1 progressors when NP-G2-044 added as combination therapy.
- Two trials anticipated to commence in 2025:
  - Phase 2B/3 study of NP-G2-044 in combination with chemo in PROC patients;
  - Phase 2B study of NP-G2-044 in combination with anti-PD-1 in specific cancer indications.
- The Sponsor wishes to thank the patients and their families who participated in this clinical trial.