Phase 2 Study of NP-G2-044, a Novel Fascin Inhibitor, in Combination with Anti-PD-1 Therapy in Patients with Solid Tumors Resistant to Prior Anti-PD-1 Therapy

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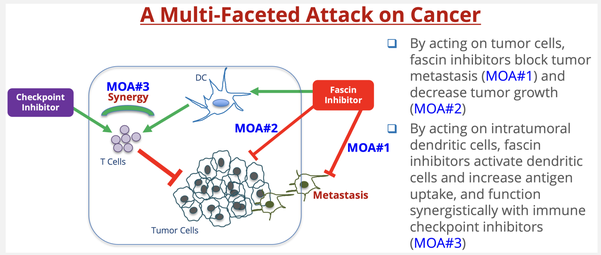
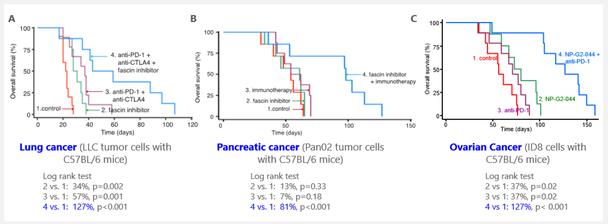
BACKGROUND

- Fascin Inhibition: NP-G2-044 is a first-in-class oral fascin inhibitor that targets fascin in both tumor cells and intratumoral dendritic cells (DCs). Fascin, the primary actin-bundling protein, is critical for cell migration and metastasis.
- Mechanism of Action: NP-G2-044 blocks tumor metastasis, reduces tumor growth, and activates intratumoral DCs. By enhancing antigen uptake and expanding activated DCs, it promotes proliferation of $CD8^+$ T cells and synergizes with immune checkpoint inhibitors (ICIs).
- Clinical Experience: Over 100 patients with treatment-refractory solid tumors have received NP-G2-044 with no dose-limiting toxicities. More than 70% did not develop new metastases on treatment.

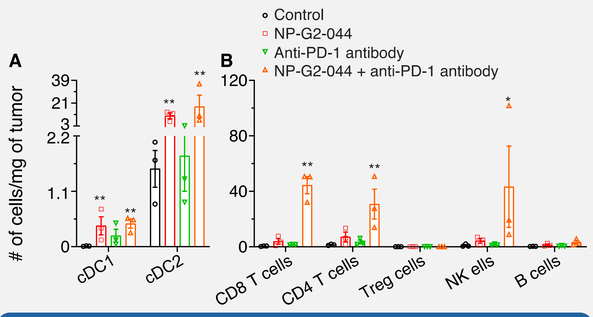


Pre-Clinical Data

NP-G2-044 synergistically increases overall survival when combined with anti-PD-1 antibody.



NP-G2-044 promotes intratumoral dendritic cell accumulation and activation.



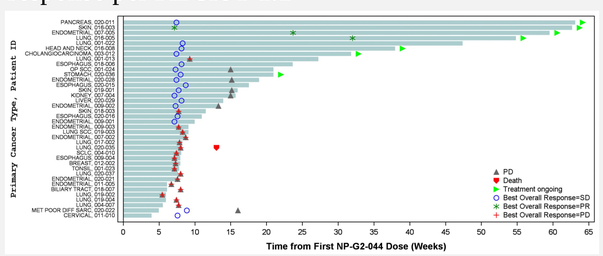
Clinical Data: Study Design

- Phase 2 Study: NP-G2-044 in combination with standard-of-care (SOC) anti–PD-1 therapy in patients with advanced solid tumors that were non-responsive or had relapsed following prior anti–PD-(L)1 treatments.
- Population: 45 patients enrolled; 80% had progressed on prior anti–PD-(L)1 and are evaluable for safety.
- Safety: Self-limiting elevations of liver enzymes (LFTs) were the most common adverse events, often preceding onset of response.

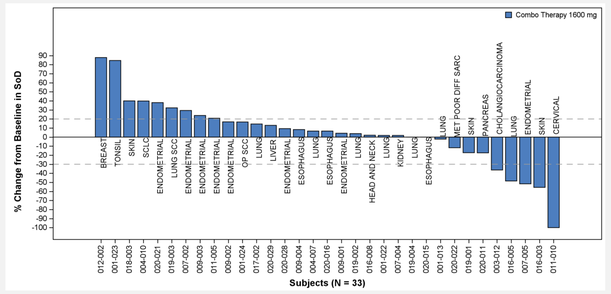
Anti-Tumor Efficacy

- Evaluable for Activity: 33 patients.
- Objective Response Rate (ORR = CR + PR): 21% (includes 2 pathological CRs).
- Disease Control Rate (DCR = SD + CR + PR): 76%.

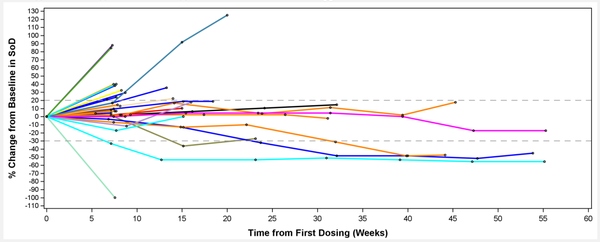
Swimmer plot of treatment duration and tumor response per RECIST 1.1



Waterfall plot of best percent change from baseline



Spider plot of percent change from baseline



Notable Responses

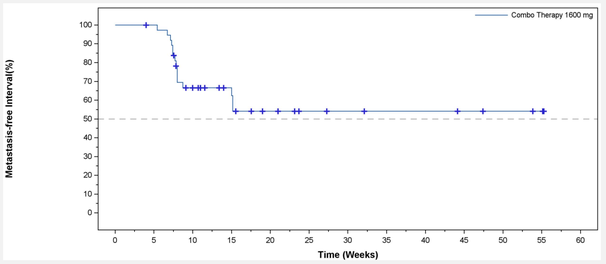
- Pancreatic Cancer: Pathological CR, PET complete metabolic response (Cycle 17).
- Endometrial Cancer: RECIST CR in target lesion (Cycle 19).
- Cutaneous Squamous Cell Carcinoma: RECIST PR (clinical CR), off study after Cycle 16.
- Stage IV NSCLC: RECIST PR, off study after Cycle 16.
- Locally Advanced Cervical Cancer: RECIST CR.
- Cholangiocarcinoma: RECIST PR (Cycle 12).
- G/E Junction Adenocarcinoma: Pathological CR, off study after 4 cycles.

CT/PET Scans (Cervical Cancer)

Baseline CT | Day 25 CT (CR) | 3-month follow-up PET/CT (CR)

Anti-Metastasis Efficacy

- Kaplan-Meier Plot for Metastasis-free Interval per RECIST 1.1
- All patients had multiple metastatic sites before study entry
- The estimated new metastasis free survival through combination at 1 year is 55%.



Safety / Adverse Events

- No DLTs observed among the patients

Subjects with Any TEAEs of >= 20% Occurrence	36(80.0)
Diarrhoea	19(42.2)
Fatigue	17(37.8)
Nausea	17(37.8)
Alanine aminotransferase increased	14(31.1)
Aspartate aminotransferase increased	14(31.1)
Vomiting	11(24.4)
Decreased appetite	9(20.0)

CONCLUSIONS

- NP-G2-044, a novel fascin inhibitor, shows promising activity in combination with ICIs for heavily pretreated, ICI-refractory solid tumors.
- Findings suggest dual benefits: inhibition of metastasis and enhancement of anti-tumor immune response.
- An amendment to this study is underway to open additional cohorts and further explore NP-G2-044's therapeutic potential across diverse tumor types.

ACKNOWLEDGEMENTS

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