2025 ASCO® ANNUAL MEETING

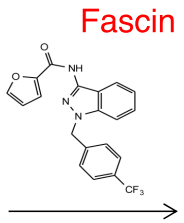
Durable responses in ICI-refractory or acquired resistance: Phase 2 study of NP-G2-044 combined with anti-PD-1 therapy

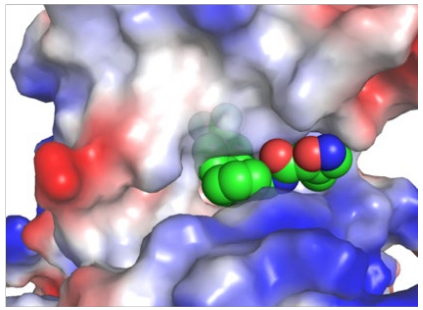
Anup Kasi, Michael J. Birrer, Jason R. Brown, Sanjay Chandrasekaran, Vincent Chung, Richard Frank, Shirish Gadgeel, Thomas J. George, Shadia I. Jalal, Alberto Mendivil, Andrew Poklepovic, Jennifer Segar, Alexander Spira, Janos Tanyi, J. Jillian Zhang, Xin-Yun Huang, Jose Jimeno, and Frank Tsai

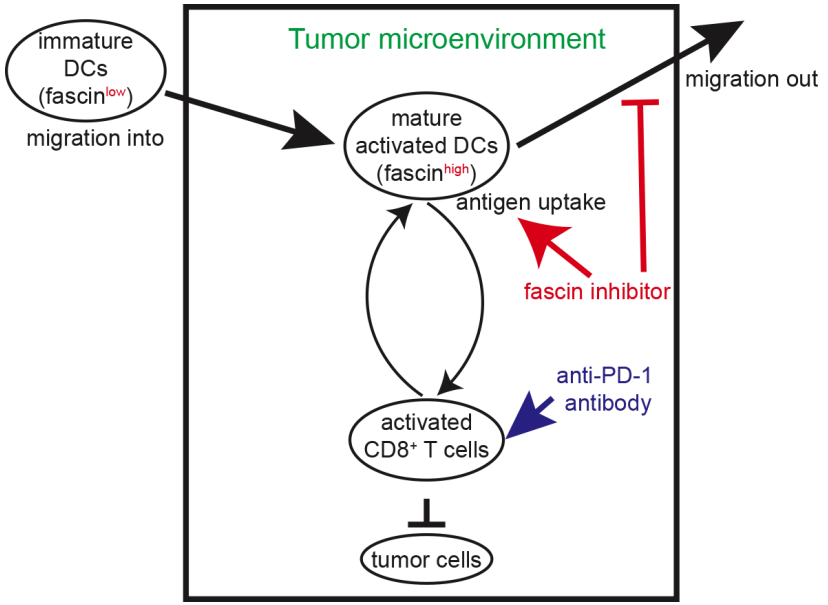
Anup Kasi, MD, University of Kansas Medical Center

Background and Rationale: NP-G2-044, a First-in-Class Fascin Inhibitor

- Small molecule oral drug
- Disrupts tumor cell motility/invasion and blocks metastasis
- Enhances intra-tumoral dendritic cell (DC) activation and CD8⁺ T-cell expansion
- Synergizes with anti–PD-1 to overcome ICI-resistance in many tumor types







Overview of Phase 2 Study IO Combo Arm

Population: Advanced/metastatic solid tumors with primary or acquired resistance to anti–PD-(L)1 therapy

Intervention: NP-G2-044 + Standard-of-Care anti–PD-1

Endpoints: Primary: ORR (RECIST); Secondary: PFS, DOR, DCR, safety

Prior lines of therapy: median 2 (range 1 – 9)

Key Takeaway Points/Conclusions

Objective Response Rate (ORR): 21% (7/33)

Disease Control Rate (DCR): 76%

Durable responses observed in seven indications:

CRs (n=4) (12%): 1 RECIST (cervical), 2 pathological (PDAC, G/E), 1 clinical (CSCC)

PRs (n=3): RECIST (endometrial, NSCLC, cholangiocarcinoma)

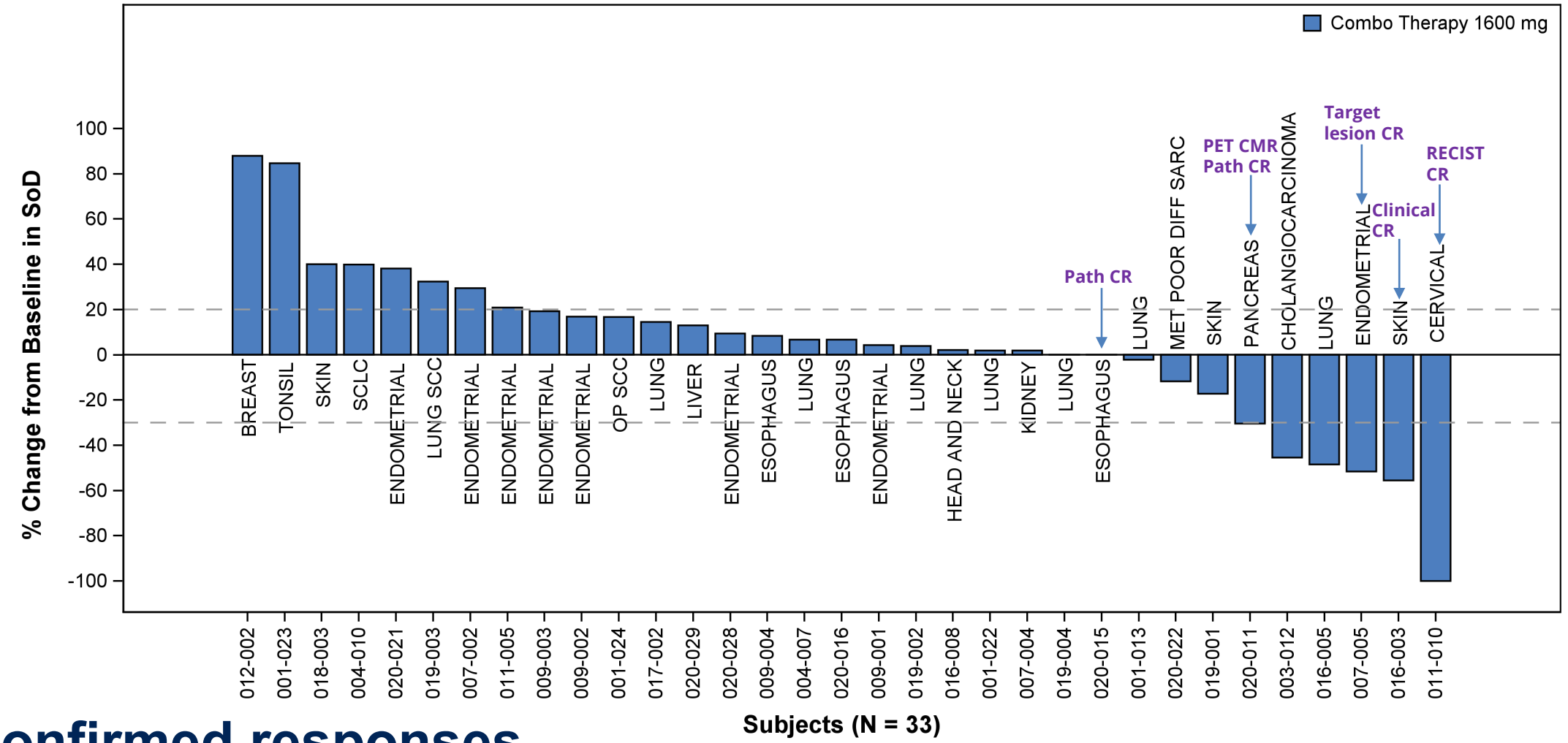
Safety profile:

No DLT

No new safety signals when combined with anti-PD-1

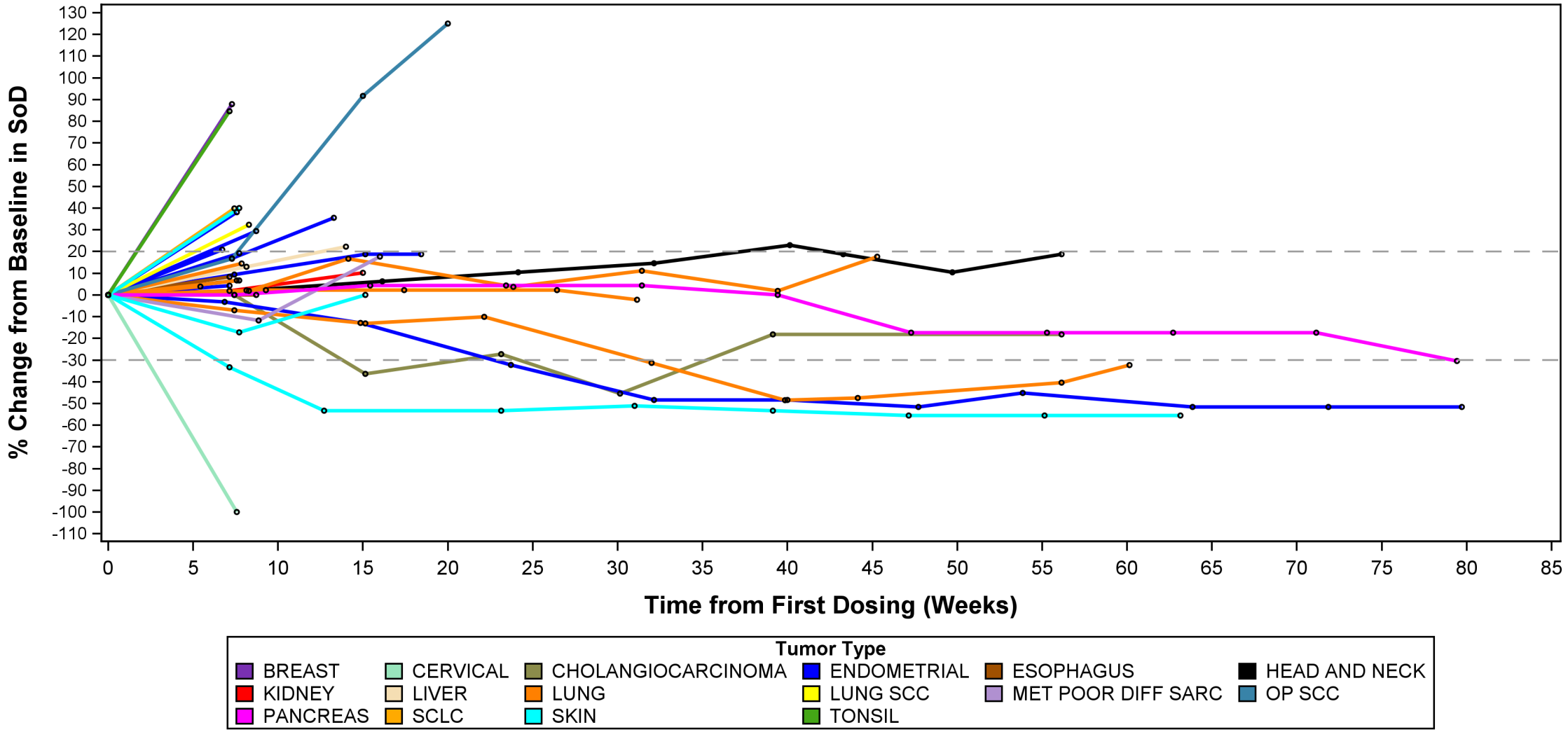
Lack of cumulative toxicities

Results: Pan-Tumor Efficacy

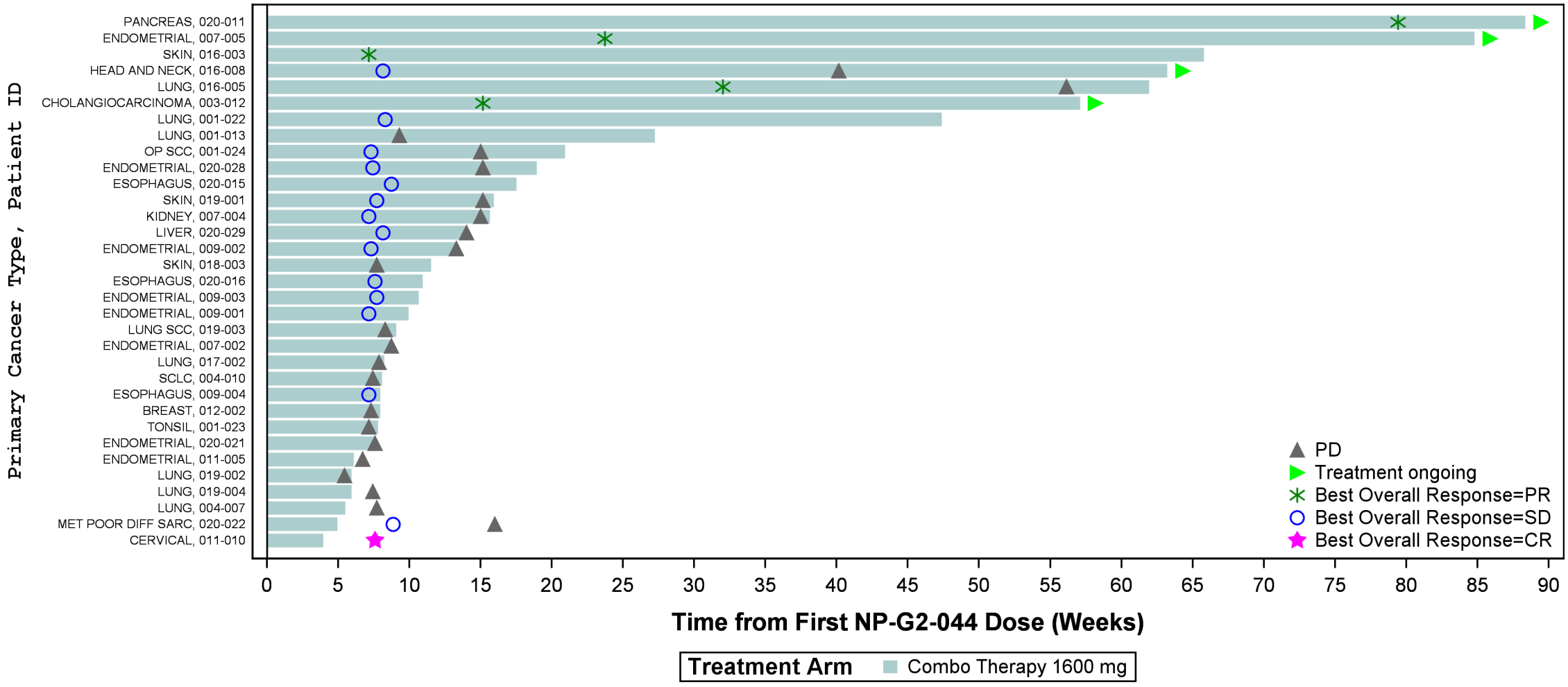


Confirmed responses

Results: Long-lasting Disease Control



Results: Durable Responses

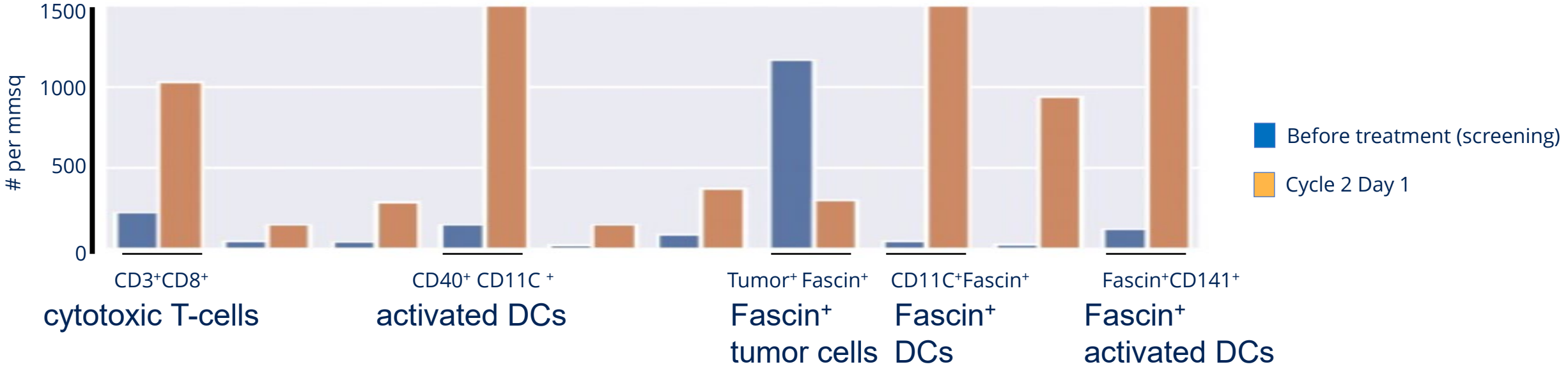


Safety Profile

NP-G2-044 + anti-PD-1 Combination Treatment-Related Adverse Events (n=45)				
	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)
Alanine aminotransferase increased	13.3	13.3	13.3	4.4
Aspartate aminotransferase increased	15.6	11.1	11.1	0
Fatigue	17.8	4.4	0	0
Diarrhea	13.3	8.9	4.4	0
Nausea	4.4	6.7	0	0
Decreased appetite	2.2	2.2	0	0
Vomiting	0	2.2	0	0
There were no Grade 5 events reported				

Mechanistic Insights

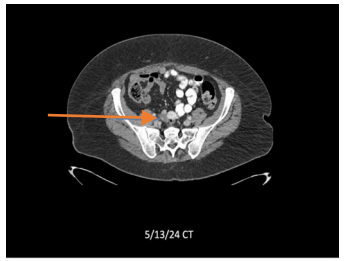
- Multiplex Immunofluorescence and Flow Cytometry (tumor biopsies):
  - Increased intratumoral cytotoxic T-cell infiltration
  - Enhanced T-cell proliferation and granzyme B expression
  - Expanded activated DCs in tumor microenvironment
- Conclusion: Supports proposed MOA of fascin inhibition + immune activation



Case Reports:

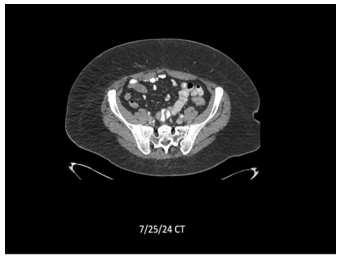
Cervical Cancer:
CR

5/2024



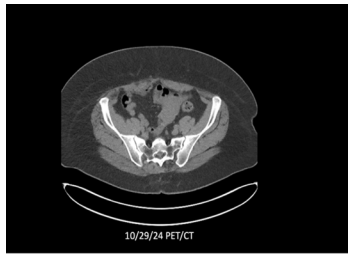
Baseline

7/2024 (CR)



CR Day 25

10/2024 (CR)

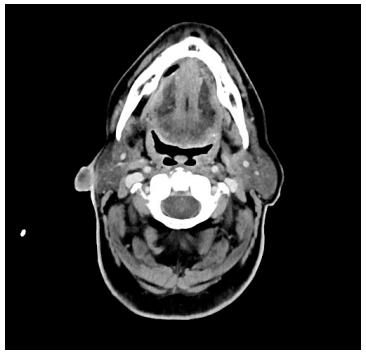


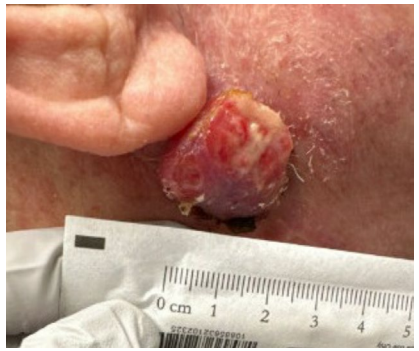
CR by PET follow-up

Still disease free (without other treatments) as of 5/2025

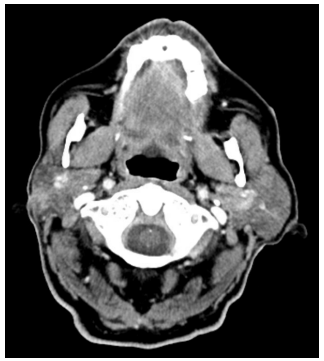
Cutaneous SCC:
Clinical CR

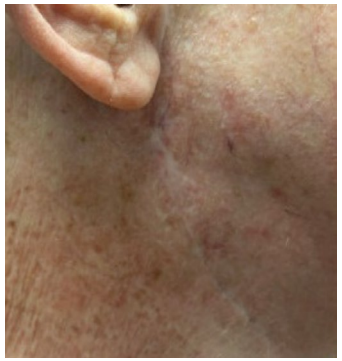
8/2023





11/2024 EOT

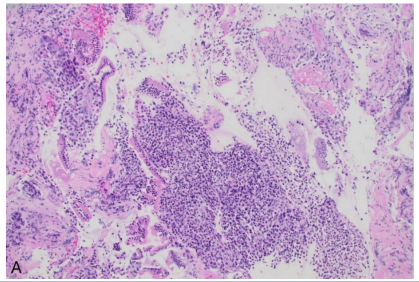




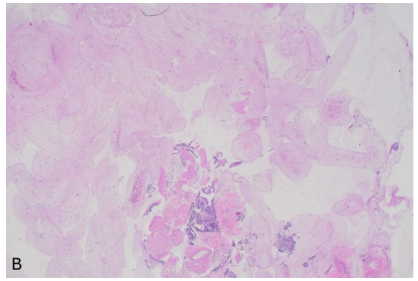
Still disease free (without other treatments)

Pancreatic cancer:
PET CR,
Path CR,
RECIST PR

Baseline



4 months after treatment



Still under treatment

Summary and Conclusion

- Efficacy: 21% ORR and 76% DCR; Overcomes ICI resistance in multiple tumor types
- Metastasis control: 55% had no new metastases; synergy with anti–PD-1
- Safety: Well tolerated with some patients on treatment approaching 2 years, Manageable and transient AEs
- Durability: Duration of response of up to 19 months

Future Directions & Acknowledgments

- Future Directions:
  Additional cohorts to refine optimal tumor types
  Correlative studies to identify predictive biomarkers

- Acknowledgments:
  Patients, families, site staff, and collaborators
  Funding source: Novita Pharmaceuticals, Inc.