Phase 2, Multi-Arm Study of Niraparib in Combination With a PD-1 Inhibitor in Patients With Non–Small Cell Lung Cancer: JASPER

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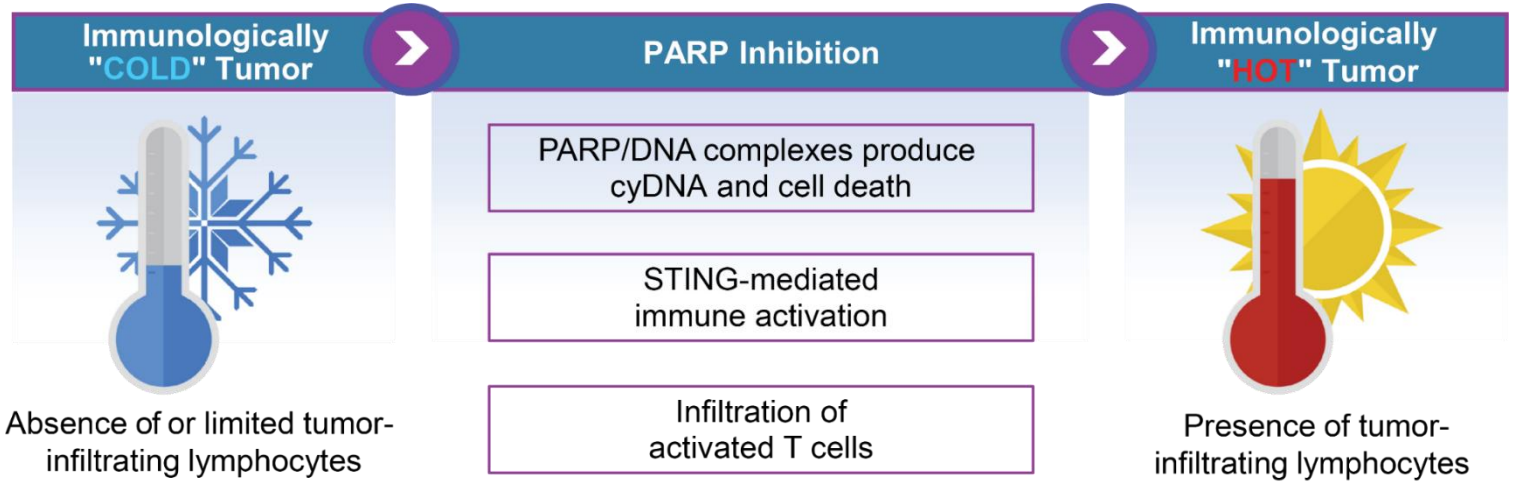
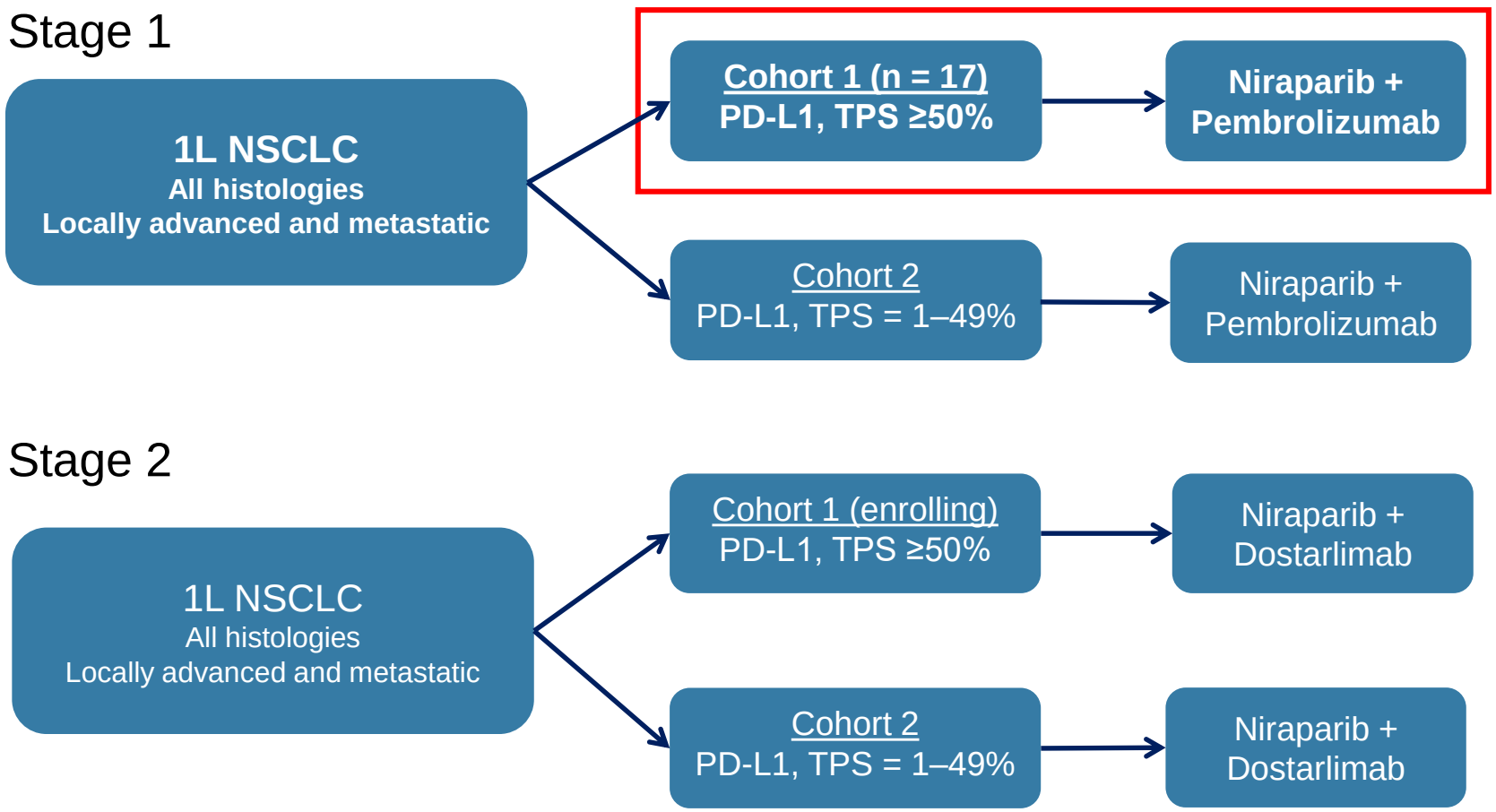
Introduction

- Poly(ADP-ribose) polymerase (PARP) is a protein involved in repairing single-strand DNA breaks
- Niraparib is a PARP inhibitor (PARPi) approved for maintenance treatment of recurrent ovarian cancer
- PARPi have been shown to enhance tumor immune response through Stimulator of Interferon Genes (STING) pathway, and synergize with anti-PD-1 therapies in both preclinical and clinical studies
- JASPER trial was designed to assess the activity of the combination of PARPi and PD-1 inhibitor (pembrolizumab or dostarlimab) in first line NSCLC
- Dostarlimab (TSR-042) is an investigational humanized PD-1 monoclonal antibody that binds with high affinity to the PD-1 receptor and effectively blocks its interaction with the PD-L1 and PD-L2; Dostarlimab has shown promising activity in several tumor types including NSCLC



JASPER Trial Design and Endpoints



Data from Stage 1/Cohort 1 will be presented today

Primary Endpoints

- Objective response rate (ORR)

Secondary Endpoints

- Safety and tolerability of niraparib + a PD-1 inhibitor
- Duration of response (DOR)
- Disease control rate (DCR)
- Progression-free survival (PFS)
- Overall survival (OS)
- Pharmacokinetics (PK)

NSCLC, non–small cell lung cancer; TPS, tumor proportion score.

Demographics and Baseline Characteristics: Stage 1/Cohort 1

Characteristic	Cohort 1 (n = 17)
Age, median, years	72
Sex, n (%)	
Female	6 (35)
Male	11 (65)
ECOG performance status, n (%)	
0	5 (29)
1	12 (71)
Overall cancer stage at enrollment, n (%)	
Stage IIIB/advanced (unresectable)	1 (6)
Stage IV/metastatic	16 (94)
Histology at diagnosis, n (%)	
Adenocarcinoma	11 (65)
Squamous cell carcinoma	5 (29)
Other	1 (6)

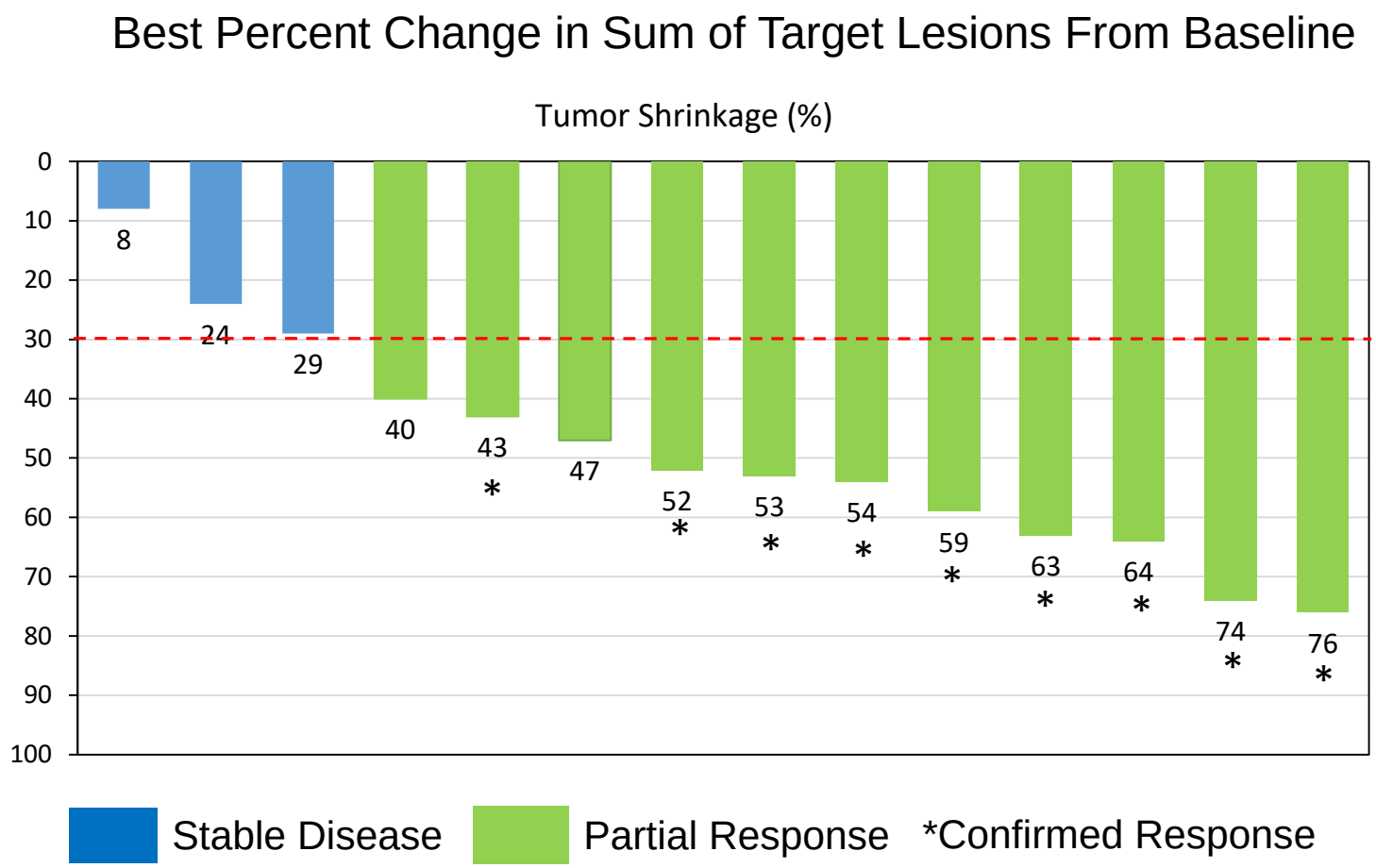
Data cut: January 28, 2019.
ECOG, Eastern Cooperative Oncology Group.

- Patients with known *EGFR* sensitizing mutation and/or *ROS1* or *ALK* translocations were excluded from the study
- Two patients were known *KRAS* mutation positive
- One patient who withdrew consent before first scan was included in safety but not in the efficacy analysis as prespecified in the study protocol

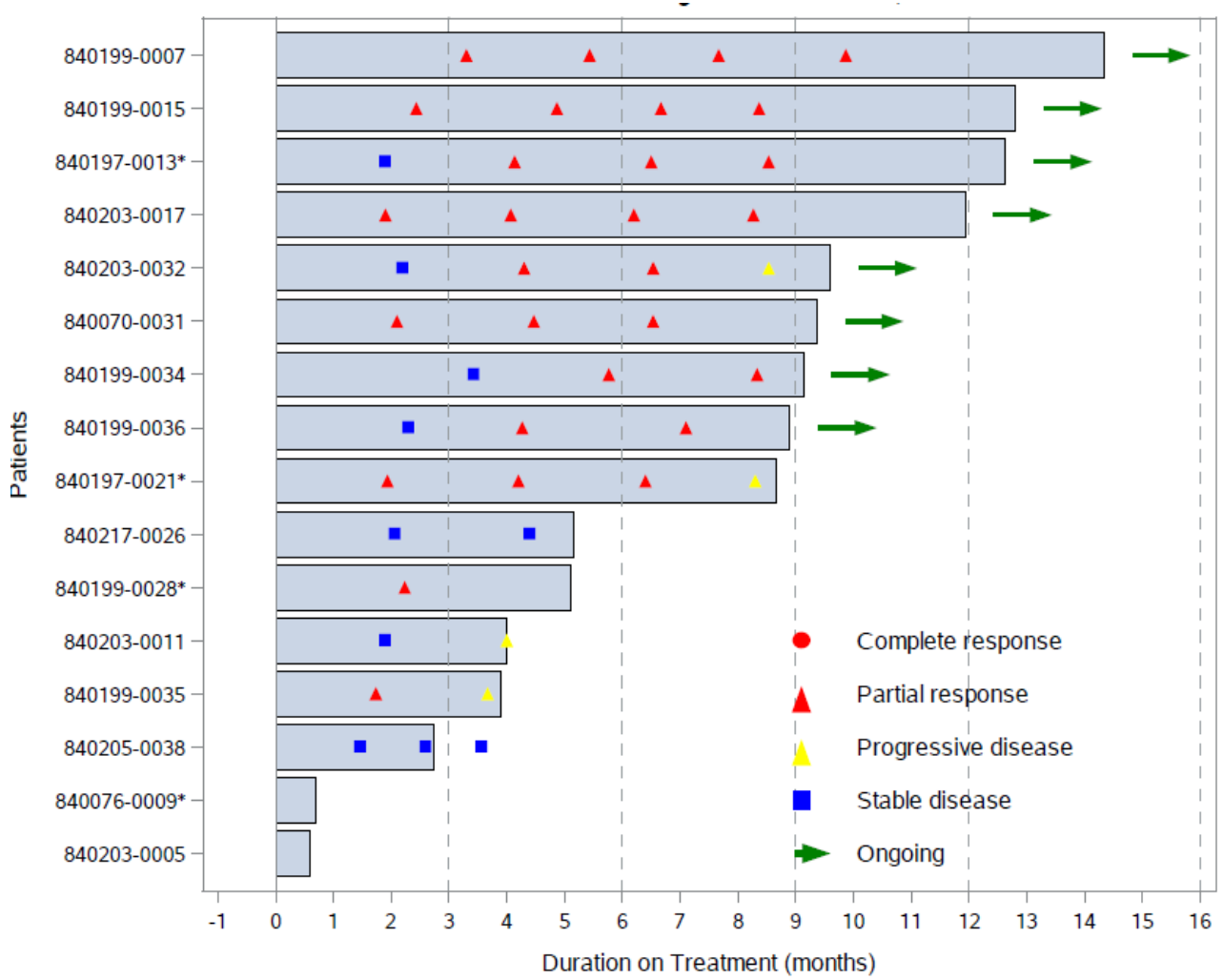
Efficacy Results: Stage 1/Cohort 1

Best Overall Response RECIST, n	Cohort 1 (n = 16)
Patients with at least 1 on-treatment scan	14†
Complete response	0
Partial response	11‡
Stable disease	3
Progressive disease	0

†Two patients discontinued before scan
‡ Includes 9 confirmed and 2 unconfirmed partial responses
RECIST, Response Evaluation Criteria in Solid Tumors.



Duration of Response: Stage 1/Cohort 1



- All 9 confirmed PRs were on treatment for >8 months; 4 have been on treatment about a year or more
- 8 patients are still on treatment

Safety: Stage 1/Cohort 1 AEs in ≥10% of patients

Preferred Term ≥ Grade 2, n (%)	Cohort 1 (n = 17)
Nausea	4 (23.5)
Fatigue	4 (23.5)
Pneumonia	4 (23.5)
Decreased appetite	4 (23.5)
Dyspnoea	4 (23.5)
Anaemia	3 (17.6)
Anxiety	3 (17.6)
Insomnia	3 (17.6)
Back pain	2 (11.8)
Weight decreased	2 (11.8)

AE, adverse event.

Preferred Term ≥Grade 3 drug-related, n (%)	Cohort 1 (n = 17)
Patients with at least 1 grade ≥3 drug-related AE	**9 (53)**
Anemia	2 (12) (Grade 3)[a]
Fatigue	1 (6) (Grade 3)[a] 1 (6) (Grade 3)[a,b]
Platelet count decreased	1 (6) (Grade 3)[a]

[a] Related to niraparib.
[b] Related to pembrolizumab.

JASPER: Enrollment initiated in stage 2 of niraparib + dostarlimab

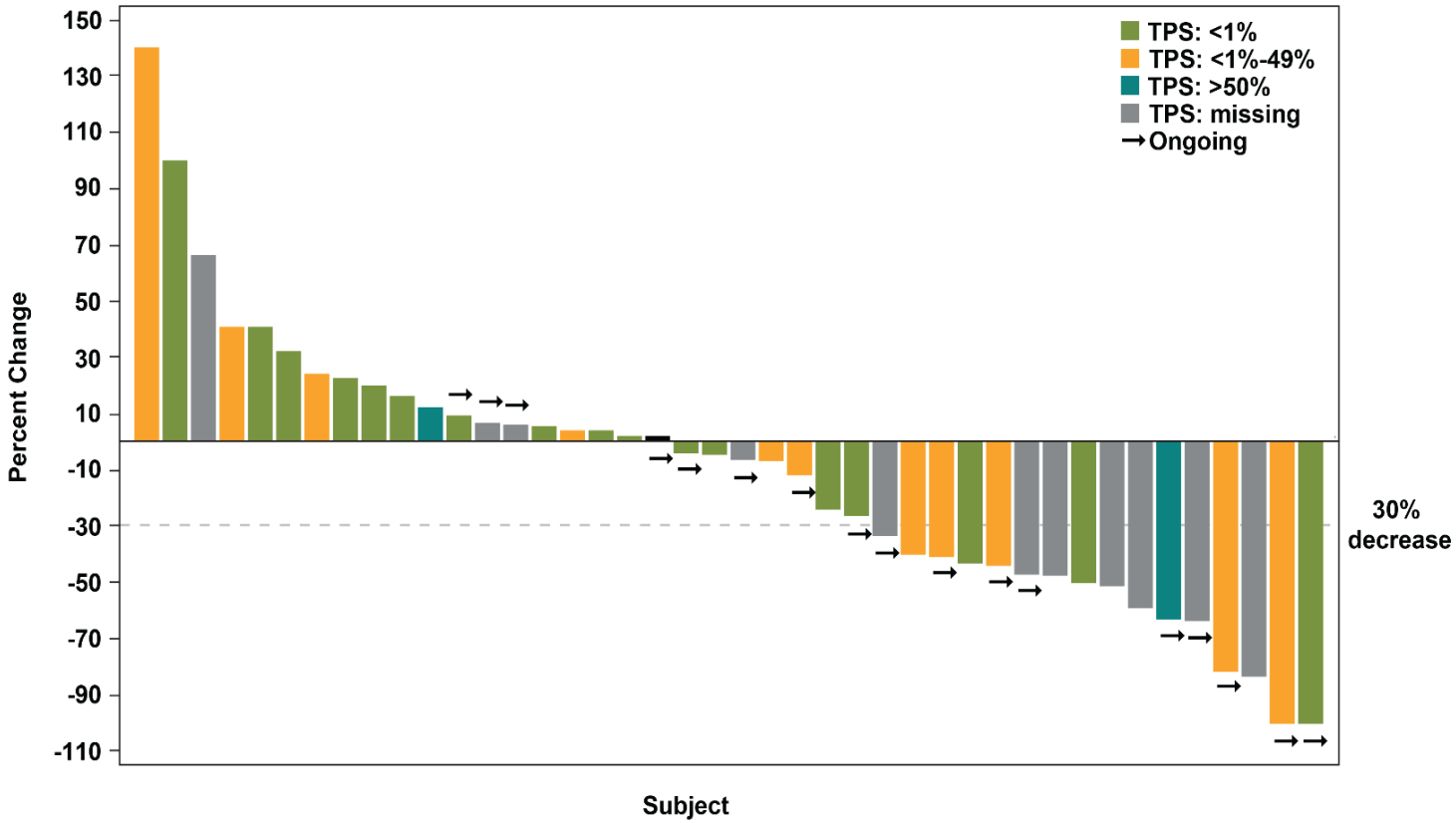
Stage 2

1L NSCLC
All histologies
Locally advanced and metastatic

Cohort 1 (enrolling)
PD-L1, TPS ≥50%

Niraparib + Dostarlimab

Best Percentage Change by PD-L1 TPS Score in Sum of Target Lesion from Baseline (irRECIST)



NSCLC, non–small cell lung cancer; TPS, tumor proportion score.

Conclusions and Future Directions

- Preliminary efficacy results for niraparib in combination with PD-1 inhibitor are encouraging
  - Responses were seen in 11 (9 confirmed) of 16 patients with TPS ≥ 50%
  - All 9 confirmed PRs were on treatment for >8 months
  - 8 patients continue on treatment
- Safety is consistent with prior clinical experience of niraparib and pembrolizumab, as monotherapy or in combination, in other tumor types
- Currently enrolling cohort of TPS ≥ 50% with combination of niraparib and dostarlimab

Acknowledgements

We thank the patients and their families for participating in this study, as well as the study teams at each of the study sites.