NextCure

NC318 PHASE 1/2 CLINICAL TRIAL: PHASE 1 DATA AND PHASE 2 PLANS

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NATIONAL HARBOR, MARYLAND

November 9, 2019

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AGENDA

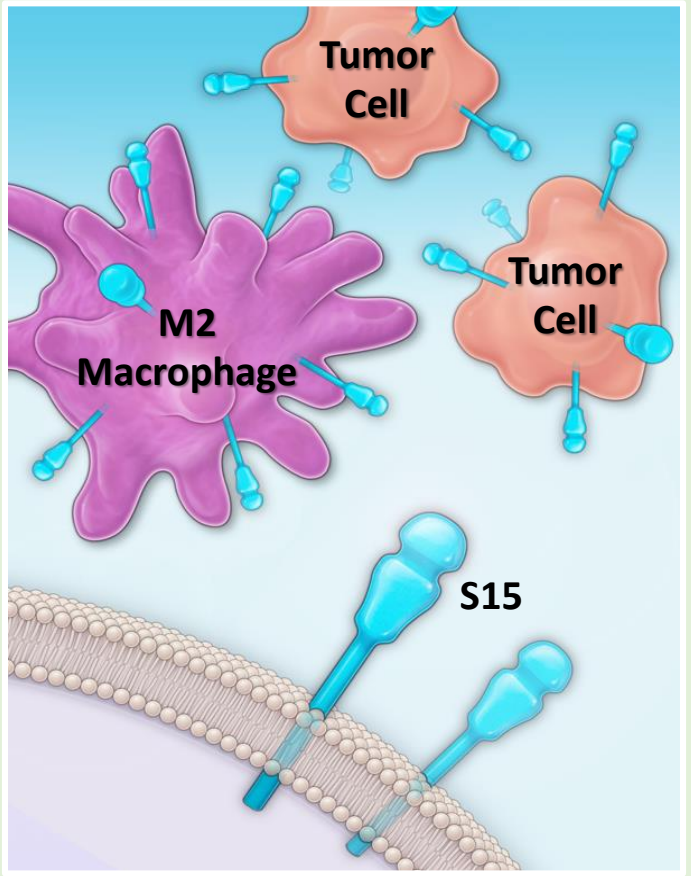
- Introductions
- Review of NC318 Phase 1 Trial Data
- Future Plans for NC318
- Q&A

Single agent anti-tumor activity in PD-1 refractory NSCLC: phase 1 data from the first-in-human trial of NC318, a Siglec-15-targeted antibody

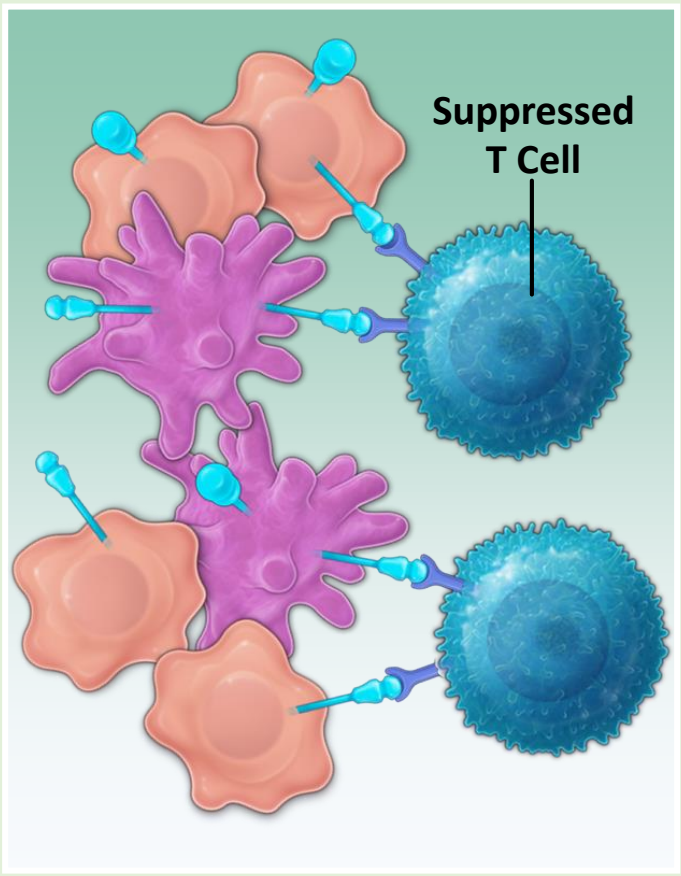
Anthony Tolcher, Omid Hamid, Jeffrey Weber, Patricia LoRusso, Kathryn Shantz, Kevin N. Heller, and Martin Gutierrez

SIGLEC-15 (S15) AS A TARGET

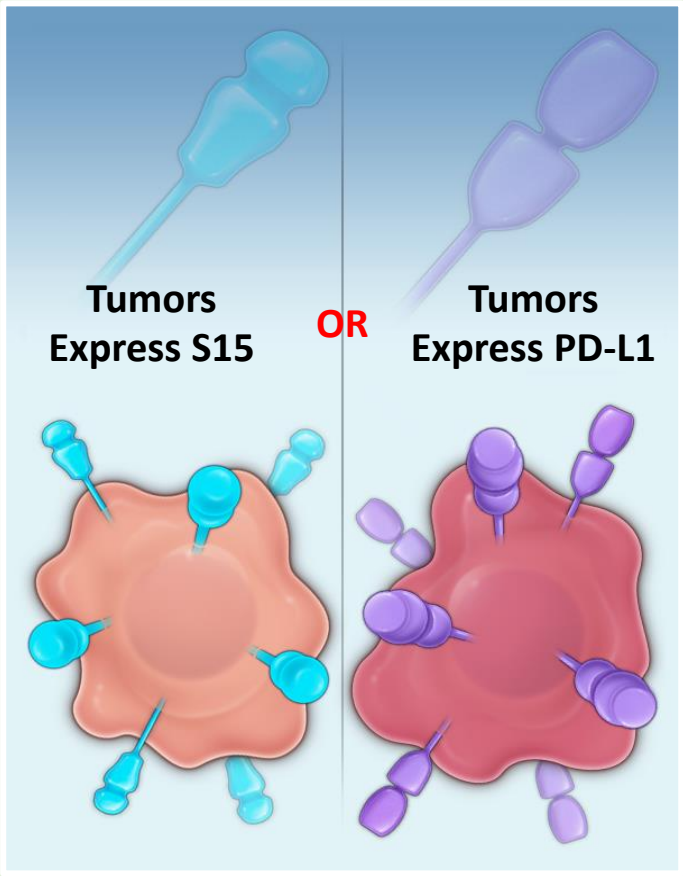
EXPRESSED ON TUMORS AND M2 MACROPHAGES



SIGLEC-15 SUPPRESSES T CELL FUNCTION

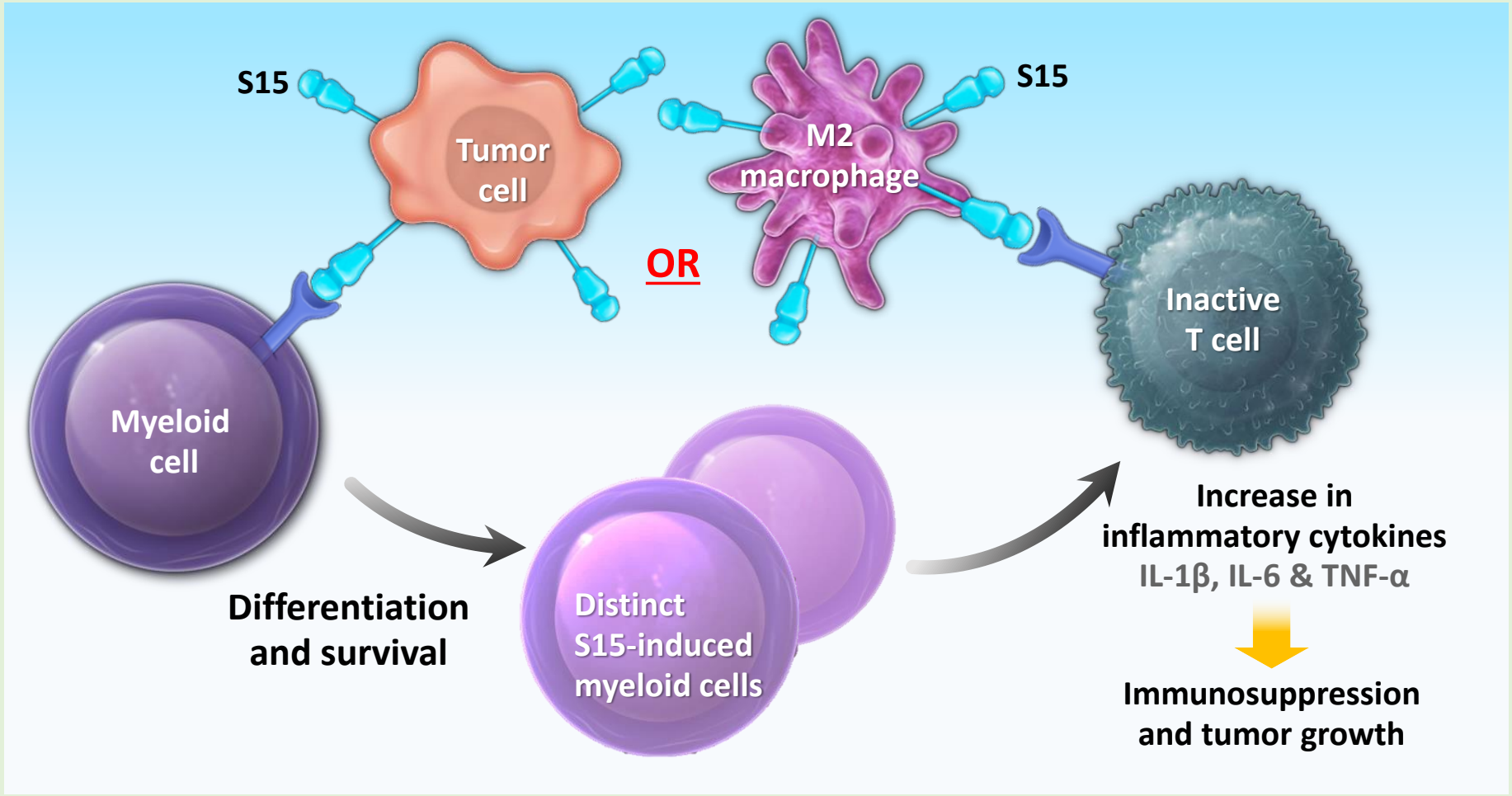


EXPRESION IS NON-OVERLAPPING WITH PD-L1



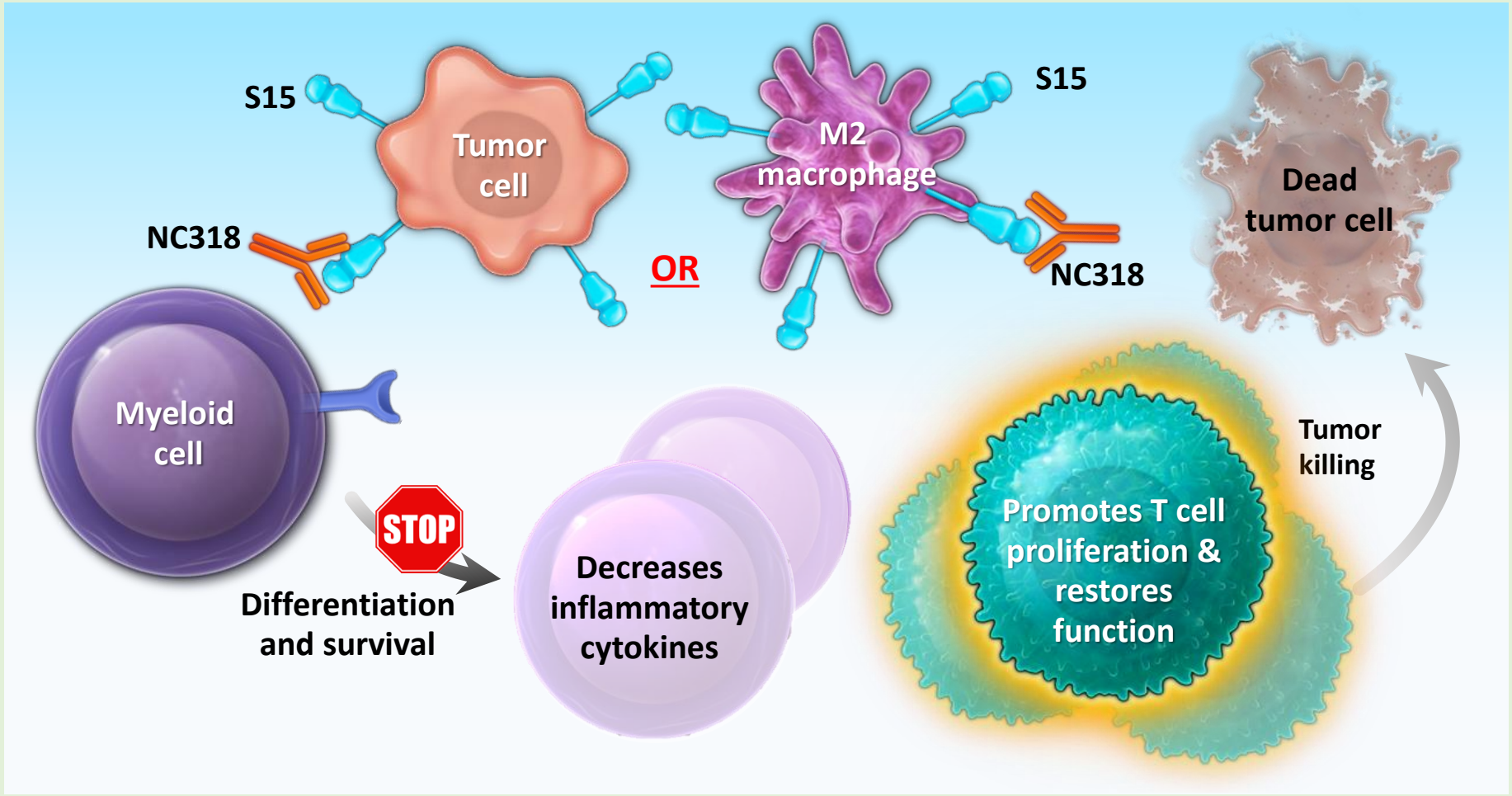
From NextCure, Inc. data on file

S15 IS HIGHLY IMMUNOSUPPRESSIVE IN THE TME IN MULTIPLE TUMORS



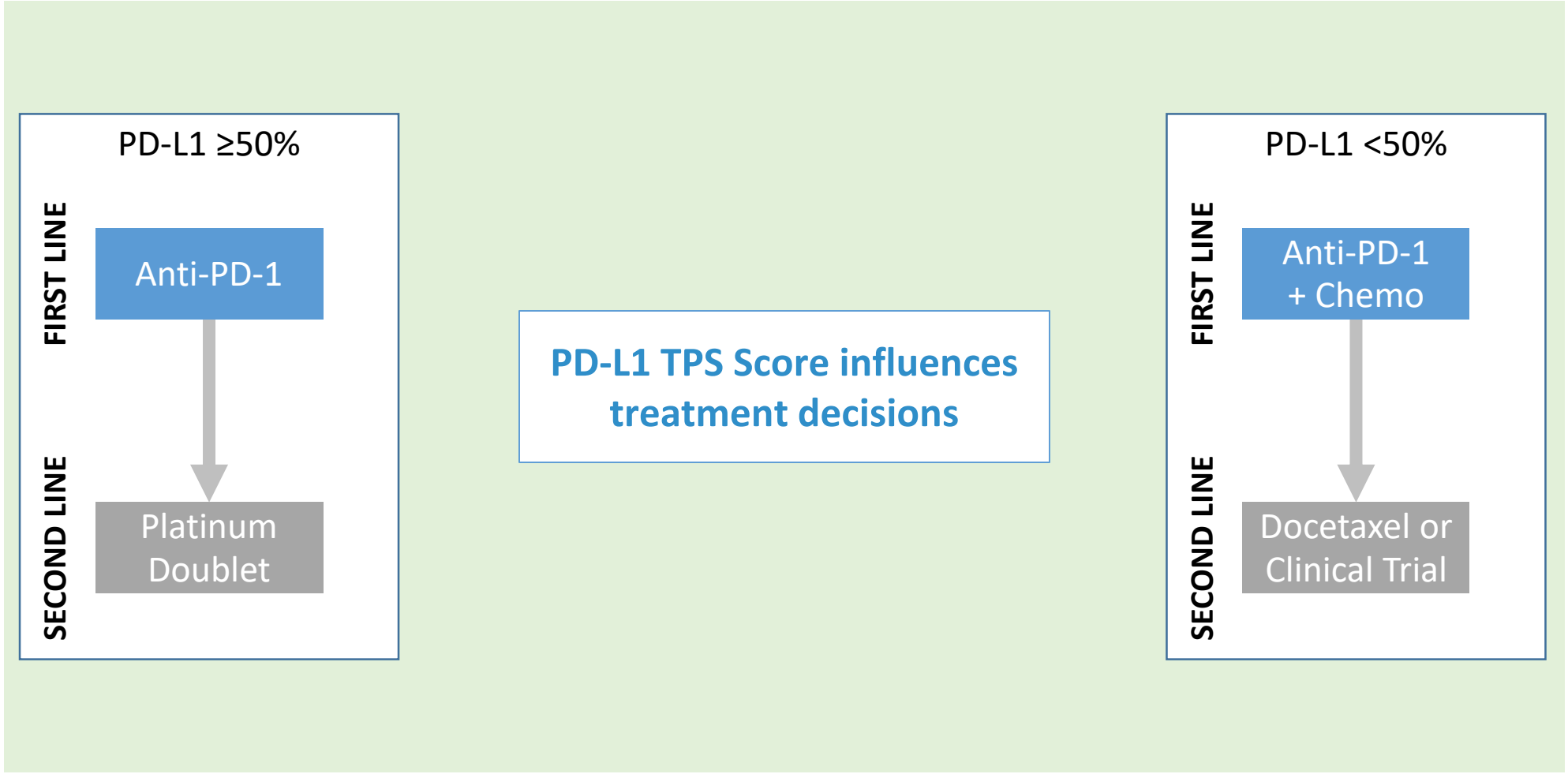
From NextCure, Inc. data on file

NC318 BLOCKS IMMUNOSUPPRESSIVE ACTIVITY INDUCED BY S15



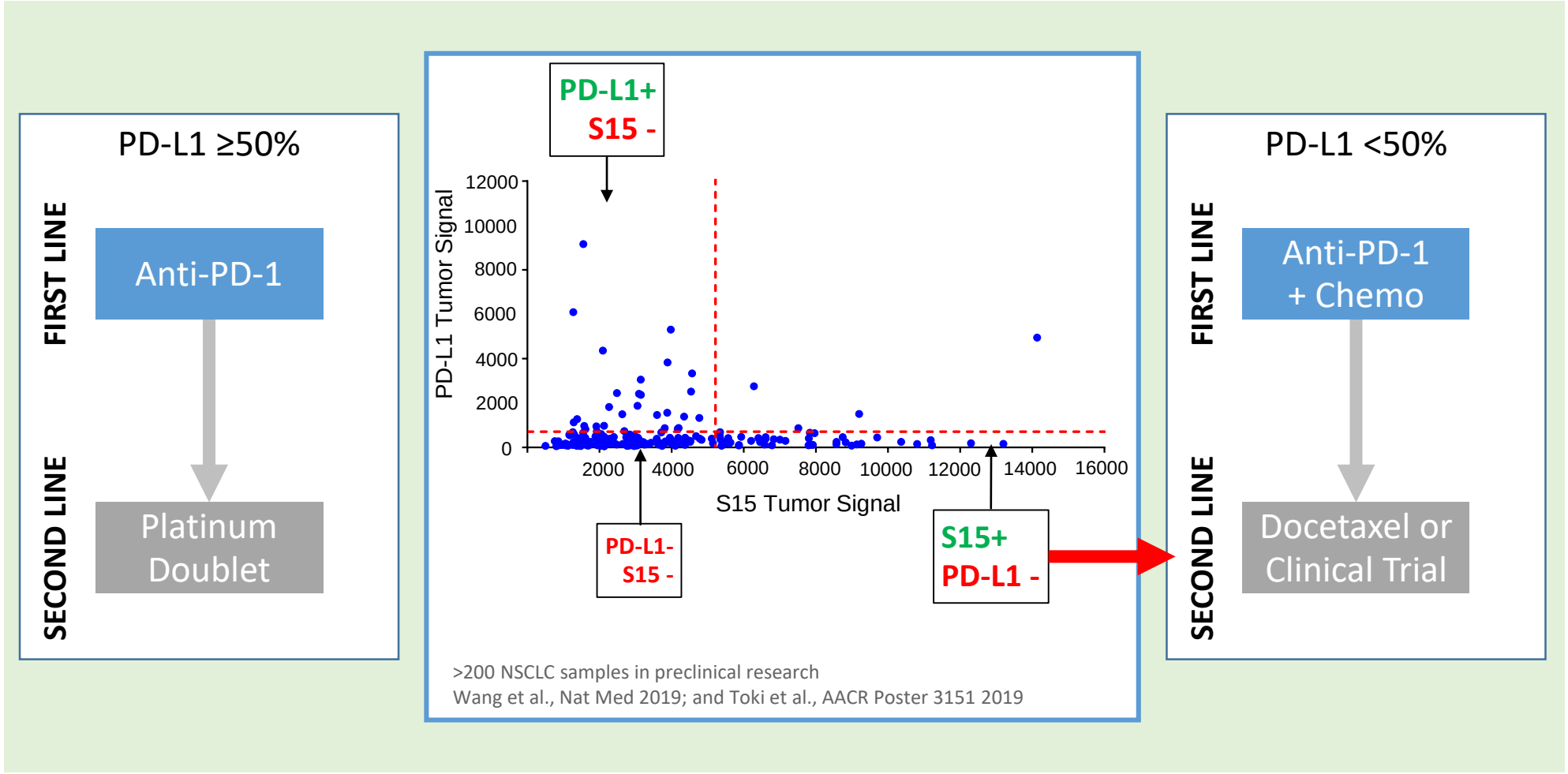
From NextCure, Inc. data on file

CURRENT TREATMENT OPTIONS FOR NSCLC WITHOUT GENETIC DRIVEN MUTATIONS



Brahmer JR et al J Immunother Cancer 2018

S15 AND PD-L1 MUTUALLY EXCLUSIVE EXPRESSION IN NSCLC
A POTENTIAL TARGET FOR PD-1 REFRACTORY NSCLC



FIRST-IN-HUMAN PHASE 1/2 CLINICAL STUDY OF NC318

Phase 1: Dose Escalation

OBJECTIVES: Safety and Tolerability of NC318

3+3 Design
- Subjects dosed every 2 weeks
- DLT period 28 days
- Additional subjects enrolled for biopsies

Eligibility:
- Men/Women ≥ 18 y/o, and PS<2
- Advanced/metastatic solid tumors (all comers)
- Refractory/intolerant to standard of care

8 mg n = 4 → **24 mg n=4** → **80 mg n= 10** → **240 mg n=12** → **400 mg n= 11** → **800 mg n=4** → **1600 mg n=4**

1600 mg cohort added after no DLTs observed through 800 mg cohort

Data as of 26-Sep-2019

Phase 2: Dose Expansion

NSCLC | **H&N** | **Ovarian** | **TNBC**

- Simon 2-Stage design
- Subject tumors must be PD-L1 TPS <50%
- Required biopsies at screening and on treatment
- S15 expression will be evaluated retrospectively

Clinical trial information: NCT03665285

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BASELINE CHARACTERISTICS OF PHASE 1 SUBJECTS

Characteristic	All subjects (N=49)*	NSCLC (n=13)*
Age, years		
Median (range)	62 (32-78)	68 (48-77)
Sex, n (%)		
Female	28 (57)	6 (46)
Male	21 (43)	7 (54)
ECOG performance status, n (%)		
0	16 (33)	2 (15)
1	33 (67)	11 (85)
Prior systemic anti-cancer regimens		
Median (range)	3 (1-15)	4 (1-7)
Prior Immunotherapy, n (%)	31 (63)	13 (100)

***All comers regardless of PD-L1 or S15 status**

Data as of 26-Sep-2019

INCIDENCE OF TREATMENT-RELATED ADVERSE EVENTS ≥5%

AE Preferred Term, n (%)	8 mg (n=4)		24 mg (n=4)		80 mg (n=10)		240 mg (n=12)		400 mg (n=11)		800 mg (n=4)		1600 mg (n=4)		Total (N=49)	
	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4
Diarrhea	0	0	1 (25)	0	4 (40)	0	1 (8)	0	1 (9)	0	1 (25)	0	0	0	8 (16)	0
Amylase increased	0	0	0	0	2 (20)	1 (10)	1 (8)	0	1 (9)	0	0	0	0	0	4 (8)	1 (2)
Infusion reaction	0	0	0	0	1 (10)	0	2 (17)	0	1 (9)	0	0	0	0	0	4 (8)	0
Fatigue	1 (25)	0	0	0	0	0	1 (8)	0	0	0	1 (25)	0	0	0	3 (6)	0
Headache	0	0	1 (25)	0	0	0	0	0	1 (9)	0	0	0	1 (25)	0	3 (6)	0
Lipase increased	0	0	0	0	2 (20)	2 (20)	0	0	1 (9)	1 (9)	0	0	0	0	3 (6)	3 (6)
Pruritis	1 (25)	0	0	0	0	0	0	0	1 (9)	0	1 (25)	0	0	0	3 (6)	0
Pruritis generalized	0	0	0	0	2 (20)	0	0	0	0	0	0	0	1 (25)	0	3 (6)	0

Data as of 26-Sep-2019

INCIDENCE OF TREATMENT-RELATED ADVERSE EVENTS ≥5%

AE Preferred Term, n (%)	8 mg (n=4)		24 mg (n=4)		80 mg (n=10)		240 mg (n=12)		400 mg (n=11)		800 mg (n=4)		1600 mg (n=4)		Total (N=49)	
	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4
Diarrhea	0	0	1 (25)	0	4 (40)	0	1 (8)	0	1 (9)	0	1 (25)	0	0	0	8 (16)	0
Amylase increased	0	0	0	0	2 (20)	1 (10)	1 (8)	0	1 (9)	0	0	0	0	0	4 (8)	1 (2)
Infusion reaction	0	0	0	0	1 (10)	0	2 (17)	0	1 (9)	0	0	0	0	0	4 (8)	0
Fatigue	1 (25)	0	0	0	0	0	1 (8)	0	0	0	1 (25)	0	0	0	3 (6)	0
Headache	0	0	1 (25)	0	0	0	0	0	1 (9)	0	0	0	1 (25)	0	3 (6)	0
Lipase increased	0	0	0	0	2 (20)	2 (20)	0	0	1 (9)	1 (9)	0	0	0	0	3 (6)	3 (6)
Pruritis	1 (25)	0	0	0	0	0	0	0	1 (9)	0	1 (25)	0	0	0	3 (6)	0
Pruritis generalized	0	0	0	0	2 (20)	0	0	0	0	0	0	0	1 (25)	0	3 (6)	0

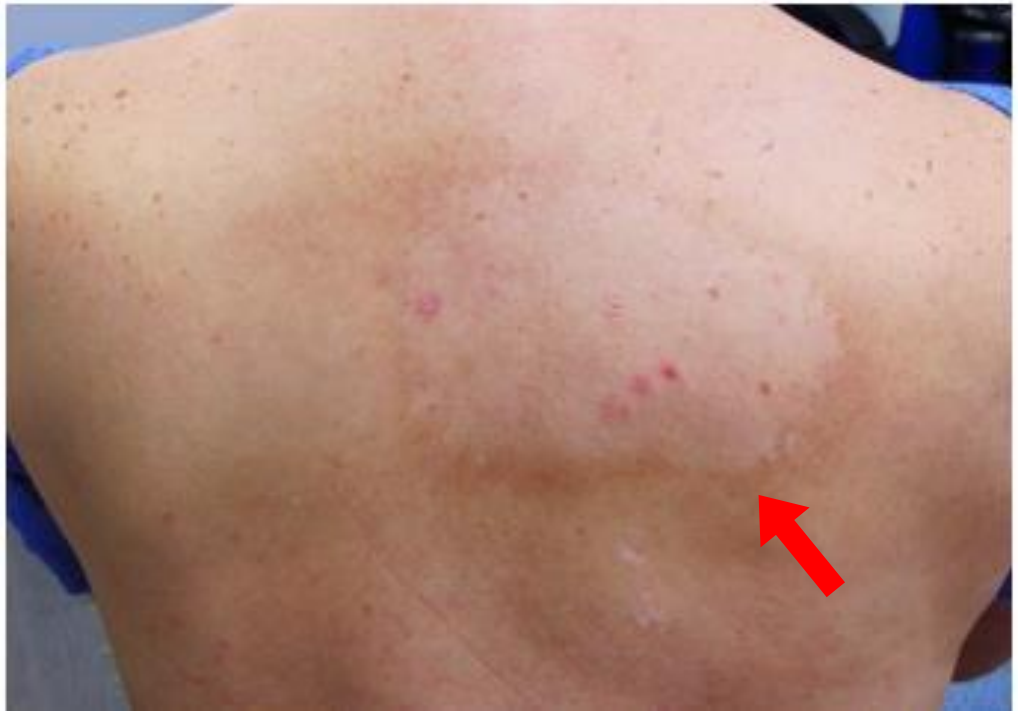
Immune-related adverse events such as uveitis (x1), pneumonitis (x2), and vitiligo (x2) also observed

Data as of 26-Sep-2019

VITILIGO IS A MARKER OF IMMUNE ACTIVATION[1]

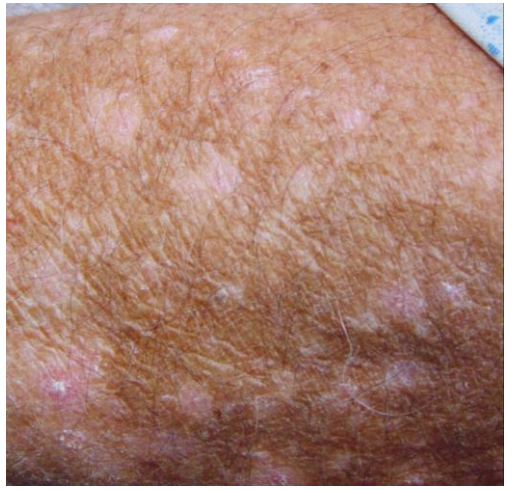
NC318 Subject 1: 80 mg dose
48 y/o NSCLC PD-L1 TPS <1%.
Vitiligo localized to radiation field, observed after 3 doses

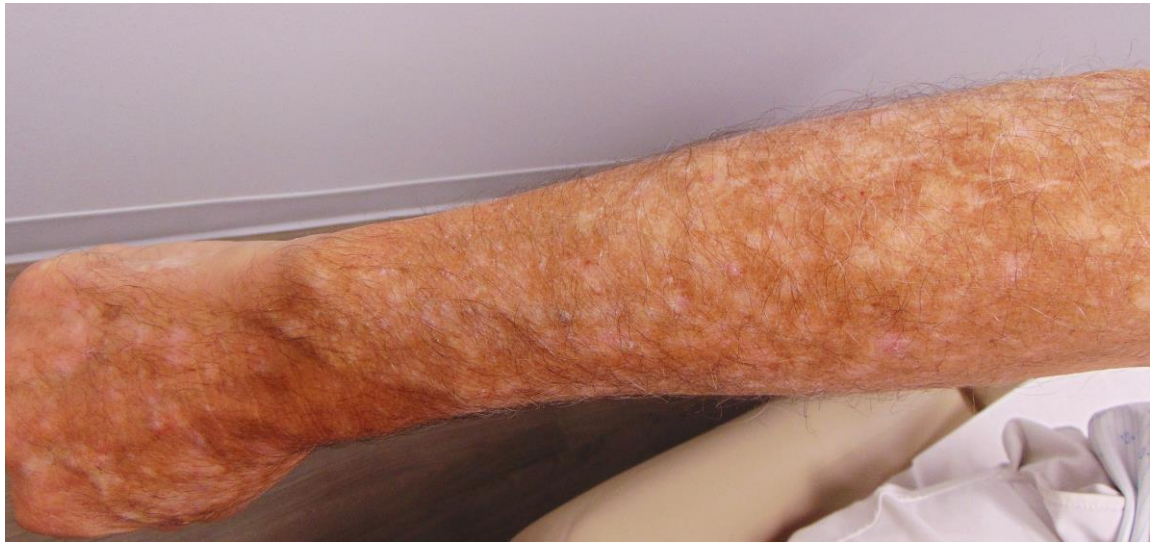
Durable SD (36+ weeks)
Images from Next Oncology



NC318 Subject 2: 400 mg dose
62 y/o Hepatocellular Carcinoma
Vitiligo observed after 3 doses

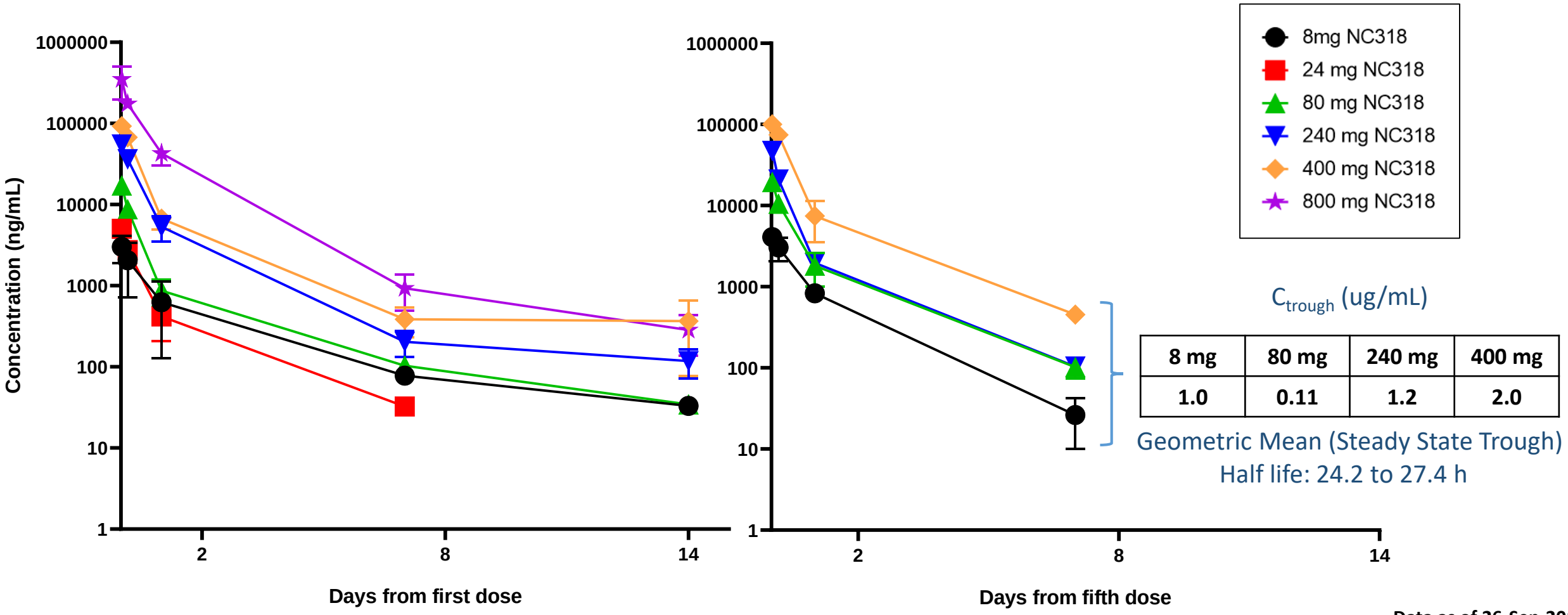
Durable SD (17+ weeks)
Images from Next Oncology





[1]*Lo JA et al JAMA Oncol. 2015 and Babai et al Drug Safety. 2019*

PHARMACOKINETICS DEMONSTRATES NC318 STEADY STATE TROUGH LEVEL



C_{trough} (ug/mL)

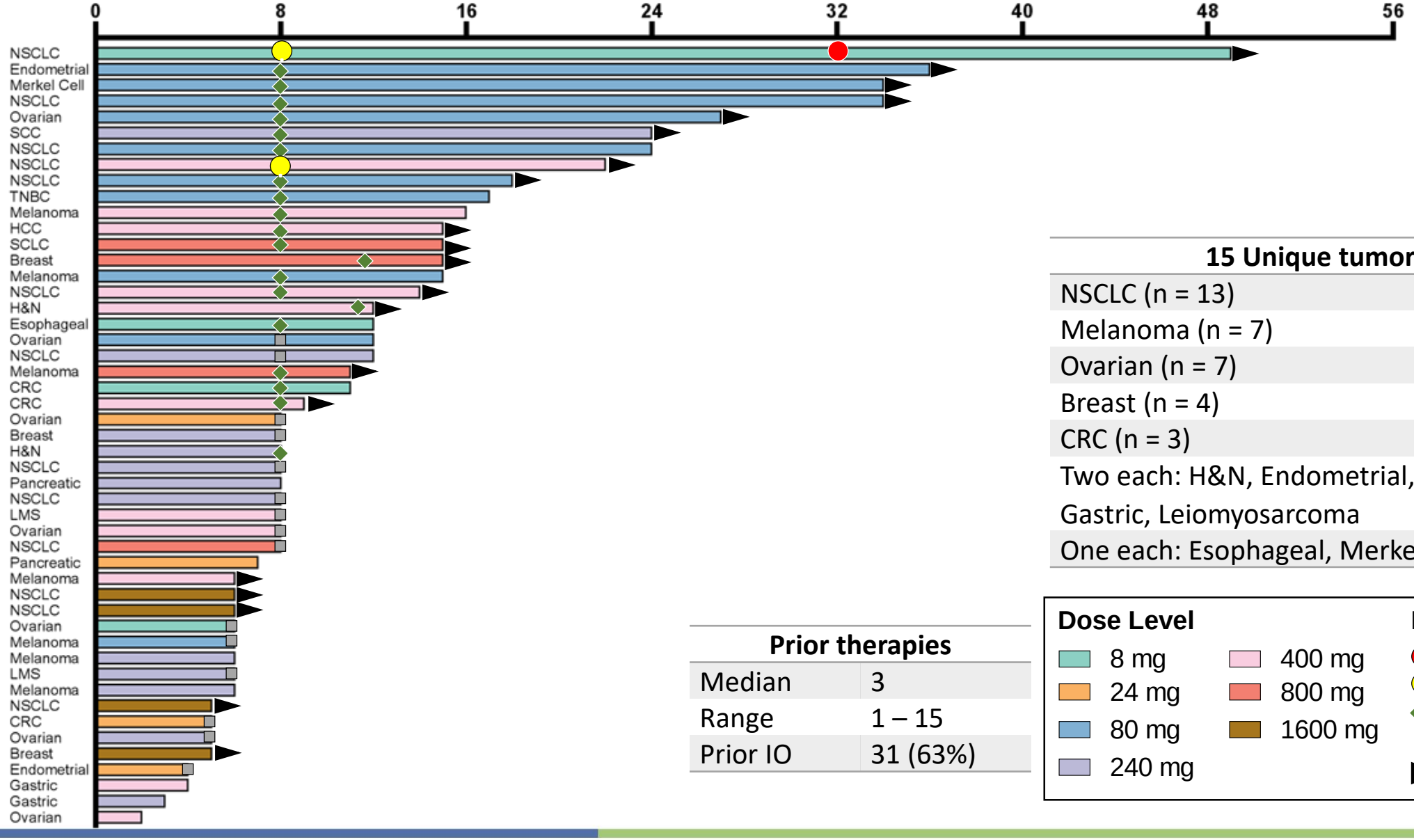
8 mg	80 mg	240 mg	400 mg
1.0	0.11	1.2	2.0

Geometric Mean (Steady State Trough)

Half life: 24.2 to 27.4 h

Data as of 26-Sep-2019

TREATMENT DURATION IN WEEKS FOR ALL PHASE 1 SUBJECTS



15 Unique tumor types
NSCLC (n = 13)
Melanoma (n = 7)
Ovarian (n = 7)
Breast (n = 4)
CRC (n = 3)
Two each: H&N, Endometrial, Pancreatic, Gastric, Leiomyosarcoma
One each: Esophageal, Merkel, SCC, HCC, SCLC

Prior therapies	
Median	3
Range	1 – 15
Prior IO	31 (63%)

Dose Level

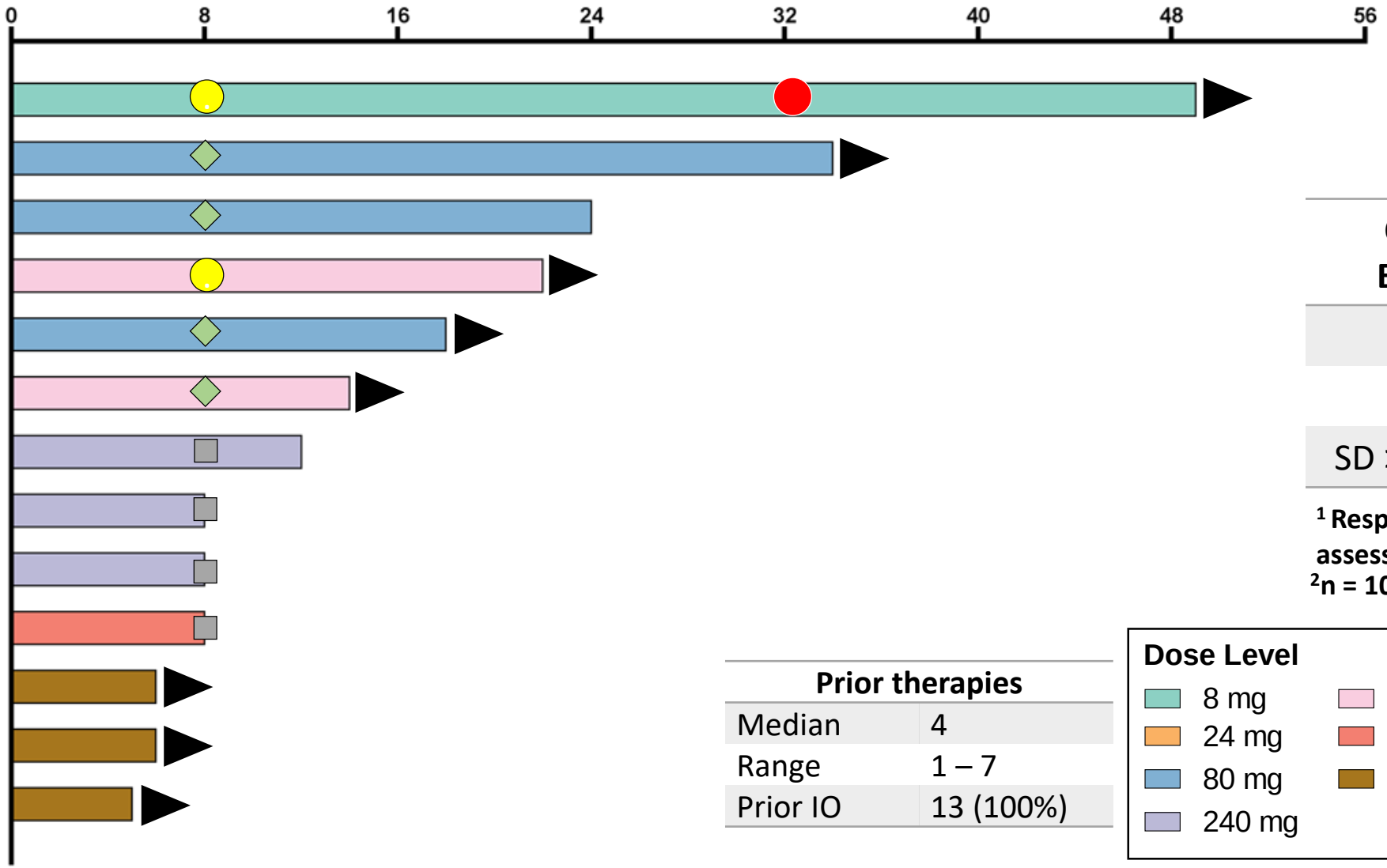
- 8 mg
- 24 mg
- 80 mg
- 240 mg
- 400 mg
- 800 mg
- 1600 mg

Best Response

- CR Start
- PR Start
- SD Start
- PD
- Treatment ongoing

Data as of 26-Sep-2019

TREATMENT DURATION IN WEEKS FOR NSCLC PHASE 1 SUBJECTS



Clinical Benefit[1]	NSCLC (n = 13)[2]
CR	1
PR	1
SD >16 weeks	3

[1] Response is based on investigator tumor assessments per RECIST v1.1
[2] n = 10 efficacy evaluable population

Prior therapies	
Median	4
Range	1 – 7
Prior IO	13 (100%)

Dose Level
- 8 mg
- 24 mg
- 80 mg
- 240 mg
- 400 mg
- 800 mg
- 1600 mg

Best Response
- CR Start
- PR Start
- SD Start
- PD
- Treatment ongoing

Data as of 26-Sep-2019

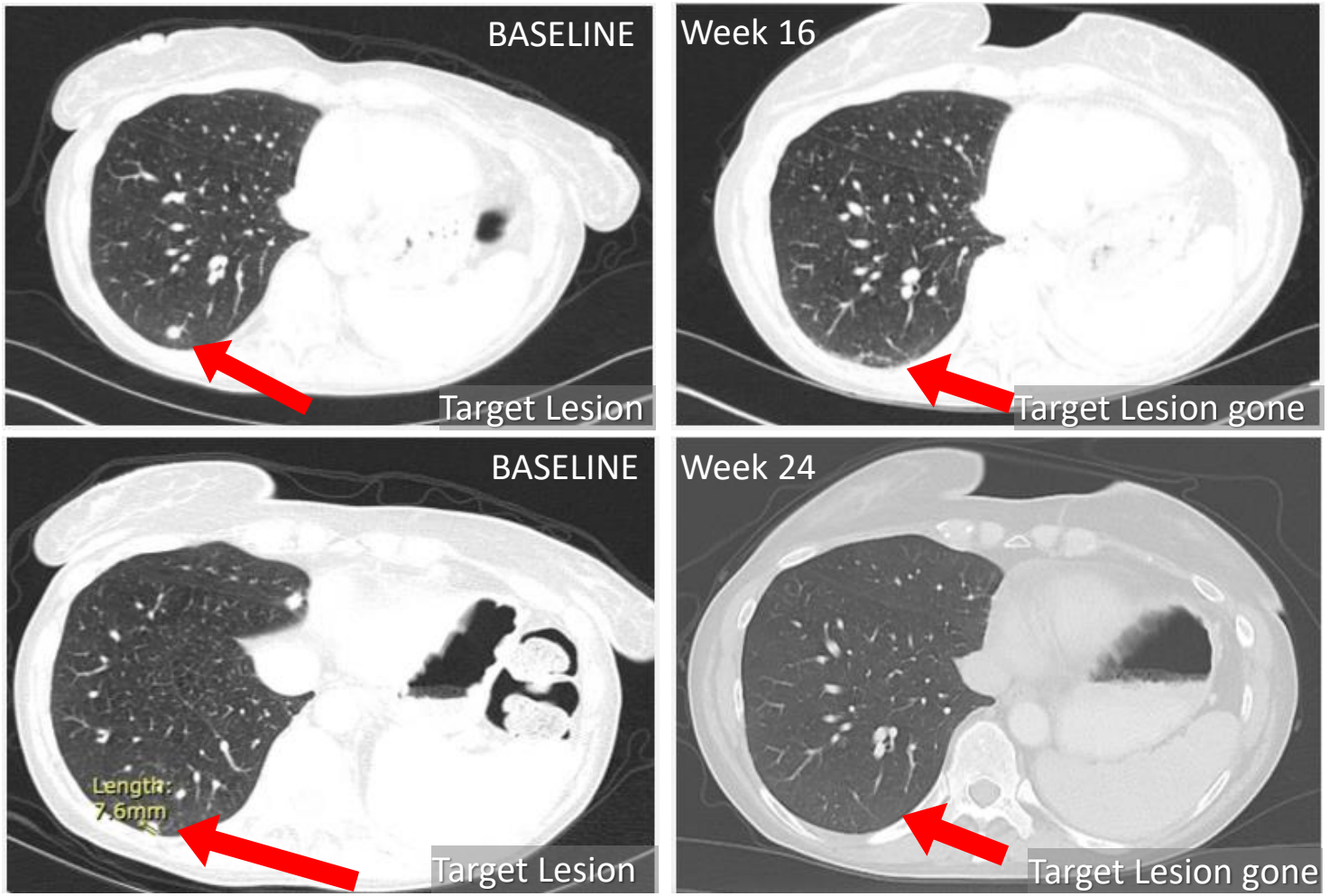
COMFIRMED COMPLETE RESPONSE

56 y/o NSCLC dosed 8 mg every 2 weeks
(with multiple lesions)

Prior therapies:
- Chemotherapy: 3 regimens (progression)
- Immunotherapy: nivolumab (best response stable disease then progression)

Diagnostic biopsy:	
S15	PD-L1 (TPS)
N/A	1-50%

Duration from PR: 41+ weeks.
Duration of CR: 13+ weeks.



Images from Next Oncology

DURATION ON STUDY 49+ WEEKS

Data as of 26-Sep-2019

CONFIRMED PARTIAL RESPONSE

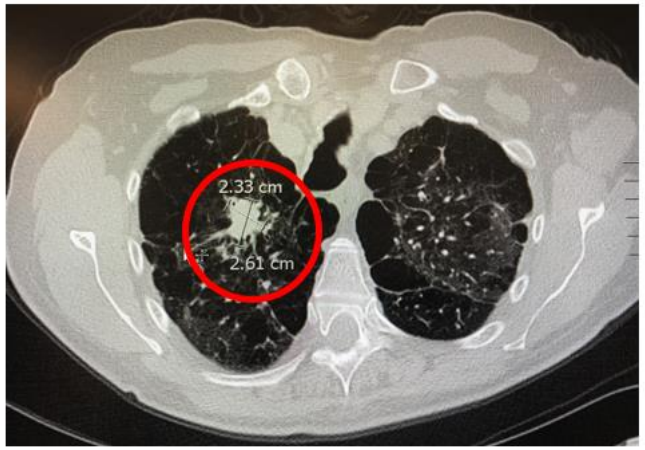
74 y/o NSCLC dosed 400 mg every 2 weeks

Prior therapies:

- Immunotherapy: "LAG3/PD-1" (best response stable disease then progression)

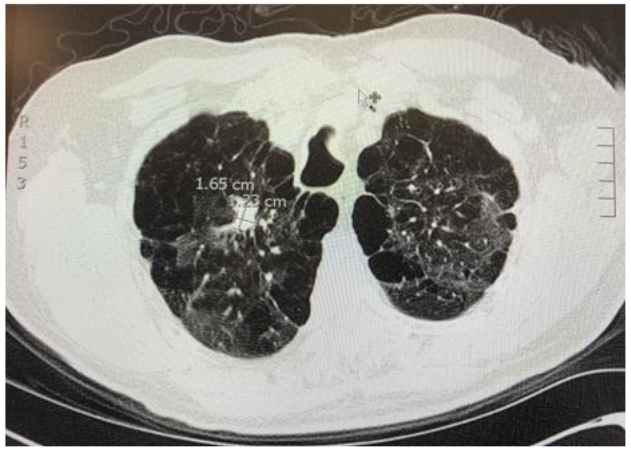
Diagnostic biopsy:	
S15	PD-L1 (TPS)
N/A	1-50%

BASELINE



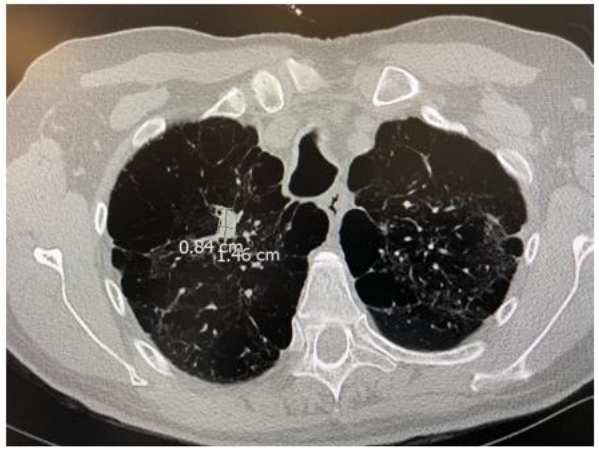
Duration of PR: 15+ weeks.

Week 8



Target lesions -41%

Week 16



Target lesions -71%

DURATION ON STUDY 24+ Weeks

Images from John Theurer Cancer Center

Data as of 26-Sep-2019

CONCLUSIONS

- NC318 has been well tolerated across multiple dose levels
- Adverse event profile consistent with other approved immunotherapies
- Predictable pharmacokinetic profile
- NC318 has shown encouraging single-agent anti-tumor activity
  - PD-1 refractory NSCLC: 1 CR, 1 PR, and stable disease in 3 patients (of 10 evaluable patients)
  - Durable stable disease (>24 weeks observed in multiple tumor types)
- Phase 2 enrollment underway

ACKNOWLEDGEMENTS

The patients and families who participated in this clinical study

NEXT Oncology
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NextCure
Sol Langermann
Linda Liu

FUTURE PLANS FOR NC318 PROGRAM

The NC318-01 Phase 1/2 clinical trial enrolling patients into the Phase 2 component

- Phase 2 tumor selection based on S15 expression demonstrated from archival biopsies
- S15 tumor expression observed in 15-25% of NSCLC, H&N, Ovarian, and TNBC biopsies

From NextCure, Inc. data on file

NSCLC

H&N

Ovarian

TNBC

- Simon 2-Stage design
- Monotherapy 400 mg every 2 weeks
- Subject tumors must be PD-L1 TPS <50%
- Required biopsies at screening and on treatment
- S15 expression will be evaluated retrospectively

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NEXT PHASE 2 STUDY PLANNED TO EVALUATE NC318 IN COMBINATION WITH STANDARD OF CARE CHEMOTHERAPIES WILL SUPPORT EVALUATION OF NC318 IN FIRST LINE INDICATIONS (1H2020)

Thank you