MEETING SUMMARY
ASCO 2019, Chicago, USA

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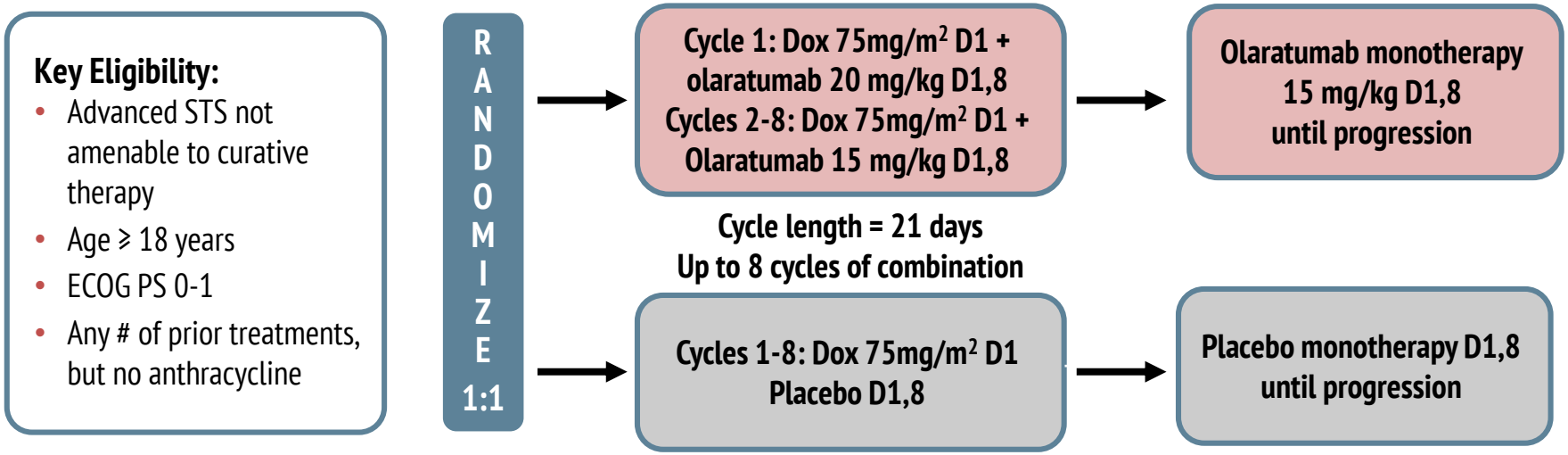
HIGHLIGHTS ON SARCOMA

ANNOUNCE: A RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, PHASE III TRIAL OF DOXORUBICIN + OLARATUMAB VS DOXORUBICIN + PLACEBO IN PATIENTS WITH ADVANCED SOFT TISSUE SARCOMAS

Tap W, et al. ASCO 2019 Abst #LBA3

ANNOUNCE STUDY DESIGN



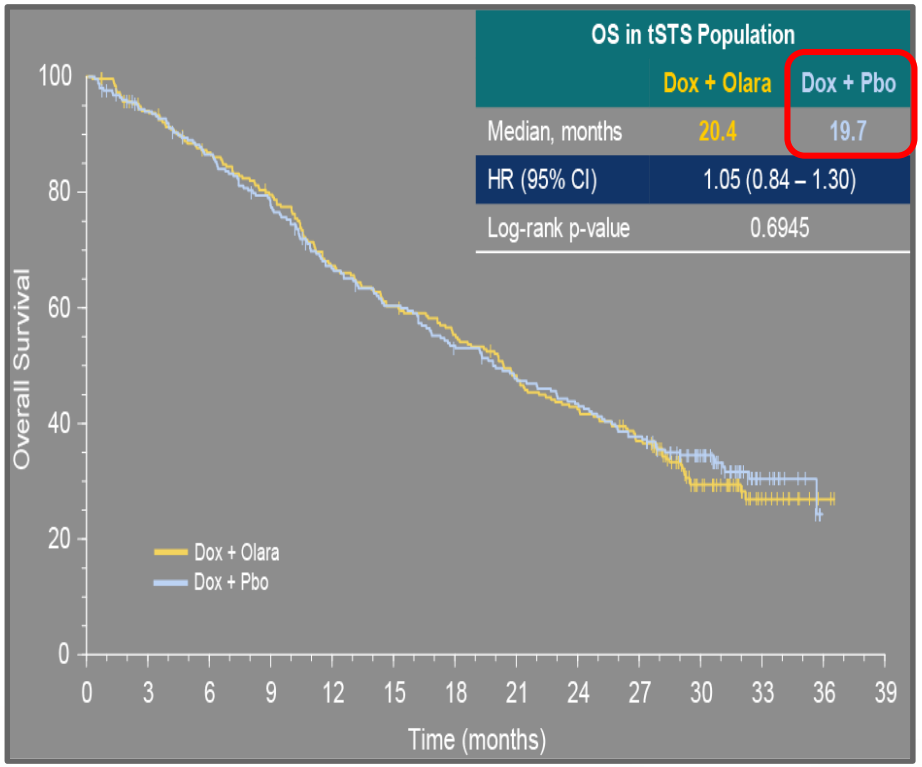
Stratification factors: Number of prior therapies (0 vs ⩾1), histology (LMS vs LPS vs UPS vs Other), ECOG PS (0 vs 1)

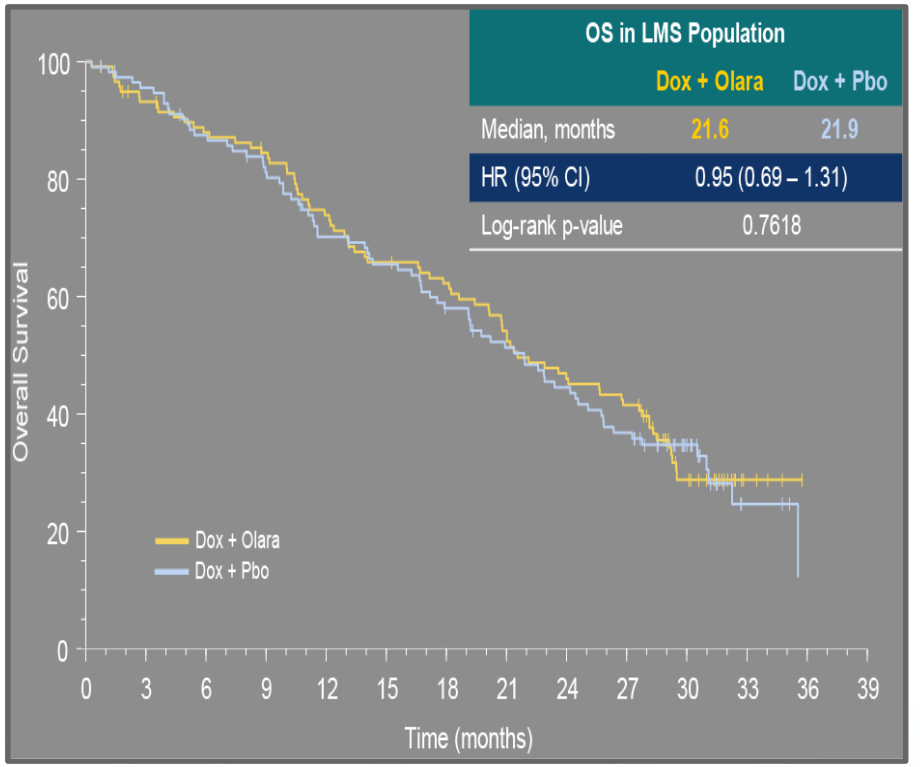
Primary endpoint: OS in the total STS & LMS populations
Key secondary endpoints: PFS, ORR, PROs, safety, PK, immunogenicity
Exploratory: Biomarkers, subgroup analyses
Other features: Dexrazoxane use allowed at any cycle, cardiac monitoring of LVEF prior to cycles 5, 7, & 9 then q3 months

D, day; Dox, doxorubicin; ECOG PS, Eastern Cooperative Oncology Group performance status; LMS, leiomyosarcoma; LVEF, left ventricular ejection fraction; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; PRO, patient-reported outcomes; q, every; STS, soft tissue sarcoma; UPS, undifferentiated pleomorphic sarcoma

Tap W, et al. presented at ASCO 2019, Abst. #LBA3

OVERALL SURVIVAL: tSTS AND LMS POPULATIONS





CI, confidence interval; Dox, doxorubicin; HR, hazard ratio; LMS, leiomyosarcoma; Olara, olaratumab; OS, overall survival; Pbo, placebo; tSTS, total Soft Tissue Sarcoma

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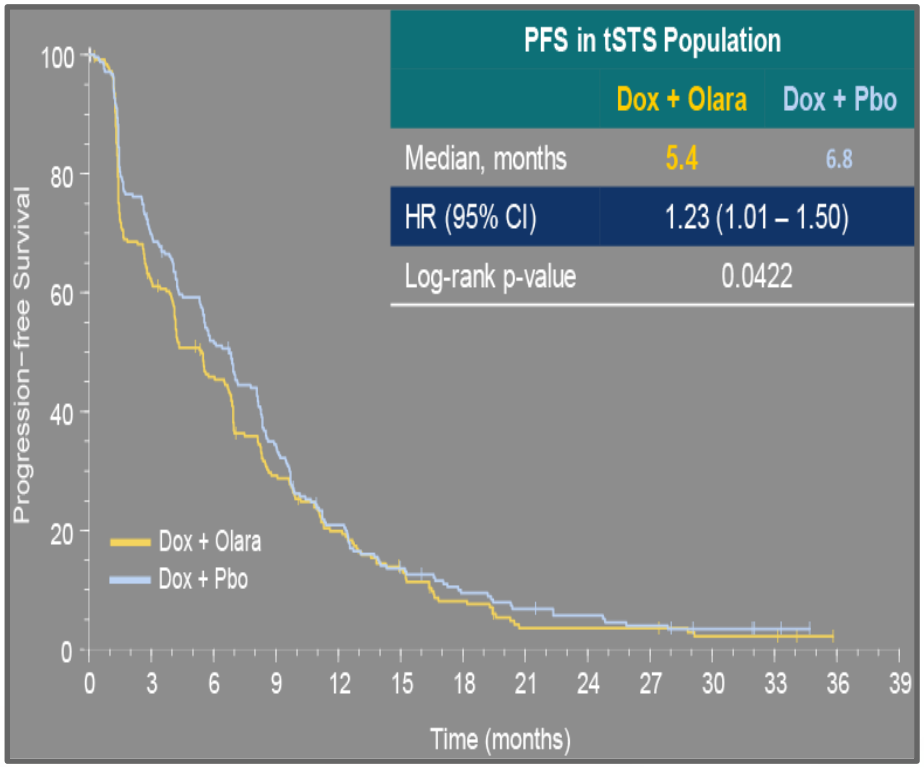
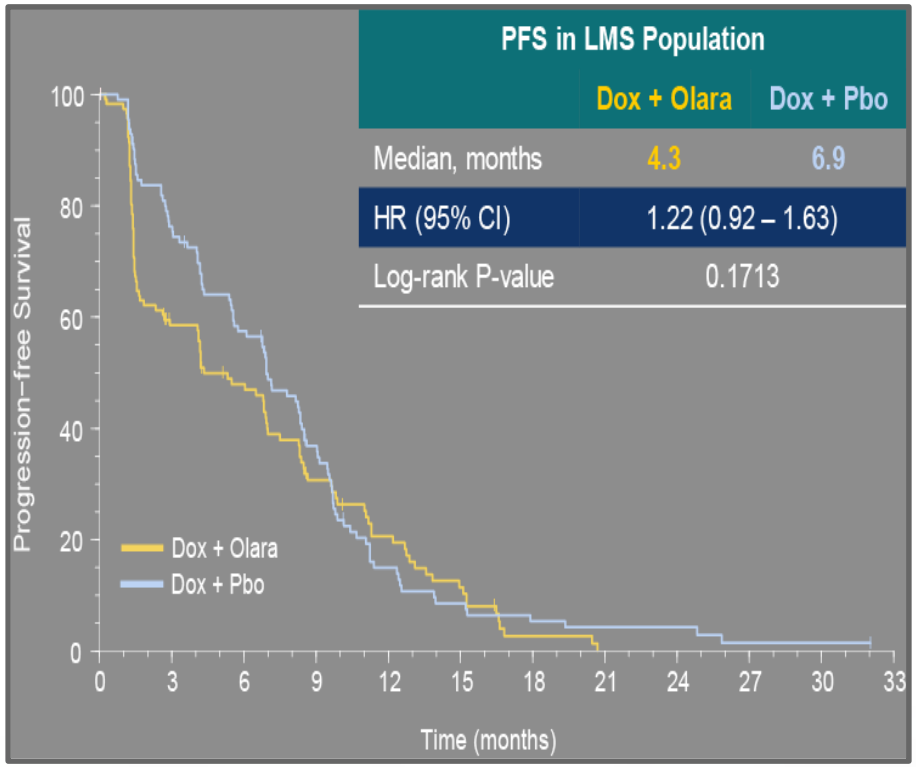
PROGRESSION-FREE SURVIVAL: tSTS AND LMS POPULATIONS





CI, confidence interval; Dox, doxorubicin; HR, hazard ratio; LMS, leiomyosarcoma; Olara, olaratumab; Pbo, placebo; PFS, progression-free survival; tSTS, total Soft Tissue Sarcoma

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ANNOUNCE TRIAL
TAKE HOME MESSAGES

- ANNOUNCE failed to meet the primary endpoint of OS in STS histologies or the LMS population
  - Benefit seen in phase Ib/II trial was not confirmed
- The control arm had the highest OS for doxorubicin in any randomized STS trial
  - Entry not limited to first line and allowed up to 600 mg/m^2 doxorubicin
- No new patients to be started on olaratumab

CI, confidence interval; LMS, leiomyosarcoma; OS, overall survival; STS, soft tissue sarcoma

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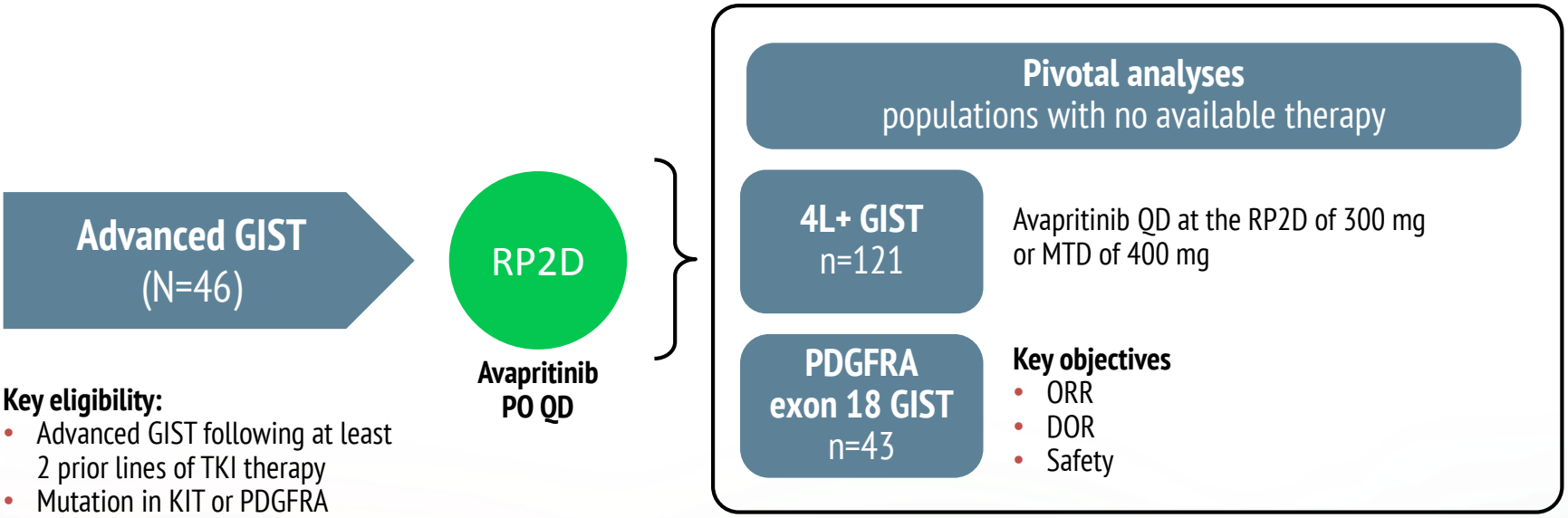
CLINICAL ACTIVITY OF AVAPRITINIB IN ⩾4TH LINE (4L+) AND PDGFRA EXON 18 GASTROINTESTINAL STROMAL TUMORS (GIST)

Heinrich M, et al. ASCO 2019, Abst. #11022

PHASE I STUDY IN GIST: THE NAVIGATOR TRIAL

- NAVIGATOR is an open-label dose escalation/dose expansion phase I study of avapritinib (NCT02508532)

Study design, amendments, and objectives

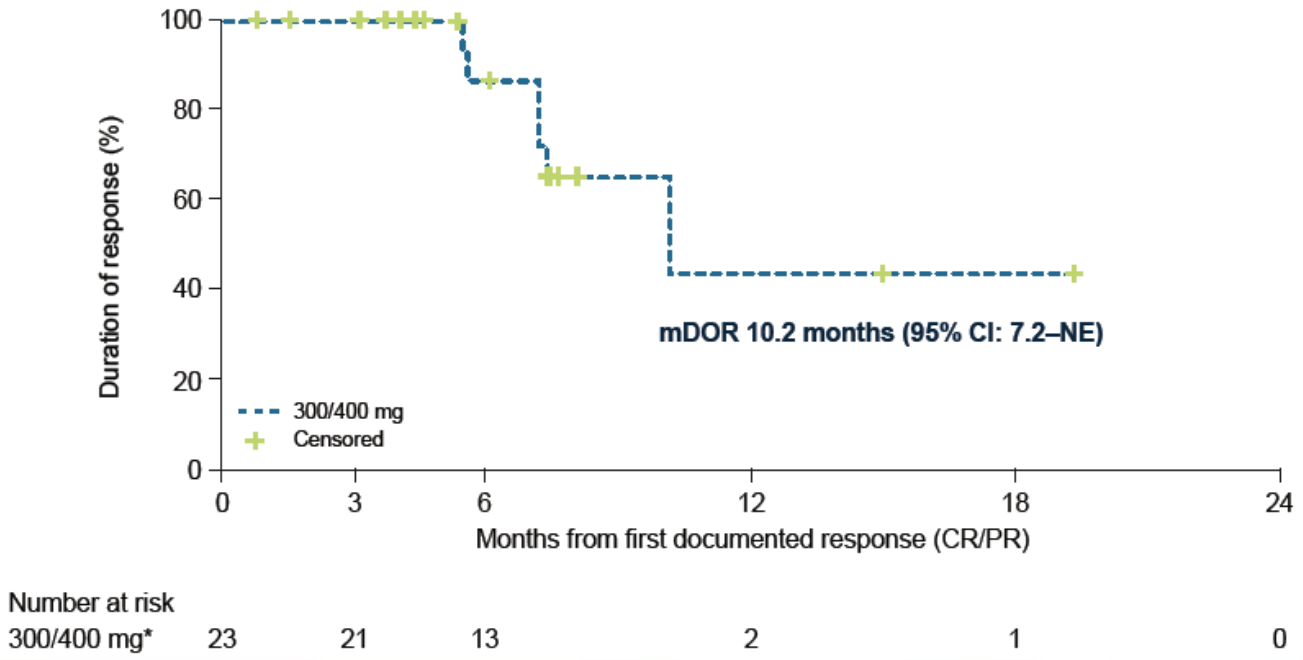


*While enrollment criteria in the study protocol specified that patients in expansion group 1 were required to have received only at least 2 prior lines of TKI therapy, equating to an analysis population of 3L+, the observed enrollment more greatly reflected a population more heavily pretreated.

DOR, duration of response; GIST, gastrointestinal stromal tumors; N, number; ORR, objective response rate; QD, everyday
Heinrich M, et al. presented at ASCO 2019 Abst. #11022

PATIENTS TREATED IN 4TH LINE +

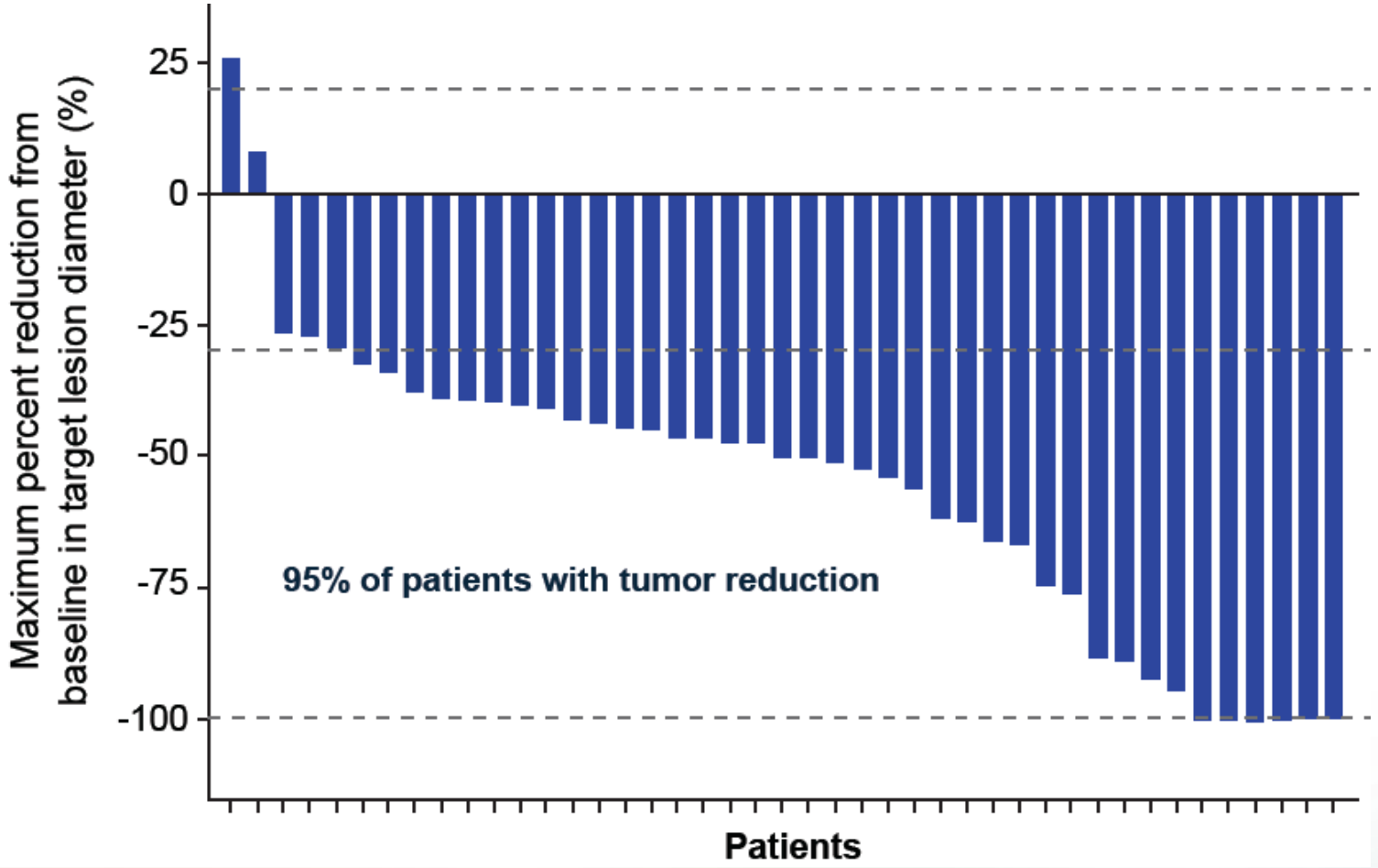
- Median follow-up was 10.8 months across all 4L+ patients



4L, fourth line; CI, confidence Interval; CR, Complete Response; PR, Partial Response; mDOR, median duration of response

Heinrich M, et al. presented at ASCO 2019 Abst. #11022

PATIENTS WITH TUMORS HARBORING PDGFRA D842V MUTATION



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ADVERSE EVENTS STRATIFICATION

Most Common AEs Occurring in ⩾15% of Patients % (n)	300/400 mg Starting Dose (N=204)			
	All AEs		Treatment-related AEs	
	All grades	Grade ⩾3	All	Grade ⩾3
Nausea	64.2 (131)	2.5 (5)	59.3 (121)	–
Fatigue	55.4 (113)	7.4 (15)	47.1 (96)	6.4 (13)
Amemia	50.0 (102)	28.4 (58)	36.3 (74)	16.2 (33)
Cognitive effects*	41.2 (84)	3.9 (8)	41.2 (84)	3.9 (8)
Periorbital edema	40.7 (83)	–	40.2 (82)	–
Vomiting	38.2 (78)	2.0 (4)	31.9 (65)	–
Decreased appetite	37.7 (77)	2.9 (6)	28.4 (58)	–
Diarrhea	37.3 (76)	4.9 (10)	31.9 (65)	2.9 (6)
Increased lacrimation	32.8 (67)	–	30.4 (62)	–
Peripheral edema	30.9 (63)	–	27.0 (55)	–
Face edema	24.5 (50)	–	24.0 (49)	–
Constipation	22.5 (46)	–	–	–
Dizziness	22.1 (45)	–	–	–
Hair color changes	21.1 (43)	–	20.6 (42)	–
Blood bilirubin increased	21.1 (43)	4.4 (9)	18.6 (38)	3.9 (8)
Abdominal pain	20.1 (41)	5.4 (11)	–	–
Headache	16.7 (34)	–	–	–
Dyspnea	16.7 (34)	2.5 (5)	–	–
Dyspepsia	15.7 (32)	–	–	–
Hypokalemia	15.7 (32)	2.9 (6)	–	–
Dysgeusia	15.2 (31)	–	15.2 (31)	–

*Cognitive effects include pooled terms of memory impairment (29.4%), cognitive disorder (10.8%), confusional state (7.4%), and encephalopathy (1.5%). The sponsor considered all cognitivie effect AEs as treatment-related in this analysis.
Note: 3 events of intracranial hemorrhage occurred, 1 at the 90 mg dose level; 2 were grade 3, 1 was grade 1. AEs are sorted by decreasing incidence in the All AEs All grades group. All grades AEs occuring in ⩾15% of patients. Grade ⩾3 AEs occuring in ⩾2% of patients.

AEs, adverse events

Heinrich M, et al. presented at ASCO 2019 Abst. #11022

A RANDOMIZED PHASE II TRIAL OF NIVOLUMAB MONOTHERAPY VS NIVOLUMAB + IPILIMUMAB IN ADVANCED GIST

Singh AS, et al. ASCO 2019, Abst. #11017

TOPLINE STUDY RESULTS

Study population (NCT02880020)

- 29 patients (27 evaluable)
- Median of 3 (1-7) lines of prior therapies

Efficacy Outcomes

- Nivolumab arm
  - 8/16: best response of SD for a CBR of 50.0%
  - Median PFS 12.1 weeks
  - 6 grade 3/4 AEs (hyperglycemia, DKA, weakness 2x, abdominal pain, rash)

- Nivolumab + ipilimumab arm
  - 1/13 had a PR and 2/13 SD for a CBR of 23.1%
  - Median PFS of 8.3 weeks
  - 6 Grade 3/4 AEs (diarrhea 3x, weakness, hyperglycemia, AST elevation)

- 8 patients on therapy >6 months
- 2 patients with a KIT Exon 17 mutation had radiographic disease shrinkage

Safety Outcomes

- Most AEs were grades 1-2 with fatigue (37%) being the most common

AEs,Adverse events; CBR, Clinical Benefit Rate; CI, Confidence Interval; DKA, Diabetic ketoacidosis; PFS, Progression Free Survival; SD, Stable Disease

Singh AS, et al. presented at ASCO 2019 Abst #11017

APATINIB PLUS CAMRELIZUMAB (SHR-1210) FOR UNRESECTABLE HIGH-GRADE OSTEOSARCOMA (APFAO) PROGRESSING AFTER CHEMOTHERAPY: A PROSPECTIVE, OPEN LABEL, PHASE II TRIAL

Xie L, et al. ASCO 2019, Abst. #11013

TOPLINE STUDY RESULTS

- JAN 1 – Sep 4, 2018: 41 patients

Efficacy Outcomes

- Objective response rate: 21.95% (9/41)
- 20/ 41 patients (48.8%, 95%CI: 32.8%-64.8%) progression free at 6 months
  - 6-month PFS rate: 54.32% (95% CI 37.62%-68.33%)
  - 4-month PFS rate: 70.00% (95% CI 53.24%–81.73%)
- Median PFS: 6.50 (95% CI 4.23–7.50) months
- Median OS: not reached
- No statistical difference in response rate or PFS between different PD-L1 expression groups (*P=0.153 and 0.231*)

Safety Outcomes

- Toxic effects led to dose reductions, or short interruptions, or both in 20/ 41 patients (48.78%)

CI, confidence Interval; OS, Overall survival; PFS, Progression Free Survival

Xie L, et al. presented at ASCO 2019 Abst. #11013

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