2024 ASCO® ANNUAL MEETING

Updated results from the Phase 1b/2 **HERKULES-3** study: **ERAS-007 plus encorafenib and cetuximab (EC)** in patients (pts) with EC-naïve metastatic BRAF V600E colorectal cancer (CRC)

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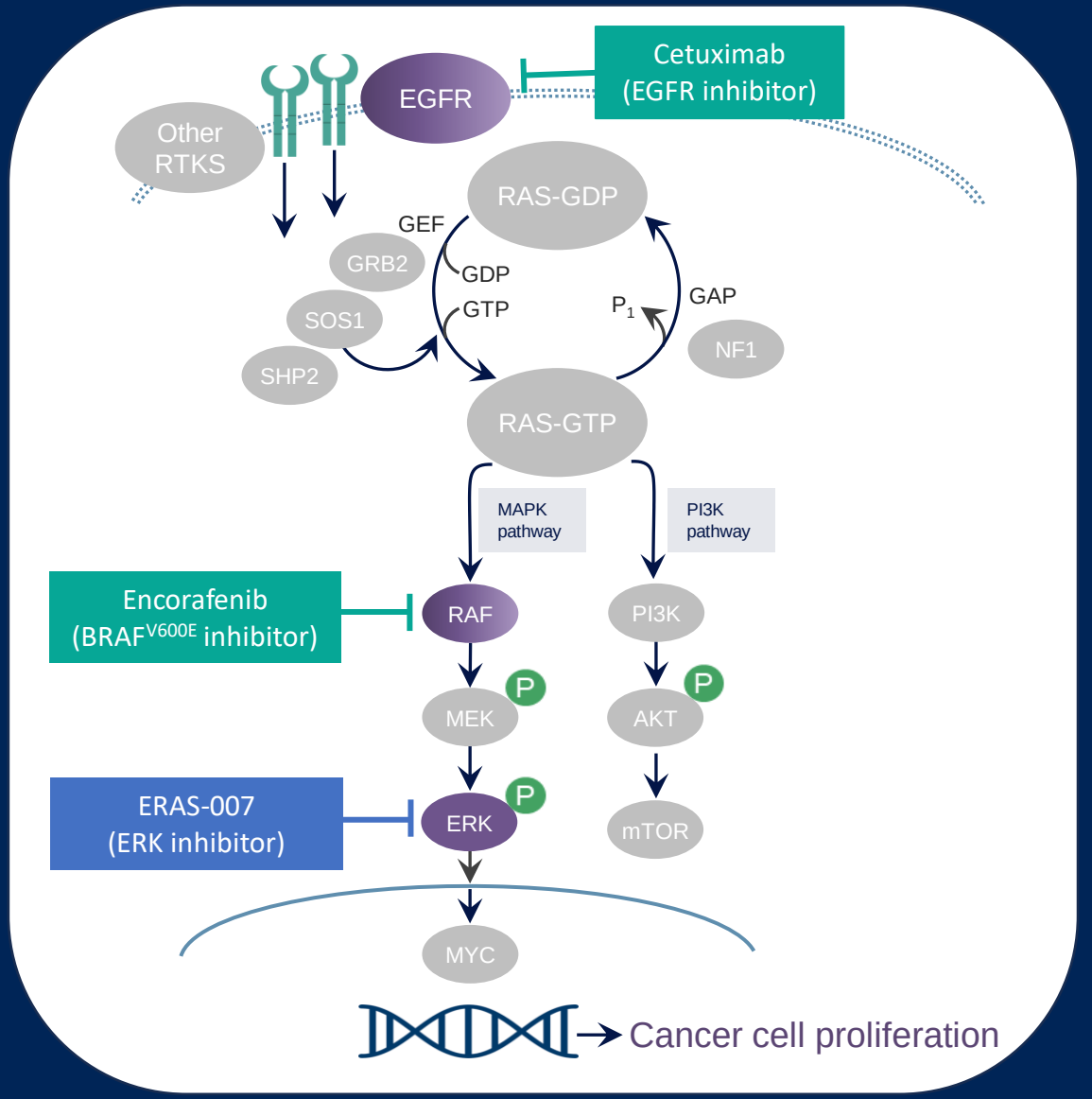
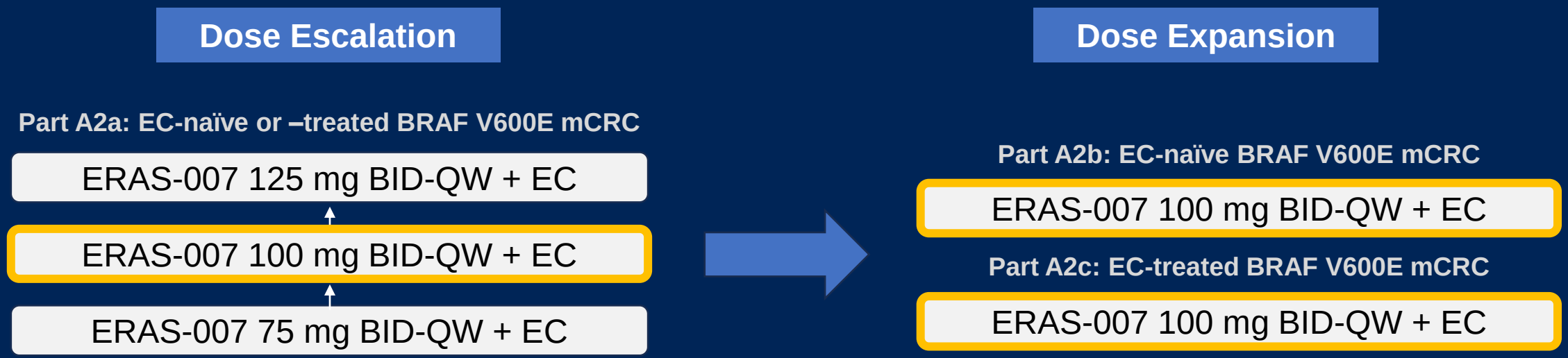
Background

- RAS/MAPK pathway (including BRAF) dysregulation results in downstream activation of ERK1/2
- BRAF V600E CRC has worse survival than non-BRAF V600E–mutated CRC, and novel therapies are needed
- ERAS-007 is a novel, potent, orally bioavailable inhibitor of ERK1/2
- Adding ERAS-007 to encorafenib and cetuximab (EC) may prevent resistance to BRAF/EGFR inhibition by inhibiting ERK
- ERAS-007 alone or in combination with EC showed promising in vitro and in vivo activity in BRAF V600E mCRC models



Study Design (NCT05039177)



- The MTD was not established, rather the maximum administered dose (MAD) was identified as 100 mg BID-QW ERAS-007 in combination with EC
- There was no clinically relevant drug-drug interaction identified for ERAS-007 and EC

BID-QW: twice a day once per week; DLT: dose limiting toxicity; EC: encorafenib (300 mg, oral daily) + cetuximab (500 mg/m^2, intravenous infusion once every 2 weeks); MTD: maximum tolerated dose; EC naïve = pts that had no prior EC treatment before study; EC-treated = pts treated with EC prior to the study

Demographics, Baseline Tumor Characteristics, and Disposition

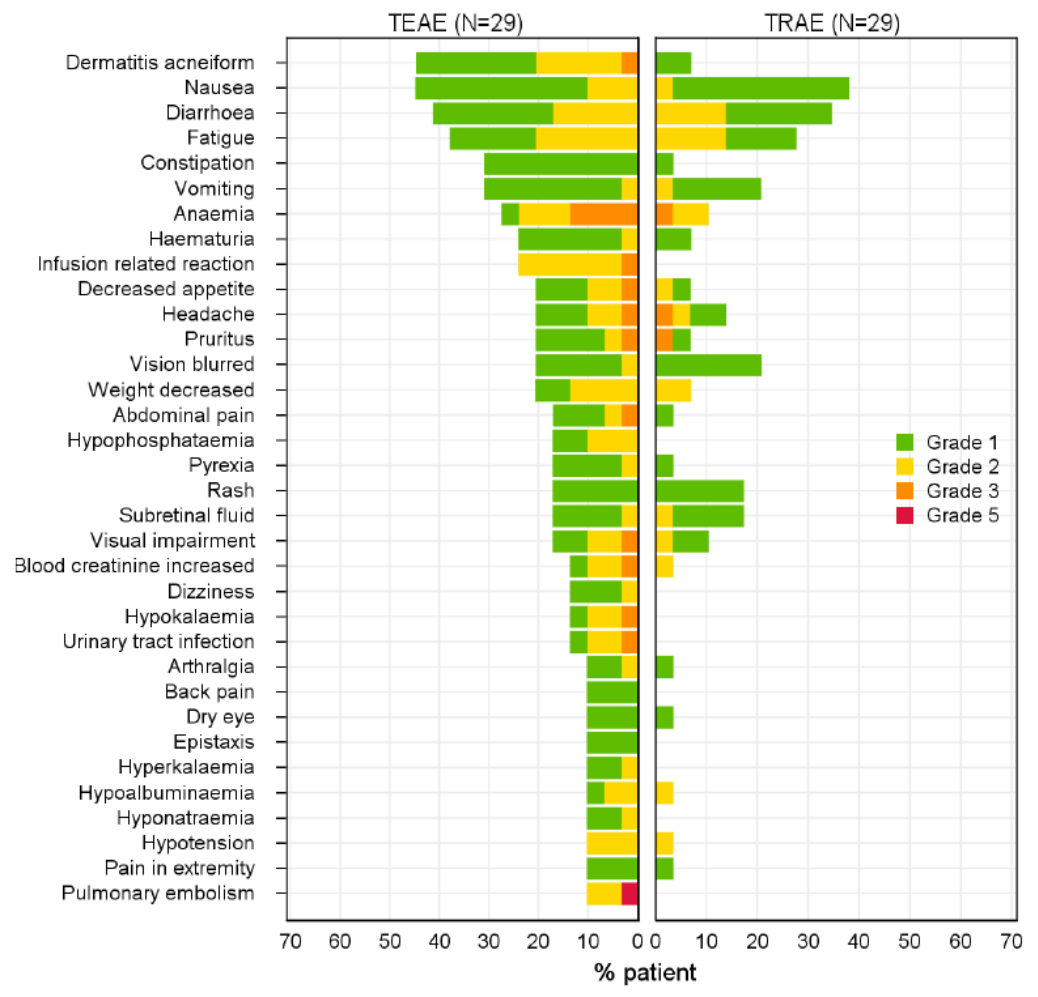
ERAS-007 100 mg BID-QW + EC pts	EC Naïve (N = 20)	All (N = 29)
Median age (range)	64.0 (39, 79)	63.0 (39, 86)
Sex (n %)		
Male	8(40.0)	14 (48.3)
Female	12 (60.0)	15 (51.7)
Race (n %)		
Asian	1 (5.0)	2 (6.9)
White	19 (95.0)	25 (86.2)
Not reported	0	2 (6.9)
ECOG (n %)		
0	7 (35.0)	11 (37.9)
1	12 (60.0)	17 (58.6)
2	1 (5.0)	1 (3.4)

ERAS-007 100 mg BID-QW + EC pts	EC Naïve (N = 20)	All (N = 29)
Microsatellite instability status (n %)		
High	3 (15.0)	6 (20.7)
Stable	17 (85.0)	23 (79.3)
Location of primary tumor (n %)		
Both right and left side of colon	2 (10.0)	2 (6.9)
Left side of colon, including rectum	6 (30.0)	8 (27.6)
Right side of colon	12 (60.0)	19 (65.5)
# of lines of prior systemic therapy (n %)		
Median (min, max)	2 (1, 3)	2 (1, 6)
1	9 (45.0)	9 (31.0)
2	9 (45.0)	12 (41.4)
≥3	2(10.0)	8 (27.6)

- As of April 23, 2024, 22 (75.9%) patients have discontinued treatment with the most common reason being disease progression (n=15; 51.7%) and withdrawal of consent (n=4; 13.8%)

Safety-Evaluable population includes all patients who received at least 1 dose of ERAS-007; EC = encorafenib (300 mg, oral daily) + cetuximab (500 mg/m^2, intravenous infusion once every 2 weeks); BID-QW = twice a day once per week; EC naïve = pts that had no prior EC treatment before study; All = naïve group + pts treated with EC prior to the study; Data extraction date: 23 April 2024

Safety and Tolerability – TEAEs in ≥10% Pts and Incidence of TRAEs for ERAS-007*



- One DLT of Grade 3 macular edema was reported during dose escalation
- TRAEs for ERAS-007 were reported in 89.7% of patients; most events were Grade 1-2 severity (72.4%)
- No patients discontinued ERAS-007 or encorafenib due to TRAE
  - 2 patients discontinued cetuximab due to infusion related reactions (IRR)
- AE leading to dose reduction of any study treatment occurred in 24.1% of patients
  - Events reported in ≥2 patients were skin reactions for cetuximab and ocular AEs for ERAS-007
- One unrelated Grade 5 event of pulmonary embolism was reported

*ERAS-007 dosed at 100 mg twice a day once per week in combination with encorafenib (300 mg, oral daily) + cetuximab (500 mg/m^2, intravenous infusion once every 2 weeks); Safety-evaluable population includes all patients who received at least 1 dose of ERAS-007; TEAEs: Treatment-emergent adverse events; TRAEs: = TEAE related to ERAS-007; Data extraction date: 23 April 2024

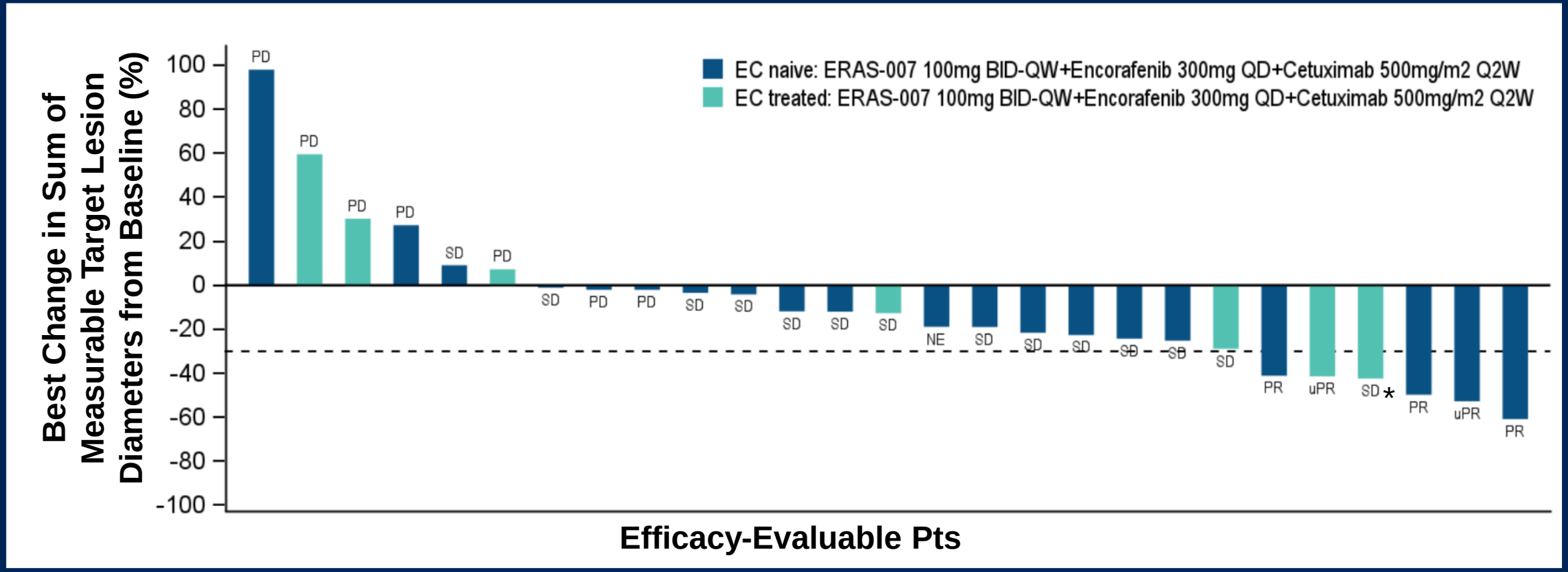
Severity CTCAE Grade: Grade 1=Mild; Grade 2=Moderate; Grade 3=Severe; Grade 4=Life-Threatening; Grade 5=Fatal

Objective Response Rate

ERAS-007 100 mg BID-QW + EC pts	EC Naïve (N = 20)	All (N = 27)
Objective response per RECIST (n %)		
Complete Response (CR)	0	0
Partial Response (PR)	3 (15.0)	3 (11.1)
Stable Disease (SD)	12 (60.0)	16 (59.3)
Progressive Disease (PD)	4(20.0)	7 (25.9)
Not Evaluable (NE)	1 (5.0)	1 (3.7)
Confirmed responders	3 (15.0)	3 (11.1)
95% CI for objective response rates	(3.21, 37.89)	(2.35, 29.16)
Confirmed and unconfirmed responders	4 (20.0)	5 (18.5)
95% CI for objective response rates	(5.73, 43.66)	(6.30, 38.08)
Disease control rate (CR+PR+SD)	15 (75.0)	19 (70.4)

Efficacy-evaluable population includes safety-evaluable pts with a measurable disease at baseline and at least one post-dose response assessment. EC naïve = pts that had no prior EC treatment before study; All = naïve group + pts treated with EC prior to the study

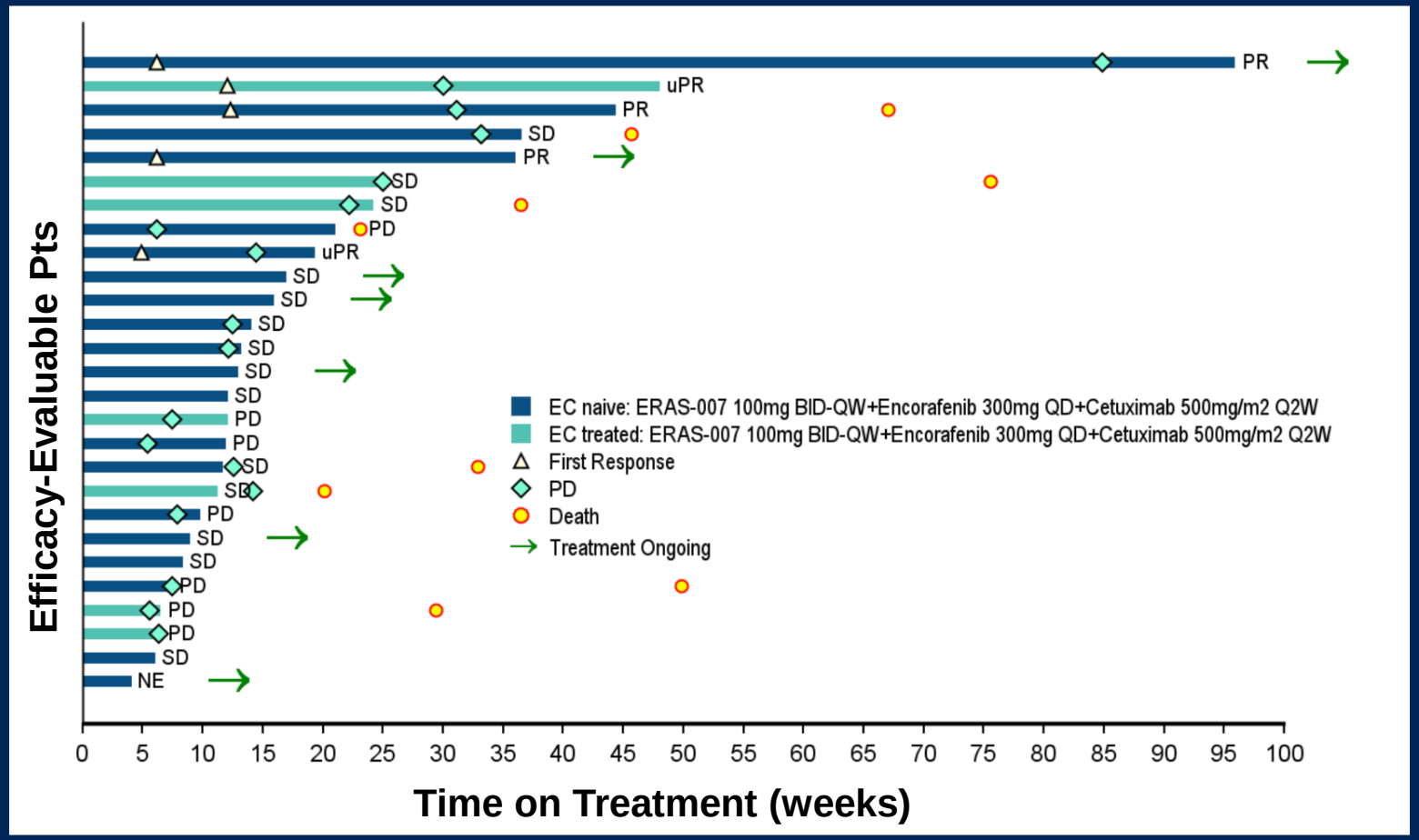
Best % Change in Target Lesions in All and EC Naïve Pts



* Patient had best overall response of SD prior to the % change in target lesions reaching > -30% at which point the patient had PD; Efficacy-evaluable population includes safety-evaluable pts with a measurable disease at baseline and at least one post-dose response assessment. Response on the bar represents the best overall response based on investigator assessment.

BID-QW: twice a day once a week; PD: progressive disease; PR: partial response; SD: stable disease. uPR: unconfirmed partial response; Data extraction date: 23 April 2024

Duration of Treatment in All and EC Naïve Pts



Median duration of treatment exposure (weeks):

All pts - **12.9 (4.0 to 95.9)**

EC Naïve - **13.0 (4.0 to 95.9)**

Efficacy-evaluable population includes safety-evaluable pts with a measurable disease at baseline and at least one post-dose response assessment. PD: progressive disease; PR: partial response; Pts: Patients; SD: stable disease; uPR: unconfirmed partial response

Key Results and Conclusions

- ERAS-007 (100 mg BID-QW) combined with EC has demonstrated an acceptable safety profile and tolerability in clinical trials, with the majority of ERAS-007-related adverse events being low-grade.
- The objective response rate for the ERAS-007 + EC triplet in EC-naïve patients with BRAF-mutant CRC was comparable to historical controls for EC alone[1].
- BRAFV600E mCRC continues to be a disease with a poor prognosis in need of novel therapeutic approaches.

1 Kopetz et al 2019 NEJM

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  - Alexander I. Spira - *Virginia Cancer Specialists, Fairfax, VA*
  - David R. Spigel - *Sarah Cannon Research Institute, Nashville, TN*
  - Susanna V. Ulahannan - *University of Oklahoma Health Sciences Center, Oklahoma City, OK*

THANK YOU