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THE BEACON STUDY

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UNMET MEDICAL NEED IN BRAF-MUTATED mCRC PATIENTS

- BRAF mutations (nearly always V600E) are found in the tumours of between 8% and 15% of patients with mCRC[1]
- BRAF mutations are a significant negative prognostic marker for patients with mCRC[1]
- Tumour BRAF mutation status should be determined for every case of CRC, ideally at the time of diagnosis
- FOLFOXIRI plus bevacizumab might be a reasonable option for the first-line treatment of BRAF mutant mCRC (Subgroup analysis of TRIBE study)[2,3]
- Up to now there is no standard of care therapy (particulary not beyond 1st line therapy) for BRAF V600E mutated-mCRC patients.

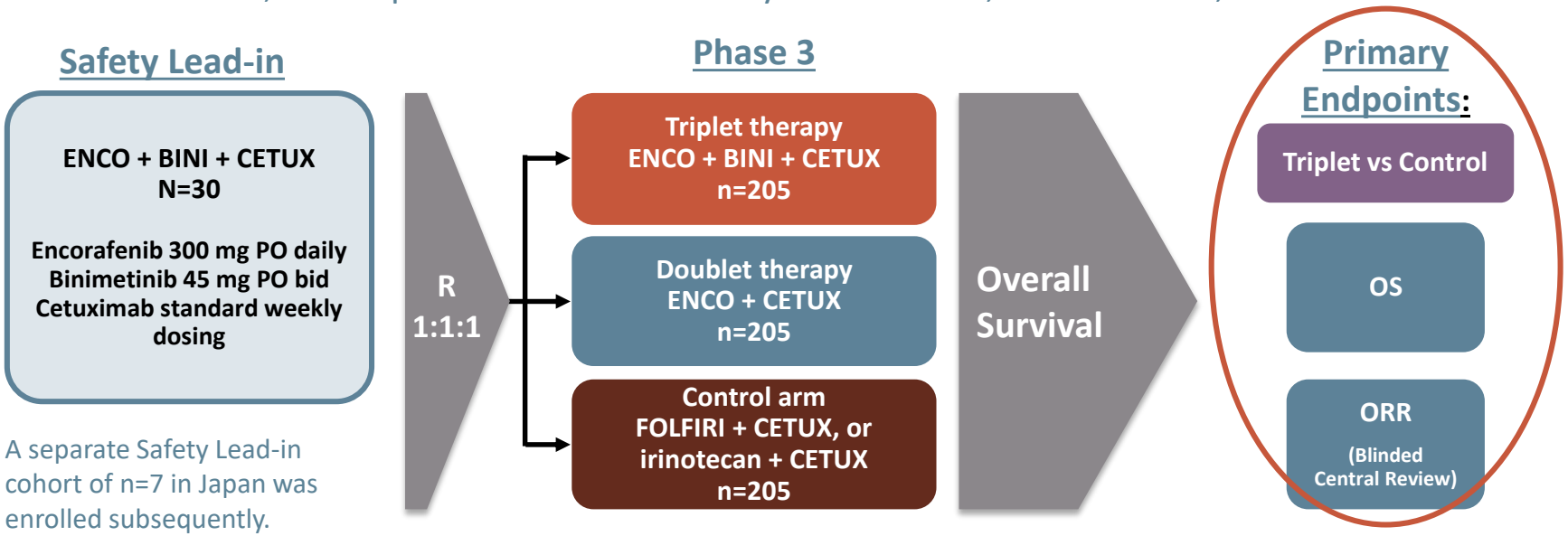
FOLFOXIRI, folinic acid + fluorouracil + oxaliplatin + irinotecan; mCRC, metastatic colorectal cancer;

[1]Tran B. et al. Cancer 2011; 117: 4623-32.
[2]Cremolini C, et al. Lancet Oncol 2015; 16: 1306–1315
[3]Van Cutsem E. et al. Ann Oncol. 2016; 27(8):1386-422

BEACON STUDY DESIGN

NCT02928224: Phase III, open-label, randomised study

Eligibility: Patients with BRAFV600E mCRC with disease progression after 1 or 2 prior regimens; ECOG PS of 0 or 1;and no prior treatment with any RAF inhibitor, MEK inhibitor, or EFGR inhibitor



A separate Safety Lead-in cohort of n=7 in Japan was enrolled subsequently. Results will be reported at a later time.

Randomization was stratified by ECOG PS (0 vs. 1), prior use of irinotecan (yes vs. no), and cetuximab source (US-licensed vs. EU-approved).

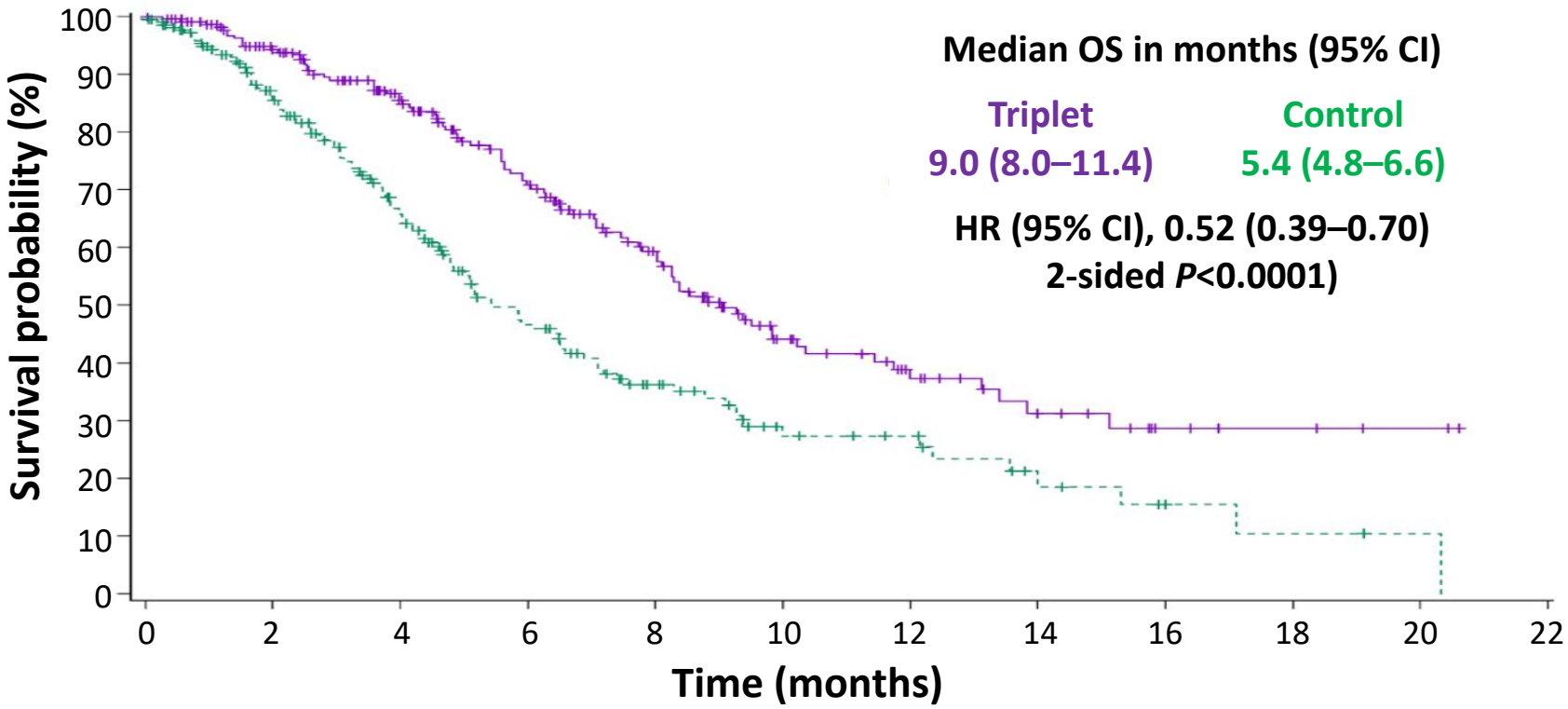
Secondary Endpoints: Doublet vs. Control OS & ORR, PFS, Safety

ECOG PS: Eastern Cooperative Oncology Group performance status; FOLFIRI, folinic acid + fluorouracil + irinotecan; mCRC, metastatic colorectal cancer; ORR, obective response rate; OS, overall survival; PFS, progression-free survival: PO, per os;

Van Cutsem E. et al. J Clin Oncol. 2019;37(17):1460-1469; Kopetz S. et al. N Engl J Med. 2019;381(17):1632-1643; Tabernero J, et al. ESMO 2019 Abstract LBA32

BEACON STUDY
PRIMARY ENDPOINT

= Overall survival: Triplet therapy vs control arm (all randomized patients)



Triplet	224	186	141	103	69	37	24	14	6	4	2	0
Control	221	158	102	60	34	18	15	7	4	2	1	0

CI, Confident interval; HR, hazard ratio; OS, overall survival;
Kopetz S. et al. N Engl J Med. 2019;381(17):1632-1643; Tabernero J, et al. ESMO 2019 Abstract LBA32

BEACON STUDY
ADVERSE EVENTS AND LABORATORY ABNORMALITIES*

Events	Triplet N=222 Grade ≥3	Doublet N=216 Grade ≥3	Control N=193 Grade ≥3
Diarrhea	10%	2%	10%
Abdominal pain	6%	2%	5%
Nausea	5%	<1%	1%
Vomiting	4%	1%	3%
Pulmonary embolism	4%	1%	3%
Intestinal obstruction	3%	4%	3%
Asthenia	3%	3%	5%
Acute kidney injury	3%	2%	<1%
Fatigue	2%	4%	4%
Dermatitis acneiform	1%	2%	1%
Illeus	2%	1%	2%
Urinary tract infection	1%	2%	1%
Cancer pain	<1%	2%	<1%
Laboratory abnormality			
Hemoglobin (g/L), hypo	10%	5%	4%
Creatinine (µmol/L), hyper	4%	2%	1%
Bilirubin (µmol/L), hyper	2%	2%	3%
Creatinine Kinase (IU/L), hyper	2%	0	0

*Occurring in at least 2% of patients in either triplet or doublet arms

BEACON STUDY
CONCLUSIONS

- Encorafenib, cetuximab and binimetinib (triplet), and encorafenib and cetuximab (doublet), significantly improved OS and ORR relative to the current standard of care (control) in patients with BRAFV600E mutant mCRC
- The safety and tolerability profile of both combinations allow maintenance of high dose intensity for most patients and are consistent with the known profiles of the component agents

First evidence of survival benefit for a chemotherapy-free targeted treatment regimen in prospective biomarker-defined patients with metastatic colorectal cancer, defining a new standard of care

mCRC, metastatic colorectal cancer; ORR, obective response rate; OS, overall survival;
Kopetz S. et al. N Engl J Med. 2019;381(17):1632-1643; Tabernero J, et al. ESMO 2019 Abstract LBA32

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