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MEETING SUMMARY
ESMO 2019, Barcelona, Spain

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HEPATOBILIARY CANCER AND COLORECTAL CANCER

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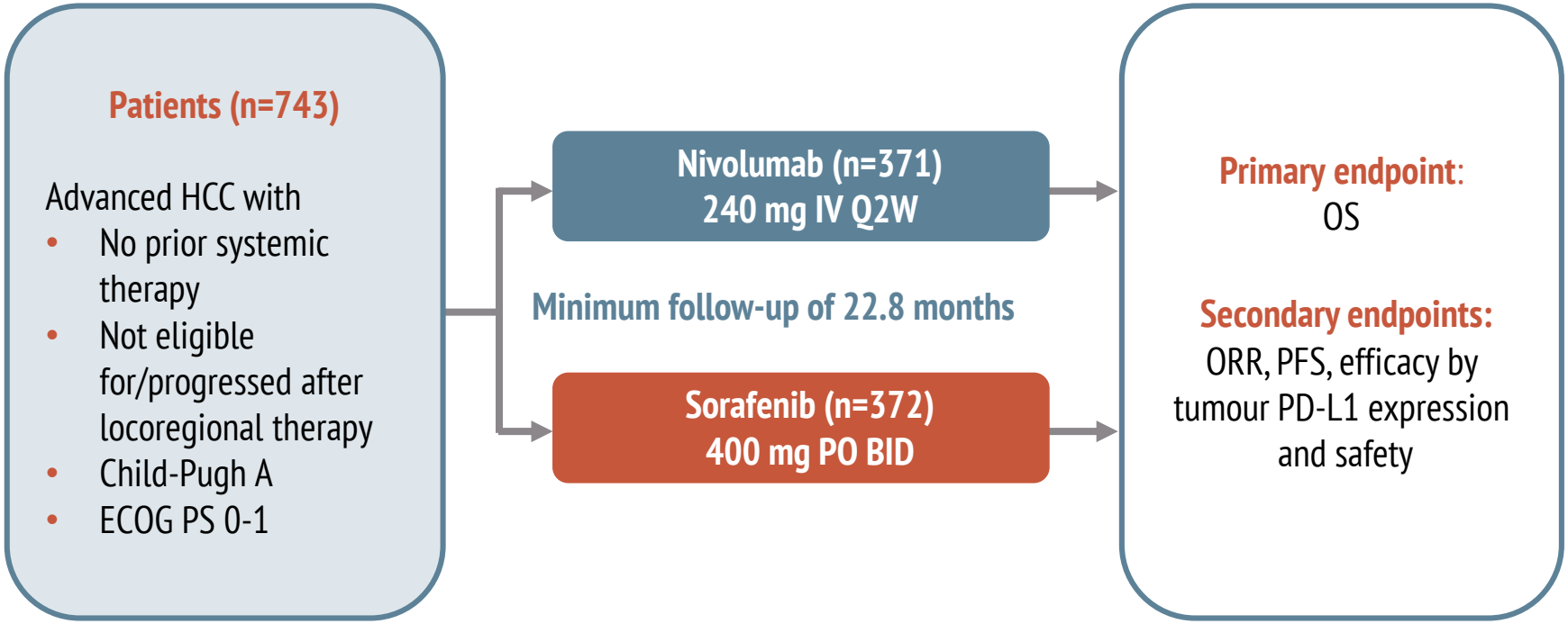
CHECKMATE 459: A RANDOMIZED, MULTI-CENTER PHASE 3 STUDY OF NIVOLUMAB VS SORAFENIB AS FIRST-LINE TREATMENT IN PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA

Yau T, et al. ESMO 2019 Abstract #LBA38_PR

CHECKMATE 459 STUDY DESIGN

NCT02576509: Phase III, randomized, multicentre, open-label study



BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group – performance status; HCC; hepatocellular carcinoma; IV, intravenous; ORR, overall response rate; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; PO, *per os*; Q2W, twice a week

Yau T, et al. ESMO 2019 Abstract LBA38_PR.

CHECKMATE 459 STUDY
RESULTS: EFFICACY AND SAFETY

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- Overall survival (OS) did not meet the predefined threshold of statistical significance (HR 0.84, P=0.0419)

	Nivolumab (n=371)	Sorafenib (n=372)
Median OS, months (95% CI)	16.4 (13.9-18.4)	14.7 (11.9-17.2)
12-months OS rate, % (95% CI)	59.7 (54.4-64.6)	55.1 (49.8-60.1)
24-months OS rate, % (95% CI)	36.8 (31.8-41.8)	33.1 (28.3-38.0)
Median Progression-free survival, months (95% CI)	3.7 (3.1-3.9)	3.8 (3.7-4.5)
Objective response rate, n (%)	57 (15)	26 (7)
Best overall response, n (%)		
Complete response	14 (4)	5 (1)
Partial response	43 (12)	21 (6)
ORR by baseline tumour PD-L1 expression, n/n (%)		
PD-L1 ⩾1%	20/71 (28)	6/64 (9)
PD-L1 <1%	36/295 (12)	20/300 (7)
Grade 3/4 treatment related adverse events, n (%)	81 (22)	179 (49%)
Discontinuation, n (%)	16 (4)	29 (8%)

HR; hazard ratio; OS, overall survival; PD-L1, programmed death ligand 1

Yau T, et al. ESMO 2019 Abstract LBA38_PR.

CHECKMATE 459 STUDY
CONCLUSIONS

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- Though the primary endpoint of overall survival did not achieve statistical significance versus sorafenib, nivolumab showed clinically meaningful improvements in overall survival, objective response rate, and complete response rate as first-line treatment for advanced hepatocellular carcinoma
- Nivolumab demonstrated a favorable safety profile consistent with previous reports

RANDOMIZED EFFICACY AND SAFETY RESULTS FOR ATEZOLIZUMAB + BEVACIZUMAB IN PATIENTS WITH PREVIOUSLY UNTREATED, UNRESECTABLE HEPATOCELLULAR CARCINOMA

Lee M, et al. ESMO 2019 Abstract #LBA39

GO30140 STUDY DESIGN

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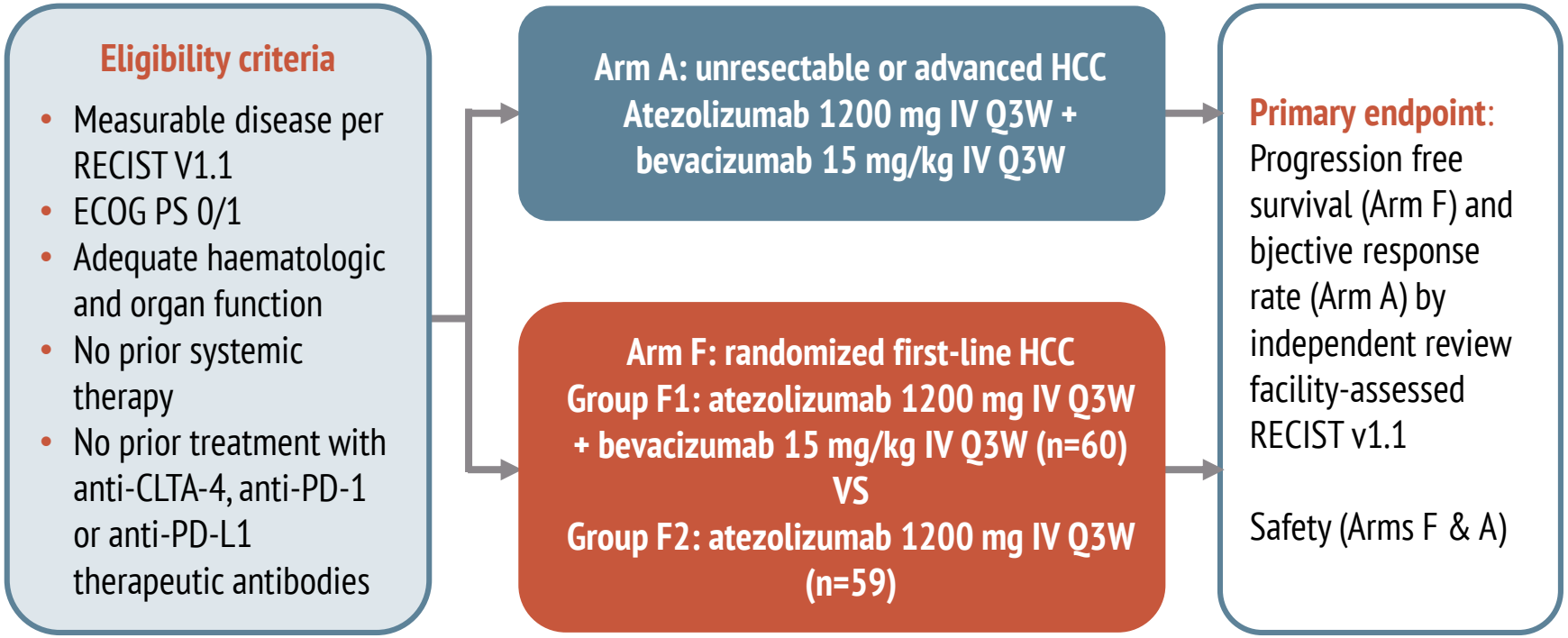
NCT02715531: Phase Ib, multicentre, open-label study



CTLA-4, cytotoxic T-lymphocyte-associated protein 4; ECOG PS, Eastern Cooperative Oncology Group – performance status; HCC; hepatocellular carcinoma; IV, intravenous; ORR, overall response rate; PD-1, programmed cell death 1; PD-L1, programmed death ligand 1; Q3W, three time a week

Lee M, et al. ESMO 2019 Abstract LBA39.

GO30140 STUDY
RESULTS: EFFICACY AND SAFETY + CONCLUSION

	Arm A (n=104)
Primary endpoint ORR, n (%)	37 (36%)
Any grade TRAEs, n (%)	91 (88%)
Grade 3-4 TRAEs, n (%)	41 (39%)
Grade 5 TRAEs, n (%)	3 (3%)

Arm F	Group F1 (n=60)	Group F2 (n=59)	HR, p value
Median progression-free survival, months	5.6	3.4	HR 0.55, 80% CI, 0.40-0.74, p= 0.0108
Any grade TRAEs, n (%)	41 (68%)	24 (41%)	–
Grade 3-4 TRAEs, n (%)	12 (20%)	3 (5%)	
Grade 5 TRAEs, n (%)	0 (0%)	0 (0%)	

- Coupled with a tolerable safety profile, these data suggest that atezolizumab + bevacizumab could become a promising first-line treatment option for unresectable HCC if further studies confirm the efficacy data shown in this study

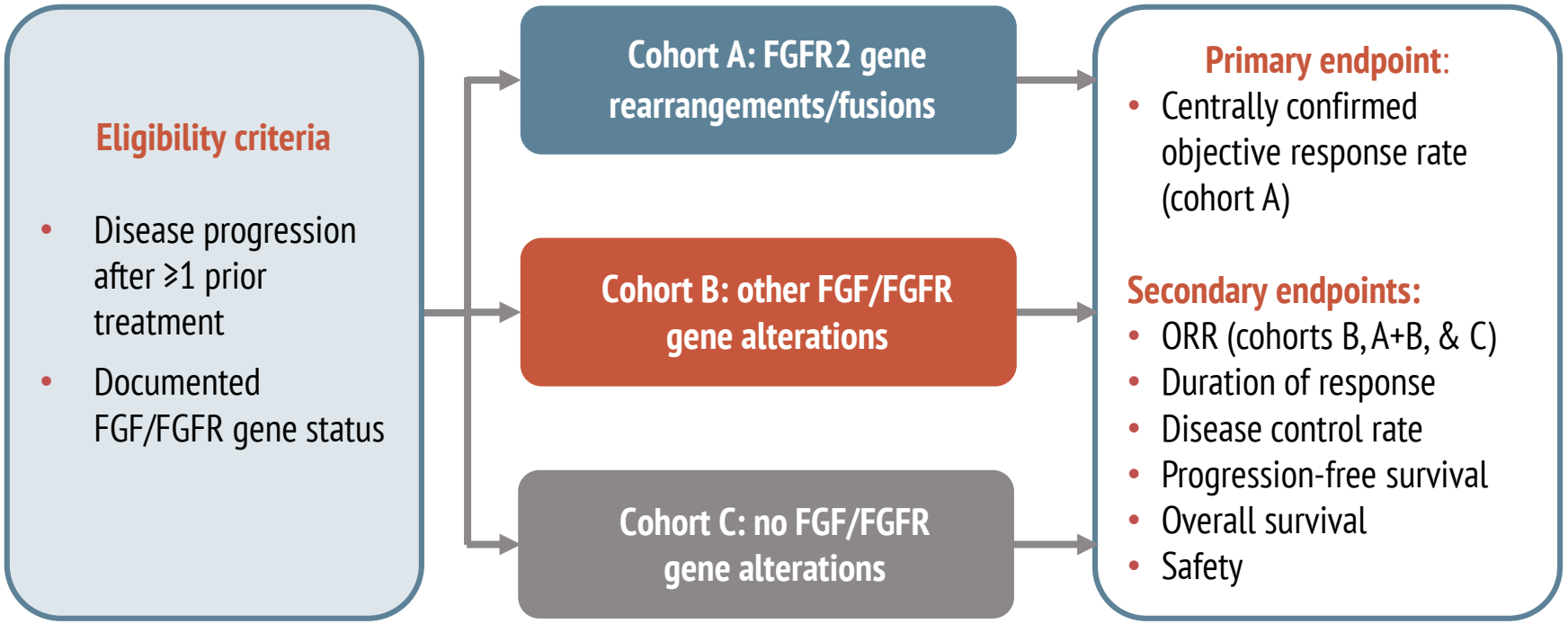
CI, confidence interval; HCC; hepatocellular carcinoma; HR, hazard ratio; ORR, overall response rate; TRAEs, treatment-related adverse events
Lee M, et al. ESMO 2019 Abstract LBA39.

FIGHT-202: A PHASE II STUDY OF PEMIGATINIB IN PATIENTS WITH PREVIOUSLY TREATED LOCALLY ADVANCED OR METASTATIC CHOLANGIOCARCINOMA

Vogel A, et al. ESMO 2019 Abstract #LBA40

FIGHT-202 STUDY DESIGN

NCT02924376 : Phase II, open label, single arm study



- Patients in each cohort received oral pemigatinib 13.5 mg QD (21-day cycle; 2 weeks on, 1 week off) until disease progression/unacceptable toxicity

FGF, Fibroblast growth factor; FGFR, Fibroblast growth factor receptor; ORR, objective response rate; QD, every day

Vogel A, et al. ESMO 2019 Abstract LBA40.

FIGHT-202 STUDY (CUT OFF DATE: MARCH 22, 2019)
RESULTS: EFFICACY AND SAFETY + CONCLUSION

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- 146 patients were enrolled (cohort A, n=107; B, n=20; C, n =18; 1 undetermined)
- ORR in cohort A was 35.5% (95% CI, 26.5%–45.4%), with 3 complete responses
- Median DOR was 7.5 months (95% CI, 5.7–14.5)
- DCR was 82% (95% CI, 74%–89%)
- mPFS and mOS were 6.9 months (95% CI, 6.2–9.6) and 21.1 months (14.8–not reached) (OS not mature at cutoff)
- In cohorts B and C, no patient achieved a response
- Overall, most common adverse events were hyperphosphatemia (60%; grade ≥3, 0%), alopecia (49%; 0%), diarrhea (47%; 3%), fatigue (42%; 5%), nail toxicities (42%; 2%), and dysgeusia (40%; 0%). Hyperphosphatemia was managed with diet modifications, phosphate binders, if needed; diuretics or dose reductions/interruptions
- Discontinuation, dose reduction and interruption due to AEs occurred in 9%, 14% and 42% of patients, respectively

→ These data support pemigatinib as a potential treatment option for previously treated patients with CCA harbouring FGFR2 gene rearrangements/fusions

AEs, adverse events; CCA, cholangiocarcinoma; DCR, disease control rate; DOR, duration of response; FGFR2, Fibroblast growth factor receptor 2; mOS, median overall survival; mPFS, median progression-free survival; ORR, overall response rate; OS, overall survival

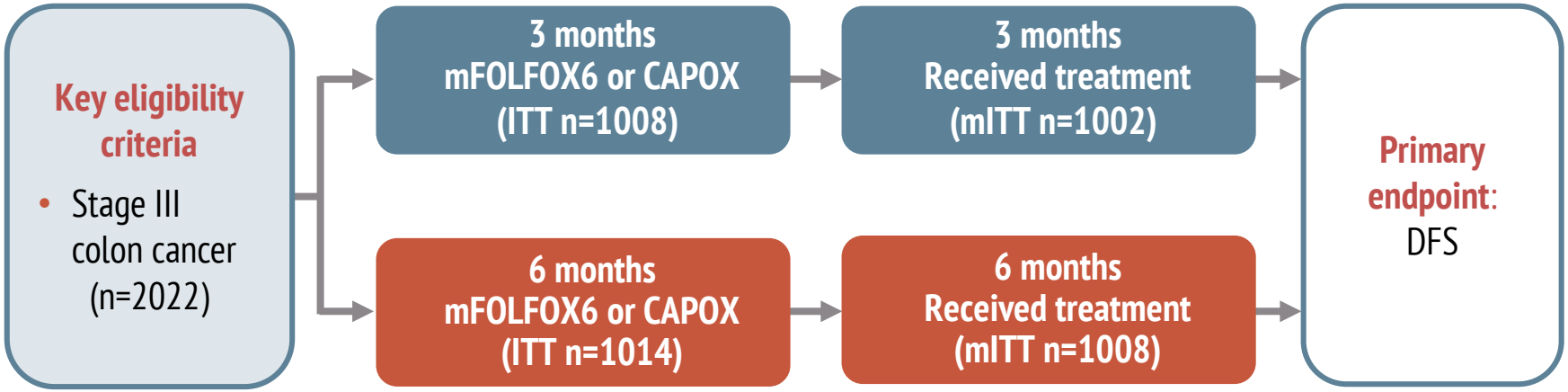
Vogel A, et al. ESMO 2019 Abstract LBA40.

ANALYSIS OF CIRCULATING TUMOUR DNA (ctDNA) FROM PATIENTS ENROLLED IN THE IDEA-FRANCE PHASE III TRIAL: PROGNOSTIC AND PREDICTIVE VALUE FOR ADJUVANT TREATMENT DURATION

Taieb J, et al. ESMO 2019 Abstract #LBA30_PR

IDEA STUDY DESIGN

NCT00958737: Phase III, open-label, randomised study[1]



Background

ctDNA = major prognostic factor in resected stage II and III colon cancer patients[2,3]

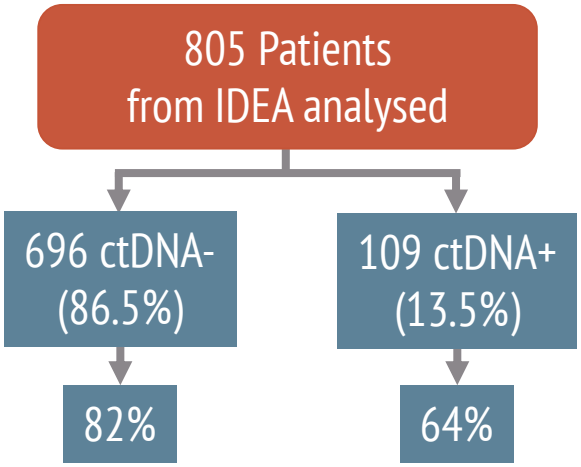
Objective

Analysing ctDNA from patients enrolled in the IDEA-FRANCE trial for its prognostic value and its predictive value for treatment duration

CAPOX, capecitabine plus oxaliplatin; DFS, disease-free survival; ITT, intent to treat; mITT, modified intent to treat; mFOLFOX6, fluorouracil, leucovorin, and oxaliplatin

[1]Andre T. et al. J Clin Oncol. 2018;36(15):1469-1477; [2]Tie J, et al. Sci Transl Med. 2016;8(346):346ra92;
[3]Schøler LV, et al. Clin Cancer Res. 2017;15;23(18):5437-5445; Taieb J, et al. ESMO 2019 Abstract LBA30_PR.

ctDNA ASSESSMENT FROM IDEA STUDY
RESULTS + CONCLUSION



2-year DFS

HR: 1.75 (95% CI 1.25-2.45)
p=0.001

- In multivariate analysis including age, gender, MSI, perforation, T stage, N stage and treatment arm, ctDNA was confirmed as an independent prognostic marker (adj.HR: 1.85 (95%CI 1.31 to 2.61) **p < 0.001**)
- Adjuvant treatment for 6 months was superior to 3 months in both ctDNA– (HR: 0.69 (95%CI 0.52 to 0.93) p=0.015) and ctDNA+ pts (HR: 0.50 (95%CI 0.27 to 0.95) p=0.033)
- Interestingly ctDNA+ pts treated 6 months had a similar prognosis to ctDNA- pts treated 3 months

→ ctDNA was confirmed as an independent prognostic marker.

CI, confidence interval; ctDNA, circulating tumour DNA; DFS, disease-free survival; HR, hazard ratio; MSI, microsatellite instable
Taieb J, et al. ESMO 2019 Abstract LBA30_PR.

ENCORAFENIB PLUS CETUXIMAB WITH OR WITHOUT BINIMETINIB FOR BRAF V600E MUTANT METASTATIC COLORECTAL CANCER: EXPANDED RESULTS FROM A RANDOMIZED, 3-ARM, PHASE III STUDY VS THE CHOICE OF EITHER IRINOTECAN OR FOLFIRI PLUS CETUXIMAB (BEACON CRC)

Tabernero J, et al. ESMO 2019 Abstract #LBA32

BEACON STUDY
DESIGN AND CURRENT STATUS

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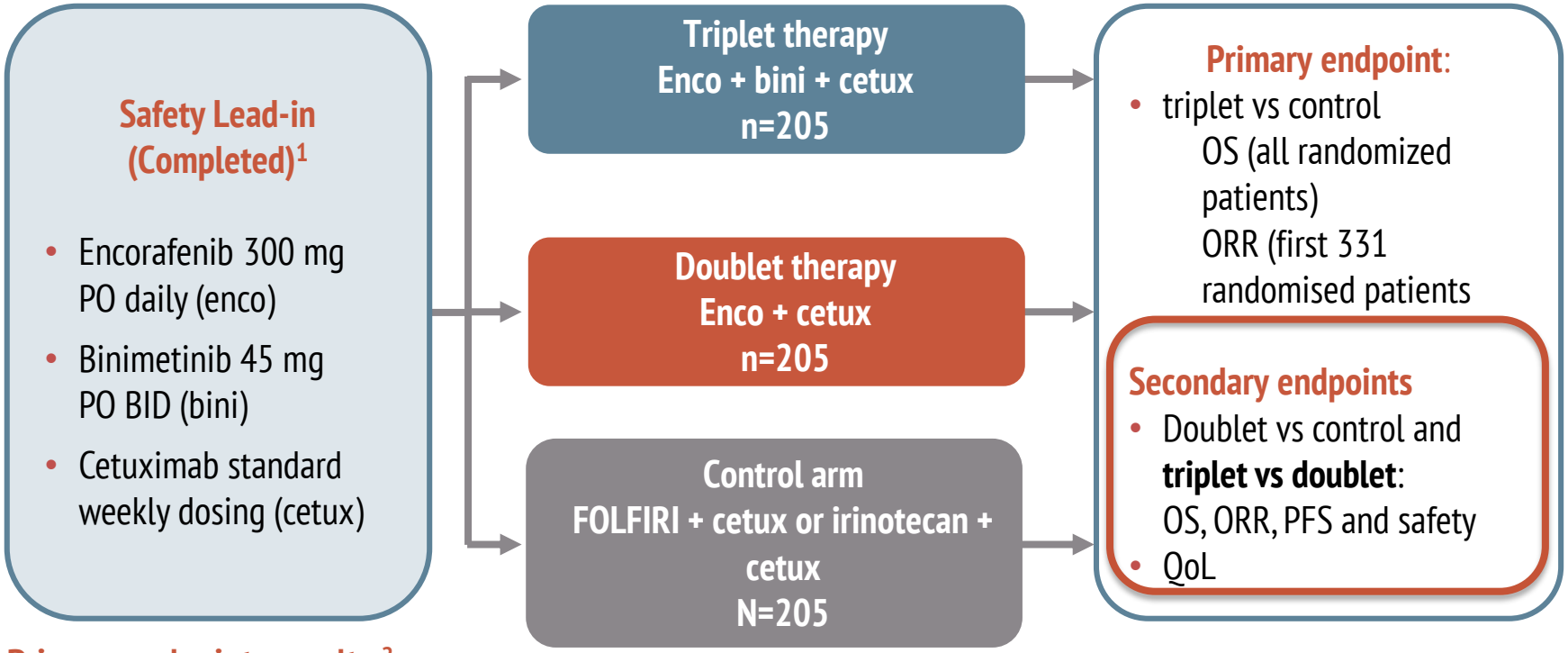
NCT02928224: Phase III, open-label, randomised study



Primary endpoints results:[2]

Triplet therapy significantly improved overall survival (HR:0.52, P<0.001) and ORR (26% in triplet arm vs 2% in control arm, P<0.001) in patients with BRAFV600E mCRC compared with current standard of care

BID, twice a day; FOLFIRI, folinic acid + fluorouracil + irinotecan; mCRC, metastatic colorectal cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival: PO, *per os*; QoL, quality of life

[1]Van Cutsem E. et al. J Clin Oncol. 2019;37(17):1460-1469; [2]Kopetz S. et al. N Engl J Med. 2019 (Epub ahead of print); Tabernero J, et al. ESMO 2019 Abstract LBA32

BEACON STUDY – SECONDARY ENDPOINTS

TRIPLET VS DOUBLET: RESULTS AND CONCLUSIONS

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	Triplet therapy (n=224)	Doublet therapy (n=220)	HR (95% CI)
Median OS, months (95% CI)	9.0 (8.0-11.4)	8.4 (7.5-11.0)	0.79 (0.59-1.06)
Overall response rate, % (95% CI)	26 (18-35)	20 (13-29)	–
Patients with one prior therapy			
ORR, % (95% CI)	34 (23-47)	22 (14-33)	–
Grade ≥3 adverse events, %	58	50	–
Rate of discontinuation, %	7	8	–

There were no differences in QoL across all used instruments

Median follow up: 7.8 months

→ Triplet therapy compared to doublet therapy has some improved efficacy with a modest increase in toxicities and no detrimental effect in QoL

CI, confidence interval; HR, hazard ratio; OS, overall survival, ORR; objective response rate; QoL; quality of life
Tabernero J, et al. ESMO 2019 Abstract LBA32; Kopetz S. et al. N Engl J Med. 2019 (Epub ahead of print).

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