Supplemental Material

Table S1 Baseline patient characteristics[1,2]

Characteristic	Encorafenib + cetuximab (n=220)	Encorafenib + binimetinib + cetuximab (n=224)	Control (n=221)
Female, %	48	53	57
Age, median (range), years	61 (30, 91)	62 (26, 85)	60 (27, 91)
ECOG PS=0, %	51	52	49
Location of primary tumour,[a] %			
Left side of colon (including rectum)	38	35	31
Right side of colon	50	56	54
≥3 organs involved, %	47	49	44
Presence of liver metastases, %	61	65	58
Prior lines of therapy, %			
1	66	65	66
2[b]	34	35	34
MSI-H,[c] %	9	10	5
CEA baseline value > 5 µg/L, %	70	80	81
CRP baseline value > 10 mg/L, %	36	42	41

[a]Remaining patients had primary tumour in both left and right sides of colon and those with unknown location of primary tumour; [b]Includes one patient in the encorafenib + binimetinib + cetuximab group and one patient in the control group who received >2 prior lines of therapy; [c]Based on assessment by polymerase chain reaction; MSI status is missing in 23% of patients.[3]

CEA, carcinoembryonic antigen; CRP, C-reactive protein; ECOG PS, European Cooperative Oncology Group Performance Status; MSI-H, microsatellite instability-high.

Table S2 Cetuximab dose reduction and modification guidance for dermatologic AEs[4,5a]

AE	Dose modification
Dermatologic toxicities and infectious sequelae (eg, acneiform rash, mucocutaneous disease)	First occurrence, grade 3 or 4 • Delay cetuximab infusion for 1–2 weeks; if condition improves continue at 250 mg/m^2 • If no improvement, discontinue cetuximab[b] Second occurrence, grade 3 or 4 • Delay cetuximab infusion for 1–2 weeks; if condition improves continue at 200 mg/m^2 • If no improvement, discontinue cetuximab[b] Third occurrence, grade 3 or 4 • Delay cetuximab infusion for 1–2 weeks; if condition improves continue at 150 mg/m^2 • If no improvement, discontinue cetuximab[b] Fourth occurrence, grade 3 or 4 • Discontinue cetuximab[b]

[a]For full details on dosage modifications, please consult the Prescribing Information or Summary of Product Characteristics[4,5]; [b]If cetuximab is discontinued, encorafenib should also be discontinued.[6,7] AE, adverse event.

REFERENCES FOR SUPPLEMENTARY TABLES

1. Kopetz S, Grothey A, Yaeger R*, et al.* Encorafenib, binimetinib, and cetuximab in BRAF V600E-mutated colorectal cancer. *N Engl J Med* 2019;381:1632-43.
2. Tabernero J, Grothey A, Van Cutsem E*, et al.* Encorafenib Plus Cetuximab as a New Standard of Care for Previously Treated BRAF V600E–Mutant Metastatic Colorectal Cancer: Updated Survival Results and Subgroup Analyses from the BEACON Study. *J Clin Oncol* 2021;39:273-84.
3. Kopetz S, Grothey A, Van Cutsem E*, et al.* Encorafenib plus cetuximab with or without binimetinib for BRAF V600E-mutant metastatic colorectal cancer: Quality-of-life results from a randomized, three-arm, phase III study versus the choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC). Presented at: American Society of Clinical Oncology; 2020; abstract 8.
4. Eli Lilly and Company. ERBITUX® Prescribing Information; Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/125084s273lbl.pdf [accessed 17 June 2020].
5. Erbitux 5 mg/mL solution for infusion Summary of Product Characteristics. January 2020. https://www.ema.europa.eu/en/medicines/human/EPAR/erbitux#product-information-section. [accessed 17 June 2020].
6. Array BioPharma Inc. BRAFTOVI® (encorafenib) prescribing information; Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/210496s006lbl.pdf [accessed 14 July 2020].
7. Pierre Fabre Médicament. BRAFTOVI® (encorafenib) summary of product characteristics; Available from: https://www.ema.europa.eu/en/documents/product-information/braftovi-epar-product-information_en.pdf [accessed 14 July 2020].