

Supplement: Plain Language Summary

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Managing side effects in patients who are being treated with encorafenib and cetuximab for advanced colorectal cancer

Date of summary: June 2021 [placeholder – to be updated with month of publication upon acceptance]

Study number: NCT02928224; <https://clinicaltrials.gov/ct2/show/NCT02928224>

Study start date: October 2016

Study end date: May 2022

The full title of this article is: Management of adverse events from the treatment of encorafenib plus cetuximab for patients with *BRAF* V600E-mutant metastatic colorectal cancer: insights from the BEACON CRC study

Encorafenib is pronounced “en koe RAF e nib”.

Cetuximab is pronounced “se TUK see mab”.

The purpose of this plain language summary is to explain the findings from recent research.

- This summary reports the results of a single study. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, not on the results of a single study. The study described here is still ongoing and the final results may be different from the outcomes described in this summary.
- Encorafenib plus cetuximab is approved in the United States and Europe to treat people with a specific type of colorectal cancer (CRC).

What did this study look at?

- CRC is cancer in the large intestines, also known as the colon and rectum. When cancer spreads to other locations in the body, such as the liver, it is called metastatic. This study looked at patients with metastatic CRC (mCRC).
- This summary is based on research that looked at the most common side effects that occur when patients with mCRC take encorafenib and cetuximab together. This summary also suggests the best ways to manage these side effects.

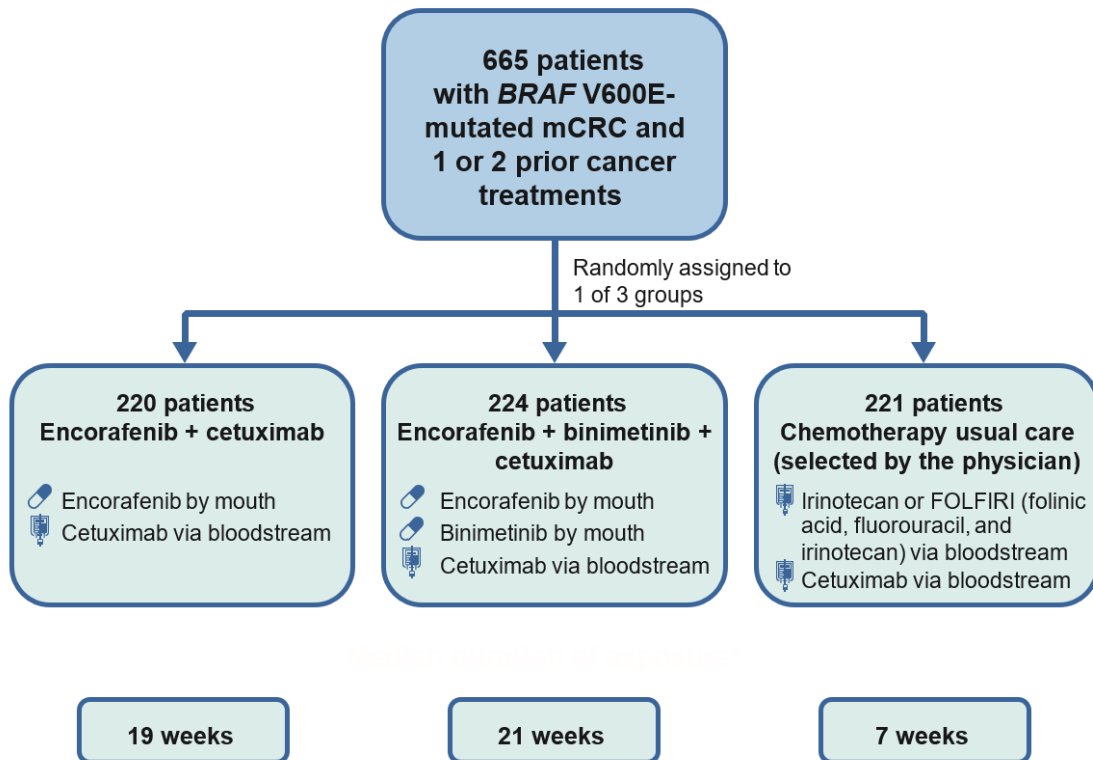
Description of Drugs used in This Study

- Encorafenib plus cetuximab is a treatment option for people with *BRAF* V600E-mutated mCRC.
 - Encorafenib is a *BRAF* inhibitor, meaning it blocks the action of a gene (a gene is a section of DNA that tells the cell how to make a specific molecule, such as a protein) called *BRAF* which increases the growth and spread of cancer.
 - Cetuximab is an EGFR, or epidermal growth factor receptor, inhibitor. EGFR is a protein that acts with *BRAF* to increase the growth and spread of cancer cells. Cetuximab blocks the action of EGFR, and together with encorafenib, the treatment aims to block the growth and spread of cancer cells.
- Binimetinib is an inhibitor that blocks proteins called MEK1 and MEK2. MEK1 and MEK2 proteins act with *BRAF* to increase the growth and spread of cancer cells. Binimetinib together with encorafenib and cetuximab aims to block the growth and spread of cancer cells.
 - Binimetinib, either when used alone or with other drugs, is not approved for the treatment of mCRC.
- The approvals of encorafenib and cetuximab in the US and Europe were based on the results of a study called BEACON CRC, which is still ongoing. The study is looking at how well the therapy works and is also examining any medical problems or side effects that happen during treatment.
 - Medical problems may be caused by reasons not related to the study (for example, caused by an underlying disease or by chance) or they may be caused by a study treatment or by another medicine the patient is taking.
 - A side effect is something (expected or unexpected) that is thought to be caused by a medicine or treatment taken by a patient.
 - The BEACON CRC study results showed that the group of patients who took encorafenib plus cetuximab had fewer medical problems and lived longer than the patients who took the previous standard treatment for this type of cancer (chemo plus cetuximab).

Who took part in this study?

- Researchers studied 665 patients with *BRAF* V600E-mutated mCRC who had already received one or two treatments before this study and whose cancer came back.
- The patients in this study were between 26 and 91 years old when they started the study, with the average age being about 60 years old. About half of the patients involved were men and half were women.
- Patients involved in this study were put into 1 of 3 possible treatment groups (**Figure 2**):
 1. Encorafenib plus cetuximab
 2. Encorafenib plus cetuximab plus binimetinib
 3. Standard chemo plus cetuximab
 - Previously, this was the standard treatment used for this type of cancer.
 - People in this group received what their physician believed was the best possible usual care for their disease.
- Chemo and cetuximab are administered directly into the bloodstream; encorafenib and binimetinib are taken as tablets.

Figure 2. Treatment groups in the study



What were the results of this study?

- The most common medical problems with the encorafenib and cetuximab combination involved the stomach and intestines and included diarrhea, nausea, decreased appetite, pain, and vomiting. Other common medical problems were feeling tired and achy, having acne-like bumps on the skin, and getting headaches (**Table 1**).
- The number of serious medical problems that came up during treatment was about the same for both groups. A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems. Less than half of the people in the study (40%) had serious medical problems.

Table 1. Common medical problems reported by patients in the study

Medical problem	Encorafenib + cetuximab (216 patients total)	Chemotherapy usual care (193 patients total)
	Number of patients (%)	
Diarrhea	83 of 216 (38%)	94 of 193 (49%)
Nausea	82 of 216 (38%)	84 of 193 (44%)
Fatigue/weakness	72 of 216 (33%)	54 of 193 (28%)
Decreased appetite	67 of 216 (31%)	56 of 193 (29%)
Acne-like bumps on skin	65 of 216 (30%)	77 of 193 (40%)
Abdominal pain	60 of 216 (28%)	54 of 193 (28%)
Vomiting	59 of 216 (27%)	61 of 193 (32%)
Muscle/joint pain	49 of 216 (23%)	4 of 193 (2%)
Headache	43 of 216 (20%)	5 of 193 (3%)
Fever	40 of 216 (19%)	28 of 193 (15%)
Anemia	42 of 216 (19%)	36 of 193 (19%)
Constipation	39 of 216 (18%)	39 of 193 (20%)
Mole/skin tag	34 of 216 (16%)	0
Rash	32 of 216 (15%)	28 of 193 (15%)
Dry skin/itch	28 of 216 (13%)	16 of 193 (8%)
Shortness of breath	28 of 216 (13%)	20 of 193 (10%)
Back pain	28 of 216 (13%)	27 of 193 (14%)
Pain in extremity/swelling	25 of 216 (12%)	14 of 193 (7%)
Weight decreased	24 of 216 (11%)	12 of 193 (6%)
Insomnia	24 of 216 (11%)	13 of 193 (7%)

Tips for understanding the table

- The first column of **Table 1** lists the medical problems that were commonly reported during the trial. All medical problems reported by more than 10% of patients are listed.
- The second column shows how many patients taking encorafenib plus cetuximab reported each medical problem, as well as what percentage of the group this equates to.
- The third column shows how many patients taking chemotherapy usual care reported each medical problem, as well as what percentage of the group this equates to.
- Using these tips, in the first row you can see that 82 out of 216 patients taking encorafenib plus cetuximab (38% of that group) had diarrhea. A total of 94 out of 193 patients (49%) taking chemotherapy usual care had diarrhea.

What is the best way to handle common medical problems that may happen during treatment?

- When starting a patient on a new cancer treatment, healthcare providers should tell patients and their caregivers about the medical problems that may occur and how to deal with them. They should also encourage patients to tell their cancer team and other healthcare professionals if a medical problem lasts a long time or if any symptoms change or worsen. **Figure 3** shows medical problems that are common when people take these kinds of medications. The figure lists the signs and symptoms and ways to handle each problem.

Figure 3. Common medical problems that may happen during mCRC treatment and

Problem	Signs and Symptoms	Suggestions for what to do
Diarrhea	Feeling hungry and thirsty, swelling, stomach ache	<ul style="list-style-type: none"> • Could there be other causes (such as infection)? • Change your diet (small meals, more often) • Eat less fiber • Drink more fluids • Replace lost salts with food or drinks (sports drink, soup, etc.) • Ask your doctor about taking an anti-diarrhea medication
Nausea/vomiting	Feeling hungry and thirsty, weakness, weight loss	<ul style="list-style-type: none"> • Avoid fried and spicy foods • Eat small meals, more often • Eat lukewarm or cold foods • Stay sitting up or standing for about an hour after eating • Brush and floss your teeth regularly • Drink fluids • Ask your doctor about taking anti-nausea medication
Skin reaction	Acne-like bumps on the skin, rash, itching	<ul style="list-style-type: none"> • Plan ahead: use gentle soaps, sun protection, and dry-skin lotion • Stay out of the sun • Check with your doctor about using a corticosteroid cream and/or antibiotic
Muscle/joint pain	Muscle pain, joint pain	<ul style="list-style-type: none"> • Rest the area that hurts • Consider using a pain reliever (check with your doctor) • Consider stretching • Ask your doctor about using low dose corticosteroids
Kidney problems	Urinating less frequently	<ul style="list-style-type: none"> • Drink enough fluids • Ask your doctor about any medications you are taking that could cause harm to the kidneys • Contact your doctor to see if you have a urinary tract infection
Fever, headache, feeling tired, weak	Fever, headache, feeling tired, weak	<ul style="list-style-type: none"> • Drink enough fluid • Eat a healthy diet • Exercise regularly if possible • Rest when needed • Consider using a pain reliever (check with your doctor) • Your doctor may consider other causes, such as infection

suggestions on how to handle them

mCRC, metastatic colorectal cancer.

What was the main conclusion reported by the researchers?

- Medical problems that patients have when they take encorafenib plus cetuximab are generally mild or moderate, and most patients can handle the problems with help from their cancer team. Knowing what the common medical problems are and preparing for them in advance might help lessen the discomfort they cause.

Are there any plans for further studies or publications?

- This study also measured other results of the treatment, such as changes to quality of life, which will be published in a separate paper.
- Because this study is not complete, more analyses of the data are planned to provide information to help doctors understand the best way to use the treatment to care for their patients.

Who sponsored this study?

- The BEACON CRC trial was sponsored by Array BioPharma in collaboration with Merck KGaA Darmstadt, Germany (for sites outside of North America), ONO Pharmaceutical, and Pierre Fabre. Array BioPharma was acquired by Pfizer in July 2019. The study was also supported by the Cancer Center Core Grant P30 CA 008748 to Memorial Sloan Kettering Cancer Center.

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