# Encorafenib in combination with cetuximab in BRAF<sup>V600E</sup>-mutant metastatic colorectal cancer: a pooled analysis of European observational studies



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## Introduction

- Encorafenib in combination with cetuximab (EC) has become the standard of care for patients with BRAF<sup>V600E</sup>-mutant metastatic colorectal cancer (mCRC) after prior systemic therapy.<sup>1–2</sup>
- The *BRAF<sup>V600E</sup>* mutation is estimated to occur in 8% to 12% of mCRCs and several real-world studies have collected data in this relatively rare patient population.<sup>1, 3–7</sup>
- Centralizing all the data in a unique database might allow a better understanding of the disease and the management of these patients.
- Therefore, we aimed to pool the available data on *BRAF<sup>V600E</sup>*-mutant mCRC patients treated with encorafenib-based regimens in a real-world setting in Europe to better understand BRAF testing, monitoring, disease characteristics and treatment strategies in these patients, as well as the patterns of use, effectiveness, and safety of this treatment.

#### Table 2. Variables across real-world evidence studies.

	BERING CRC	CONFIDENCE	B-REAL	Italian GONO Cohort	CATAMARAN
	NCT04673955	Retrospective	Retrospective	Retrospective	Retrospective
Adults ≥18 years	X	X	Х	Х	X
Demographics					
Sex	Х	X	X	Х	Х
Weight/height	X	X			
Race Employment status	X				
Medical history comorbidities	× ×	X			X
Country	X	X	Х	Х	X
Clinical characteristics			1		1
Initial CRC diagnosis					
Diagnosis date	X	X	X	X	
Primary tumor location	X	X	X	X	X
Sidedness	X	x	x	X	X
Surgery of primary tumor	X	X	X	X	X
TNM stage	Х	Х	Х	Х	Х
Diagnosis of mCRC					
Metastatic date	Х	Х	Х	Х	
Synchronous or metachronous lesions			X		Х
Site	X	X	X	X	X
	X	X	X	X	Χ.
Test date			X		x
Testing method	Х		X	Х	
Kind of material used	Х				
Result	Х	Х	Х	Х	Х
Biomarkers					
MSI/MMR test date			X		
IVISI high/low/stable/unknown	X	X	X	X	X
Prior reatment for CKC	Y		Y		
Start date	x		^		
End date	X				
Reason for end of treatment	Х				
Prior chemotherapy					
Start date			Х	Х	Х
End date					
Reason for end of treatment	v				
Start date	X				
End date	X				
Reason for end of treatment					
Prior primary surgery	Х	Х	Х		Х
Start date	Х	Х	Х		
End date					
Results	Х	X			Х
Reason for end of treatment	V				
Prior paillative therapies	X				
End date	X				
Reason for end of treatment	X				
Microscopic findings	X				
ECOG PS	Х	Х	Х	Х	Х
QoL EQ5D	X (QLQ–C30)				
Concomitant medication	X	X			Х
Adverse events	X	X	X	X	
Start uale End date	X	X			
Grade	X	X	x	X	
Relationship	X	X			
Action taken	Х	Х			
Seriousness	Х	Х			
Outcome	Х	Х			
Special situation reported	Χ				
Efficacy data		~	V	V.	
best response date	X	X	X	X	
Date of first disease progression	x	X	X	x	
Date of death	X	X	X	x	
Current treatment: Treatment E/C					
Start and end date of the lines	Х	Х	Х	Х	
Date of cycles					
Initial dosage	X	X	X	X	
Dosage modification (Y/N)	X	X	X	X	
Duse modification	X	X	X	X	
Dose modification	^	X	X	x	
Discontinuation	х	X	X	x	
Permanent discontinuation reason	X	X	X	X	
Temporary discontinuation reason	X	Х		Х	
Laboratory test results	Х				X (CEA and CRP leve
Subsequent treatment	Х	Х	Х	Х	Х
Start date	X	X	X	X	
End date	X	X		X	
Reason for end of treatment	X		X	X	

## Methods

- This is a retrospective, longitudinal, pooled data analysis of real-world observational studies conducted across Europe between 2020–2024.
- Adult patients (aged ≥18 years) who received an encorafenib-based regimen for BRAF<sup>V600E</sup>-mutant mCRC in each study will be included in the present pooled database.
- Data collected from the date of encorafenib-based treatment initiation (including treatment history and baseline demographics at initial diagnosis) until the end of the observation period in each study (end of follow-up or death, whichever occurred first) will be pooled in a unique *BRAF<sup>V600E</sup>* mCRC pooled database, as per the data pooling process (Figure 1).
- The pooling process will follow six steps (Figure 2).

#### Figure 1. The data program pooling process.

#### Figure 2. The steps of the data pooling process.



 The objectives of this pooling are to describe the demography and clinical characteristics, the treatment patterns, BRAF testing, effectiveness and safety of encorafenib-based regimen. Subgoups analyses of MSI-H and elderly population will be performed when data are available.

Resu	ts

- The pooled database will compile data from more than 800 patients across several studies, including BERING CRC (Austria/Germany/Switzerland; NCT04673955), B-REAL (France), CATAMARAN (the Netherlands), CONFIDENCE (Spain), Italian GONO Cohort (Italy).
- See **Table 1** for a summary of the studies and **Table 2** for a description of study variables.

#### Table 1. Studies included in the pooled analysis.

Study	Design	Countries	Patients	Outcomes	Ν	Status
BERING CRC	Prospective, longitudinal NIS	Austria, Germany, Switzerland	Adult patients with <i>BRAF<sup>V600E</sup>-</i> mutant mCRC treated with E/C	Effectiveness, baseline clinical and demographic characteristics, treatment patterns, safety and QoL	217/300	Ongoing

CA 19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; CRC, colorectal cancer; CRP, C-reactive protein; E/C, encorafenib plus cetuximab; ECOG PS, Eastern Cooperative Oncology Group Performance Scale; EQ5D, EuroQol-5 Dimension; mCRC, metastatic colorectal cancer; MMR, mismatch repair; MSI, microsatellite instability; QLQ-C30, European Organisation for the Research and Treatment of Cancer (EORTC) Core Quality of Life questionnaire; QoL, quality of life; TNM, tumour/node/metastasis.

## Conclusions

- Pooling data from multiple European studies into a single European retrospective study provides opportunities to increase the statistical power of a study and answer novel research questions.
- The results from the analyses will help to better understand patient characteristics and prognostic factors from adult patients with BRAF<sup>V600E</sup>-mutant mCRC who were treated with encorafenib in combination with cetuximab.

#### Acknowledgments

B-REAL	Retrospective NIS	France, Austria, Germany, Italy, Spain, Belgium*, USA†	Adult patients with <i>BRAF<sup>V600E</sup></i> -mutant mCRC treated with E/C	Baseline clinical and demographic characteristics, effectiveness, treatment patterns and safety	201	Completed
CATAMARAN	Retrospective NIS	The Netherlands	Adult patients with <i>BRAF<sup>V600E</sup></i> -mutant mCRC treated with E/C or EBC	Baseline clinical and demographic characteristics, effectiveness	162	Completed
CONFIDENCE	Retrospective NIS	Spain	Adult patients with BRAF <sup>V600E</sup> -mutant mCRC treated in 2nd line with E/C	Effectiveness, baseline clinical and demographic characteristics, treatment patterns and safety	80	Completed
Italian GONO Cohort	Retrospective NIS	Italy	<i>BRAF<sup>v600E</sup></i> -mutant mCRC patients treated with E/C or EBC	Baseline clinical and demographic characteristics, effectiveness, treatment patterns and safety	211	Completed

E/C, encorafenib plus cetuximab; EBC, encorafenib plus binimetinib plus cetuximab; mCRC, metastatic colorectal cancer; NIS, non-interventional study; QoL, quality of life. \*Patients from Belgium who received treatment under compassionate use were excluded from the pooling. \*Patients from the USA are excluded from the pooling because only the European population is included.

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