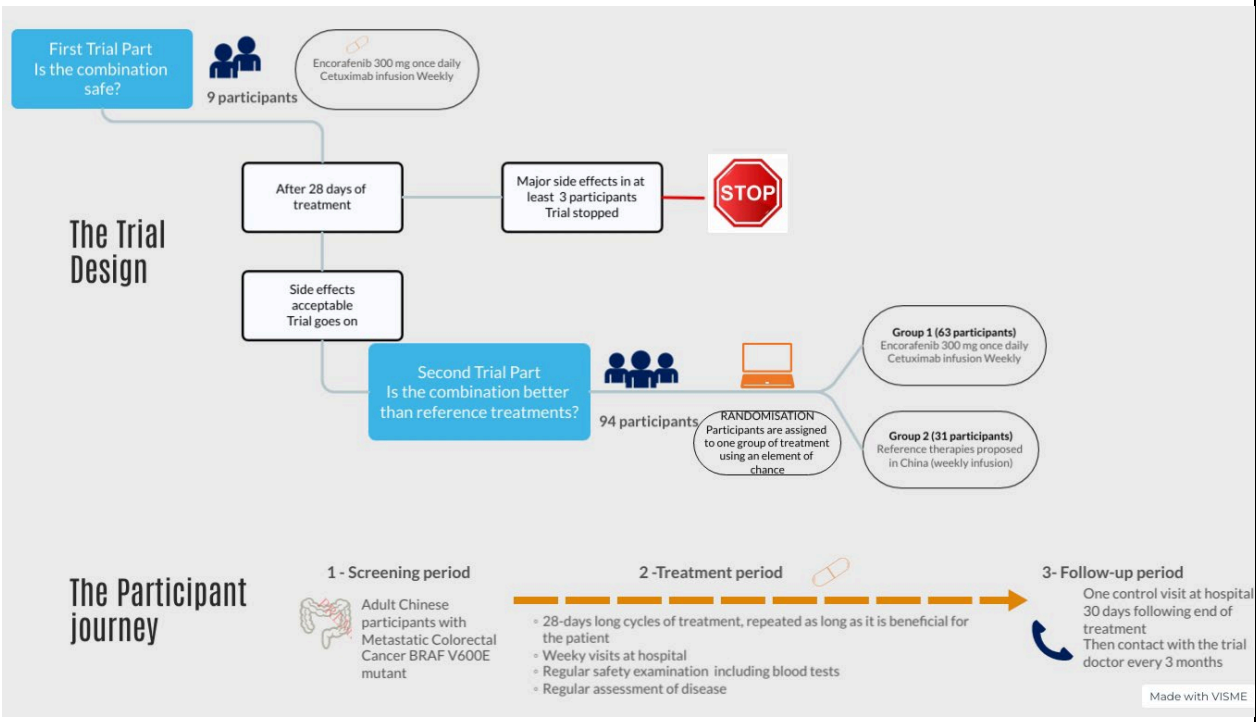
Trial title	A trial to evaluate whether encorafenib in combination with cetuximab is safe and effective in the Chinese mainland population with *BRAF*^{V600E} mutant metastatic Colorectal Cancer.
Disease 	*BRAF*^{V600E} Metastatic Colorectal Cancer
Treatment 	Encorafenib (BRAFTOVI®) in combination with cetuximab (Erbitux®)
Participants 	Mainland adult Chinese participants with *BRAF*^{V600E} mutant metastatic colorectal cancer whose disease had progressed following prior therapies
Trial dates 	From 02 September 2021 (first participant first visit) to September 2024 (approximate end of the trial)
Trial Locations 	China
We do research to improve patient care. This trial will help us to answer important questions about treatment of metastatic colorectal cancer	

This document is a brief summary of a clinical trial protocol. It is written in plain language for the general public, providing answers to the following questions:

- What is the purpose of the trial?
- What are the objectives of the trial and how are they evaluated?
- How is the trial conducted?
- Who can take part in the trial?
- What are the trial treatments and how are they administered?
- What are the possible benefits and risks in taking part in the trial?

What is the purpose of the trial?	. Previous clinical trials have shown that encorafenib in combination with cetuximab is effective to treat patients with metastatic colorectal cancer carrying a specific mutation in the *BRAF* gene (*BRAF*^{V600E}). Encorafenib is a marketed drug (Braftovi®). It is used in combination with cetuximab (Erbitux®) in several countries (European Union, USA, Australia, Japan, Switzerland…) for patients whose disease had worsened following prior systemic therapies. The purpose of this trial is to prove that this combination would present the same benefits for the Chinese patients.
What are the objectives of the trial and how are they evaluated?	There are 2 main objectives assessed in two consecutive parts of the trial: • The purpose of the first part is to evaluate whether the combination of encorafenib and cetuximab is safe by primarily counting the number of participants who had major side effect during the first 28 days of treatment. • The purpose of the second part is to compare the combination with the reference treatments. Efficacy is primarily assessed by analysing the period of time between the start of treatment and the disease worsens In addition, thanks to the trial, researcher intend to :

	• Describe the side effects in Chinese population and compare the combination with the reference treatments in term of tolerance. • Describe how encorafenib enters the body, circulates in the bloodstream and is finally eliminated. • Compare the combination with the reference treatments in term of survival that is to say the period of time between treatment assignement and the participant's death (overall survival) • Compare the combination with the reference treatments in term of response rate that is to say the proportion of participants for whom the tumors shrink or completely disappear after treatment.
How is the trial conducted?	This is a Phase 2 trial with 103 participants. During the first part of the trial, nine (9) participants are treated with the combination of encorafenib and cetuximab. After 28 days (one cycle) of treatment, an analysis is performed to check whether the combination is safe. If at least three (3) participants have a major side effect, the combination is considered not safe, and the trial is stopped. If the combination is considered safe with less than three (3) participants having a major side effect, the trial proceeds to the second part. Ninety-four (94) additional participants enter the second part of the trial and are splitted in two groups using an element of chance (randomization): • Two-thirds of participants (63) receive the combination • One-third of participants (31) receive the reference treatments Both parts of the trial start with a screening phase to assess wether the participants fulfills all the conditions to enter the trial. The treatment period starts with the first dose received and consists in:

	• Successive cycles of treatments, 28 days long each during which therapies are administrered according to the trial protocol • Regular assessments to control participant's safety including physical examinations and blood tests • Regular assessments including imaging tests to control the size of the tumors and the evolution of the disease. All participants are treated as long as they benefit from the treatment received. That means as long as the tumors do not worsen (disease progression) and the treatment is tolerated. When the participant stops the treatment, the follow-up period begins. This period consists of monitoring the participant's health over time, which may include information on their health status, physical examinations, blood tests and radiological imaging. The schema summarizes the information presented above:
	
Who can take part in the trial?	To be part of the trial, participant must fulfill several conditions including the following: The participant is Mainland Chinese with age ≥ 18 years old

	The tumor cannot be removed by surgery (unresectable) The tumor has a specific genetic mutation called *BRAF*^{V600E} mutation The participant has been treated once or twice for his/her metastatic cancer before The participant has never been treated with the treatments studied in the trial
What are the trial treatments and how are they administered ?	Participants treated with the combination receive : • 4 capsules of encorafenib to be taken once a day in the morning. The total daily dose of encorafenib is 300mg. • Cetuximab by intravenous infusion performed once a week at the hospital. Participants treated with the reference treatments receive either irinotecan and cetuximab or FOLFIRI and cetuximab at the investigator's discretion. All these treatments are administered by intravenous infusion performed at the hospital (once a week for Cetuximab and every two weeks for irinotecan and FOLFIRI).
What are the possible benefits and risks in taking part in the trial?	Previous clinical studies in the non-Chinese population have demonstrated that the combination of encorafenib and cetuximab is effective to treat patients with *BRAF*^{V600E} mutant metastatic colorectal cancer. It is anticipated that the combination is also effective in the Chinese population. The combination is approved and used since 2020 in several countries such as USA and European Union. Information gathered show that tolerance to therapy is similar for patients of Asian origin than for other patients. The trial may have potential discomforts and constraints for the participants requiring regular visits at hospital, blood sampling and imaging examinations. Encorafenib and cetuximab can cause side effects for which participants are informed by trial doctors at trial entry and are closely monitors for all the duration of the trial.

Cinical Trial identification	
Protocol Number	W00090GE202
Protocol version	3.0 dated 10 January 2022
Full trial title	A multicenter, randomized, open-label, 2-arm, Phase II trial with a safety lead-in phase evaluating the combination of encorafenib and cetuximab versus irinotecan/cetuximab or infusional 5-fluorouracil (5-FU)/folinic acid (FA)/irinotecan (FOLFIRI)/cetuximab in Chinese patients with *BRAF*^{V600E} mutant metastatic colorectal cancer.
Registry ID	ClinicalTrials.gov: NCT05004350 Nautical - ClinicalTrials.gov
Who sponsors this trial?	
Name and contact details of the sponsor	Pierre Fabre Médicament Les Cauquillous 81500 Lavaur-France .
Additional Information	

Glossary	
BRAFV600E	All humans have a gene called *BRA*F. The *BRAF* gene makes a protein that helps control cell growth. In some patients with colorectal cancer, this gene mutates (V600E mutation) and makes the tumor grow faster.
Metastatic colorectal cancer (mCRC)	Metastatic colorectal cancer is a cancer that initially develops in the colon (the longest part of the large intestine) and/or the rectum (the last several inches of the large intestine before the anus) and has spread to other place(s) of the body
Side effects	Side effects are unwanted medical events (such as headache) that happen during the trial and that are related or possibly related to trial treatment.
Overall survival (OS)	Overall survival is the time period between the treatment start and the participant's death
Phase II trials	Phase II trials are designed to assess whether an experimental treatment is safe and whether it works.
Randomization	Randomization is the assignment to one of the treatment groups using an element of chance
Disease Progression	Cancer that continues to grow or spread.