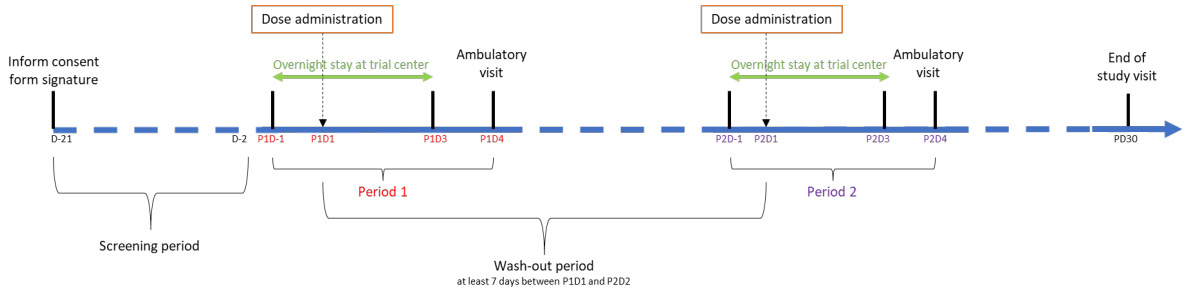
Trial title	A trial to demonstrate that administration of binimetinib treatment using a 45 mg strength tablet is equivalent to 3 tablets of 15 mg.
Disease 	Healthy volunteers
Treatment 	binimetinib (MEKTOVI®)
Participants 	Healthy volunteers aged between 18 and 65 years except pregnant women and women of childbearing potential
Trial dates 	From 31 August 2022 (first participant first visit) to December 2022 (estimated End of trial)
Trial Locations 	Biotrial center, Rennes - France
We do research to improve patient care. This trial will help us to ease cancer therapy for patients treated with binimetinib.	

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?	Binimitenib (MEKTOVI®) is a marketed drug for the treatment of adults' patients with unresectable or metastatic melanoma presenting a specific mutation (BRAF V600 mutation). In order to facilitate treatment administration, a new strength tablet containing 45 mg of binimetinib is being developed. As a result, the number of binimetinib tablets to be taken by the patients will be reduced from 6 tablets (6 x 15 mg) to 2 tablets (2 x 45 mg) per day. The purpose of the trial is to demonstrate the bioequivalence of the two formulations; it means that binimetinib treatment is delivered in the body in the same way (in quantity and speed) with a 45 mg-tablet than with 3 tablets of 15 mg.
What are the objectives of the trial and how are they evaluated?	The primary objective of the trial is to compare the concentration of binimetinib in the blood after administration of both formulations. Measure of concentration at different time points following administration provides estimation for : • the total exposure to binimetinib experienced by the participant. The total exposure is the amount of treatment circulating in the blood from administration to elimination. • the maximal concentration observed in the blood These are primary pharmacokinetics parameters used to assess bioequivalence. In addition, the trial will allow:

	• To compare additional pharmacokinectic parameters such as the time between treatment administration and observation of the maximal concentration in the blood • To evaluate the safety of both formulations of binimetinib according to the number and type of side effects
How is the trial conducted?	This is a randomized, crossover Phase I trial. Randomized means that healthy volunteers will be split in two groups using an element of chance: • one group will receive the reference formulation first (3 tablets of 15 mg) then the test formulation (one tablet of 45 mg) • one group will receive the test formulation first then the reference formulation. Crossover means that each healthy volunteer will sequentially receive both formulations. The trial will consist of: • A screening period before the first treatment administration to check that participant fulfills all conditions to enter the trial • A first treatment period of 5 days, requiring overnight stay at trial center for the first 3 days following the first administration. • A washout period of at least 7 days required for the body to eliminate drug from first administration. • A second treatment period of 5 days, requiring overnight stay at trial center for the first 3 days following the second administration. • An End-of-Study visit to be performed 1 month after last administration for a final examination of the participant. The trial will be carried out in a center specialized in phase 1 trials with experienced medical staff and adequate facilities. The schema summarizes the information presented above:



P1D1 stands for "Period 1 Day 1"and corresponds to the day of administration during this first period

P2D1 stands for "Period 2 Day 1"and corresponds to the day of administration during this second period

Who can take part in the trial?	To be part of the trial, participant must fulfill several conditions including the following: • Healthy volunteer as assessed by clinical examinations during screening period (including blood test) and medical history • Aged between ≥ 18 and ≤ 65 years, except pregnant women and women of childbearing potential
What are the trial treatments and how are they administered?	Participants will receive 2 single oral administrations of 45 mg binimetinib, separated by a period of at least 7 days between intakes. • One administration will be performed using 1 tablet of 45 mg (the test formulation) • One administration will be performed using 3 tablets of 15 mg (the reference formulation currently marketed)
What are the possible benefits and risks in taking part in the trial?	Healthy volunteers in phase 1 clinical trials contribute to the development of safe drugs and accept risks and constraints without anticipated health benefits from participation. By contributing to the advance of knowledge, participants will be compensated. The trial has potential discomforts and constraints requiring participants to stay 3-day periods at the trial center (twice during trial conduct) with serial blood samplings and dietary restrictions. Binimetinib can cause side effects which are well documented and for which participants are informed by trial doctor at trial

	entry. Participants are closely monitored for all the duration of the trial. Exposure to binimetinib is limited to 2 single oral administrations separated by a week limiting the risk of side effects that can be observed for daily administrations.

Cinical Trial identification	
Protocol Number	W00074CI103
Protocol Version	1.2 dated 22 June 2022
Full trial title	A randomized, single-center, open-label, single dose, two-period, crossover pivotal bioequivalence study comparing binimetinib 3 x 15 mg and 45 mg tablets in healthy participants
Registry ID	EudraCT Number: 2022-000610-34

Who sponsors this trial?	
Name and contact details of the sponsor	Pierre Fabre Médicament Les Cauquillous 81500 Lavaur-France .

Additional Information

Glossary	
Healthy volunteers	Healthy volunteers in phase 1 clinical trials contribute to the development of safe drugs and accept risks and constraints without anticipated health benefits from participation.
Unresectable	that cannot be removed by surgery
BRAF^{V600E}	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	Metastasic means that cancer has spread to a different part of the body than where it started
Randomization	Randomization is the assignment to one of the treatment groups using an element of chance
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.
Pharmacokinetic	The pharmacokinetic of a drug is how the body absorbs, transforms, and eliminates this drug.
Phase I trials	Phase I trials test an experimental drug, in a small group of people to evaluate safety, identify side effects and determine safe dosages.
Crossover trials	Crossover trials are trials in which participants do not only receive one intervention, but multiple, and the effect of the interventions are measured on the same individuals