Encorafenib/binimetiib master protocol: an open-label continuation study for participants continuing from encorafenib/binimetinib clinical studies. ;Sub-study 1:
An open-label study for continued treatment access for participants from the C4211001 (Array CMEK162X2201) and the C4211003 (Array-162-311, MILO) Binimetinib studies.;Sub-study 2:
An open-label study for continued treatment access for participants from the C4221004 (Array CMEK162B2301, Columbus) Encorafenib and Binimetinib study;Sub-s

Published: 19-04-2022
Last updated: 10-01-2025

This study has been transitioned to CTIS with ID 2023-509408-13-00 check the CTIS register for the current data. - To monitor the safety and tolerability of binimetinib- To monitor the safety and tolerability of encorafenib

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53566

Source
ToetsingOnline

Brief title
FLOTILLA

Condition

- Other condition

Synonym
cancer

Health condition

(Maligne) solide tumoren, niet-reseceerbare huidkanker, niet-kleincellige longkanker

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Pfizer Inc.

Intervention

Keyword: Lung cancer, Skin cancer, Solid tumors

Outcome measures

Primary outcome

• AEs leading to permanent discontinuation of binimetinib or encorafenib

• SAEs

Secondary outcome

NA

Study description

Background summary

Sub-study 1:

The C4211001 Parent Study was a Phase 2, open-label study to assess the safety and efficacy of binimetinib (also known as MEK162) in adults with locally advanced and unresectable or metastatic malignant cutaneous melanoma, harboring BRAFV600 or NRAS mutations. The PCD was reached on 07 January 2014. Two participants remained on binimetinib treatment
in the Parent Study as of 30 September 2021.

The C4211003 Parent Study was a multinational, randomized, open-label Phase 3 study to evaluate binimetinib versus physician*s choice of selected chemotherapies in participants with LGS carcinomas of the ovary, fallopian tube or primary peritoneum who had recurrent
or persistent disease following at least 1 prior platinum-based chemotherapy treatment and no more than 3 prior lines of chemotherapy. The PCD was reached on 20 January 2016.
Two participants remained on binimetinib treatment in the Parent Study as of 30 September
2021.

Participants who are deriving benefit from study intervention as determined by the respective investigator may continue to receive treatment on this Continuation Sub-Study. All
The ongoing participants in the Parent Studies are receiving treatment with binimetinib; thus, this protocol only describes the procedures for study intervention of binimetinib. The investigator is to follow the guidance below for the conduct of this Continuation Study.

Sub-study 2:

The C4221004 Parent Study was a 2-part, multi-center, randomized, open-label, Phase 3 study comparing the efficacy and safety of encorafenib plus binimetinib to vemurafenib and encorafenib monotherapy in participants with locally advanced unresectable or metastatic melanoma with BRAFV600 mutation. Part 1 of the study evaluated the activity of Combo 450 (encorafenib 450 mg QD plus binimetinib 45 mg BID). Part 2 further defined the contribution of binimetinib to the combination using a lower encorafenib dose, 300 mg QD, in the combination. PCD was achieved on 09 November 2016. As of 28 March 2022, 62 participants are on active treatment, including 30 participants in Part 1 and 32 participants in Part 2.
Participants who are deriving benefit from study intervention as determined by

the respective investigator may continue to receive treatment on this Continuation Sub-Study. This protocol only describes the procedures for these potential participants from the parent study. The rollover of eligible participants to this Continuation Sub-Study will occur when 80% of randomized participants in each part of the study have died, withdrawn consent for survival follow-up, or are lost to follow-up, as needed for the final OS update to be performed in the parent study.

Sub-study 3:
The C4221008 Parent Study was an open-label, multicenter, non-randomized, Phase 2 study to determine the safety, tolerability and efficacy of encorafenib given in combination with binimetinib in treatment-naïve and previously treated participants with BRAF V600E-mutant metastatic NSCLC. Participants who are deriving benefit from study intervention(s) as determined by the respective investigator may continue to receive treatment on this Continuation Sub-Study. This protocol only describes the procedures for these potential participants from the Parent Study.

Study objective

This study has been transitioned to CTIS with ID 2023-509408-13-00 check the CTIS register for the current data.

- To monitor the safety and tolerability of binimetinib
- To monitor the safety and tolerability of encorafenib

Study design

As an Encorafenib/Binimetinib Continuation Sub-Study, this study does not have a separate design apart from what has been described in the Master Protocol for Encorafenib/Binimetinib Continuation Sub-Studie:

This is an open-label, master protocol for encorafenib/binimetinib continuation sub-studies for participants receiving study intervention(s) in an encorafenib/binimetinib Parent Study. The study is being conducted under this Master Protocol for Encorafenib/Binimetinib Continuation Sub-Studies with an individual encorafenib/binimetinib continuation sub-study protocol for each eligible Parent Study (see Section 4.1.1).

Approximately 75 participants from potentially qualifying Parent Studies will be included in this Master Protocol for Encorafenib/Binimetinib Continuation Sub-Studies.

The following terminology will be used throughout this protocol:
• Master Protocol for Encorafenib/Binimetinib Continuation Sub-Studies: Includes a description of study procedures and assessments that are to be

performed for all participants. • Parent Study: original encorafenib/binimetinib study meeting the criteria provided in Section 4.1.1. • Encorafenib/Binimetinib Continuation Sub-Study Protocol: Includes the specific aspects of the respective Parent Study, which includes and is not limited to, schedule of activities, dosing, toxicity management, dose modification, drug storage/handling, and additional safety data collection (if required).

4.1.1. Qualified Studies for This Protocol
For inclusion in this Master Protocol for Encorafenib/Binimetinib Continuation Sub-Studies, the Parent Study must be an encorafenib/binimetinib study, with adequate drug supply of the investigational product for clinical use, and which meets at least one of the following criteria:
• The main analyses, at minimum primary analysis, have been completed as defined by the encorafenib/binimetinib Parent Study.
• Study was terminated early following a population level futility analysis or sponsor business decision, and the study intervention for the proposed indication is not otherwise available outside of a clinical study for individual participants who may continue to derive clinical benefit from the treatment as determined by the principal investigator.

For more information, please refer to the master protocol, dated 03Nov2021

Intervention

Oral administration of binimetinib or encorafenib, BID, same dose level as in the parent study.

Study burden and risks

Participants enrolled in this Continuation Sub-Study have been determined by the investigators to have derived clinical benefit from study intervention. More detailed information about the known and expected benefits and risks and reasonably expected AEs of binimetinib or encorafenib may be found in the IB's, which are the SRSD's for this study.

Contacts

Public
Pfizer

Hudson Boulevard East 66
New York NY 10001
US

Scientific
Pfizer

Hudson Boulevard East 66
New York NY 10001
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Any participant who is receiving study intervention and deriving clinical benefit (as determined by the principal investigator) in an encorafenib/binimetinib Parent Study, with no ongoing NCI CTCAE version 4.03 Grade >=3 or intolerable Grade 2 AEs considered to be related to study treatment.

Exclusion criteria

1. Any medical reason that, in the opinion of the investigator or sponsor, precludes the participant from inclusion in the study

Study design

Design

Study phase: 4

Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-01-2023
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Braftovi
Generic name:	Encorafenib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Mektovi
Generic name:	Binimetinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	19-04-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-07-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-07-2022
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-12-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-07-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-08-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-05-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-06-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-509408-13-00
EudraCT	EUCTR2021-004395-34-NL
ClinicalTrials.gov	NCT05203172
CCMO	NL80817.091.22