Study of Alpelisib (BYL719) in Combination With Trastuzumab and Pertuzumab as Maintenance Therapy in Patients With HER2-positive Advanced Breast Cancer With a PIK3CA Mutation

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Main Information

Primary registry identifying number
LBCTR2022054889

Protocol number
CBYL719G12301

MOH registration number

Study registered at the country of origin
Yes

Study registered at the country of origin: Specify

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency

Primary sponsor
Novartis Pharmaceuticals

Primary sponsor: Country of origin
Novartis Pharmaceuticals

Date of registration in primary registry
16/12/2022

Date of registration in national regulatory agency

Public title
Study of Alpelisib (BYL719) in Combination With Trastuzumab and Pertuzumab as Maintenance Therapy in Patients With HER2-positive Advanced Breast Cancer With a PIK3CA Mutation

Acronym

Scientific title
EPIK-B2: A Two Part, Phase III, Multicenter, Randomized (1:1), Double-blind, Placebo-controlled Study to Assess the Efficacy and Safety of Alpelisib (BYL719) in Combination With Trastuzumab and Pertuzumab as Maintenance Therapy in Patients With HER2-positive Advanced Breast Cancer With a PIK3CA Mutation

Acronym
EPIK-B2

Brief summary of the study: English
The purpose of this two parts multicenter, randomized, double-blind, placebo-controlled, Phase III study is to evaluate the efficacy and safety of alpelisib compared to alpelisib matching-placebo in combination with trastuzumab and pertuzumab as maintenance treatment of patients with HER2-positive advanced breast cancer whose tumor harbors a PIK3CA mutation following induction therapy with a taxane in combination with trastuzumab and pertuzumab. Part 1 is the open-label, safety run-in part of the study, designed to confirm the recommended phase 3 dose (RP3D) dose of alpelisib in combination with trastuzumab and pertuzumab. Following Part 1, Part 2 will be initiated, which is the randomized, Phase III part of the study.

Brief summary of the study: Arabic
هدف هذه الدراسة هو معرفة ما إذا كان دواء ألبيليسيب عندما يُضاف إلى تراستوزوماب وبرتوزوماب يساعد على الحدّ من نموّ خلايا سرطان الثدي لدى المرضى المصابين بسرطان الثدي المتقدّم إيجابي البروتين "هير2" HER2.

Health conditions/problem studied: Specify

Advanced HER2+Breast Cancer

Interventions: Specify

Drug: Alpelisib
Alpelisib - continuous once daily, in a 21-day cycle
Other Name: BYL719

Drug: Alpelisib matching Placebo
Alpelisib matching placebo: continuous once daily, in a 21-day cycle

Drug: Trastuzumab
Trastuzumab - Day 1 of Cycle 1, and on Day 1 (+/- 3 days) of every cycle thereafter

Drug: Pertuzumab
Pertuzumab - Day 1 of Cycle 1, and on Day 1 (+/- 3 days) of every cycle thereafter

Key inclusion and exclusion criteria: Inclusion criteria

- Participant has histologically-confirmed HER2-positive breast cancer that is advanced (loco-regionally not amenable to surgery or is metastatic).
- Participant has received pre-study induction therapy with up to and including a maximum of 6 cycles of a taxane (docetaxel, paclitaxel, or nab-paclitaxel), plus trastuzumab and pertuzumab. 4 or 5 cycles of induction therapy are permitted if discontinuation of taxane was due to taxane toxicity.
- Participant has an Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1
- Participant has adequate bone marrow and organ function
- Applies only to Part 2: Participant has a PIK3CA mutation(s) present in tumor tissue prior to enrollment, as determined by a Novartis designated central laboratory.

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

18

Key inclusion and exclusion criteria: Age maximum

99

Key inclusion and exclusion criteria: Exclusion criteria

Exclusion Criteria:

- Participant with inflammatory breast cancer at screening.
- Participant with evidence of disease progression during the pre-study induction therapy and prior to first dose of alpelisib (or alpelisib/alpelisib matching-placebo for Part 2)
- Participant with an established diagnosis of diabetes mellitus type I or uncontrolled type II based on fasting plasma glucose (FPG) and HbA1c.
- Participant has a known history of acute pancreatitis within 1 year of screening or past medical history of chronic pancreatitis
- Participant has clinically significant, uncontrolled heart disease and/or recent cardiac events
- Participant has a history of Steven-Johnson Syndrome (SJS), erythema multiforme (EM) or Toxic Epidermal Necrolysis (TEN).
- Participant has currently documented pneumonitis/interstitial lung disease

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Therapy

Trial scope: Specify scope

N/A

Study design: Allocation

Randomized controlled trial

Study design: Masking

Blinded (masking used)

Study design: Control

Placebo

Study phase

3

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Study design: Specify assignment

Other

sequential

IMP has market authorization

Yes, Worldwide

IMP has market authorization: Specify

USA, Europe

Name of IMP

Alpelisib

Year of authorization

2019

Month of authorization

5

Type of IMP

Gene therapy

Pharmaceutical class

phosphatidylinositol 3-kinase (PI3K) inhibitor

Therapeutic indication

Patients with HER2-positive Advanced Breast Cancer with a PIK3CA Mutation

Therapeutic benefit

Progression Free Survival

Study model

N/A

Study model: Explain model

N/A

Study model: Specify model

N/A

Time perspective

N/A

Time perspective: Explain time perspective

N/A

Time perspective: Specify perspective

N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention

Samples with DNA**

Biospecimen description

Samples will be shipped to Q2 solutions lab

Target sample size

8

Actual enrollment target size

Date of first enrollment: Type

Anticipated

Date of first enrollment: Date

28/12/2022

Date of study closure: Type

Date of study closure: Date

Anticipated

29/09/2031

Recruitment status

Suspended

Recruitment status: Specify

Date of completion

IPD sharing statement plan

Yes

IPD sharing statement description

Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent expert panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

This trial data is currently available according to the process described on www.clinicalstudydatarequest.com. https://www.clinicalstudydatarequest.com

Additional data URL

https://clinicaltrials.gov/ct2/show/record/NCT04208178?term=CBYL719G12301&draw=2&rank=1

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinical trials.gov	NCT04208178

Sources of Monetary or Material Support

Name
Novartis Pharma Services Inc.

Secondary Sponsors

Name
NA

Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Fadi Farhat	Saida	Lebanon	+961 3 753155	drfadi.trials@gmail.com	Hammoud Hospital University Medical Center
Scientific	Hind Khairallah	Beirut	Lebanon	+961 1 512002 Ext. 271	hind.khairallah@fattal.com.lb	Khalil Fattal et Fils s.a.l
Public	Marwan Ghosn	Beirut	Lebanon	+961 3 226842	marwan.ghosn@usj.edu.lb	Hotel Dieu de France Hospital
Public	Hampig Raphael Kourie	Dora	Lebanon	+961 3 321899	hampig.kourie@usj.edu.lb	Hopital Saint Joseph

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hammoud Hospital University Medical Center	Fadi Farhat	Hematology Oncology	Approved
Hotel Dieu de France	Marwan Ghosn	Hematology Oncology	Approved
Hopital Saint Joseph	Hampig Raphael Kourie	Oncology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hammoud Hospital University Medical Center	30/06/2021	Ibrahim Omeis	iomeis@hammoudhospital.org	+961 (0) 7 723111 ext 1222/1223
Hotel Dieu de France	29/09/2021	Nancy Alam	nancy.alam@usj.edu.lb	+961 (0) 1 421000 ext 2335
Psychiatric Hospital of the Cross	08/09/2022	Christiane Abi Elias	irghpc@gmail.com	+961 (0) 3 953794

Countries of Recruitment

Name
Belgium
China
France
Spain
United States of America
Lebanon

Health Conditions or Problems Studied

Condition	Code	Keyword
Advanced HER2+Breast Cancer	Malignant neoplasm of breast (C50)	Advanced HER2+Breast Cancer

Interventions

Intervention	Description	Keyword
IMP administration , ICF, visit assessment and schedule	IMP administration , ICF, visit assessment and schedule	IMP administration , ICF, visit assessment and schedule

Primary Outcomes

Name	Time Points	Measure
Part 1	6 weeks	Incidence of dose limiting toxicities (DLTs) for each dose level
Part 2	Up to approximately 38 months	Progression Free Survival (PFS)

Key Secondary Outcomes

Name	Time Points	Measure
Part 1	Day 8 of Cycle 1 and then Day 1 of Cycle 2, Cycle 4, Cycle 6 and Cycle 10 (Each cycle = 21 days)	Summary statistics of alpelisib concentrations by timepoint and dose level
Part 2	Up to approximately 70 months	Overall survival (OS)
Part 2	Day 8 of Cycle 1 and then Day 1 of Cycle 2, Cycle 4, Cycle 6 and Cycle 10 (Each cycle = 21 days)	Summary statistics of alpelisib concentrations by timepoint and dose level
Part 2	Up to approximately 38 months	Overall response rate (ORR) with confirmed response
Part 2	Up to approximately 38 months	Clinical Benefit Rate (CBR) with confirmed response
Part 2	Up to approximately 38 months	Time to response (TTR) based on local radiology assessments
Part 2	Up to approximately 38 months	Duration of response (DOR) with confirmed response
Part 2	Baseline, approximately 38 months	Change in Functional Assessment of Cancer Therapy - Breast (FACT-B) treatment outcomes index (TOI) from baseline
Part 2	Up to approximately 38 months	Time to deterioration in FACT-B TOI (defined as a ≥ 5 point decrease from baseline)
Part 2	Up to approximately 38 months	PFS based on local radiology assessments
Part 2	Baseline, up to approximately 38 months	Time to definitive deterioration of Eastern Cooperative Group of Oncology Group (ECOG) performance status

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files