



# 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**

13/09/2023

**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 البيليسيب عندما يُضاف إلى تراستوزوماب وپرتوزوماب يساعد على الحد من نمو خلايا سرطان HER2 "التدي 2" لدى المرضى المصابين بسرطان الثدي المتقدم إيجابي البروتين "هير

**Health conditions/problem studied: Specify**





Advanced HER2+Breast Cancer

**Interventions: Specify**

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

Drug: Apelisib matching Placebo  
Apelisib 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 apelisib (or apelisib/apelisib 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	07/06/2023
<b>Recruitment status</b> Suspended	<b>Recruitment status: Specify</b>
<b>Date of completion</b>	
<b>IPD sharing statement plan</b> Yes	<b>IPD sharing statement description</b> 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 <a href="http://www.clinicalstudydatarequest.com">www.clinicalstudydatarequest.com</a> . <a href="https://www.clinicalstudydatarequest.com">https://www.clinicalstudydatarequest.com</a>
<b>Additional data URL</b> <a href="https://clinicaltrials.gov/ct2/show/record/NCT04208178?term=CBYL719G12301&amp;draw=2&amp;rank=1">https://clinicaltrials.gov/ct2/show/record/NCT04208178?term=CBYL719G12301&amp;draw=2&amp;rank=1</a>	
<b>Admin comments</b>	
<b>Trial status</b> 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
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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 $\geq 5$ 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**