Study Assessing the Efficacy and Safety of Alpelisib + Nab-paclitaxel in Subjects With Advanced TNBC Who Carry Either a PIK3CA Mutation or Have PTEN Loss Without PIK3CA Mutation

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Main Information

Primary registry identifying number
LBCTR2021044784

Protocol number
CBYL719H12301

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 Pharma Services inc.

Primary sponsor: Country of origin
Novartis Pharmaceuticals

Date of registration in primary registry
22/01/2024

Date of registration in national regulatory agency

Public title
Study Assessing the Efficacy and Safety of Alpelisib + Nab-paclitaxel in Subjects With Advanced TNBC Who Carry Either a PIK3CA Mutation or Have PTEN Loss Without PIK3CA Mutation

Acronym

Scientific title
A Phase III, Multicenter, Randomized, Double-blind, Placebo-controlled Study to Assess the Efficacy and Safety of Alpelisib (BYL719) in Combination With Nab-paclitaxel in Patients With Advanced Triple Negative Breast Cancer With Either Phosphoinositide-3-kinase Catalytic Subunit Alpha (PIK3CA) Mutation or Phosphatase and Tensin Homolog Protein (PTEN) Loss Without PIK3CA Mutation

Acronym

Brief summary of the study: English
The purpose of this study is to determine whether treatment with alpelisib in combination with nab-paclitaxel is safe and effective in subjects with advanced triple negative breast cancer (aTNBC) who carry either a PIK3CA mutation (Study Part A) or have PTEN loss without PIK3CA mutation (Study Parts B1 and B2)

Brief summary of the study: Arabic
دراسة متعددة المراكز، عشوائيّة التوزيع، مزدوجة التعمية، مرتكزة على المقارنة بدواء وهمي في المرحلة الثالثة، لتقييم فعاليّة وسلامة ألبيليسيب (BYL719) بالاشتراك مع ناب-باكليتاكسيل (nab-paclitaxel) لدى المرضى المصابين بسرطان الثدي الثلاثي السلبي المتقدم إمّا مع طفرة PIK3CA في جين أو مع فقدان البروتين مماثل الفوسفاتاز والتنسين PTEN بدون طفرة في جين PIK3CA

Health conditions/problem studied: Specify
Triple Negative Breast Neoplasms

Interventions: Specify

Drug: alpelisib
300 mg orally once per day (QD)
Other Name: BYL719
Drug: placebo
300 mg orally once per day (QD)
Other Name: alpelisib matching placebo
Drug: nab-paclitaxel
100 mg/m² as IV infusion on Days 1, 8 and 15 of a 28-day cycle
Other Name: abraxane

Key inclusion and exclusion criteria: Inclusion criteria

Subject has histologically confirmed diagnosis of advanced (loco-regionally recurrent and not amenable to curative therapy, or metastatic (stage IV)) TNBC
Subject has either a measurable disease per RECIST 1.1 criteria or, if no measurable disease is present, then at least one predominantly lytic bone lesion or mixed lytic-blastic bone lesion with identifiable soft tissue component (that can be evaluated by CT/MRI) must be present Part B1: patients must have measurable disease
Subject has adequate tumor tissue to identify the PIK3CA mutation status (either carrying a mutation or without a mutation) and the PTEN loss status; both of which will determine whether the subject can be allocated to Part A - PIK3CA mutation regardless of PTEN status; or to Part B - PTEN loss without a PIK3CA mutation
Subject has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
Subject has received no more than one line of therapy for metastatic disease.
Subject has adequate bone marrow and organ function

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

Subject has received prior treatment with any PI3K, mTOR or AKT inhibitor
Subject has a known hypersensitivity to alpelisib, nab-paclitaxel or to any of their excipients
Subject has not recovered from all toxicities related to prior anticancer therapies to NCI CTCAE version 4.03 Grade ≤1; with the exception of alopecia
Subject has central nervous system (CNS) involvement
Subject with an established diagnosis of diabetes mellitus type I or uncontrolled type II based on Fasting Plasma Glucose and HbA1c
Subject has impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of the study drugs (e.g., ulcerative diseases, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome, or small bowel resection) based on investigator discretion
Subject has a history of acute pancreatitis within 1 year of screening or past medical history of chronic pancreatitis
Subject has currently documented pneumonitis/interstitial lung disease
Subject has a history of severe cutaneous reactions, such as Steven-Johnson Syndrome (SJS), erythema multiforme (EM),Toxic Epidermal Necrolysis (TEN) or Drug Reaction with Eosinophilia and Systemic Syndrome (DRESS)
Subject with unresolved osteonecrosis of the jaw
Other protocol-defined inclusion/exclusion criteria apply.

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Safety

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

Parallel

N/A

IMP has market authorization

Yes, Lebanon and Worldwide

IMP has market authorization: Specify

Lebanon and Worldwide

Name of IMP

Alpelisib

Year of authorization

2020

Month of authorization

12

Type of IMP

Gene therapy

Pharmaceutical class

Class I α-specific PI3K inhibitor

Therapeutic indication

Advanced Triple Negative Breast Cancer

Therapeutic benefit

to determine whether treatment with alpelisib in combination with nab-paclitaxel is safe and effective in subjects with advanced triple negative breast cancer (aTNBC) who carry either a PIK3CA mutation (Study Part A) or have PTEN loss without PIK3CA mutation (Study Parts B1 and B2)

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

Standard laboratory samples and biomarkers will be shipped to central labs : Navigate pharma in US and to Q2 solutions in UK

Target sample size

5

Actual enrollment target size

Date of first enrollment: Type

Anticipated

Date of first enrollment: Date

03/04/2023

Date of study closure: Type

Anticipated

Date of study closure: Date

09/01/2026

Recruitment status

Suspended

Recruitment status: Specify

Date of completion

10/11/2022

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 review 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 availability is according to the criteria and process described on www.clinicalstudydatarequest.com

Additional data URL

https://www.clinicaltrials.gov/ct2/show/study/NCT04251533?term=CBYL719H12301&draw=2&rank=1

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinical trials. gov	NCT04251533

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	Jawad Makarem	Al Chouf	Lebanon	03484288	Jawad.Makarem@awmedicalvillage.org	Ain Wazein Medical Village
Scientific	Hind Khairallah	Sinelfil	Lebanon	01512002#271	Hind.khairallah@fattal.com.lb	Khalil Fattal et Fils s.a.l.
Public	Joseph Kattan	Ashrafieh	Lebanon	009613635913	jkattan62@hotmail.com	Hotel-Dieu de France
Public	Nagi El Saghir	Beirut	Lebanon	009613827955	ns23@aub.edu.lb	American University of Beirut Medical Center

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Ain Wazein Medical Village	Jawad Makarem	Hematology oncology	Approved
Hotel-Dieu de France	Joseph Kattan	Hematology and Oncology	Approved
American University of Beirut Medical Center	Nagi El Saghir	Hematology and Oncology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Ain w Zein Medical Village	14/01/2021	Hayat Kamaleddine	irb@awmedicalvillage.org	+961 (0) 5 509 001 ext 2014
Hotel Dieu de France	03/11/2020	Nancy Alam	nancy.alam@usj.edu.lb	+961 1 421 000 ext 2335
American University of Beirut Medical Center	03/08/2021	Fuad Ziyadeh	fz05@aub.edu.lb	+9611350000 ext 5445

Countries of Recruitment

Name
Lebanon
Australia
Austria
Brazil
Bulgaria
Colombia
Croatia
France
Germany
Hungary
India
Italy
Republic of Korea
Malaysia
Norway
Poland
Russian Federation
Slovakia
Spain
Switzerland
Taiwan
Turkey
United Kingdom
United States of America

Health Conditions or Problems Studied

Condition	Code	Keyword
Triple Negative Breast Neoplasms	Malignant neoplasm of breast (C50)	Triple Negative Breast Neoplasms

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
Progression-free Survival (PFS) Per Investigator Assessment in Study part A	Once approximately 192 PFS events in Study Part A had been observed	up to 35 months
Progression-free Survival (PFS) Per Investigator Assessment in Study part B2	Once approximately 192 PFS events in Study Part B2 had been observed	up to 22 months
Overall Response Rate (ORR) based on local radiology assessments in subjects with measurable disease at baseline in study Part B1	Up to 6 months	Up to 6 months

Key Secondary Outcomes

Name	Time Points	Measure
Overall Survival (OS) in Study Part A	Up to 66 months	Up to 66 months
Overall Survival (OS) in Study Part B2	Up to 41 months	Up to 41 months
Overall response rate (ORR) with confirmed response in Study Part A	Up to 35 months	Up to 35 months
Overall response rate (ORR) with confirmed response in Study Part B2	Up to 22 months	Up to 22 months
Clinical benefit rate (CBR) with confirmed response in Study Part A	Up to 35 months	Up to 35 months
Clinical benefit rate (CBR) with confirmed response in Study Part B1	Up to 6 months	Up to 6 months
Clinical benefit rate (CBR) with confirmed response in Study Part B2	Up to 22 months	Up to 22 months
Time to response (TTR) in Study Part A	Up to 35 months	Up to 35 months
Time to response (TTR) in Study Part B1	Up to 6 months	Up to 6 months
Time to response (TTR) in Study Part B2	Up to 22 months	Up to 22 months
Duration of Response (DOR) with confirmed response in Study Part A	Up to 35 months	Up to 35 months

Duration of Response (DOR) with confirmed response in Study Part B1	Up to 6 months	Up to 6 months
Duration of Response (DOR) with confirmed response in Study Part B2	Up to 22 months	Up to 22 months
Overall Survival (OS) in Study Part B1	Up to 6 months	Up to 6 months
Progression-free Survival (PFS) Per Investigator Assessment in Study part B1	Up to 6 months	Up to 6 months
Plasma concentrations of alpelisib - Part A	Up to 35 months	Up to 35 months
Plasma concentrations of alpelisib - Part B1	Up to 6 months	Up to 6 months
Plasma concentrations of alpelisib -Part B2	up to 22 months	up to 22 months
Plasma concentrations of paclitaxel - Part A	Up to 35 months	Up to 35 months
Plasma concentrations of paclitaxel - Part B1	up to 6 months	up to 6 months
Change from baseline in the global health status/Quality of life (QoL) scale score of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire 30-item Core Module (EORTC QLQ-C30) in study Part A	Up to 35 months	Up to 35 months
Change from baseline in the global health status/QoL scale score of the EORTC QLQ-C30 in study Part B2	Up to 22 months	Up to 22 months
Time to 10% definitive deterioration in the global health status/QOL scale score of the EORTC QLQ-C30 in study Part A	Up to 35 months	Up to 35 months
Time to 10% definitive deterioration in the global health status/QOL scale score of the EORTC QLQ-C30 in study Part B2	Up to 22 months	Up to 22 months
PFS based on local radiology assessments using RECIST 1.1 criteria for subjects by PIK3CA mutation status measured in baseline ctDNA in study Part A	Up to 35 months	Up to 35 months
PFS based on local radiology assessments using RECIST 1.1 criteria for subjects by PIK3CA mutation status measured in baseline ctDNA in study Part B2	Up to 22 months	Up to 22 months
Time to definitive deterioration of the Eastern Cooperative Oncology Group (ECOG) performance status (PS) from baseline in Study Part A	Up to 35 months	Up to 35 months
Time to definitive deterioration of the ECOG performance status from baseline in Study Part B2	Up to 22 months	Up to 22 months

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