



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

29/08/2021

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، عشوائية التوزيع، مزدوجة التعمية، مرتكزة على المقارنة بدواء وهمي في المرحلة الثالثة، لتقييم فعالية وسلامة ألبيليسيب (BYL719) بالاشتراك مع ناب-باكليتاكسيل (nab-paclitaxel) لدى المرضى المصابين بسرطان الثدي الثلاثي السلبي المتقدم إما مع طفرة (PIK3CA) أو مع فقدان البروتين مماثل الفوسفاتاز والتسيتين (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 | IMP has market authorization: Specify | |
| Yes, Worldwide | US, EMEA, Australia, Lebanon | |
| Name of IMP | Year of authorization | Month of authorization |
| Alpelisib | 2020 | 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 | Study model: Explain model | |
| N/A | N/A | |
| Study model: Specify model | | |
| N/A | | |
| Time perspective | Time perspective: Explain time perspective | |
| N/A | N/A | |
| Time perspective: Specify perspective | | |
| N/A | | |
| Target follow-up duration | Target follow-up duration: Unit | |
| | | |
| Number of groups/cohorts | | |
| | | |
| Biospecimen retention | Biospecimen description | |
| Samples with DNA** | Standard laboratory samples and biomarkers will be shipped to central labs : Navigate pharma in US and to Q2 solutions in UK | |
| Target sample size | Actual enrollment target size | |
| 5 | | |
| Date of first enrollment: Type | Date of first enrollment: Date | |
| Anticipated | 17/05/2021 | |

**Date of study closure: Type**

Anticipated

Date of study closure: Date

09/01/2026

Recruitment status

Pending

Recruitment status: Specify**Date of completion**

24/08/2023

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 |

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 |

Ethics Review

| Ethics approval obtained | Approval date | Contact name | Contact email | Contact phone |
|----------------------------|---------------|------------------|--------------------------|-----------------------------|
| Ain w Zein Medical Village | 14/01/2021 | Hayat Kamaledine | 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 |



| 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