A phase II open label, randomized, three-arm, multicenter study of LAG525 given in combination with spartalizumab (PDR001), or with spartalizumab and carboplatin, or with carboplatin, as first or second line therapy in patients with advanced triple-negative breast cancer

22/11/2024 13:23:55

Main Information

Primary registry identifying number
LBCTR2019020196

Protocol number
CLAG525B2101

MOH registration number
33223/2018

Study registered at the country of origin
Yes

Study registered at the country of origin: Specify

Type of registration
Retrospective

Type of registration: Justify
LCTR was recently initiated, original file was previously submitted by Paper

Date of registration in national regulatory agency
06/08/2018

Primary sponsor
Novartis Pharma Services Inc.

Primary sponsor: Country of origin
Novartis Pharmaceuticals

Date of registration in primary registry
04/01/2021

Date of registration in national regulatory agency
06/08/2018

Public title
A phase II open label, randomized, three-arm, multicenter study of LAG525 given in combination with spartalizumab (PDR001), or with spartalizumab and carboplatin, or with carboplatin, as first or second line therapy in patients with advanced triple-negative breast cancer

Acronym

Scientific title
A phase II open label, randomized, three-arm, multicenter study of LAG525 given in combination with spartalizumab (PDR001), or with spartalizumab and carboplatin, or with carboplatin, as first or second line therapy in patients with advanced triple-negative breast cancer

Acronym

Brief summary of the study: English
The purpose of this study is to assess the efficacy, safety, and PK characteristics of the following three combinations: i) LAG525 + spartalizumab; ii) LAG525 + spartalizumab + carboplatin, and iii) LAG525 + carboplatin in subjects with advanced TNBC and up to one prior line of systemic treatment for metastatic disease. A thorough biomarker strategy to address key aspects of tumor immunogenicity will be implemented in the study.

Brief summary of the study: Arabic

دراسة مرحلة ثانية مفتوحة اللصاقة وعشوائيّة التوزيع ومتعددة المراكز من ثلاث مجموعات حول دواء LAG525 المعطى بالاشتراك مع دواء سبارتاليزوماب (PDR001) أو مع سبارتاليزوماب وكاربوبلاتين، أو مع كاربوبلاتين، كعلاج أساسي أو كعلاج خيار ثان لدى المرضى المصابين بسرطان الثدي الثلاثيّ السلبيّ المتقدّم

Health conditions/problem studied: Specify

Triple Negative Breast Cancer

Interventions: Specify

LAG525/ PDR001/ Carboplatin

Key inclusion and exclusion criteria: Inclusion criteria

1-Patient has advanced (loco-regionally recurrent not amenable to curative therapy or metastatic) breast cancer.
2-Patient must have measurable disease, i.e., at least one measurable lesion as per RECIST 1.1 criteria (Tumor lesions previously irradiated or subjected to other loco-regional therapy will only be considered measurable if disease progression at the treated site after completion of therapy is clearly documented)
3-Patient progressed after adjuvant or 1 prior systemic treatment in the metastatic setting. Patients with de novo metastatic disease are eligible if they received 1 prior line of therapy
4-Patient must have received prior systemic treatment that included taxane-based chemotherapy for adjuvant or metastatic disease
5-Patient must have a site of disease amenable to biopsy, and must be willing to undergo a new tumor biopsy at screening and during therapy on this study, the latter if medically feasible. Patients with an available archival tumor tissue do not need to perform a tumor biopsy at screening if patient has not received anti-cancer therapy since the biopsy was taken.
6-Patient has histologically and/or cytologically confirmed diagnosis of advanced TNBC (based on most recently analyzed biopsy, local lab) meeting the following criteria: HER2 negative in situ hybridization test or an IHC status of 0 or 1+, and ER and PR expression is <1 percent as determined by immunohistochemistry (IHC)

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

90

Key inclusion and exclusion criteria: Exclusion criteria

1-Patient has received prior immunotherapy as anticancer treatment such as anti-LAG-3, anti-PD-1, anti-PD-L1, or anti-PD-L2 antibody (any line of therapy).
2-Patient received prior neoadjuvant or adjuvant therapy with a platinum agent or mitomycin and experienced recurrence within 12 months after the end of the platinum-based or mitomycin containing therapy or received Platinum or mitomycin for metastatic disease
3-Patient has had major surgery within 14 days prior to starting study treatment or has not recovered to grade 1 or less from major side effects.
4-Patient with presence of CTCAE grade 2 toxicity or higher due to prior cancer therapy. Exception to this criterion; patients with any grade of alopecia are allowed to enter the study..
5-Patient has received radiotherapy ≤ 4 weeks prior to randomization (≤ 2 weeks for limited field radiation for palliation), and has not recovered to grade 1 or better from related side effects of such therapy (with the exception of alopecia).
6-Patient has a known hypersensitivity to other monoclonal antibodies, platinum-containing compounds, or to any of the excipients of LAG525, spartalizumab, or carboplatin.
7-Patient has symptomatic central nervous system (CNS) metastases or CNS metastases that require local CNS-directed therapy (such as radiotherapy or surgery), or increasing doses of corticosteroids within the 2 weeks prior to first dose of study treatment. Patients with treated brain metastases should be neurologically stable and witout CNS progression for at least 12 weeks prior to randomization and have discontinued corticosteroid treatment (with the exception of < 10 mg/day of prednisone or equivalent for an indication other than CNS metastases) for at least 4 weeks before first dose of any study treatment.

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Other

Trial scope: Specify scope

Study design: Allocation

Randomized controlled trial

Study design: Masking

Open (masking not used)

Study design: Control

Active

Study phase

2

Study design: Purpose
Treatment

Study design: Specify purpose
N/A

Study design: Assignment
Parallel

Study design: Specify assignment
N/A

IMP has market authorization
No

IMP has market authorization: Specify

Name of IMP
LAG525

Year of authorization

Month of authorization

Type of IMP
Immunological

Pharmaceutical class
LAG525 is a high-affinity, ligand-blocking humanized IgG4 antibody (stabilized hinge, S228P) against LAG-3 that blocks the binding of MHC Class II to LAG-3.

Therapeutic indication
Patients with triple negative breast cancer

Therapeutic benefit
'Overall response rate (ORR) per RECIST v1.1 per investigators' assessment up to 8 cycles

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

Central Laboratory Q2 Solutions, The Alba Campus, Rosebank, Livingston, EH54 7EG, United Kingdom

Lab Tests to be done:
Hematology Hematocrit, Hemoglobin, Platelets, White blood cells, Differential (Basophils, Eosinophils, Lymphocytes, Monocytes, Neutrophils, Bands
Chemistry Albumin, Alkaline phosphatase, ALT , AST , Gamma-glutamyl-transferase (GGT), Lactate dehydrogenase (LDH), Calcium, Magnesium, Phosphorus, Chloride, Sodium, Potassium, Creatinine, Creatinine clearance, Creatine kinase, Direct Bilirubin, Indirect Bilirubin, Total Bilirubin, Total Cholesterol, Blood Urea Nitrogen (BUN) or Urea, Uric Acid, Amylase, Lipase, Glucose
Coagulation International normalized ratio [INR]), Activated partial thromboplastin time (APTT)
Thyroid TSH, Free T3 and Free T4
Hepatitis markers HBV-DNA, HBsAg, HBsAb, HBcAb, HCV RNA-PCR
Cytokines IFN-γ, IL-6, IL-1,TNF-α
Pregnancy Test serum pregnancy hCG test

Target sample size

6

Actual enrollment target size

6

Date of first enrollment: Type

Actual

Date of first enrollment: Date

31/10/2018

Date of study closure: Type

Actual

Date of study closure: Date

23/07/2020

Recruitment status

Complete

Recruitment status: Specify

On Hold

Date of completion

13/09/2019

IPD sharing statement plan

No

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.

Additional data URL

https://clinicaltrials.gov/ct2/show/record/NCT03499899?term=CLAG525B2101&rank=1

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinical Trials. gov	NCT03499899

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	Joseph Kattan	Beirut	Lebanon	009613635913	jkattan62@hotmail.com	Hotel Dieu De France
Scientific	Hind Khairallah	Sin El Fil	Lebanon	+961 1 512002 Ext. 271	Hind.Khairallah@fattal.com.lb	Khalil Fattal et Fils s.a.l.
Public	Dany Abi Gerges	Bsalim	Lebanon	+9613341960	abgerges@idm.net.lb	Middle East Institute Of Health
Public	Fadi Farhat	Saida	Lebanon	+9613753155	drfadi.trials@gmail.com	Hammoud Hospital

Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu De France	Dr Joseph Kattan	Hematology Oncology	Approved
Middle East Institute of Health	Dr Dany ABi Gerges	Hematology Oncology	Approved
Hammoud Hospital University Medical Center	Dr Fadi Farhat	Hematology Oncology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hotel Dieu de France	03/07/2018	Nancy Alam	nancy.alam@usj.edu.lb	+961 1421000 ext 2335
Middle East Institute of Health	16/08/2018	Ahmad Ibrahim	ahmad_O_Ibrahim@hotmail.com	+961 (0) 3 233 560
Hammoud Hospital University Medical Center	16/07/2018	Ahmad Zaatari	zaatari@hammoudhospital.com	+961 (0) 7 723111 ext 1160

Countries of Recruitment

Name
Australia
Belgium
Canada
France
Germany
Hungary
Italy
Japan
Lebanon
Singapore
Spain
Thailand
United States of America

Health Conditions or Problems Studied

Condition	Code	Keyword
breast cancer	Breast, unspecified (C50.9)	Tripple negative ABC

Interventions

Intervention	Description	Keyword
Physical examination, height, weight, Hematology, Chemistry, Ferritin, Creatinine, Cleatinine Clearance, Hepatitis, Pregnancy Test, Urine Dipstick, Microscopic Urinalysis, Proteinuria, Urine Pregnancy Test, Liver function test, Ocular exam, audiometry, ECG, Electrocardiogram, PK sampling, vital signs, Growth and development	Physical examination, height, weight, Hematology, Chemistry, Ferritin, Creatinine, Cleatinine Clearance, Hepatitis, Pregnancy Test, Urine Dipstick, Microscopic Urinalysis, Proteinuria, Urine Pregnancy Test, Liver function test, Ocular exam, audiometry, ECG, Electrocardiogram, PK sampling, vital signs, Growth and development	Physical examination, height, weight, Hematology, Chemistry, Ferritin, Creatinine, Cleatinine Clearance, Hepatitis, Pregnancy Test, Urine Dipstick, Microscopic Urinalysis, Proteinuria, Urine Pregnancy Test, Liver function test, Ocular exam, audiometry, ECG, Electrocardiogram, PK sampling, vital signs, Growth and development

Primary Outcomes

Name	Time Points	Measure
Overall response rate (ORR) per RECIST v1.1 per investigators' assessment	24 months	24 Months

Key Secondary Outcomes

Name	Time Points	Measure
Duration of response (DOR)	3 years	3 years
Overall Survival (OS)	3 years	3 years
Clinical Benefit Rate (CBR)	24 months	24 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