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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

Main Information	
Primary registry identifying number	Protocol number
LBCTR2019020196	CLAG525B2101
MOH registration number	
33223/2018	
Study registered at the country of origin	Study registered at the country of origin: Specify
Yes	
Type of registration	Type of registration: Justify
Retrospective	LCTR was recently initiated, original file was previously submitted by Paper
Date of registration in national regulatory agency	
06/08/2018	
Primary sponsor	Primary sponsor: Country of origin
Novartis Pharma Services Inc.	Novartis Pharmaceuticals
Date of registration in primary registry	Date of registration in national regulatory agency
29/05/2021	06/08/2018
Public title	Acronym
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	
Scientific title	Acronym
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	
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	

Lebanon Clinical Trials Registry

در اسة مرحلة ثانية مفتوحة اللصاقة وعشوائيّة التوزيع ومتعددة المراكز من ثلاث مجموعات حول دواء

REPUBLIC OF LEBANON

MINISTRY OF PUBLIC HEALTH

(PDR001) المعطى بالاشتراك مع دواء سبارتاليزوماب LAG525

أو مع سبار تاليز وماب وكار بوبلاتين، أو مع كار بوبلاتين، كعلاج أساسي أو كعلاج خيار ثان لذى المرضى المصابين بسرطان الثدي الثلاثي ، السلبي المتقدم

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

Key inclusion and exclusion criteria: Specify gender

18

Key inclusion and exclusion criteria: Age minimum

Key inclusion and exclusion crit	eria: 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).

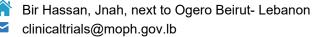
6-Patient has a known hypersensitivity to other monoclonal antibodies, platinum-containing compounds, or to any of the excipients of LAG525, spartalizumab, or carboplatin.

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	Type of intervention: Specify type
Pharmaceutical	N/A
Trial scope Other	Trial scope: Specify scope
Study design: Allocation	Study design: Masking
Randomized controlled trial	Open (masking not used)
Study design: Control	Study phase
Active	2



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Study design: Purpose Treatment	Study design: Specify purpose N/A	
Study design: Assignment Parallel	Study design: Specify assignm N/A	ent
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 (stabilize LAG-3 that blocks the binding of MHC Class II to LAG-3. Therapeutic indication Patients with triple negative breast cancer	ed hinge, S228P) against	
Therapeutic benefit 'Overall response rate (ORR) per RECIST v1.1 per investigators' assessmen	t 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 N/A	perspective
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	

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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, Gammaglutamyl-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-y, IL-6, IL-1,TNF-a Pregnancy Test serum pregnancy hCG test Target sample size Actual enrollment target size 6 6 Date of first enrollment: Type Date of first enrollment: Date 31/10/2018 Actual Date of study closure: Type Date of study closure: Date Actual 23/07/2020 **Recruitment status Recruitment status: Specify** Complete On Hold Date of completion 13/09/2019 IPD sharing statement plan IPD sharing statement description Novartis is committed to sharing with qualified external No 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	009613635 913	jkattan62@hotm ail.com	Hotel Dieu De France
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Public	Dany Abi Gerges	Bsalim	Lebanon	+9613341 960	abgerges@idm.n et.lb	Middle East Institute Of Health
Public	Fadi Farhat	Saida	Lebanon	+9613753 155	drfadi.trials@gm ail.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_lbrahim@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

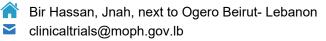




Countries of Recruitment
Name
Australia
Belgium
Canada
France
Germany
Hungary
Italy
Japan
Lebanon
Singapore
Spain
Thailand
United States of America

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	