Study of Nivolumab Versus Placebo in Combination With Neoadjuvant Chemotherapy and Adjuvant Endocrine Therapy in Participants With High-risk, Estrogen Receptor-Positive (ER+), Human Epidermal Growth Factor Receptor 2-Negative (HER2-) Primary Breast Cancer

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT04109066	RECRUITING	SEPTEMBER 30, 2019	DECEMBER 2, 2021

STUDY DESCRIPTION

Brief Summary

A randomized multi-arm study evaluating the efficacy and safety of nivolumab versus placebo in combination with neoadjuvant (pre-surgery)chemotherapy and adjuvant (post-surgery) endocrine therapy in participants with high-risk, estrogen receptor-positive, human epidermal growth factor receptor 2-negative (ER+, HER2-) early stage breast cancer.

Condition or Disease: Breast Cancer

Intervention/treatment:
Biological: nivolumab
Drug: paclitaxel (PTX)
Other: nivolumab placebo
Drug: anthracycline
Drug: cyclophosphamide
Drug: Endocrine Therapy
Procedure: Surgery

Phase: Phase 3

DETAILED DESCRIPTION

N/A

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 1200 participants

Intervention Model : Parallel Assignment

Masking: Double (Participant, Investigator)

Primary Purpose: Treatment

Official Title: A Randomized, Multicenter, Double-blind, Placebo-controlled Phase 3 Study of Nivolumab Versus Placebo in Combination With Neoadjuvant Chemotherapy and Adjuvant Endocrine Therapy in Patients With High-risk, Estrogen Receptor-Positive (ER+), Human Epidermal Growth Factor Receptor 2-Negative (HER2-) Primary Breast Cancer

Actual Study Start Date: November 2019

Estimated Primary Completion Date: June 2032

Estimated Study Completion Date: June 2032

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Arm A: Nivolumab combined with neoadjuvant CT and adjuvant ET Nivolumab with paclitaxel followed by nivolumab with anthracycline + cyclophosphamide as neoadjuvant (pre-surgery) treatment, then nivolumab with adjuvant (post-surgery) endocrine therapy of investigator's choice	Biological: nivolumab Specified Dose on Specified days Drug: paclitaxel (PTX) Specified dose on Specified days Drug: anthracycline Specified dose on Specified days Drug: cyclophosphamide Specified dose on Specified days Drug: Endocrine Therapy Variable endocrine therapy of investigators choice Procedure: Surgery Surgery for breast cancer

Placebo Comparator: Arm B: Placebo combined with neoadjuvant CT and adjuvant ET Nivolumab placebo with paclitaxel followed by nivolumab placebo with anthracycline + cyclophosphamide as neoadjuvant (pre-surgery) treatment, then nivolumab placebo with adjuvant (post-surgery) endocrine therapy of investigator's choice	Drug: paclitaxel (PTX) Specified dose on Specified days Other: nivolumab placebo Specified dose on Specified days Drug: anthracycline Specified dose on Specified days Drug: cyclophosphamide Specified dose on Specified days Drug: Endocrine Therapy Variable endocrine therapy of investigators choice Procedure: Surgery Surgery for breast cancer

OUTCOME MEASURES

Primary Outcome Measures:
1. Pathological Complete response (pCR) Using the definition of ypT0/is ypN0 [Time Frame: approximately 7 months]
2. Event-Free Survival (EFS) [Time Frame: up to 10 years]

Secondary Outcome Measures:
1. Overall Survival (OS) [Time Frame: up to 10 years]
2. Disease-free Survival (DFS) [Time Frame: up to 10 years]
3. Distant Metastasis-free survival (DMFS) [Time Frame: up to 10 years]
4. pCR using the definition of ypT0 ypN0 [Time Frame: approximately 7 months]
5. pCR rate using the definition of ypT0/is [Time Frame: approximately 7 months]
6. Objective response rate (ORR) using definition of tumor response rate per radiologic-based assessment [Time Frame: approximately 7 months]
7. ORR using definition of tumor response rate per clinic-based physical assessment [Time Frame: approximately 7 months]
8. Residual cancer burden (RCB) category status (0, I, II, III) [Time Frame: approximately 7 months]
9. Incidence of adverse events (AEs) [Time Frame: approximately 17 months]
10. Severity of AEs [Time Frame: approximately 17 months]
11. Change from baseline on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) global health status/quality of life (QOL) subscale (items 29 and 30) [Time Frame: up to 52 weeks]
12. Change from baseline on the EORTC QLQ-C30 physical functioning subscale (items 1 to 5) [Time Frame: up to 52 weeks]

ELIGIBILITY CRITERIA

Ages Eligible for Study: 18 Years and older (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

For more information regarding Bristol-Myers Squibb Clinical Trial participation, please visit www.BMSStudyConnect.com
Inclusion Criteria:
Localized invasive breast ductal carcinoma, confirmed by the local pathologist, that includes the following combined primary tumor and clinical node (cN) categories: T1c (tumor size = 2 cm)-T2 (tumor size > 2 cm), cN1-N2 OR T3-T4, cN0-cN2. Note: Axillary lymph node status must be assessed by fine needle biopsy or core biopsy. Estrogen receptor-positive (ER+) breast cancer (BC) and with or without progesterone receptor (PgR) expression (determined on the most recently analyzed tissue sample tested locally and confirmed by the central laboratory, as defined in the relevant American Society of Clinical Oncology (ASCO)-College of American Pathologists (CAP) Guidelines. Human epidermal growth factor receptor 2 (HER2-) BC tested in the local laboratory, defined as a negative in situ hybridization test or an immunohistochemistry (IHC) status of 0, 1+, or 2+. Tumor Grade 3 of ductal histology, Or Tumor Grade 2 of ductal histology having an ER expression level percentage between 1-10% Must agree to provide primary breast tumor tissue at baseline and at surgery Must be deemed eligible for surgery Males and females must agree to follow specific methods of contraception, if applicable, while participating in the trial Must have an Eastern Cooperative Oncology Group (ECOG) scale performance status of 0 or 1
Exclusion Criteria:
Breastfeeding, pregnant, or expecting to conceive or father children within the projected duration of the study, starting with the screening through 12 months for participants who receive cyclophosphamide, or 6 months for participants who do not receive cyclophosphamide, after the last dose of study treatment Prior treatment with chemotherapy, endocrine therapy (ET), targeted therapy, and/or radiation therapy for the currently diagnosed breast cancer prior to enrollment Prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, or anti-CTLA-4 antibody, or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways Significant cardiovascular disease such as left ventricular ejection fraction (LVEF) 1 tumor in different quadrants of the breast) Bilateral invasive BC
Other protocol-defined inclusion/exclusion criteria apply

CONTACTS AND LOCATIONS

Contacts

Contact: Recruiting sites have contact information.Please contact the sites directly. If there is no contact information, please email: Clinical.Trials@bms.com
Contact: First line of the email MUST contain NCT # and Site #.

Locations

United States, Alabama	University of South Alabama Mitchell Cancer Institute	Mobile
United States, California	Local Institution	Concord
United States, California	Local Institution	Duarte
United States, California	Marin Cancer Care, Inc	Greenbrae

United States, California	Local Institution	Los Angeles
United States, California	Local Institution	Orange
United States, California	Innovative Clinical Research Institute	Whittier
United States, Connecticut	Bennett Cancer Center	Stamford
United States, Florida	Cancer Specialists of North FL	Jacksonville
United States, Florida	University of Miami	Miami
United States, Florida	Local Institution	Orlando
United States, Florida	Sacred Heart Medical Group	Pensacola
United States, Florida	Tallahassee Memorial Cancer Center	Tallahassee
United States, Georgia	University Cancer Blood Ctr	Athens
United States, Georgia	Northside Hospital,Inc.- Central Research Department	Atlanta
United States, Georgia	John B. Amos Cancer Center	Columbus
United States, Illinois	Northwestern Memorial Hospital	Chicago
United States, Indiana	Fort Wayne Medical Oncology and Hematology, Inc.	Fort Wayne
United States, Kentucky	Local Institution	Louisville
United States, Maine	New England Cancer Specialists	Scarborough
United States, Maryland	American Oncology Partners of Maryland, PA	Bethesda
United States, Missouri	HCA Midwest Division	Kansas City
United States, New Jersey	Local Institution	Flemington
United States, New Jersey	Summit Medical Group	Florham Park
United States, New Jersey	The Cancer Center At Hackensack University Medical Center	Hackensack
United States, New Jersey	Rutgers Cancer Institute of New Jersey	New Brunswick
United States, New Mexico	University of New Mexico Comprehensive Cancer Center	Albuquerque
United States, New York	Montefiore Medical Center	Bronx
United States, North Carolina	Local Institution	Charlotte
United States, North Carolina	Local Institution	Durham
United States, North Carolina	Local Institution	Winston-Salem
United States, Ohio	Local Institution	Canton
United States, Ohio	Local Institution	Cincinnati
United States, Ohio	MetroHealth Medical Center	Cleveland
United States, Ohio	Local Institution	Cleveland
United States, Oregon	Local Institution	Portland
United States, Tennessee	Tennessee Oncology, PLLC - SCRI - PPDS	Chattanooga
United States, Tennessee	Local Institution	Knoxville
United States, Texas	Ft. Worth Center For Cancer Blood Disorders	Fort Worth
United States, Utah	Local Institution	Salt Lake City
United States, Virginia	Local Institution	Fairfax
United States, Virginia	Hematology-Oncology Associates Of Fredricksburg, Inc	Fredericksburg
United States, Virginia	Virginia Cancer Institute	Richmond
United States, Washington	Local Institution	Seattle
Argentina, Buenos Aires	Local Institution	Caba
Argentina, Buenos Aires	Local Institution	Ciudad Autonoma Beunos Aires
Argentina, Buenos Aires	Hospital Britanico De Buenos Aires	Ciudad Autónoma de Buenos Aires
Argentina, Buenos Aires	Local Institution	La Plata
Argentina, Cordoba	Local Institution	Río Cuarto

Argentina, Santa FE	Local Institution	Rosario
Argentina	Clinica Adventista Belgrano	Buenos Aires
Argentina	Instituto Medico Especialazado Alexander Fleming	Caba
Argentina	Local Institution	Cordoba
Argentina	Local Institution	Cordoba
Argentina	Local Institution	La Rioja
Argentina	Local Institution	Viedma
Australia, New South Wales	Mater Hospital	North Sydney
Australia, New South Wales	Port Macquarie Base Hospital	Port Macquarie
Australia, New South Wales	Local Institution	Sydney
Australia, Queensland	Royal Brisbane and Womens Hospital	Herston
Australia, South Australia	Calvary Central Districts Hospital	Elizabeth Vale
Australia, Victoria	Monash Medical Centre Clayton	Clayton
Australia, Victoria	Austin Hospital	Heidelberg
Australia, Victoria	Peter MacCallum Cancer Centre	Melbourne
Australia, Victoria	Ballarat Base Hospital	North Ballarat
Austria	Universitaetsklinik F. Frauenheilkunde / Geburtshilfe	Graz
Austria	Med. Universitaet Innsbruck	Innsbruck
Austria	Landeskrankenhaus-Universitaetsklinik fuer Innere Medizin III	Salzburg
Austria	Medizinische Universitaet Wien	Wien
Austria	Medizinische Universitaet Wien	Wien
Belgium	Local Institution	Charleroi
Belgium	Universitair Ziekenhuis Antwerpen	Edegem
Belgium	UZ Gent-Medical oncology	Gent
Belgium	Universitair Ziekenhuis Brussel - PIN	Jette
Belgium	CHU de Liège	Liege
Brazil, Ceara	Oncocentro Servico Medicos e Hospitalares Ltda	Fortaleza
Brazil, Distrito Federal	Hospital Sirio Libanes	Brasilia
Brazil, Goias	Local Institution	Goiania
Brazil, Minas Gerais	Universidade Federal De Minas Gerais	Belo Horizonte - Mg
Brazil, Minas Gerais	Local Institution	Juiz de Fora
Brazil, RIO Grande DO SUL	ONCOSITE - Centro de Pesquisa Clinica em Oncologia	Ijui
Brazil, RIO Grande DO SUL	Irmandade da Santa Casa de Misericordia de Porto Alegre - Hospital Santa Rita	Port Alegre
Brazil, RIO Grande DO SUL	Local Institution	Porto Alegre
Brazil, Rio Grande Do Sul	Hospital Sao Lucas Da Pucrs	Porto Alegre
Brazil, RIO Grande DO SUL	Local Institution	Santa Cruz do Sul
Brazil, Sao Paulo	Fundacao Pio Xii Hosp Cancer De Barretos	Barretos
Brazil, SAO Paulo	Faculdade de Medicina do ABC	Santo Andre
Brazil, SAO Paulo	Local Institution	São Paulo
Brazil	COI Clinicas Oncologicas Integradas SA	Rio de Janeiro
Brazil	Centro de Pesquisa e Centro de Estudos em Oncologia Ginecologica e Mamaria	Sao Paulo
Brazil	Hospital Municipal Vila Santa Catarina	Sao Paulo
Canada, Nova Scotia	Local Institution	Halifax
Canada, Ontario	Local Institution	Thunder Bay
Canada, Ontario	Local Institution	Toronto

Canada, Ontario	Local Institution	Toronto
Canada, Quebec	Local Institution	Montreal
Canada, Quebec	Local Institution	Montreal
Canada, Quebec	Centre Hospitalier de l'Université de Montréal-Breast Cancer	Montréal
Canada, Quebec	Centre integre universitaire de sante et de service sociaux de l'estrie - CHUS	Sherbrooke
Chile, Coquimbo	Local Institution	La Serena
Chile, Metropolitana	Centro de Investigacion Clinica Bradford Hill	Santiago de Chile
Chile, Metropolitana	Hospital Clinico Pontificia Universidad Catolica De Chile	Santiago Region Metropolitana
Chile, Valparaiso	Oncocentro Apys	Vina del Mar
China, Anhui	Local Institution	Bengbu
China, Anhui	Local Institution	Hefei
China, Beijing	Local Institution	Beijing
China, Beijing	Local Institution	Beijing
China, Chongqing	Local Institution	Chongqing
China, Guangdong	Local Institution	Guangzhou
China, Guangdong	Local Institution	Guangzhou
China, Guangdong	Local Institution	Guangzhou
China, Hebei	Local Institution	Shjiazhuang
China, Heilongjiang	Local Institution	Harbin
China, Henan	Local Institution	Zhengzhou
China, Hubei	Local Institution	Wuhan
China, Jilin	Local Institution	Changchun
China, Jilin	Local Institution	Changchun
China, Liaoning	Local Institution	Shenyang
China, Shan1xi	Local Institution	XiAn
China, Shandong	Local Institution	Jinan
China, Shandong	Local Institution	Qingdao
China, Shandong	Local Institution	YanTai
China, Shanghai	Local Institution	Shanghai
China, Sichuan	Local Institution	Chengdu
China, Tianjin	Local Institution	Tianjin
China, Xinjiang	Local Institution	Urumqi
China, Zhejiang	Local Institution	Hangzhou
China, Zhejiang	Local Institution	Hangzhou
China, Zhejiang	Local Institution	Hangzhou
China	Local Institution	Chengdu
China	Local Institution	Xiamen
Colombia, Bogota	Local Institution	Colombia
Colombia	Local Institution	Barranquilla
Colombia	Local Institution	Bogotá
Colombia	Local Institution	Cali
Colombia	Local Institution	Floridablanca
Colombia	Local Institution	Monteria
Colombia	Local Institution	Pereira
Colombia	Local Institution	Rionegro, Antioquia

Czechia	Local Institution	Chomutov
Czechia	Klinika onkologie a radioterapie	Hradec Kralove
Czechia	Komplexni onkologicke centrum	Novy Jicin
Czechia	Onkologicka klinika	Olomouc
Czechia	Radioterapeuticka a onkologicka klinika FNKV	Praha 10
Denmark	Local Institution	Aarhus N
Denmark	Local Institution	Herlev
Denmark	Local Institution	Kobenhavn O
Denmark	Local Institution	Naestved
Finland	Local Institution	Helsinki
Finland	Local Institution	Tampere
France	Local Institution	Bayonne
France	Chu Jean Minjoz	Besancon
France	Hopital Morvan	Brest
France	Centre Jean Perrin	Clermont-ferrand
France	Clinique Victor Hugo	Le Mans
France	Hopital Prive Jean Mermoz	Lyon
France	Institut du Cancer de Montpellier	Montpellier Cedex 5
France	Hopital Europeen Georges Pompidou	Paris
France	Hôpital Privé Des Côtes d'Armor	Plerin
France	Institut De Cancerologie De L Ouest	Saint Herblain Cedex
France	Clinique Sainte Anne	Strasbourg
France	Centre Hospitalier intercommunal de Toulon La Seyne sur Mer	Toulon
France	Institut Gustave Roussy	Villejuif
Germany	Helios Klinikum Berlin-Buch	Berlin
Germany	Local Institution	Berlin
Germany	Universitaetsklinikum Carl Gustav Carus	Dresden
Germany	Local Institution	Erlangen
Germany	Universitaetsklinikum Essen	Essen
Germany	Universitatsklinikum Frankfurt	Frankfurt
Germany	Agaplesion Diakonieklinikum	Hamburg
Germany	Universitaetsklinik Heidelberg	Heidelberg
Germany	Universitaetsklinikum d. Saarlandes	Homburg
Germany	Universitaetsklinikum Koeln	Koeln
Germany	Universitatsklinikum Leipzig	Leipzig
Germany	Evang. Krankenhaus Bethesda	Moenchengladbach
Germany	LMU Klinikum der Universität München	Muenchen
Germany	Uni Frauenklinikum Suedstadt	Rostock
Germany	CaritasKlinikum Saarbruecken.	Saarbruecken
Germany	MVZ-Onkologie Velbert GbR	Velbert
Germany	Universitaetsklinikum Wuerzburg	Würzburg
Hong Kong	Local Institution	Hong Kong
Ireland, Dublin	St. James'S Hospital	Dublin 8
Ireland	Cork University Hospital	Cork
Ireland	Beaumont Hospital	Dublin

Italy	Local Institution	Bergamo
Italy	Local Institution	Brindisi
Italy	Local Institution	Catania
Italy	Azienda Ospedaliero-Universitaria Mater Domini	Catanzaro
Italy	Local Institution	Milano
Italy	Azienda Ospedaliero Universitaria Federico II di Napoli	Napoli
Italy	Istituto Nazionale Tumori Fondazione Pascale	Napoli
Italy	Istituto Oncologico Veneto IOV	Padova
Italy	Fondazione Irccs - Policlinico San Matteo	Pavia
Italy	Local Institution	Prato
Italy	Local Institution	Roma
Italy	Istituto Clinico Humanitas	Rozzano (MI)
Korea, Republic of	Local Institution	Seoul
Korea, Republic of	Local Institution	Seoul
Korea, Republic of	Local Institution	Seoul
Korea, Republic of	Local Institution	Seoul
Mexico, BAJA California	Local Institution	Tijuana
Mexico, Distrito Federal	Local Institution	Mexico City
Mexico, Distrito Federal	Local Institution	Tlalpan
Mexico, Nuevo LEON	Local Institution	Monterrey
Mexico, Yucatan	Local Institution	Merida
Mexico	Local Institution	Campeche
Mexico	Local Institution	Chihuahua
Mexico	Local Institution	Colima
Mexico	Local Institution	Oaxaca
Netherlands	Antoni Van Leeuwenhoek Ziekenhuis	Amsterdam
Netherlands	Amphia Ziekenhuis	Breda
Netherlands	Deventer Ziekenhuis	Deventer
Netherlands	Local Institution	Rotterdam
Netherlands	Universitair Medisch Centrum Utrecht	Utrecht
Poland	Oddzial Dzienny Chemioterapii	Koszalin
Poland	Local Institution	Krakow
Poland	Klinika Onkologii CZMP	Lodz
Poland	Local Institution	Opole
Poland	Klinika Nowotworow Piersi i Chirurgii Rekonstrukcyjnej	Warszawa
Portugal	Local Institution	Lisboa
Portugal	Local Institution	Lisboa
Portugal	Local Institution	Porto
Puerto Rico	Ponce Medical School Foundation	Ponce
Puerto Rico	Local Institution	San Juan
Romania	Local Institution	Bucharest
Romania	Local Institution	Bucharest
Romania	Local Institution	Bucuresti
Romania	Local Institution	Craiova
Romania	Local Institution	Floresti

Romania	Local Institution	Suceava
Russian Federation	Local Institution	Krasnodar
Russian Federation	Local Institution	Moscow
Russian Federation	Local Institution	Moscow
Russian Federation	Local Institution	Moskva
Russian Federation	Local Institution	Ryazan
Russian Federation	Local Institution	Saint Petersburg
Russian Federation	Local Institution	Sankt-Peterburg
Russian Federation	Local Institution	Sochi
Singapore	Local Institution	Singapore
Singapore	Local Institution	Singapore
Singapore	Local Institution	Singapore
Spain	Local Institution	Barcelona
Spain	Local Institution	Barcelona
Spain	Local Institution	Elche (alicante)
Spain	Local Institution	Madrid
Spain	Local Institution	Madrid
Spain	Local Institution	Madrid
Spain	Local Institution	Malaga
Spain	Local Institution	Santiago Compostela
Spain	Local Institution	Sevilla
Switzerland	University Hospital Basel	Basel
Switzerland	CHUV	Lausanne
Switzerland	Onkologiezentrum Thun-Berner Oberland Spital Sts Ag	Thun
Taiwan	Local Institution	Kaohsiung
Taiwan	Local Institution	Tainan
Taiwan	Local Institution	Tainan
Taiwan	Local Institution	Taipei
Taiwan	Local Institution	Taipei
Turkey	Local Institution	Adana
Turkey	Local Institution	Ankara
Turkey	Local Institution	Antalya
Turkey	Local Institution	Istanbul
United Kingdom, Glamorgan	Local Institution	Swansea
United Kingdom, Manchester	The Christie NHS Foundation Trust	Withington
United Kingdom	Local Institution	Coventry
United Kingdom	Local Institution	Headington
United Kingdom	Local Institution	London

Sponsors and Collaborators

Bristol-Myers Squibb

Investigator

Study Director :	Bristol-Myers Squibb	Bristol-Myers Squibb

MORE INFORMATION

Responsible Party : Bristol-Myers Squibb

ClinicalTrials.gov Identifier :	NCT04109066
Other Study ID Numbers :	CA209-7FL
First Posted :	September 30, 2019
Last Update Posted :	December 2, 2021
Last Verified :	December 2021
Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Keywords provided by Bristol-Myers Squibb:	*Nivolumab* *Breast Cancer* *Cancer* *Estrogen Receptor-Positive (ER+) Human Epidermal Growth Factor 2 Negative (HER2-)* *Neoadjuvant* *Adjuvant* *Primary Breast Cancer*
Additional relevant MeSH terms :	*Breast Neoplasms* *Neoplasms by Site* *Neoplasms* *Breast Diseases* *Skin Diseases*