



The U.S. government does not review or approve the safety and science of all studies listed on this website.

Read our full [disclaimer](https://clinicaltrials.gov/about-site/disclaimer) (<https://clinicaltrials.gov/about-site/disclaimer>) for details.

Completed 

A Phase 1 Study of Nivolumab (BMS-936558) in Subjects With Advanced or Recurrent Malignancies (MDX1106-03)

ClinicalTrials.gov ID  NCT00730639

Sponsor  Bristol-Myers Squibb

Information provided by  Bristol-Myers Squibb (Responsible Party)

Last Update Posted  2021-12-03

Study Details Tab

Study Overview

Brief Summary

The purpose of this study is to determine the safety and effectiveness of MDX-1106 in patients with certain types of cancer. Another purpose is to determine how MDX-1106 is absorbed and distributed within the body, and how it's eventually eliminated.

Official Title

A Phase 1, Open-Label, Multicenter, Multidose, Dose Escalation Study of BMS-936558 (Nivolumab) in Subjects With Selected Advanced or Recurrent Malignancies

Conditions

Metastatic Castration-resistant Prostate Cancer

Renal Cell Carcinoma

Metastatic Melanoma

Non-small Cell Lung Cancer



Intervention / Treatment ⓘ

- Biological: BMS-936558 (MDX-1106)
- Biological: BMS-936558 (MDX-1106)
- Biological: BMS-936558 (MDX-1106)
- Biological: BMS-936558 (MDX-1106)
- Biological: BMS-936558 (MDX-1106)

Other Study ID Numbers ⓘ

- MDX1106-03 (Other Identifier) (OTHER: BMS)

Study Start (Actual) ⓘ

2008-10-30

Primary Completion (Actual) ⓘ

2013-02-04

Study Completion (Actual) ⓘ

2020-12-22

Enrollment (Actual) ⓘ

395

Study Type ⓘ

Interventional

Phase ⓘ

Phase 1

Resource links provided by the National Library of Medicine

[MedlinePlus Genetics](https://medlineplus.gov/genetics/) (<https://medlineplus.gov/genetics/>), related topics:

[Melanoma](https://medlineplus.gov/genetics/condition/melanoma) (<https://medlineplus.gov/genetics/condition/melanoma>), [Lung cancer](https://medlineplus.gov/genetics/condition/lung-cancer) (<https://medlineplus.gov/genetics/condition/lung-cancer>).

[Genetic and Rare Diseases Information Center](https://rarediseases.info.nih.gov/gard) (<https://rarediseases.info.nih.gov/gard>), resources:
[Renal Cell Carcinoma](https://rarediseases.info.nih.gov/diseases/13215/renal-cell-carcinoma) (<https://rarediseases.info.nih.gov/diseases/13215/renal-cell-carcinoma>),
[Clear Cell Renal Cell Carcinoma](https://rarediseases.info.nih.gov/diseases/9574/clear-cell-renal-cell-carcinoma) (<https://rarediseases.info.nih.gov/diseases/9574/clear-cell-renal-cell-carcinoma>).

[Drug Information](https://dailymed.nlm.nih.gov/dailymed/) (<https://dailymed.nlm.nih.gov/dailymed/>), available for:
[Nivolumab](https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Nivolumab) (<https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Nivolumab>).

[FDA Drug and Device Resources](https://clinicaltrials.gov/fda-links) (<https://clinicaltrials.gov/fda-links>).

Contacts and Locations

This section provides contact details for people who can answer questions about joining this study, and information on where this study is taking place.

To learn more, please see the [Contacts and Locations section in How to Read a Study Record](https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations) (<https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations>).

This study has 13 locations

United States

Arizona Locations

-  **Scottsdale, Arizona, United States, 85258**
Pinnacle Oncology Hematology

Connecticut Locations

-  **New Haven, Connecticut, United States, 06520**
Yale University School Of Medicine

Florida Locations

-  **Tampa, Florida, United States, 33612-9497**
H. Lee Moffitt Cancer Center & Research
Institute

Maryland Locations

-  **Baltimore, Maryland, United States, 21231**
Johns Hopkins University

Massachusetts Locations

-  **Boston, Massachusetts, United States, 02215**
Beth Israel Deaconess Medical Center
-  **Boston, Massachusetts, United States, 02215**

Dana Farber Cancer Institute

 **Boston, Massachusetts, United States, 02215**
Massachusetts General Hospital

Michigan Locations

 **Ann Arbor, Michigan, United States, 48109**
University Of Michigan Cancer Center

New York Locations

 **New York, New York, United States, 10065**
Memorial Sloan Kettering Nassau

North Carolina Locations

 **Huntersville, North Carolina, United States, 28078**
Carolina Biooncology Institute

Ohio Locations

 **Cincinnati, Ohio, United States, 45219**
Christ Hospital

Tennessee Locations

 **Nashville, Tennessee, United States, 37203**
Sarah Cannon Research Institute

 **Nashville, Tennessee, United States, 37232**
Vanderbilt-Ingram Cancer Ctr

Participation Criteria

Researchers look for people who fit a certain description, called [eligibility criteria](#). Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read [Learn About Studies](#) (<https://clinicaltrials.gov/study-basics/learn-about-studies>).

Eligibility Criteria

Description

For more information regarding BMS clinical trial participation, please visit www.BMSStudyConnect.com

Inclusion Criteria:

- Subjects must have mCRPC, RCC, MEL, Non-small-cell lung cancer (NSCLC), or Colorectal Cancer (CRC), that is advanced (non-resectable), or recurrent and for which no alternative, curative standard exists
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2
- Must have at least 1 measurable lesion
- Subjects with mCRPC and with only non-measurable bone lesions must have either progression new lesions or have Prostate-specific antigen (PSA) progression within the 6-week period before study administration
- At least 1 and up to 5 prior systemic therapies for advanced/recurrent disease
- Prior treated brain or meningeal metastases must be without Magnetic resonance imaging (MRI) evidence of progression for at least 8 weeks and off immunosuppressive doses of systemic steroids for at least 2 weeks before study drug administration
- Prior systemic radiation therapy must have been completed at least 4 weeks before study drug administration. Prior focal radiotherapy completed at least 2 weeks prior to study drug administration
- Immunosuppressive doses of systemic medications, such as steroids or absorbed topical steroids must be discontinued at least 2 weeks before study drug administration
- Prior surgery that required general anesthesia must be completed at least 2 weeks before study drug administration. Surgery requiring local/epidural anesthesia must be completed at least 72 hours before study drug administration

Exclusion Criteria:

- History of severe hypersensitivity reactions to other Monoclonal antibody (mAb)s
- Subjects with any active autoimmune disease or a documented history of autoimmune disease, or history of syndrome that required systemic steroids or immunosuppressive medications, except for subjects with vitiligo or resolved childhood asthma/atopy
- Prior therapy with an anti-Programmed death-1 (PD-1), anti-PD-L1, anti-PD-L2, or anti-Cytotoxic t-lymphocyte antigen-4 (CTLA-4) antibody (or any other antibody targeting T cell co-stimulation pathways)
- Known history of Human Immunodeficiency Virus
- Active infection requiring therapy, positive tests for Hepatitis B surface antigen or Hepatitis C ribonucleic acid (RNA)
- Underlying medical conditions that will make the administration of study drug hazardous

- Concurrent medical condition requiring the use of immunosuppressive medications, or immunosuppressive doses of systemic or absorbable topical corticosteroids
- Use of other investigational drugs (drugs not marketed for any indication) within 28 days or at least 5 half-lives (whichever is longer) before study drug administration

Ages Eligible for Study ⓘ

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study ⓘ

All

Accepts Healthy Volunteers ⓘ

No

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose ⓘ : Treatment

Allocation ⓘ : Non-Randomized

Interventional Model ⓘ : Single Group Assignment

Masking ⓘ : None (Open Label)

Arms and Interventions

Participant Group/Arm i	Intervention/Treatment i
Experimental: Melanoma - BMS-936558 (MDX-1106)	Biological: BMS-936558 (MDX-1106) • Solution, Intravenous, 0.1 mg/kg - 10 mg/kg, Every 2 weeks, 3 years depending on response • Other Names: ◦ BMS-936558
Experimental: RCC - BMS-936558 (MDX-1106)	Biological: BMS-936558 (MDX-1106) • Solution, Intravenous, 1 - 10 mg/kg, Every 2 weeks, 3 years depending on response • Other Names: ◦ BMS-936558
Experimental: mCRPC - BMS-936558 (MDX-1106)	Biological: BMS-936558 (MDX-1106) • Solution, Intravenous, 10 mg/kg, Every 2 weeks, 3 years depending on response • Other Names: ◦ BMS-936558
Experimental: NSCLC - BMS-936558 (MDX-1106)	Biological: BMS-936558 (MDX-1106) • Solution, Intravenous, 1 - 10 mg/kg, Every 2 weeks, 3 years depending on response • Other Names: ◦ BMS-936558
Experimental: CRC - BMS-936558 (MDX-	Biological: BMS-936558 (MDX-1106)

1106)

- Solution, Intravenous, 10 mg/kg, Every 2 weeks, 3 years depending on response
- Other Names:
 - BMS-936558

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Number of Participants With Severe Adverse Events (AEs), Serious Adverse Events (SAEs), Treatment-Related AEs, Deaths, Discontinuation of Study Drug Due to AEs	AE=any new unfavorable symptom, sign or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity or drug dependency/abuse; is life-threatening, an important medical event or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Treatment-related=having certain, probable, possible or missing relationship to study drug. Death=during the study and up to 28 days past study discontinuation. The select AEs were determined using the Medical Dictionary for Regulatory Activities (MedDRA, v15.1) and graded using the Cancer Therapy Evaluation Program Common Terminology Criteria for Adverse Events (CTCAE), Version 3.0.	Day 1 to 70 days following last dose of study drug up to June 2013, approximately 4 years
Number of Participants	Alkaline phosphatase (ALP), Alanine Aminotransferase (ALT), Aspartate	Day 1 up to

With Abnormal Serum Chemistry Laboratory Values	Aminotransferase (AST), Creatinine and Total Bilirubin. National Cancer Institute Common Terminology Criteria (CTC) version (v) 3.0 was used to determine Grade (Gr). Abnormal values for ALP, ALT and AST were based on grades; Gr 1: > 1.0 - 2.5 * upper limits of normal (ULN); Gr 2: > 2.5 - 5.0 * ULN; Gr 3: > 5.0 - 20.0 * ULN; Gr 4: > 20.0 * ULN. Abnormal values for Creatinine were based on Gr 1: > 1.0 - 1.5*ULN; Gr 2: > 1.5 - 3.0*ULN; Gr 3: > 3.0 - 6.0*ULN; Gr 4: > 6.0*ULN. Abnormal values for Total Bilirubin were based on Gr 1: > 1.0 - 1.5 * upper limits of normal (ULN); Gr 2: > 1.5 - 3.0 * ULN; Gr 3: > 3.0 - 10.0 * ULN; Gr 4: > 10.0 * ULN.	June 2013, approximately 4 years
Number of Participants With Abnormal Hematology Laboratory Values	Hemoglobin, Lymphocytes, Neutrophils, Platelets and Leukocytes. National Cancer Institute Common Terminology Criteria (CTC) version (v) 3.0 was used to determine Grade (Gr). Abnormal values for Hemoglobin were based on Gr 1: 10.0 - less than (<) lower limit of normal (LLN); Gr 2: 8.0 - < 10.0; Gr 3: 6.5 - < 8.0; Gr 4: < 6.5. Abnormal values for Lymphocytes were based on Gr 1: 0.8 - < 1.5; Gr 2: 0.5 - < 0.8; Gr 3): 0.2 - < 0.5; Gr 4: < 0.2. Abnormal values for Neutrophils were based on Gr 1: 1.5 - < 2.0; Gr 2: 1.0 - < 1.5; Gr 3: 0.5 - < 1.0; Gr 4: < 0.5. Abnormal values for Platelets were based on Gr 1: 75.0 - < lower limits of normal (LLN); Gr 2: 50.0 - < 75.0; Gr 3: 25.0 - < 50.0; Gr 4: < 25.0. Abnormal values for Leukocytes were based on Gr 1: 3.0 - < LLN; Gr 2: 2.0 - < 3.0; Gr 3: 1.0 - < 2.0; Gr4: < 1.0.	Day 1 up to June 2013, approximately 4 years

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
-----------------	---------------------	------------

Immunogenicity Assessment	Classification of participants host immune response was based on the following definitions: Anti-Drug Antibody (ADA) Positive Subjects have with at least one ADA positive sample at any time after initiation of treatment. ADA positive subjects were further classified into categories with Persistent Positive defined as an ADA positive sample at 2 or more sequential timepoints at least 8 weeks apart.	Day 1 up to June 2013, approximately 4 years
Objective Response Rate	Tumor response was evaluated by the sponsor based on tumor assessments by the investigator according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.0. Objective response rate (ORR) was defined as the proportion of participants who's confirmed best overall response (BOR) is either complete (CR) or partial (PR), where the denominator is the number of treated participants in the population of interest. Response was based on tumor measurements. Responders= complete response (CR) or partial response (PR). CR=disappearance of all target and non-target lesions; PR=at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference the screening sum longest diameter. 95% Confidence intervals (CIs) were computed using the Clopper Pearson method.	Day 1 up to June 2013, approximately 4 years
Duration of Tumor Response	Duration of tumor response (DOR) was calculated from the first date of response of complete response (CR) or partial response (PR) to the date of the first progressive disease (PD) or the date of death. Duration of response was censored at the last tumor assessment date if a responder did not have PD or death. Nonresponders were not included in the	Day 1 up to June 2013, approximately 4 years

	analysis. Median DOR was estimated by Kaplan-Meier analysis.	
Geometric Mean Maximum Serum Concentration (Cmax)	Nivolumab in human serum was assayed by PPD® (Richmond, Virginia) using a cross-validated enzyme-linked immunosorbent assay (ELISA). Blood samples were assessed at all doses from a subset of participants. The pharmacokinetic (PK) parameter of Cmax was measured in micrograms per milliliter (µg/mL).	1,4,8,24, 48 and 96 hours post-dose timepoints on Day 1 of cycles 1 and 3
Median Time of Maximum Serum Concentration (Tmax)	Nivolumab in human serum was assayed by PPD® (Richmond, Virginia) using a cross-validated ELISA. Blood samples were assessed at all doses from a subset of participants. The PK parameter of Tmax was measured in hours (h).	1,4,8,24, 48 and 96 hours post-dose timepoints on Day 1 of cycles 1 and 3
Geometric Mean Area Under the Curve (AUC[TAU]) in One Dosing Interval Observed Post-Single Dose	Nivolumab in human serum was assayed by PPD® (Richmond, Virginia) using a cross-validated ELISA. Blood samples were assessed at all doses from a subset of participants. The PK parameter of AUC was measured in micrograms*hours per milliliter (µg*h/mL).	1,4,8,24, 48 and 96 hours post-dose timepoints on Day 1 of

		cycles 1 and 3
Geometric Mean Total Body Clearance of Drug From Serum (CLT)	Nivolumab in human serum was assayed by PPD® (Richmond, Virginia) using a cross-validated ELISA. Blood samples were assessed at all doses from a subset of participants. The PK parameter of CLT was measured in milliliters per hour (mL/h).	1,4,8,24, 48 and 96 hours post-dose timepoints on Day 1 of cycle 3
Mean Effective Half-life (T-HALFeff)	Nivolumab in human serum was assayed by PPD® (Richmond, Virginia) using a cross-validated ELISA. Blood samples were assessed at all doses from a subset of participants. The PK parameter of T-HALFeff was measured in hours (h).	1,4,8,24, 48 and 96 hours post-dose timepoints on Day 1 of cycle 3

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor ⓘ

Bristol-Myers Squibb

Collaborators ⓘ

- Ono Pharmaceutical Co. Ltd

Investigators ⓘ

- Study Director: Bristol-Myers Squibb, Bristol-Myers Squibb

Publications

From PubMed

These publications come from PubMed, a public database of scientific and medical articles. This list is automatically created by ClinicalTrials.gov Identifier (NCT Number), and these articles may or may not be about the study.

- [Topalian SL, Hodi FS, Brahmer JR, Gettinger SN, Smith DC, McDermott DF, Powderly JD, Sosman JA, Atkins MB, Leming PD, Spigel DR, Antonia SJ, Drilon A, Wolchok JD, Carvajal RD, McHenry MB, Hosenl F, Harbison CT, Grosso JF, Sznol M. Five-Year Survival and Correlates Among Patients With Advanced Melanoma, Renal Cell Carcinoma, or Non-Small Cell Lung Cancer Treated With Nivolumab. JAMA Oncol. 2019 Oct 1;5\(10\):1411-1420. doi: 10.1001/jamaoncol.2019.2187. \(https://pubmed.ncbi.nlm.nih.gov/31343665\).](https://pubmed.ncbi.nlm.nih.gov/31343665)
- [Topalian SL, Sznol M, McDermott DF, Kluger HM, Carvajal RD, Sharfman WH, Brahmer JR, Lawrence DP, Atkins MB, Powderly JD, Leming PD, Lipson EJ, Puzanov I, Smith DC, Taube JM, Wigginton JM, Kollia GD, Gupta A, Pardoll DM, Sosman JA, Hodi FS. Survival, durable tumor remission, and long-term safety in patients with advanced melanoma receiving nivolumab. J Clin Oncol. 2014 Apr 1;32\(10\):1020-30. doi: 10.1200/JCO.2013.53.0105. Epub 2014 Mar 3. \(https://pubmed.ncbi.nlm.nih.gov/24590637\).](https://pubmed.ncbi.nlm.nih.gov/24590637)
- [Topalian SL, Hodi FS, Brahmer JR, Gettinger SN, Smith DC, McDermott DF, Powderly JD, Carvajal RD, Sosman JA, Atkins MB, Leming PD, Spigel DR, Antonia SJ, Horn L, Drake CG, Pardoll DM, Chen L, Sharfman WH, Anders RA, Taube JM, McMiller TL, Xu H, Korman AJ, Jure-Kunkel M, Agrawal S, McDonald D, Kollia GD, Gupta A, Wigginton JM, Sznol M. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. N Engl J Med. 2012 Jun 28;366\(26\):2443-54. doi: 10.1056/NEJMoa1200690. Epub 2012 Jun 2. \(https://pubmed.ncbi.nlm.nih.gov/22658127\).](https://pubmed.ncbi.nlm.nih.gov/22658127)

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted ⓘ

2008-08-04

First Submitted that Met QC Criteria ⓘ

2008-08-07

First Posted (Estimated) ⓘ

2008-08-08

Results Reporting Dates**Results First Submitted** ⓘ

2016-02-22

Results First Submitted that Met QC Criteria ⓘ

2016-03-24

Results First Posted (Estimated) ⓘ

2016-04-15

Study Record Updates**Last Update Submitted that met QC Criteria** ⓘ

2021-12-01

Last Update Posted ⓘ

2021-12-03

Last Verified ⓘ

2021-11

More Information**Terms related to this study****Additional Relevant MeSH Terms**

Neoplasms by Site

Neoplasms

Neoplasms by Histologic Type

Adenocarcinoma

Carcinoma

Neoplasms, Glandular and Epithelial

Kidney Neoplasms

Urologic Neoplasms

Urogenital Neoplasms

Female Urogenital Diseases

Female Urogenital Diseases and Pregnancy Complications

Urogenital Diseases

Kidney Diseases

Urologic Diseases

Male Urogenital Diseases

Carcinoma, Renal Cell

Antineoplastic Agents, Immunological

Antineoplastic Agents

Immune Checkpoint Inhibitors

Molecular Mechanisms of Pharmacological Action

Nivolumab

Drug and device information, study documents, and helpful links

Studies a U.S. FDA-Regulated Drug Product

Yes

Studies a U.S. FDA-Regulated Device Product

No

Helpful Links Provided by Bristol-Myers Squibb

[BMS Clinical Trial Information](https://www.bms.com/researchers-and-partners/clinical-trials-and-research.html) (<https://www.bms.com/researchers-and-partners/clinical-trials-and-research.html>).

[BMS Clinical Trial Patient](https://www.bmsstudyconnect.com/s/US/English/USenHome)

[Recruiting](https://www.bmsstudyconnect.com/s/US/English/USenHome) (<https://www.bmsstudyconnect.com/s/US/English/USenHome>).

[Investigator Inquiry Form](https://www.bms.com/researchers-and-partners/clinical-trials-and-research.html) (<https://www.bms.com/researchers-and-partners/clinical-trials-and-research.html>).

[FDA Safety Alerts and](https://www.fda.gov/Safety/MedWatch/SafetyInformation/default.htm)

[Recalls](https://www.fda.gov/Safety/MedWatch/SafetyInformation/default.htm) (<https://www.fda.gov/Safety/MedWatch/SafetyInformation/default.htm>).