A Phase 3, Randomized, Double blind Study of Neoadjuvant Chemotherapy plus Nivolumab versus Neoadjuvant Chemotherapy plus Placebo, followed by Surgical Resection and Adjuvant Treatment with Nivolumab or Placebo for Participants with Resectable Stage II-IIIB Non-small Cell Lung Cancer

Published: 17-09-2019
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This study has been transitioned to CTIS with ID 2022-502658-15-00 check the CTIS register for the current data. Primary Objective• To compare the event-free survival (EFS) by blinded independent central review (BICR) in Arm A (vs Arm B…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON55271

Source
ToetsingOnline

Brief title
CA209-77T

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: Adjuvant treatment, Neoadjuvant chemotherapy, Nivolumab, Surgical Resection

Outcome measures

Primary outcome

EFS is defined as the length of time from randomization to any of the following events: progression of disease precluding surgery, progression or recurrence of disease after surgery, or death due to any cause. Progression/recurrence will be assessed by BICR per RECIST 1.1.

Secondary outcome

• OS is defined as the time between the date of randomization and the date of death due to any cause. OS will be censored on the last date a subject was known to be alive.

• pCR is defined as the number of randomized participants with absence of residual viable tumor in lung and lymph nodes as evaluated by blinded independent pathology review (BIPR), divided by the number of randomized participants for each treatment group.

Study description

Background summary

Approximately 80% of lung cancer cases are NSCLC, with most patients presenting with late stage disease. Of these patients with NSCLC, 20% present with stage I or II disease, whereas 30% present with stage III disease and 50% with stage IV disease. Patients with pathologic stage I NSCLC have a 5-year survival of approximately 70%. Stage II to III NSCLC patients have a 5-year survival of approximately 25% to 50%. The early-stage (II-IIIB) NSCLC represents a population of high unmet need with poor 5-year survival. Surgical resection remains the mainstay of treatment for Stage I and II patients and resectable IIIB. Despite potential curative surgery, 50% of stage IIA-IIIB NSCLC patients will relapse and eventually die of their disease. This study aims to improve survival in these patients by eradicating micrometastatic disease and to minimize the risk of relapse with adjuvant or neoadjuvant chemotherapy.

Study objective

This study has been transitioned to CTIS with ID 2022-502658-15-00 check the CTIS register for the current data.

Primary Objective
• To compare the event-free survival (EFS) by blinded independent central review (BICR) in Arm A (vs Arm B participants

Secondary Objectives
• To compare the overall survival (OS) in Arm A vs Arm B participants
• To assess the pathologic complete response (pCR) rate by blinded independent pathology review (BIPR) in Arm A vs Arm B participants

Study design

This is a randomized, double blind, multicenter phase 3 study for participants with early stage (Stage IIA [>= 4 cm] to IIIB [T3N2 only]) NSCLC evaluating Arm A with the comparator arm (Arm B). This study will examine if periadjuvant (neoadjuvant, then adjuvant) immunotherapy will prolong event free survival in participants with early stage (Stage IIA [>= 4 cm] to IIIB [T3N2 only]) NSCLC.

Participants will be randomized (1:1 ratio) across 2 treatment arms:

) platinum-based doublet chemotherapy Q3W x 4 cycles as neoadjuvant treatment followed by surgery; then post surgery nivolumab 480 mg Q4W adjuvant treatment for up to 13 cycles (approximately 1 year) post surgery.

• Arm B: placebo Q3W + SOC platinum-based doublet chemotherapy Q3W x 4 cycles as neoadjuvant treatment followed by surgery, then post-surgery placebo Q4W for up to 13 cycles (approximately 1 year) post surgery.

The choice of platinum-based doublet regimens is dependent on NSCLC histology:
• Squamous histology: carboplatin (AUC 5 or AUC 6) + paclitaxel (175 mg/m2 or 200 mg/m2)
• Non-squamous histology:
- carboplatin (AUC 5 or AUC 6) + pemetrexed 500 mg/m2
- cisplatin 75 mg/m2 + pemetrexed 500 mg/m2

After completing treatment with protocol specified adjuvant study treatment, participants will have follow-up assessments (FU1 and FU2) and disease surveillance (Year 2 through year 5).

Intervention

Participants will be randomized (1:1 ratio) across 2 treatment arms:

• Arm A: nivolumab 360 mg Q3W + SOC platinum-based doublet chemotherapy Q3W x 4 cycles as neoadjuvant treatment followed by surgery; then post surgery nivolumab 480 mg
Q4W adjuvant treatment for up to 13 cycles (approximately 1 year) post surgery.

• Arm B: placebo Q3W + SOC platinum-based doublet chemotherapy Q3W x 4 cycles as neoadjuvant treatment followed by surgery, then post-surgery placebo Q4W for up to 13 cycles
(approximately 1 year) post surgery.

The choice of platinum-based doublet regimens is dependent on NSCLC histology:
• Squamous histology: carboplatin (AUC 5 or AUC 6) + paclitaxel (175 mg/m2 or 200 mg/m2)
• Non-squamous histology:
- carboplatin (AUC 5 or AUC 6) + pemetrexed 500 mg/m2
- cisplatin 75 mg/m2 + pemetrexed 500 mg/m2

All study drugs will be provided by the sponsor.

Study burden and risks

As part of the trial, patients will be expected to attend multiple clinic visits where they will undergo physical examinations, vital sign measurements, blood tests for safety assessment, pregnancy testing (for females of child bearing potential) and monitoring for adverse events & serious adverse events. Patients will be asked to complete questionnaire*s (NSCLC-SAQ, PGIS, PROMIS PF 8c, FACT-L & EQ-5Q-3L) about their quality of life. Blood will also be

collected at certain visits for research purposes (PK, immunogenicity and biomarker studies). If there is no archival tumour tissue (10 tumor slides) available or the sample was taken too long ago (>= 3 months), patients need to have a fresh tumor biopsy. Surgery will be performed on patients post completion of neo-adjuvant therapy. A tumour biopsy will also be performed at disease progression, if clinically possible. Patients will undergo radiographic assessment of their tumors by CT and within 1 week prior to initiation of adjuvant study treatment. PET-CT scans will be performed prior to start of the study and 14 days prior to surgery. Subsequent imaging assessments will be performed every 12 weeks for 2 years, then every 6 months for up to a maximum of 5 years until disease recurrence or progression (confirmed by blinded independent central review). Brain MRI will be performed prior to start of the study and thereafter only if clinically indicated. The frequency of visits and number of procedures carried out during this trial would be typically considered over and above standard of care. The procedures are carried out by trained medical professionals and every effort will be made to minimise any risks or discomfort to the patient.
Treatment for cancer often has side effects, including some that are life threatening. To assure an ongoing favourable risk/benefit assessment for patients enrolled onto the study, an Independent Data Monitoring Committee (DMC) will be established to provide oversight of safety and efficacy considerations. Additionally, the DMC will provide advice to the sponsor regarding actions the committee deems necessary for the continuing protection of patients enrolled in the study.
BMS will conduct rigorous safety monitoring to ensure patients safety by regularly & systematically reviewing safety data; the reported safety events will be closely followed-up; sites and study investigators will receive training on the implementation of nivolumab toxicity management strategies. New immune system targeted therapy (immunotherapies) such as nivolumab could potentially provide clinical benefit and improvements in the outcomes for patients with this disease. However, with all experimental drugs and clinical trials, there are known and unknown risks. Study medication and procedure related risks are outlined in the patient information sheet in detail to ensure the patients are fully informed before agreeing to take part in the study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Males and females >= 18 years
• Suspected or histologically confirmed, resectable Stage IIA (>= 4cm) to IIIB (T3N2) NSCLC with disease that is considered resectable. Staging should be based on the 8th edition of the AJCC/UICC staging system.
• No brain metastasis
• Participants must be eligible for complete resection and must agree to undergo standard of care surgery for complete resection of NSCLC after neoadjuvant therapy
• Treatment-naïve (no prior systemic anti-cancer treatment)
• Eastern Cooperative Oncology Group (ECOG) performance status <= 1
• Ability to provide tumor tissue for biomarker testing
• Women must not be pregnant or breastfeeding

Exclusion criteria

• Non-squamous NSCLC histology with known ALK and EGFR mutation
• Grade >= 2 peripheral neuropathy
• Participants with an active, known or suspected auto-immune disease
• Participants with a condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednison equivalent) or other immunosuppresive medications within 14 days of randomization
• Participants with interstitial lung disease or active, non-infectious

pneumonitis
• Previous malignancies are excluded unless a complete remission was achieved at least 2 years prior to first treatment an no additional therapy is required or anticipated during the study
• Positive for active HBV and HCV at screening
• Known history of positive test for HIV or acquired immunodeficiency syndrome (AIDS) at screening
• Any previous anti-cancer treatment including cytotoxic, IO treatment, targeted agents or radiotherapy
• History or allergy or hypersensitivity to platinum-containing compounds (if deemed chemotherapy eligible) or study drug components

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-01-2020
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Abiplatin
Generic name:	Cisplatin
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Alimta
Generic name:	Pemetrexed
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Opdivo
Generic name:	Nivolumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Paraplatin
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxol
Generic name:	Paclitaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	17-09-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-09-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-06-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	17-06-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-08-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-08-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-01-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-01-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-08-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-10-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-01-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-04-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	18-11-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-02-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2022-502658-15-00
EudraCT	EUCTR2019-000262-38-NL
CCMO	NL69737.042.19
Other	U1111-1226-5321