

# NICO - CA209-891: Neoadjuvant and adjuvant nivolumab as Immune Checkpoint inhibition in Oral cavity cancer

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<b>Registration date</b> 06/07/2018	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 11/01/2021	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-of-nivolumab-and-usual-treatment-for-mouth-cancer-nico-ca209-891> (added 11/06/2019)

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### EudraCT/CTIS number

2017-005015-13

**IRAS number**

ClinicalTrials.gov number  
NCT03721757

Secondary identifying numbers  
37191

## Study information

**Scientific Title**

NICO - CA209-891: Neoadjuvant and adjuvant nivolumab as Immune Checkpoint inhibition in Oral cavity cancer

**Acronym**

NICO - CA209-891

**Study objectives**

Mouth cancer is usually treated with surgery, often followed by radiation therapy with or without chemotherapy. Unfortunately despite this treatment, it recurs or spreads in about half of patients. Recently, a drug called nivolumab which is given into a vein via a drip, has been shown to be of benefit where the cancer has spread and worsened following treatment with chemotherapy. This drug stimulates the immune system and when it works, often does so for a long period of time. In this trial the aim is to use this drug to reduce the chances of the cancer coming back after surgery and radiotherapy. The study will assess if this treatment leads to a reduction in the cancer recurring.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

London - Harrow Research Ethics Committee 18/LO/0368; First MREC approval date 18/05/2018

**Study design**

Non-randomised; Interventional; Design type: Treatment, Drug, Radiotherapy, Immunotherapy, Surgery

**Primary study design**

Interventional

**Secondary study design**

Non randomised study

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use the contact details to request a patient information sheet

## **Health condition(s) or problem(s) studied**

Mouth cancer

## **Interventions**

This is a non-randomised phase II study of nivolumab in high risk oral cavity cancer for whom resection is the primary treatment. Patients will be assigned to one of two cohorts based on pathological findings following surgery.

Following initial biopsy and confirmation of eligibility, patients will be enrolled and treated with a single dose of nivolumab (240 mg flat dose), followed by surgery to remove their tumour within 1-2 weeks.

Based on pathological risk factors determined following surgery, patients will be assigned to undergo adjuvant radiotherapy or chemoradiotherapy. Patients with high risk criteria (extracapsular spread, involved margins) as determined on pathological review following surgery will be assigned to chemoradiotherapy.

A further single dose of nivolumab (240 mg flat dose) will be given between surgery and commencement of chemoradiotherapy or radiotherapy (1-2 weeks prior).

Radiotherapy will be administered over 30 fractions i.e. over 30 days (Monday to Friday for 6 consecutive weeks). Patients receiving chemoradiotherapy will receive concomitant Cisplatin (100mg/m<sup>2</sup>) on day 1 and day 21 of radiotherapy treatment.

Following completion of chemo/radiation (within 1-2 weeks), patients will commence adjuvant nivolumab, with a total of 6 doses (480mg flat dose) given at 4 weekly intervals.

On completion of chemoradiotherapy or radiotherapy, all patients will have imaging of the head & neck and chest using CT and/or MRI. Further scans will be performed at 8 and 12 months post surgery, with an end of study visit after the last scan. Patients will then be followed up for survival until the final study definition is reached.

## **Intervention Type**

Mixed

## **Primary outcome measure**

1. 1-year disease free survival  $\geq$  75% in high-risk population. The endpoint is disease recurrence at 12 months measured as a 1 for patients who have disease recurrence (or death by any cause) and 0 for those that do not
2. Feasibility of recruitment to both cohorts, predominantly assessed using the recruitment rate as the endpoint of interest measured as the number of patients/site/month

## **Secondary outcome measures**

1. Safety, measured and categorised based on CTCAE (version 4). Interest will predominantly be on the number of grade 3/4 adverse events
2. Time to recurrence, measured as the time from surgery until disease recurrence or death by any cause
3. Overall survival, measured as the time from registration until death by any cause

4. Quality of life, measured using Quality of Life Questionnaire–Core 30 module (QLQ-C30) and the head-and-neck–specific module (QLQ-H&N35) at:
- 4.1. Prior to surgery and initial nivolumab treatment
  - 4.2. Post surgery but pre-radiotherapy/chemoradiotherapy
  - 4.3. First administration of nivolumab post radiotherapy/chemoradiotherapy
  - 4.4. Third administration of nivolumab post radiotherapy/chemoradiotherapy
  - 4.5. Sixth administration of nivolumab post radiotherapy/chemoradiotherapy
  - 4.6. End of study treatment/safety visit
5. Surgical complications: infection rate, length of hospital admission, free flap failure, perioperative (30-day) mortality

**Overall study start date**

01/12/2017

**Completion date**

01/09/2021

**Reason abandoned (if study stopped)**

Participant recruitment issue

## **Eligibility**

**Key inclusion criteria**

1. Signed, written informed consent
2. Subjects must be willing and able to comply with scheduled visits and procedures
3. Histologically confirmed squamous cell carcinoma of the oral cavity (oral tongue (anterior 2 /3), gingiva/alveolus, floor of mouth, buccal sulcus, retromolar trigone, and hard palate as defined by ICD-10 codes)
4. Subjects willing to have a fresh biopsy performed, or archival tissue available from diagnostic biopsy meeting requirements set out in laboratory manual
5. Clinically and/or radiologically staged as T1-4 N1-3 or any T3-4 N0 (unless T4 on the basis of bone invasion only). Staging based upon the AJCC/UICC TNM 8th Edition
6. Surgery planned as primary treatment modality with patients fit for major resection ± reconstruction surgical procedure
7. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
8. 18 years or over at time of provision of consent for trial inclusion
9. Screening laboratory values must meet the following criteria:  
WBC ≥ 2000/μL  
Neutrophils ≥ 1500/uL  
Platelets ≥ 100x103/uL  
Hemoglobin ≥ 9.0 g/dL  
Serum creatinine ≤1.5 x ULN or calculated creatinine clearance > 40 mL/min (using the Cockcroft-Gault formula)  
AST ≤ 3.0 x ULN  
ALT ≤ 3.0 x ULN  
Total Bilirubin ≤ 1.5 x ULN (except subjects with Gilbert Syndrome who must have a total bilirubin level of < 3.0x ULN)
10. Women of childbearing potential (WOCBP) must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 24 hours prior to the start of study drug
11. Women must not be breastfeeding

12. WOCBP must agree to follow instructions for method(s) of contraception for a period of 30 days (duration of ovulatory cycle) plus the time required for the investigational drug to undergo approximately five half-lives. WOCBP randomized/assigned to receive nivolumab should use an adequate method to avoid pregnancy for 5 months (30 days plus the time required for nivolumab to undergo approximately five half-lives) after the last dose of investigational drug

13. Males who are sexually active with WOCBP must agree to follow instructions for method(s) of contraception for a period of 90 days (duration of sperm turnover) plus the time required for the investigational drug to undergo approximately five half-lives

14. Males randomized to receive nivolumab who are sexually active with WOCBP must continue contraception for 7 months (90 days plus the time required for nivolumab to undergo approximately five half-lives) after the last dose of investigational drug. Azoospermic males and WOCBP who are continuously not heterosexually active are exempt from contraceptive requirements. However, they must still undergo pregnancy testing as described in these sections. Investigators shall counsel WOCBP and male subjects who are sexually active with WOCBP on the importance of pregnancy prevention and the implications of an unexpected pregnancy. Investigators shall advise WOCBP and male subjects who are sexually active with WOCBP on the use of highly effective methods of contraception. Highly effective methods of contraception which have a failure rate of < 1% when used consistently and correctly

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

Both

### **Target number of participants**

Planned Sample Size: 120; UK Sample Size: 120

### **Total final enrolment**

23

### **Key exclusion criteria**

1. Tumours staged as T4 on the basis of bone invasion only and in the absence of nodal metastases
2. Distant metastases detected, or suspected on imaging
3. Unfit for chemoradiotherapy, due to comorbidity
4. Previous malignancy requiring treatment within the last 3 years (with the exception of non-melanoma skin cancers, and the following in situ cancers: bladder, gastric, colon, oesophageal endometrial, cervical/dysplasia, melanoma, or breast). Prior head and neck cancer within the last three years is allowed if the tumour was treated with surgery only, and did not require radiotherapy
5. Prior head and neck radiotherapy
6. On immunosuppressive medication (including steroids at dose equivalent to prednisolone > 10mg/day unless used as replacement therapy)
7. Subjects with an active, known or suspected autoimmune disease. Subjects with type I

diabetes mellitus, hypothyroidism only requiring hormone replacement, skin disorders (such as vitiligo, psoriasis, or alopecia) not requiring systemic treatment, lichen planus or other conditions not expected to recur in the absence of an external trigger are permitted to enrol

8. Known human immunodeficiency virus (HIV) or viral hepatitis infection
9. Women who are pregnant or breastfeeding
10. Known medical condition that, in the investigator's opinion, would increase the risk associated with study participation or study drug administration or interfere with the interpretation of safety results

**Date of first enrolment**

01/09/2018

**Date of final enrolment**

01/03/2020

## **Locations**

**Countries of recruitment**

England

Scotland

United Kingdom

Wales

**Study participating centre**

**Clatterbridge Cancer Centre (lead centre)**

Clatterbridge Road

Bebington

Wirral

United Kingdom

CH63 4JY

**Study participating centre**

**University Hospital Aintree**

Fazakerley Hospital

Lower Lane

Liverpool

United Kingdom

L9 7AL

**Study participating centre**

**NHS Greater Glasgow and Clyde**

Beatson West of Scotland Cancer Centre

1055 Great Western Road  
Glasgow  
United Kingdom  
G12 0XH

**Study participating centre**  
**University College London Hospital**  
250 Euston Road  
London  
United Kingdom  
NW1 2PG

**Study participating centre**  
**The Christie Hospital**  
550 Wilmslow Road  
Withington  
Manchester  
United Kingdom  
M20 4BX

**Study participating centre**  
**Queen Victoria Hospital**  
Holtye Road  
East Grinstead  
United Kingdom  
RH19 3DZ

**Study participating centre**  
**Northern General Hospital**  
Sheffield Teaching Hospitals NHS Foundation Trust  
Herries Road  
Sheffield  
United Kingdom  
S5 7AU

**Study participating centre**  
**Velindre Cancer Centre**  
Velindre Road  
Cardiff  
United Kingdom  
CF14 2TL

**Study participating centre**  
**Royal Sussex County Hospital**  
Eastern Road  
Brighton  
United Kingdom  
BN2 5BE

**Study participating centre**  
**Royal Surrey County Hospital**  
Egerton Road  
Guildford  
United Kingdom  
GU2 7XX

## **Sponsor information**

### **Organisation**

The Clatterbridge Cancer Centre NHS Foundation Trust

### **Sponsor details**

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Bebington  
Wirral  
England  
United Kingdom  
CH63 4JY  
+44 (0)151 482 7804 ext 4740  
Jennifer.almond@nhs.net

### **Sponsor type**

Hospital/treatment centre

### **ROR**

<https://ror.org/05gcq4j10>

## **Funder(s)**

### **Funder type**

Industry



**Funder Name**

Bristol-Myers Squibb International Corporation; Grant Codes: CA209-891

**Alternative Name(s)**

Bristol-Myers Squibb Company, BMS

**Funding Body Type**

Government organisation

**Funding Body Subtype**

For-profit companies (industry)

**Location**

United States of America

## Results and Publications

**Publication and dissemination plan**

Additional documents will not be publicly available but requests for them will be considered upon receipt of an emailed request to the NICO Trial Coordinator. Planned publication of the study results in a high impact peer reviewed journal.

**Intention to publish date**

01/09/2022

**Individual participant data (IPD) sharing plan**

The data sharing plans for the current study are unknown and will be made available at a later date.

**IPD sharing plan summary**

Data sharing statement to be made available at a later date

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No