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

Submission date 02/07/2018	**Recruitment status** Stopped	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 06/07/2018	**Overall study status** Stopped	
Last Edited 11/01/2021	**Condition category** Cancer	

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
Mr Robert Hanson

ORCID ID
https://orcid.org/0000-0002-5084-9622

Contact details
Cancer Research UK Liverpool Cancer Trials Unit
1st Floor, MerseyBio
Crown Street
Liverpool
United Kingdom
L69 7ZB
+44 (0)151 794 8852
r.hanson@liverpool.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2017-005015-13

ClinicalTrials.gov (NCT)
NCT03721757

Protocol serial number
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

Study type(s)
Treatment

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/m2) 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(s)
1. 1-year disease free survival ≥ 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

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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
United Kingdom

England

Scotland

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

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, Bristol Myers Squibb, Bristol-Myers Company, BMS

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

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?
HRA research summary			28/06/2023	No	No