ISRCTN87831050 https://doi.org/10.1186/ISRCTN87831050

A mouthwash medicine for the reduction or prevention of mouth ulceration caused by radiotherapy for head and neck cancer

Submission date 25/10/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 13/02/2023	**Overall study status** Completed	
Last Edited 04/10/2024	**Condition category** Oral Health	

Plain English Summary
Background and study aims
This study is looking at a new medication called NG11-2 to see if it can reduce a side effect called severe Radiation-induced Oral Mucositis (RIOM) that can happen to people getting radiation treatment for head and neck cancer. Severe RIOM can make patients very sick and make it hard for them to finish their cancer treatment. Right now, there are no approved drugs that can prevent or treat severe RIOM. This study will test different doses of NG11-2 to find the best one, and then more patients will take that dose to see if it works. This study is being done at multiple hospitals.

Who can participate?
Patients aged 18 years or older, with head and neck cancer.

What does the study involve?
Daily treatment with NG11-2 will occur prior to radiotherapy for 5 days/week for up to 7 weeks. Throughout the radiotherapy regimen, no more than 60 minutes prior to the completion of radiotherapy, on each weekday the patient will be instructed to
a) rinse their mouth twice with room temperature water in the 5 minutes prior to NG11-2 treatment then
b) rinse their mouth with 12.5ml of NG11-2 for between 90 & 120 seconds duration, gargling twice for approximately three seconds each if possible during this period then
c) expectorate the solution
Treatment will continue for up to 7 weeks with a 6-week follow-up period.

What are the possible benefits and risks of participating?
Benefits:
Possibly prevention/ reduction in severe Radiation-induced Oral Mucositis during the patient's radiotherapy treatment
Risks:
The study will fit in with the usual treatment and the only additional things that patients will have to do are: give a small number of extra blood samples, have some patches put on their

chest for an electrocardiogram (ECG), and fill out a short questionnaire a few times. Patients will also have to rinse their mouths with the NG11-2 solution before each radiation treatment. The study drug is made with adrenaline, which is a well-understood drug, but it may cause some mild side effects like irritation in the mouth or a temporary change in heart rate. The study team will closely monitor patients for any side effects and will stop treatment if needed.
Although the scientific rationale and earlier laboratory studies suggest that NG11-2 treatment is unlikely to have a negative impact on your tumour treatment, we cannot yet exclude the risk of a negative impact on your anticancer therapy when treated with NG11-2.

Where is the study run from?
VasoDynamics Ltd (UK)

When is the study starting and how long is it expected to run for?
October 2022 to August 2024

Who is funding the study?
VasoDynamics Ltd (UK)

Who is the main contact?
Dr Mary Lei, Mary.Lei@gstt.nhs.uk

Study website
https://vasodynamics.co.uk/ng11/

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2022-002409-99

IRAS number
1004528

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
NG11-2 P1b, IRAS 1004528, CPMS 54459

Study information

Scientific Title
A phase-1b dose escalation study to assess the effect of NG11-2 on radiation induced oral mucositis in patients with head & neck cancer

Acronym
NG11-2-P1b

Study hypothesis
The main objective of the trial is to see if the use of vasoconstrictors (such as Adrenaline), when administered as a mouthwash in head and neck cancer patients prior to their radiotherapy, is

tolerable and can reduce or prevent the development of severe radiation induced oral mucositis. More specifically, the trial aims to identify an appropriate dose of NG11-2 IMP based on safety and activity/preliminary efficacy for subsequent assessment in follow-up clinical trials.

Although the primary objective of the trial is to evaluate the safety & tolerability of NG11-2 mouthwash, the secondary objective is to obtain preliminary data on the activity/efficacy of NG11-2 mouthwash in the reduction of severe RIOM.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/01/2023, (West Midlands - Coventry & Warwickshire Research Ethics Committee, The Old Chapel, Royal Standard Place , Nottingham, NG1 6FS, UK; +44 207 104 8184; coventryandwarwick.rec@hra.nhs.uk), ref: 22/WM/0262

Study design
Interventional non-randomized dose escalation study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

Condition
Reduction of radiation-induced oral mucositis in head & neck cancer patients undergoing radiotherapy with or without concomitant chemotherapy

Interventions
This is an unblinded, single-arm study. Patients will undergo daily treatment with NG11-2 immediately prior to radiotherapy for 5 days/week (Mon-Fri) for up to 7 weeks. The dose level will vary from 0.92 mg/mL to 5.5 mg/mL during the dose escalation process. The NG11-2 is given as an oral rinse.
Throughout the radiotherapy regimen, no more than 60 minutes prior to the completion of radiotherapy, on each weekday the patient will be instructed to a) rinse their mouth twice with room temperature water in the 5 minutes prior to NG11-2 treatment then b) rinse their mouth with 12.5 ml of NG11-2 for between 90 & 120 seconds duration, gargling twice for approximately three seconds each if possible during this period then c) expectorate the solution. Treatment will continue for up to 7 weeks with a 6-week follow-up period.

Intervention Type

Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
NG11-2 Mouthwash, 0.92 – 5.50 mg/mL [L-adrenaline base]

Primary outcome measure
Occurence of Dose Limiting Toxicities (DLT) & Serious Adverse Events (SAE). Serious Adverse Events will be evaluated throughout the study from time of patient consent until 42 days after last IMP dose. Dose limiting toxicities will be evaluated from time of first dose until 42 days after last IMP dose. Additionally all available safety data (AEs, SAEs and DLTs) will be reviewed and evaluated by a Safety Committee (Sponsor CMO, Study Medical Monitor & Chief Investigator) before each dose escalation.

Secondary outcome measures
1. Duration of severe RIOM (WHO, RTOG and NCI-CTCAE v5 Gr 3 or above) evaluated by Oral Mucositis assessments at screening and twice weekly in each week of study treatment in weeks 1-7, and then at 7, 14, 28 and 42 days post end of Radiotherapy, in the follow-up period.
2. Incidence & Time to onset of severe RIOM (WHO, RTOG and NCI-CTCAE v5 Gr 3 or above)
3. Patient Reported Outcome Measure - Oral Mucositis (PROM-OM) evaluated at the same timepoints as the clinical Oral Mucositis assessments, namely screening and twice weekly in each week of study treatment in weeks 1-7, and then at 7, 14, 28 and 42 days post end of Radiotherapy, in the follow-up period.

Overall study start date
21/10/2022

Overall study end date
20/08/2024

Eligibility

Participant inclusion criteria
1. Male or female head and neck cancer patients scheduled for radiotherapy, aged 18 or over on day of signing informed consent;
2. Histologically confirmed head and neck cancer with or without previous resective surgery, having not been previously treated with radiation therapy
3. Scheduled to receive a mean radiation dose of no less than 30 Gy on either (a) Extended Oral Cavity, or (b) Buccal Mucosa, or (c) Lips, according to CT-based delineation of Organ-At-Risk (OAR) Guideline, with or without concurrent chemotherapy (Section 13.8 for guidance);
4. Rendered dentally fit for radiotherapy;
5. Have a Performance Status >60 on the Karnofsy scale
6. No evidence of active systemic infections at the time of screening;
7. No oral fungal infection by visual examination or swab test;
8. Body Mass Index >=18.5 kg/m²
9. Normalcy of diet evaluated with the Performance Status Scale for Head and Neck cancer patients (PSSHN) >=30;
10. Ability to retain and swill liquid inside the oral cavity for at least 90 seconds;
11. Female patients of childbearing potential must have a negative urine or serum pregnancy

test during the 2 week Screening period
12. Provide written informed consent for the trial.
13. Consent to utilize medically acceptable methods of contraception throughout the study period if of child-bearing potential;
14. Be able to comply with protocol procedures (such as Oral Mucositis assessment and swish /spit) and study schedule

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Up to 32 maximum - estimated 20-24

Total final enrolment
15

Participant exclusion criteria
1. Tumour of the larynx
2. Mentally or legally incapacitated, in the opinion of the PI, which could interfere with the ability of the patient to understand or adhere to the requirements of the study;
3. Open or unhealed non-cancerous wounds or ulcers in the oral cavity;
4. WHO Oral Mucositis grade of 2 or more
5. Uncontrolled Hypertension, defined as blood pressure in adults >150/100mm Hg at screening;
6. A known clinically significant abnormal ECG, such as arrhythmia and active ischemia,within 6 months prior to treatment;
7. Xerostomia or hyposalivation;
8. Known allergy or intolerance to sympathomimetic drugs (e.g., pseudoephedrine, epinephrine), alcohol, or any NG11-2 excipient;
9. Receiving monoamine oxidase (MAO) inhibitors or antidepressants (triptyline or imipramine types); Use of MAO inhibitor in the 14 days prior to treatment, such as isocarboxazid, linezolid, methylene blue injection, phenelzine, rasagiline, selegiline, or tranylcypromine;
10. History or current evidence of clinically significant laboratory abnormality or any disease condition that might confound the results of the study, or interfere with the patient's participation for the full duration of the study
11. Current participation in any other oral mucositis studies or completion/ withdrawal from any other oral mucositis studies within the last 3 months
12. Patient is, at the time of signing informed consent, a regular user of any illicit drugs, which would interfere with cooperation with the requirements of the trial;
13. Patient is pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the study;
14. Any other condition which, in the opinion of the Investigator, means that the patient is not a good candidate for study enrolment

Recruitment start date
01/05/2023

Recruitment end date
30/06/2024

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Study participating centre
Guys Hospital
Guys Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
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United Kingdom
EH4 2XU

Study participating centre
Aberdeen Royal Infirmary
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AB25 2ZN

Study participating centre

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Sponsor information

Organisation
VasoDynamics Ltd

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Vasodynamics

Results and Publications

Publication and dissemination plan

Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Other publication
Submission to regulatory authorities
The study database will not be shared outside of the Sponsor group.
The overall study results will be disseminated on publicly available websites

Intention to publish date

31/12/2024

Individual participant data (IPD) sharing plan

Datasets are not expected to be made available due to Sponsor commercial confidentiality and the early phase nature of the study.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.2		12/05/2023	No	Yes
HRA research summary			28/06/2023	No	No
Participant information sheet	version 2.0		20/12/2023	No	Yes