ISRCTN53390753 https://doi.org/10.1186/ISRCTN53390753

PEARL: PET-based adaptive radiotherapy clinical trial

Submission date 22/07/2019	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 10/09/2019	**Overall study status** Completed	
Last Edited 13/01/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-using-a-scan-to-improve-treatment-for-oropharyngeal-cancer-during-chemoradiotherapy-pearl

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT03935672

Protocol serial number
42228

Study information

Scientific Title
PEARL: A Phase 1 trial of PET-based adaptive radiotherapy in patients undergoing radical chemoradiotherapy for Human Papilloma Virus (HPV)-positive oropharyngeal cancer.

Acronym
PEARL

Study objectives
Patients receiving biologically-based adaptive radiotherapy will have comparable two year PFS to patients undergoing standard treatment

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/12/2018, Wales research ethics committee 2, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB; 02920785738; Wales.REC2@wales.nhs.uk), ref: 18/WA/0391

Study design
Non-randomised; Interventional; Design type: Treatment, Radiotherapy

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Human Papilloma Virus (HPV)-positive oropharyngeal cancer.

Interventions
After informed consent, HPV-positivity will be confirmed by central testing of the diagnostic biopsy specimen. Patients who have had HPV-positivity confirmed locally can undergo baseline assessment of QOL and swallowing function prior to the central laboratory results.

Patients will undergo baseline plasma and saliva tests for the presence of biomarkers.

Patients will then undergo baseline planning FDG-PET-CT scan which ATLAAS software will use to generate a GTV. The GTV will be reviewed by a team of clinical oncologists who will also take into account the diagnostic MRI, CT and clinical findings on panendoscopy.

All patients will undergo swallowing and saliva-sparing RT, delivered using Volumetric Arc Therapy (VMAT) (RapdidArc), which the UK DARS clinical trial team demonstrated reduced RT dose to the pharyngeal constrictors more effectively than IMRT.

Patients will start their 6 weeks of CCRT two to three weeks following the planning scans. Cisplatin chemotherapy will be administered as per site-specific protocols. 30 daily fractions of radiotherapy will be delivered over 6 weeks.

A second FDG-PET-CT scan and repeat plasma and saliva tests will be carried out after 2 weeks of CRT and the PET assessed for residual FDG-avid disease. The GTV will be re-defined based on the avid region of the tumour. The new GTVb will continue to receive the maximum dose of 66Gy /30F but the non-avid region will receive a total dose of 60Gy/30F.

At the end of treatment, plasma and saliva tests will be repeated and will be then carried out on a 4 weekly basis until the 3-month post-treatment PET-CT.

Swallowing and QoL assessments will be repeated 4 weeks after treatment.

At 3 months post-treatment, a repeat PET-CT will be carried out to look for response. In those patients who have equivocal findings on PET, repeat imaging will be carried out 8 (+/- 2) weeks later to check for resolution.

Swallowing panel, QoL assessments, plasma and saliva samples will be repeated at 6, 12 and 24 months posttreatment. The plasma and saliva samples will also be repeated at 18 months.

Clinical follow up will be for 5 years as per standard practice.

Intervention Type
Other

Primary outcome(s)
Progression free survival at 2 years

Key secondary outcome(s)
1. Recruitment rates will be monitored annually
2. Percentage reduction in dose to organs at risk (OARs) will be recorded and plans where there was 10% or greater reduction in dose OARs categorised as significantly changed. This will be done after the second PET scan following 2 weeks of chemo radiotherapy treatment
3. Swallowing panel measurements including qualitative and quantitative swallowing assessments (MDADI, PSS-H&N, water swallow test) and feeding tube rate dependency at 1 year
4. Quality of life (QOL) (EORTC QLQ C30, HN35 and UW-QOL questionnaires). QoL will be collected at baseline, 1, 3, 6, 12 and 24 months post concurrent chemo-radiation
5. Acute and late toxicity (NCI CTCAE criteria v4.03). Collected at baseline, weekly during treatment and 3, 6, 12 and 24 months post concurrent chemo-radiation
6. Complete metabolic response rate as per PERCIST criteria on PET-CT scan (postPET) 3 months after treatment

Completion date
31/01/2025

Eligibility

Key inclusion criteria
1. Histologically confirmed squamous cell carcinoma of the oropharynx
2. Positive p16 Immunohistochemistry on local testing
3. UICC TNM (8th edition) stage T1 – T3 N0 – N1 M0
4. Multidisciplinary team (MDT) decision to treat with primary chemoradiotherapy
5. Patients considered fit for radical treatment with primary chemoradiotherapy
6. Aged 18 years or older

7. Not smoked in the last 2 years
8. Written informed consent provided
9. Patients with reproductive potential (male or female), who are sexually active during the duration of the trial consent
to using a highly effective method of contraception for at least six months after the last dose of chemoradiotherapy

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Known HPV negative squamous cell carcinoma of the head and neck
2. T1 – T3 tumours where primary treatment with concomitant chemo-radiotherapy is not considered appropriate
3. T4 disease
4. N2 (TMN8) nodal disease
5. Distant metastatic disease
6. Current smokers or smokers who have stopped within the past 2 years
7. Diabetes mellitus
8. Any pre-existing medical condition likely to impair swallowing function and/ or a history of pre-existing swallowing
dysfunction prior to index oropharyngeal cancer
9. Previous radiotherapy to the head and neck
10. History of malignancy in the last 5 years, except basal cell carcinoma of the skin, or carcinoma in situ of the cervix
11. Women who are pregnant or breastfeeding and patients with reproductive potential (male or female) who are
sexually active during the duration of the trial and do not consent to use highly effective method of contraception for at
least 6 months after the last dose of chemoradiotherapy
12. Tumour non-avid on PET-CT or not visible on cross sectional imaging

Date of first enrolment
15/01/2020

Date of final enrolment
30/01/2023

Locations

Countries of recruitment
United Kingdom

England

Wales

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

Study participating centre
Abertawe Bro Morgannwg University LHB
One Talbot Gateway
Seaway Drive
Seaway Parade Industrial Estate
Baglan
Port Talbot
United Kingdom
SA12 7BR

Study participating centre
University Hospitals Bristol NHS Foundation Trust
Marlborough Street
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BS1 3NU

Sponsor information

Organisation
Velindre NHS Trust

ROR
https://ror.org/05ntqkc30

Funder(s)

Funder type
Government

Funder Name
Cancer Research Wales; Grant Codes: .12345

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request by contacting the CTR (pearl@cardiff.ac.uk). A process is then followed to ensure request is scientifically credible, within regulatory guidelines and within patient consent. Data may be requested at any pint during the trial. Application approvals will be subject to review by key members including trial Sponsor, TSC, TMG and IDMC where relevant.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes