# Personalized elective neck irradiation guided by sentinel lymph node biopsy in patients with squamous cell carcinoma of the oropharynx, larynx or hypopharynx with a clinically negative neck: (chemo)radiotherapy to the PRIMary tumor Only. The PRIMO study.

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To compare safety and efficacy of treatment with sentinel lymph node biopsy guided elective neck irradiation versus standard elective neck irradiation in patients receiving definitive (chemo)radiotherapy for squamous cell carcinoma of the oropharynx...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Miscellaneous and site unspecified neoplasms malignant and unspecified |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON56453

**Source**
ToetsingOnline

**Brief title**
PRIMO

### Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

**Synonym**

1 - Personalized elective neck irradiation guided by sentinel lymph node biopsy in p ... 8-05-2025

head and neck cancer, laryngeal cancer, oropharyngeal cancer, pharyngeal cancer, squamous cell carcinoma

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Radboud Universitair Medisch Centrum
**Source(s) of monetary or material Support:** Dutch National Health Care Institute. Research program veelbelovende zorg Project number: 2022012900,Alpe d'HuZes / Dutch Cancer society (KWF). Project number: 2023-1 DEV / 15046

## Intervention

**Keyword:** elective neck irradiation, head and neck cancer, sentinel lymph node biopsy

## Outcome measures

### Primary outcome

The primary safety endpoint is the number of patients with recurrence in regional lymph nodes (in the absence of synchronous recurrence of the primary tumor or second primary tumor) within 2 years after treatment. The primary efficacy endpoint is patient reported xerostomia-related quality of life measured by the xerostomia symptom scale of the EORTC QLQ-H&N35 at 6 months after treatment.

### Secondary outcome

Acute and late radiation toxicity, quality of life after treatment with focus on xerostomia and dysphagia, local and regional control rates, disease specific and overall survival, and cost-effectiveness.

# Study description

### Background summary

Squamous cell carcinoma of the upper aerodigestive tract comes with a substantial risk for cervical lymph node metastases. Elective neck irradiation is performed in patients receiving (chemo)radiotherapy aiming to eradicate nodal metastases that are under the diagnostic detection level. Most toxicity and permanent long-term radiation side effects are caused by elective neck irradiation. In particular xerostomia and dysphagia are notoriously known to negatively and permanently affect quality of life. Sentinel lymph node biopsy has emerged as a staging procedure that can reliably detect microscopic metastases by histopathological examination of sentinel lymph nodes and the pathologic status of the sentinel lymph node accurately reflects the status of the remaining nodal basin. A recent meta-analysis demonstrated an excellent diagnostic test accuracy of sentinel lymph node biopsy in patients with cancer of the oropharynx, larynx and hypopharynx (sensitivity 0.93 and negative predictive value 0.97). It is conceivable that personalized elective neck irradiation can be performed guided by the results of sentinel lymph node biopsy. With this approach it is expected that elective neck irradiation can be omitted in the majority of patients with a clinically negative neck because occult nodal metastases are present approximately in 3 out of 10. This will enable better sparing of normal tissues from radiation and consequentially result in less permanent long-term radiation side effects with better quality of life after treatment.

## Study objective

To compare safety and efficacy of treatment with sentinel lymph node biopsy guided elective neck irradiation versus standard elective neck irradiation in patients receiving definitive (chemo)radiotherapy for squamous cell carcinoma of the oropharynx, larynx or hypopharynx.

## Study design

This is a multicenter, randomized controlled trial. In total 242 patients will be randomized in ratio 1:1 to the control arm with standard bilateral elective neck irradiation or to the interventional arm with sentinel lymph node biopsy guided personalized elective neck irradiation. During a 2 year follow-up, data on toxicity, quality of life and oncologic outcomes will be collected.
If this trial demonstrates that the interventional treatment is non-inferior to the standard treatment in terms of regional recurrence and is superior in terms of xerostomia-related quality of life, this will become the new standard of care.

## Intervention

Patients randomized to the intervention arm will undergo sentinel lymph node biopsy. Based on the histopathologic status of the sentinel lymph node(s), patients will receive no elective neck irradiation (if all sentinel lymph nodes

are negative), unilateral only (if a sentinel lymph node is positive at one side of the neck) or bilateral (if sentinel lymph nodes are positive at both sides of the neck). For patients randomized to the control arm sentinel lymph node biopsy will not be performed and all will receive standard bilateral elective neck irradiation.

### Study burden and risks

Burden associated with participation | Patients randomized to the intervention arm will undergo sentinel lymph node biopsy (flexible endoscopic tracer injection under topical anesthesia in the outpatient clinic, SPECT/CT-scan and surgical removal of identified sentinel lymph nodes under general anesthesia). These procedures will not be performed in patients in the control arm. For patients randomized to the intervention arm there is a potential increased risk for regional recurrence because elective neck irradiation is omitted based on the histopathologic status of the sentinel lymph node(s). However this risk is expected to be very small (3.1% versus 2.0% in the control arm). Because regional recurrences can be cured in 70-90% of the patients with salvage neck dissection, the effect on overall survival is expected to be negligible. Independent of randomization, participants will undergo non-invasive procedures to objectify radiation sequelae and will be asked to complete quality of life questionnaires.
Benefit associated with participation | With sentinel lymph node biopsy, it is expected that futile elective neck irradiation can be omitted to one or both sides of the neck in 9 out of 10 patients. This will enable better sparing of normal tissues from radiation and it is expected that this will result in a major decrease of permanent long-term radiation side effects (such as xerostomia and dysphagia) with better quality of life after treatment compared to standard elective neck irradiation.

## Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

- Adult patients with newly diagnosed cT1-4N0M0 squamous cell carcinoma of the oropharynx, larynx or hypopharynx.
- Histopathological diagnosis of squamous cell carcinoma in the primary tumor.
- Adequate staging of the neck including CT or MRI, and PET/CT demonstrating cN0.
- Recommendation for curative intent external beam (chemo)radiotherapy made by a multidisciplinary head and neck oncology team
- Bilateral elective neck irradiation is indicated according to Dutch consensus guidelines (LPHHRT)
- Procedures for sentinel lymph node biopsy are deemed feasible by the head and neck surgeon.

## Exclusion criteria

- Recurrent disease or previous anticancer treatment to the head and neck area except for endoscopic glottic laser micro surgery.
- Well lateralized oropharyngeal cancers and early stage laryngeal cancers requiring no or unilateral elective neck irradiation according to Dutch consensus guidelines (LPHHRT).
- Patients receiving concomitant non-platinum-based systemic agents (e.g. cetuximab).
- Patients that qualify for proton therapy and want to be treated accordingly.
- Compromised airway or tracheostomy.
- Any active invasive malignancy within the last 3 years except for early stage basal/squamous cell carcinoma of the skin and incidental finding of stage T1N0M0 prostate cancer.
- Any somatic, psychological, familial, sociological or geographical condition

potentially hampering compliance with the study protocol or follow-up schedule.

# Study design

## Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Diagnostic

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 06-12-2023 |
| Enrollment: | 242 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 09-08-2023 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 14-12-2023 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 15-01-2025 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

# 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 |
|---|---|
| ClinicalTrials.gov | NCT05333523 |
| CCMO | NL83850.091.23 |