



Catholic University of Louvain, St - Luc University Hospital
Head and Neck Oncology Programme

Carcinoma of unknown primary (CUP)



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- Work-up procedure
- TNM staging
- Primary treatment
- Follow-up
- Treatment of recurrent and/or metastatic disease
- References



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Clinical evaluation

- Complete history of the disease
- Weight and weight loss
- Performance status (Karnofsky / WHO scale)
- Fiberoptic examination of H&N mucosa
- Neck examination
- Drawing of any lesions

Evidence Option

Type C	Std.
Type C	Std.
Type C	Std.
Type C	Std.
Type C	Std.
Type C	Std.



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Endoscopic evaluation	Evidence	Option
• Fine needle aspirate (FNA). To be repeated in case of no diagnosis	Type C	Std.
• Endoscopy under general anesthesia with biopsies of any suspicious site; if no abnormal mucosa, blind biopsies of nasopharynx, base of tongue and pyriform sinus; ipsilateral tonsillectomy	Type C	Std.
• Oesogastroscopy	Type C	Std.
• Endoscopy with PET-directed biopsies	Type 3	Invest.



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Advanced clinical evaluation

- Dental examination by oral surgeon
- Nutritional assessment
- Others (if required)

Evidence	Option
Type C	Std.
Type C	Std.
Type C	Indiv.



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Laboratory tests

- Hemogram, coagulation tests, liver enzymes, kidney function
- Thyroid function: TSH

Evidence

Option

Type C

Std.

Type C

Std.



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Imaging	Evidence	Option
• Regional: CT scan (or MRI) ¹	Type C	Std.
• Metastatic work-up: chest X-ray, thoracic spiral CT scan	Type C	Std.
• Additional examination depending on previous findings	Type C	Std.
• PET scan	Type 3	Invest.

¹See guidelines for loco-regional imaging



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Pathologic examination	Evidence	Option
Standards of the British Royal College of Pathologists (endorsed by EORTC) ¹	Type C	Std.

¹See pathology guidelines



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Staging	Evidence	Option
• TNM classification (5 th ed., 1997)	Type C	Std.
• WHO International Classification of Diseases for Oncology (ICD-O 9 or ICD-O 10)	Type C	Std.



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TNM/AJCC 1997 Staging

- T0: patients with unknown primary tumor
- Tx: patients whose tumor cannot be assessed or is not assessed



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TNM/AJCC 1997 Staging

- N0: no regional node metastasis
- Nx: regional nodes cannot be assessed
- N1: single ipsilateral node, ≤ 3 cm
- N2a: single ipsilateral node, > 3 cm and ≤ 6 cm
- N2b: multiple ipsilateral nodes, ≤ 6 cm
- N2c: contralateral or bilateral nodes, ≤ 6 cm
- N3: node > 6 cm



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Primary treatment: general strategy	Evidence	Option
• T0-N1 Ipsilateral ND $\pm$ RxTh (intergroup trial)¹ If previous inappropriate node excision, ipsilateral ND $\pm$ RxTh • T0-N2a/T0-N2b/T0-N3 Ipsilateral ND + RxTh (intergroup trial) • T0-N2c Bilateral ND + RxTh	Type 3 Type C Type 3 Type 3	Std. Std. Std. Std.

¹See detailed protocol



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Primary treatment: surgical procedure

Evidence

Option

- Unilateral or bilateral (N2c) ND¹
Radical modified or radical ND¹

Type 3

Std.

¹ extended radical ND may be required, e.g.N3



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Primary treatment: pathologic examination	Evidence	Option
Standards of the British Royal College of Pathologists (endorsed by EORTC)	Type C	Std.

¹See pathology guidelines



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Primary treatment: RxTh regimen

- Target volumes (intergroup trial)¹
 - Levels I-V $\pm$ pharyngeal and laryngeal mucosa according to randomization
- Target volumes (outside trial)
 - ipsilateral levels I-V (bilateral for pN2c)
- Technique
 - conformal radiotherapy
 - IMRT radiotherapy
- Dose
 - Level I-V: 60 Gy (64 Gy if high risk)²
 - mucosa: 50 Gy
- Fractionation
 - daily 2Gy/fraction
- Concomitant chemo

Evidence

Option

-

Invest.

Type 3

Std.

Type 3

Std.

Type 3

Invest.

Type 2

Std.

Type 3

Std.

Type 3

Std.

Type 2

Invest.

¹See detailed protocol

²See guidelines for post-operative radiotherapy



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Follow-up	Evidence	Option
● Clinical examination -fiberoptic examination and neck palpation every 2 months (first 2 years), every 6 months (3rd-5th year), then every year (> 5 years) -dental examination every 6 months ● Imaging -chest X-ray every year ● Laboratory tests -thyroid function (TSH) every year ● Evolution of late toxicity (EORTC/RTOG) scale	Type C Type C Type C Type C	Std. Std. Std. Std.



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Salvage treatment for recurrent disease	Evidence	Option
- anyT-N0-M0 -Surgery ± RxTh -RxTh / brachytherapy	Type 3 Type 3	Std. Std.
- T0-anyN-M0 -ND ± RxTh -RxTh -Chemotherapy	Type 3 Type 3 Type 3	Indiv. Indiv. Indiv.
- AnyT-anyN-M0 - Surgery ± RxTh - Chemotherapy - Best supportive care	Type 3 Type 3 Type 3	Indiv. Indiv. Indiv.
- Metastasis - Chemotherapy - Surgery - Best supportive care	Type 3 Type 3 Type 3	Std. Indiv. Indiv.



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