

Rare head & neck cancers: ESMO vis-a-vis NCCN Guidelines

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I HAVE NO CONFLICTS OF INTEREST TO DECLARE

clinical practice guidelines

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Nasopharyngeal cancer: EHNS–ESMO–ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up[†]

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NCCN National Comprehensive Cancer Network

NCCN Guidelines Version 1.2012
Cancer of the Nasopharynx

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CLINICAL STAGING	TREATMENT OF PRIMARY AND NECK	FOLLOW-UP
T1, N0, M0	Definitive RT to nasopharynx and elective RT to neck ^b	
T1, N1-3; T2-T4, any N	Concurrent chemo/RT (category 1) ^{b,c} → Adjuvant chemotherapy ^c or Induction chemotherapy (category 3) ^d followed by chemo/RT	Neck: Residual tumor → Neck dissection ^f Neck: Complete clinical response → Observe Follow-up (See FOLL-A) → Recurrent or Persistent Disease (See ADV-2)
Any T, any N, M1	Platinum-based combination chemotherapy ^c Concurrent chemo/RT ^{b,c,e}	RT ^b to primary and neck or Chemo/RT ^c as clinically indicated

^bSee Principles of Radiation Therapy (NASO-A).
^cSee Principles of Systemic Therapy (CHEM-A).
^dSee Discussion on induction chemotherapy.
^eCan be used for select patients with distant metastasis in limited site or with small tumor burden, or for patients with symptoms in the primary or any nodal site.
^fSee Principles of Surgery (SURG-A).

Note: All recommendations are category 2A unless otherwise indicated.
 Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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NASO-2

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Rare cancers are not so rare: The rare cancer burden in Europe

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Table 1 – Illustration of the layer structure.

Layer	Tumour	Topography code	Morphology code
1	Epithelial tumours of nasopharynx	C11	8000–8001, 8004, 8010–8011, 8020–8022, 8032, 8050–8076, 8078, 8082–8084, 8123, 8260, 8560, 8980
2	Squamous cell carcinoma with variants of nasopharynx	C11	8004, 8020–8022, 8032, 8051–8076, 8078, 8082–8084, 8123, 8560, 8980
3	Squamous carcinoma	C11	8070
3	Squamous cell carcinoma non-keratinizing, NOS	C11	8072
3	Squamous cell carcinoma keratinizing, NOS	C11	8071
3	Papillary squamous cell carcinoma	C11	8052
3	Basaloid squamous cell carcinoma	C11	8083
3	Squamous cell carcinoma, adenoid	C11	8075
3	Lymphoepithelial carcinoma	C11	8082
3	Undifferentiated carcinoma	C11	8020–8022
2	Papillary adenocarcinoma of nasopharynx	C11	8050, 8260

Table 3 – Incident cases (number and rates per million) by sex and age, and estimated number of cases arising in Europe per year.

Entity	Overall			Sex				Age (year)						Estimated number of cases arising in Europe per year ^a
				Male		Female		0–24		25–64		65+		
	Observed cases 1995–2002	Rate	SE	Rate	SE	Rate	SE	Rate	SE	Rate	SE	Rate	SE	
Rare cancers of head and neck														
1. Epithelial tumour of nasal cavity and sinuses	3555	4.42	0.07	5.87	0.12	3.04	0.09	0.05	0.01	3.31	0.09	16.77	0.36	2198
2. Squamous cell carcinoma and variants of nasal cavity and sinuses	2498	3.1	0.06	4.17	0.1	2.09	0.07	0.01	0.01	2.35	0.07	11.73	0.3	1545
2. Lymphoepithelial carcinoma of nasal cavity and sinuses	19	0.02	0.01	0.03	0.01	0.01	0.01	0.01	0.01	0.03	0.01	0.05	0.02	12
2. Undifferentiated carcinoma of nasal cavity and sinuses	139	0.17	0.01	0.22	0.02	0.13	0.02	0.00	0.00	0.17	0.02	0.5	0.06	86
2. Intestinal type adenocarcinoma nasal cavity and sinuses	20	0.02	0.01	0.05	0.01	0.00	0.00	0.00	–	0.02	0.01	0.1	0.03	12
1. Epithelial tumour of nasopharynx	3566	4.43	0.07	6.53	0.13	2.43	0.08	0.63	0.05	5.13	0.11	9.52	0.27	2205
2. Squamous cell carcinoma and variants of nasopharynx	2630	3.27	0.06	4.89	0.11	1.72	0.06	0.41	0.04	3.92	0.1	6.7	0.23	1626
2. Papillary adenocarcinoma of nasopharynx	7	0.01	0.00	0.01	0.00	0.01	0.01	0.00	–	0.01	0.01	0.01	0.01	4

H&N tumours

incidence

EPITHELIAL TUMOURS OF THE NASAL CAVITY AND SINUSES

Squamous cell carcinoma and variants of the Nasal Cavity and Sinuses

Lymphoepithelial carcinoma of the Nasal Cavity and Sinuses

Undiff carcinoma of the Nasal Cavity and Sinuses

Intestinal type adenocarcinoma the Nasal Cavity and Sinuses

1

EPITHELIAL TUMOURS OF THE NASOPHARYNX

Squamous cell carcinoma and variants of the Nasopharynx

Papillary adenocarcinoma of the Nasopharynx

EPITHELIAL TUMOURS MAJOR SAL GLANDS AND SAL GLAND TYPE TUMOURS

Epithelial tum of major Salivary glands

Salivary gland type tum of the Head and Neck

<1.5

EPITHELIAL TUMOURS OF THE HYPOPHARYNX AND LARYNX

Squamous cell carcinoma and variants of the Hypopharynx

Squamous cell carcinoma and variants of the Larynx

<6

EPITHELIAL TUMOURS OF THE OROPHARYNX

Squamous cell carcinoma and variants of the Oropharynx

<5

EPITHELIAL TUMOURS OF THE ORAL CAVITY AND LIP

Squamous cell carcinoma and variants of the Oral cavity

Squamous cell carcinoma and variants of the Lip

H&N tumours

5-year survival (%)

EPITHELIAL TUMOURS OF THE NASAL CAVITY AND SINUSES

Squamous cell carcinoma and variants of the Nasal Cav and Sinuses

50

Lymphoepithelial carcinoma of the Nasal Cavity and Sinuses

27

Undiff carcinoma of the Nasal Cavity and Sinuses

34

Intestinal type adenocarcinoma the Nasal Cavity and Sinuses

50

EPITHELIAL TUMOURS OF THE NASOPHARYNX

Squamous cell carcinoma and variants of the Nasopharynx

50

Papillary adenocarcinoma of the Nasopharynx

59

EPITHELIAL TUMOURS MAJOR SAL GLANDS AND SAL GLAND TYPE TUMOURS

Epithelial tum of major Salivary glands

66

Salivary gland type tum of the Head and Neck

69

EPITHELIAL TUMOURS OF THE HYPOPHARYNX AND LARYNX

Squamous cell carcinoma and variants of the Hypopharynx

26

Squamous cell carcinoma and variants of the Larynx

65

EPITHELIAL TUMOURS OF THE OROPHARYNX

Squamous cell carcinoma and variants of the Oropharynx

39

EPITHELIAL TUMOURS OF THE ORAL CAVITY AND LIP

Squamous cell carcinoma and variants of the Oral cavity

50

Squamous cell carcinoma and variants of the Lip

93

clinical practice guidelines

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Incidence/survival

- **European data are provided**
- **Survival 76% at 1 yr and 50% at 5 yrs**
- **Age is markedly affecting survival**

Diagnosis

NCCN	Common recommendations	ESMO
MRI	Nasopharyngoscopy + biopsy	MRI preferred (IIIB) No neck biopsy!
	PET for distant M detection based on HR clinical features	
		EBV DNA viral load is prognostic (IIIB)

Treatment

NCCN	Common recommendations	ESMO
	MDT	
IMRT or 3D (IIA)	RT mainstay	IMRT (IIA) it may reduce xerostomia and improve LC
	RT targets and dose	No >2 Gy or excessive acceleration

Treatment

NCCN	Common recommendations	ESMO
	MDT	
IMRT or 3D	RT mainstay	IMRT (IIA) it may reduce xerostomia and improve LC
	RT targets and dose	No >2 Gy or excessive acceleration
	Cisplatin concurrent	

Treatment

NCCN	Common recommendations	ESMO
	Stage I RT	
<p>II, III, IVA; IVB CT/RT + adjuvant CT (Cat I) or Induction > CT/RT (Cat III)</p> <p>If RP on nodes > neck dissection</p>		<p>II, III, IVA; IVB CT/RT <u>±</u> adjuvant CT (IA)</p> <p>Induction only in selected pts (tumor response to prevent chiasm tox)</p>
M+: CT > RT or CT/RT		M+: CT

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NCCN National Comprehensive Cancer Network **NCCN Guidelines Version 1.2012**
Very Advanced Head and Neck Cancer

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DIAGNOSIS

TREATMENT OF HEAD AND NECK CANCER

```

graph TD
    A[Recurrent or Persistent disease] --> B[Locoregional recurrence without prior RT]
    A --> C[Locoregional recurrence or Second primary with prior RT]
    A --> D[Distant metastases]
    
    B --> B1[Resectable]
    B --> B2[Unresectable]
    
    C --> C1[Resectable]
    C --> C2[Unresectable]
    
    D --> D1[Clinical trial preferred]
    D --> D2[Standard therapyb]
    
    B1 --> B1a[Surgeryd]
    B1a --> B1a1[No adverse featurese]
    B1a1 --> B1a2[Observe → Follow-up See FOLL-A]
    B1a --> B1a3[Adverse featurese]
    B1a3 --> B1a4[Extracapsular spread and/or positive margin]
    B1a4 --> B1a5[Chemo/RTb,c category 1]
    B1a3 --> B1a6[Other risk features]
    B1a6 --> B1a7[RTc or Consider chemo/RTb,c]
    
    B2 --> B2a[See Treatment of Very Advanced Head and Neck Cancer \(ADV-1\)]
    B2a --> B2a1[Salvage therapy for persistent disease as indicated]
    
    C1 --> C1a[Surgeryd ± reirradiation ± chemotherapy, clinical trial preferred]
    
    C2 --> C2a[Reirradiation ± chemotherapy, clinical trial preferred or Chemotherapy see distant metastases pathway]
    
    D1 --> D1a[Platinum + 5-FU + cetuximab category 1]
    D1a --> D1b[or Combination chemotherapyb or Single-agent chemotherapyb]
    D1b --> D1c[Chemotherapy, clinical trial preferred or Best supportive care]
    
    D2 --> D2a[PS 0-1]
    D2a --> D2a1[Single-agent chemotherapyb]
    D2a1 --> D2a2[Best supportive care]
    
    D2 --> D2b[PS 2]
    D2b --> D2b1[Single-agent chemotherapyb or Best supportive care]
    D2b1 --> D2b2[Best supportive care]
    
    D2 --> D2c[PS 3]
    D2c --> D2c1[Best supportive care]
  
```

^b See [Principles of Systemic Therapy \(CHEM-A\)](#)
^c See [Principles of Radiation Therapy \(ADV-A\)](#)
^d See [Principles of Surgery \(SURG-A\)](#)
^e Adverse features: extracapsular nodal spread, positive margins, pT3 or pT4 primary, N2 or N3 nodal disease, perineural invasion, vascular embolism ([See Discussion](#)).

Note: All recommendations are category 2A unless otherwise indicated.
 Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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ADV-2

Treatment for recurrent disease

NCCN	Common recommendations	ESMO
Same for very advanced H&N cancer		Potentially curable if small with ReRT, surgery or both Treatment tailoring according to specific individual situations
	No cetuximab	

NCCN Categories of evidence and consensus

- 1. High level of evidence and uniform NCC consensus
- 2. Lower level of evidence and uniform NCC consensus
- 3. Lower level of evidence and NCC consensus
- 4. Any level but major disagreement

United States Preventive Services Task Force: levels of evidence

- 1. RCT
- 2. Non randomized
- 3. Expert opinion

United States Preventive Services Task Force: Grading

- A. Benefit substantial
- B. Benefit moderate
- C. Not recommended
- D. Against
- I. Insufficient data

COMMENTS

- Both recognise a special place for NPC within H&N area
- ESMO: edu
- “Local” evidence has an impact
- Similar approach but:
- ESMO is including the EBV related tumors (approx 40%).
- In lack of evidences: Asian expertise has played a role