An Introduction to SCCHN

January 2023
US-NONO-00346

EMD SERONO

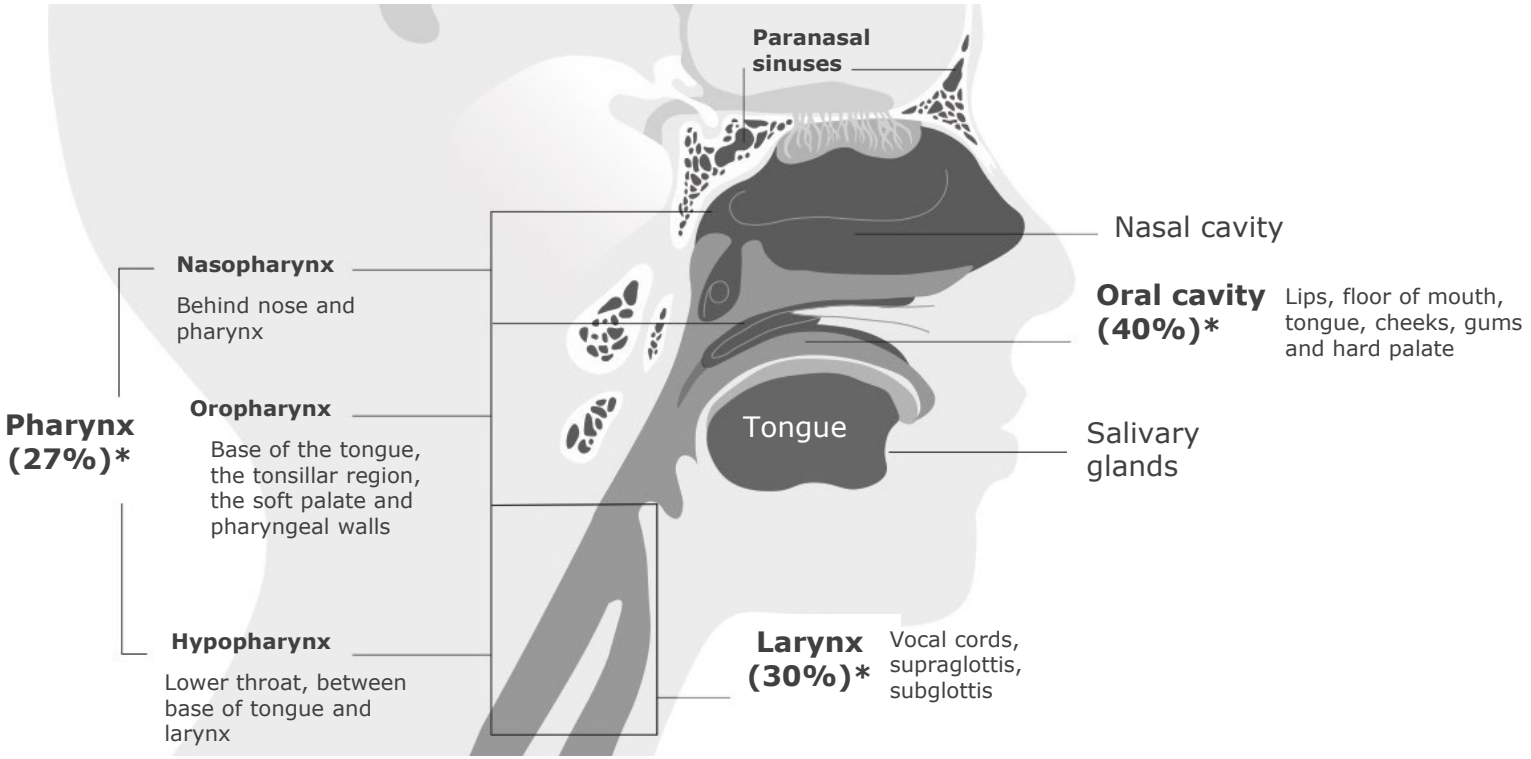
Table of Contents

Disease Background

Squamous Cell Carcinoma of the Head and Neck (SCCHN) Refers to a Group of Cancers Derived from Several Sites in the Head and Neck[1,2]

- 90% of head and neck cancers are squamous cell carcinomas (SCCs)

Anatomical distribution of head and neck cancers[1,2]



SCC: ~90%

- Oral cavity
- Larynx
- Pharynx
- Nasal cavity

Other types of head and neck cancer: ~10%

- Adenocarcinomas
- Lymphomas
- Sarcomas
- Melanomas

Typical localizations:

- Nasopharynx (NPC)†
- Salivary glands

*Main sites for SCCHN. †Most nasopharyngeal cancers are not squamous cell.
NPC, nasopharyngeal carcinoma; SCC, squamous cell carcinoma; SCCHN, squamous cell carcinoma of the head and neck.
1. Bower M, Waxman J. *Oncology Lecture Notes.* 3rd ed. Wiley; 2015; 2. Head and Neck Cancers. National Cancer Institute. https://www.cancer.gov/types/head-and-neck/head-neck-fact-sheet (accessed October 2022).

There Are a Number of Risk Factors for SCCHN

SCCHN develops in **the squamous cell epithelium** following exposure to a combination of risk factors[1,2]

- Patients with **high levels of EGFR** expression have a **worse prognosis** than those with low levels of expression[3]

Environmental factors[1,4]

Tobacco

Correlated with the duration and intensity of smoking[1]

Alcohol

Synergizes with the effect of tobacco[1]

HPV infection

Particularly associated with OPC[4]

Genetic changes[2,4,5]

EGFR **EGFR overexpression** (80–90% of patients)[5]

STAT STAT activation[5]

CD1 Cyclin D1 overexpression[5]

p16 p16 expression alteration[2]

p53 p53 mutation[4]

Other risk factors[2,6,7]

SCCHN is 2–5 times more common in men than in women[6,7]

The risk of developing SCCHN increases with age; the majority of SCCHN cases occur in patients aged ≥50 years[2,6,7]

EGFR, epidermal growth factor receptor; HPV, human papillomavirus; OPC, oropharyngeal cancer; SCCHN, squamous cell carcinoma of the head and neck; STAT, signal transducer and activator of transcription protein.

1. Pai SI, et al. Annu Rev Pathol. 2009;4:49–70; 2. Vigneswaran N, et al. Oral Maxillofac Sug Clin North Am. 2014;26:123–141; ; 3. Saada-Bouzid E, Le Tourneau C. Front Oncol. 2019;9:74; 4. Moody CA, et al. Nature Rev Canc. 2010;10:550–560; 5. Herbst RS, et al. Cancer. 2002;94:1593–1611; 6. Oropharyngeal Cancer. SEER Cancer Statistics Review. https://seer.cancer.gov/statfacts/html/oralcav.html (accessed October 2022); 7. Laryngeal Cancer. SEER Cancer Statistics Review. https://seer.cancer.gov/statfacts/html/laryn.html (accessed October 2022).

Incidence of SCCHN Globally

- Head and neck cancers are the **8th most common cancer** globally, and their incidence is predicted to rise[1,2,*]

878,348
Estimated new cases in 2020[1]

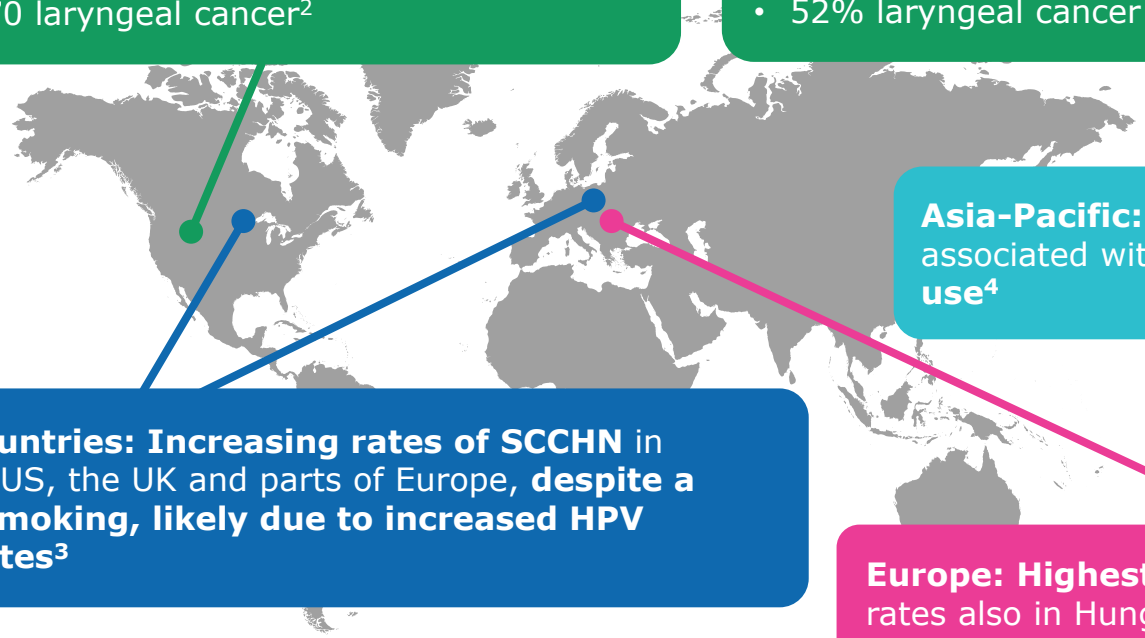
444,347
Estimated deaths in 2020[1]

*Sum of "lip, oral cavity", "larynx", "nasopharynx", "oropharynx" and "hypopharynx".
EU, European Union; SCCHN, squamous cell carcinoma of the head and neck.
1. Sung H, et al. CA Cancer J Clin. 2021;71(3):209–249; 2. Johnson DE, et al. Nat Rev Dis Primers. 2020;6(1):92.

Incidence and Risk Factors for SCCHN Vary by Geographical Region

Estimated no. new cases in the US (2022):
- 54,000 oral cavity and pharyngeal cancer[1]
- 12,470 laryngeal cancer[2]

Stage at diagnosis in the US (2012–2018):
- 28% oral cavity and pharyngeal cancer at locally advanced stage[1]
- 52% laryngeal cancer at locally advanced stage[2]



Asia-Pacific: The risk of developing SCCHN is associated with **tobacco, alcohol and areca nut use**[4]

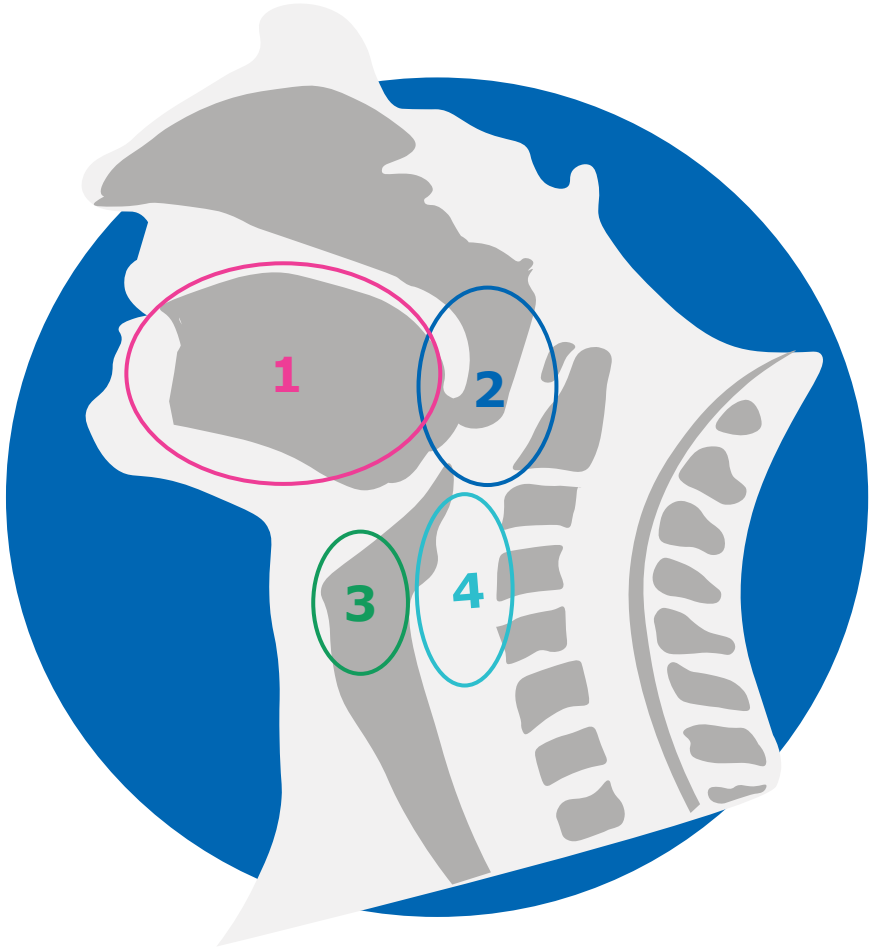
Western countries: Increasing rates of SCCHN in Canada, the US, the UK and parts of Europe, **despite a decline in smoking, likely due to increased HPV infection rates**[3]

Europe: Highest incidence of oral SCC in France (high rates also in Hungary, Slovakia and Slovenia)[4]

HPV, human papillomavirus; SCCHN, squamous cell carcinoma of the head and neck.

1. Oropharyngeal Cancer. SEER Cancer Statistics Review. https://seer.cancer.gov/statfacts/html/oralcav.html (accessed October 2022); 2. Laryngeal Cancer. SEER Cancer Statistics Review. https://seer.cancer.gov/statfacts/html/laryn.html (accessed October 2022); 3. Chaturvedi AK, et al. J Clin Oncol 2013;31:4550–4559; 4. Vigneswaran N, Williams M. Oral Maxillofac Sug Clin North Am. 2014;26:123–141.

Typical Signs and Symptoms Differ Depending on the SCCHN Site



1 Oral cavity[1]

- Patches on gums, tongue and lining of the mouth
- Bleeding
- Pain
- Ulcers

2 Oropharynx[2]

- Sore throat
- Chronic dysphagia
- Pain on swallowing
- Earache

3 Larynx[3]

- Persistent hoarseness
- Neck mass (supraglottis)
- Earache

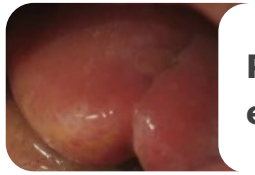
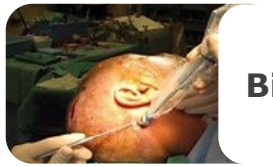
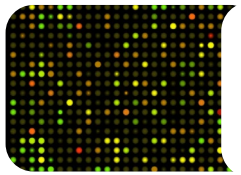
4 Hypopharynx[4]

- Soreness
- Earache
- Dysphagia
- Change in voice

SCCHN, squamous cell carcinoma of the head and neck.

1. Lip and Oral Cavity Cancer Treatment (Adult) (PDQ®)–Patient Version. National Cancer Institute. https://www.cancer.gov/types/head-and-neck/patient/adult/lip-mouth-treatment-pdq (accessed October 2022); 2. Oropharyngeal Cancer Treatment (Adult) (PDQ®)–Patient Version. National Cancer Institute. https://www.cancer.gov/types/head-and-neck/patient/adult/oropharyngeal-treatment-pdq (accessed October 2022); 3. Laryngeal Cancer Treatment (Adult) (PDQ®)–Patient Version. National Cancer Institute. https://www.cancer.gov/types/head-and-neck/patient/adult/laryngeal-treatment-pdq (accessed October 2022); 4. Hypopharyngeal Cancer Treatment (Adult) (PDQ®)–Patient Version. National Cancer Institute. https://www.cancer.gov/types/head-and-neck/patient/adult/hypopharyngeal-treatment-pdq#section/all (accessed October 2022).

Several Confirmatory Diagnostic Tests Can Be Used to Diagnose SCCHN

 **Physical examination**	Check neck, lips, gums, cheeks, nose, mouth, throat and tongue for lumps and abnormalities
 **Endoscopy**	• Visual examination of potential tumor sites • Varied terminology based on site being investigated, e.g., laryngoscopy or pharyngoscopy, or panendoscopy when combined
 **Biopsy**	Removal of tissue that is subsequently examined by a pathologist, including cytologic examination of cancer cells using microscopy
 **Molecular testing**	Laboratory tests for presence of specific genes, proteins, etc. (e.g., HPV as a favorable prognostic marker, or EGFR as a poor prognostic marker)
 **Imaging**	Radiography to detect presence of tumors • CT, PET or MRI scanning to produce detailed images and provide staging information • Bone scan to assess if tumor has metastasized to bones

CT, computed tomography; EGFR, epidermal growth factor receptor; HPV, human papillomavirus; MRI, magnetic resonance imaging; PET, positron emission tomography; SCCHN, squamous

Head and Neck Cancer: Diagnosis. Cancer.Net. https://www.cancer.net/cancer-types/head-and-neck-cancer/diagnosis (accessed October 2022).

HPV-positive OPC Is a Distinct Subtype of SCCHN

- HPV-positive and HPV-negative SCCHN are biologically different diseases, with differing risk factors, tumor sites and prognosis[1,2]

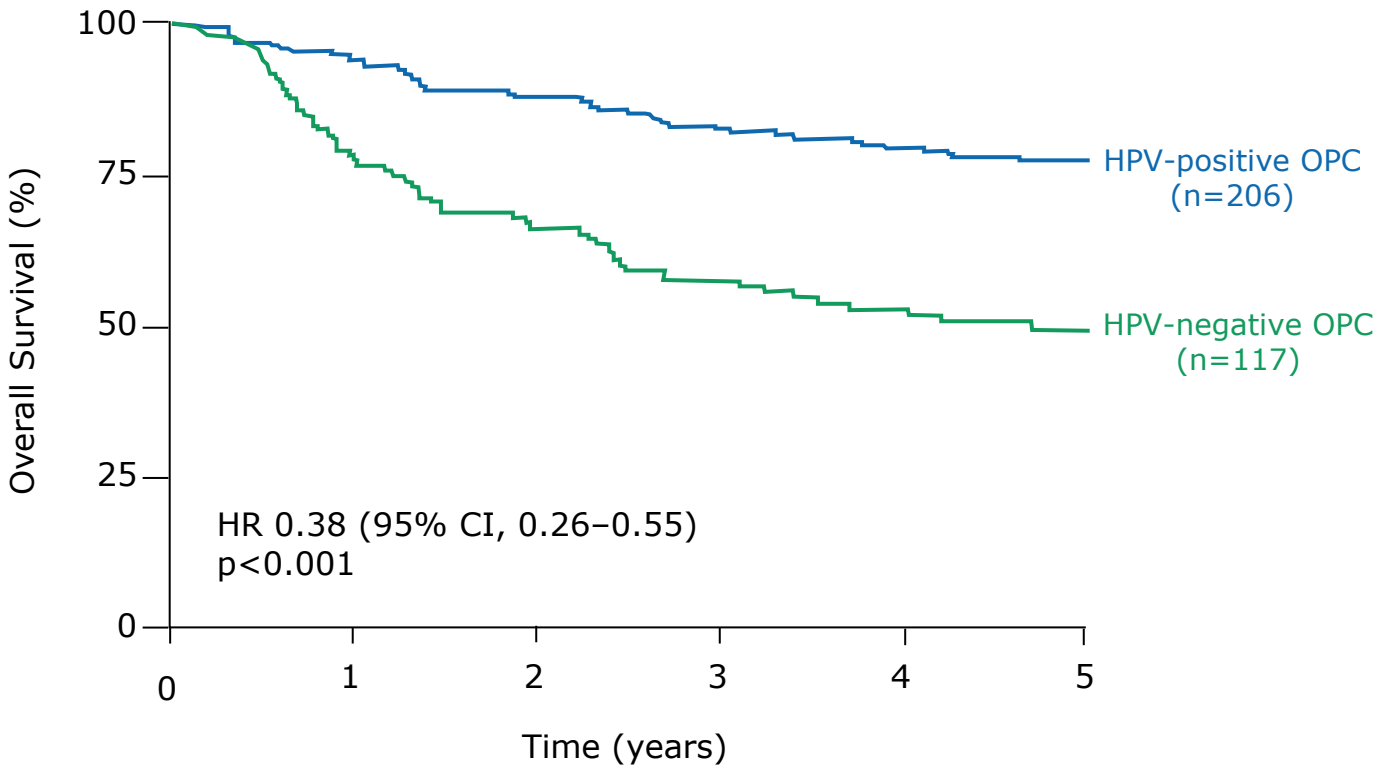
	HPV-positive SCCHN	HPV-negative SCCHN
Risk factors[1]	Sexual contact	Tobacco and alcohol use
Age[2]	Younger	Older
Tumor site[1]	Mainly oropharyngeal sites	Generally non-oropharyngeal sites
Histopathology[1]	Basaloid, non-keratinizing, poorly differentiated	Keratinizing, moderately differentiated
Relative responsiveness to CT + RT[1]	Better	Worse
Relative prognosis[1]	Better	Worse

CT, chemotherapy; HPV, human papillomavirus; OPC, oropharyngeal cancer; RT, radiotherapy; SCCHN, squamous cell carcinoma of head and neck.

1. Pai SI, Westra WH. Annu Rev Pathol. 2009;4:49–70; 2. Ringstrom E, et al. Clin Cancer Res. 2002;8:3187–3192.

Patients With HPV-positive OPC Have a Significantly Better Prognosis Than Patients With HPV-negative OPC

RTOG 0129: 5-year OS by HPV status (patients treated with high-dose cisplatin + radiotherapy)[1,*]



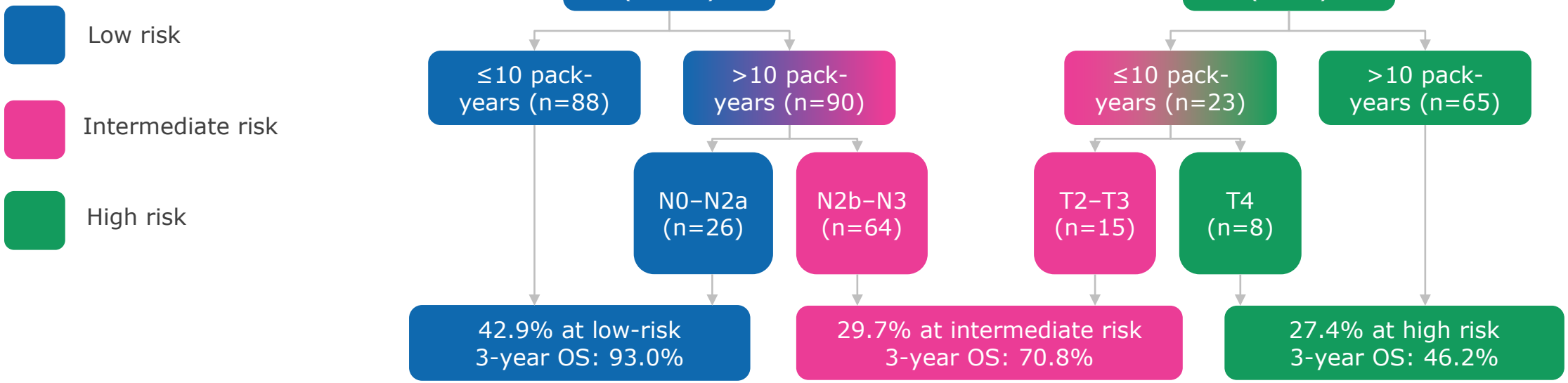
	HPV-positive OPC (n=206)	HPV-negative OPC (n=117)
3-year OS, % (95% CI)	82.4 (77.2–87.6)	57.1 (48.1–66.1)

As HPV can affect prognosis in HPV-positive OPC, less-intense or alternative treatment strategies for HPV-positive OPCs are under active investigation[2]

*The association between tumor HPV status and survival was retrospectively analyzed.
CI, confidence interval; HPV, human papillomavirus; HR, hazard ratio; NCCN, National Comprehensive Cancer Network® (NCCN ®); OPC, oropharyngeal cancer; OS, overall survival; RTOG, Radiation Therapy Oncology Group.
1. Ang KK, et al. N Engl J Med. 2010;363:24–35; 2. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Head and Neck Cancers V.2.2022.

HPV Status Plays a Role in the Prognosis of Patients With Locally Advanced SCCHN

Prognostic factors from the RTOG 0129 study



Recursive-portioning analysis identified prognostic factors with the most predictive significance

HPV, human papillomavirus; SCCHN, squamous cell carcinoma of the head and neck; N, nodal disease; OS, overall survival; T, tumor stage; RTOG, Radiation Therapy Oncology Group.

Ang KK, et al. N Engl J Med. 2010;363:24–35.

Overview of Apoptotic Pathways

Intrinsic pathway, induced by[1]:

- Intracellular stress
- DNA damage
- Anticancer therapy

Extrinsic pathway, induced by[1]:

- Extracellular stress
- Death signaling ligands

Noncanonical NF-κB pathway[2-4]

- Plays a key role in apoptosis via the release of inflammatory cytokines (eg, TNFα)

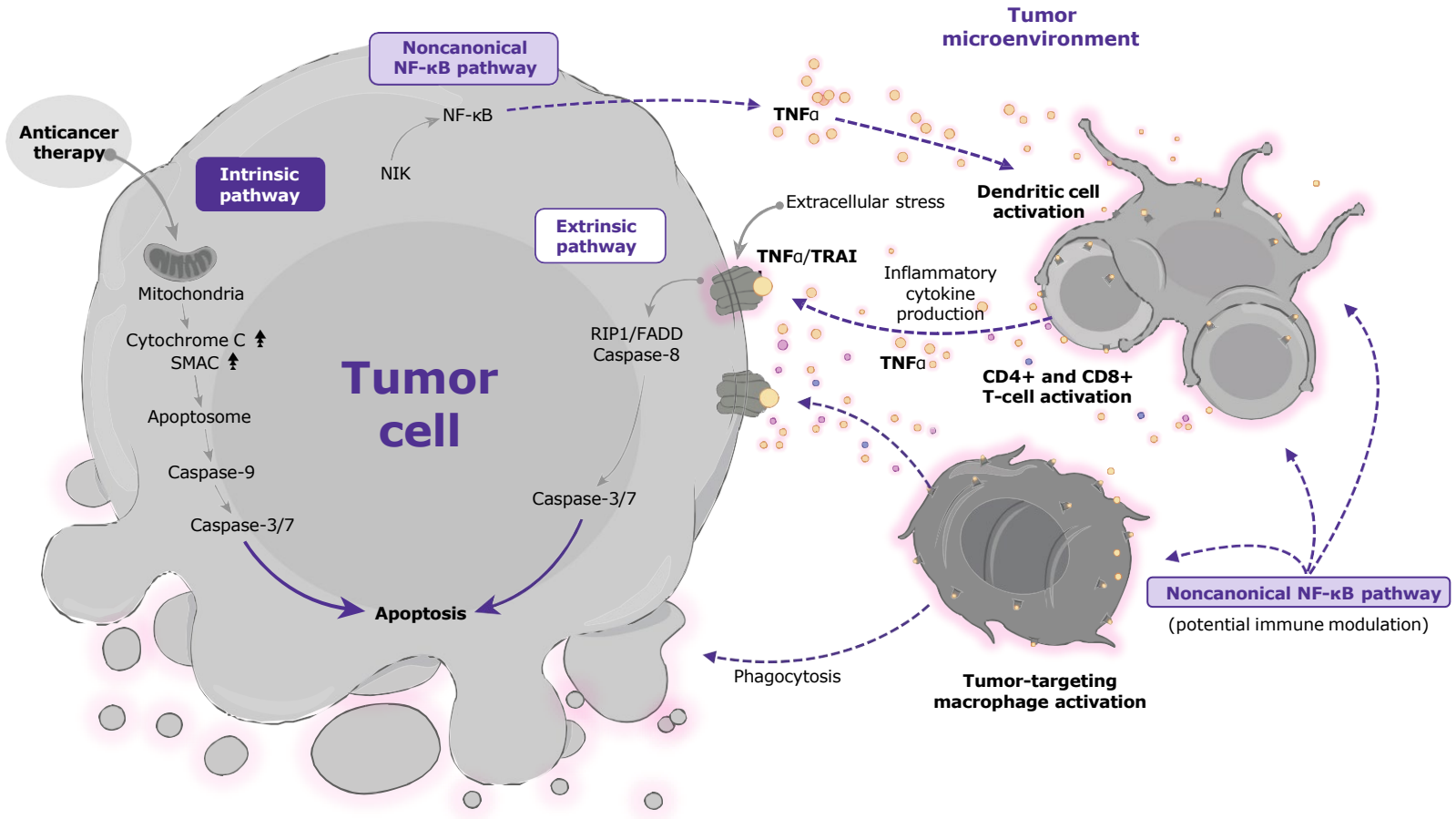
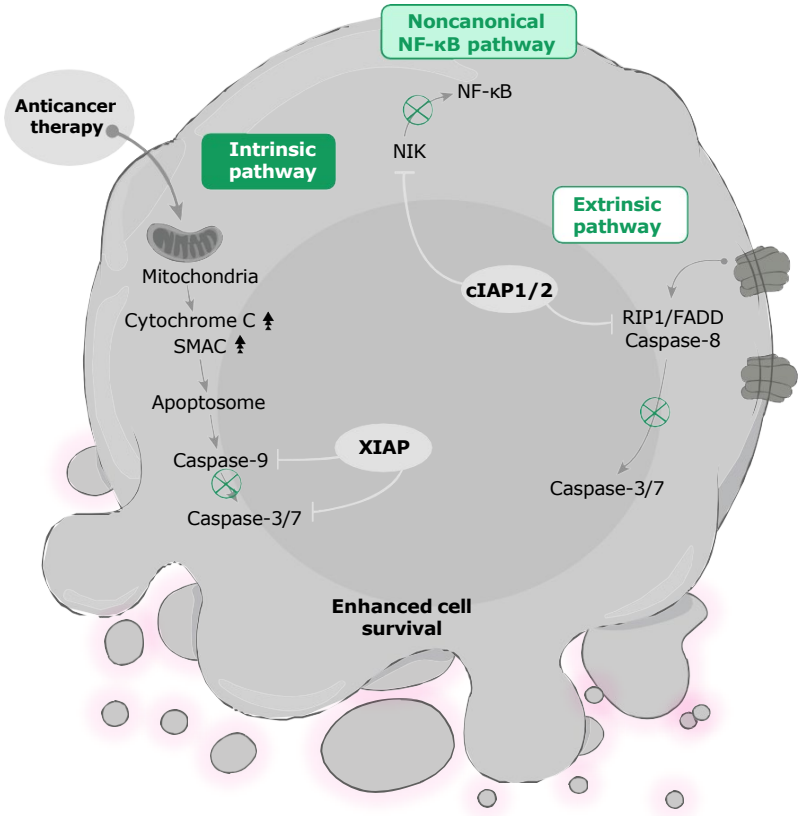


Figure adapted from: Bourhis J, et al. *Future Oncol.* 2022;18(14):1669–1678.
CD, cluster of differentiation; FADD, Fas-associated protein with death domain; MoA, mechanism of action; NF-κB, nuclear factor kappa B; NIK, NF-κB-inducing kinase; RIP1, receptor interacting serine/threonine kinase 1; SCCHN, squamous cell carcinoma of the head and neck; SMAC, second mitochondria-derived activator of caspases; TNFα, tumor necrosis factor, alpha; TRAIL, TNF-related apoptosis-inducing ligand.
1. Bourhis J, et al. *Future Oncol*. 2022;18(14):1669–1678; 2. Lau R, Pratt MA. *ISRN Oncol.* 2012;2012:928120; 3. Dougan M, et al. *J Exp Med*. 2010;207(10):2195–2206; 4. Sun S-C. *Cell Res*. 2011;21:71–85.

Role of Inhibitor of Apoptotic Proteins in Apoptosis

IAPs block apoptosis in healthy cells[2-4]



- In a genomic analysis of SCCHN tumors by the Cancer Genomic Atlas Network, **activating mutations were found in multiple genes involved in apoptosis pathways**[1]
- Inhibitor of apoptotic proteins (IAPs) are frequently **overexpressed in various cancers,** including SCCHN, and have been shown to **increase the resistance** of cancer cells to apoptosis and **prevent cell death** induced by anticancer treatments, such as CT and RT[2,3]
- **IAPs**, including cIAP1/2 and XIAP, are a class of proteins that **block apoptotic signaling pathways** induced by various intrinsic or extrinsic factors, **resulting in enhanced cell survival**[2,3]
- Resistance to apoptosis is a hallmark of cancer,[5,6] and **IAP overexpression is associated with poor prognosis** in several tumor types, including SCCHN[7,8]
- In preclinical studies, **IAP overexpression prevented cell death** induced by CT or RT in cell lines and mouse xenograft models, including SCCHN cell lines[9-11]

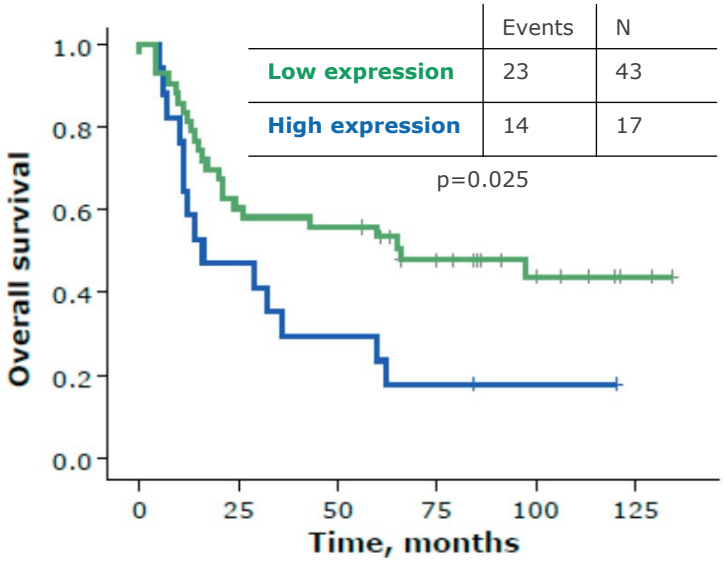
Figure adapted from: Bourhis J, et al. Future Oncol. 2022; 18(14): 1669-1678.
cIAP, cellular inhibitor of apoptosis protein; CT, chemotherapy; FADD, Fas-associated protein with death domain; IAP, inhibitor of apoptosis protein; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; NIK, NF-κB–inducing kinase; RIP1, receptor interacting protein 1; RT, radiotherapy; SCCHN, squamous cell carcinoma of the head and neck; TNF, tumor necrosis factor; XIAP, X-linked inhibitor of apoptosis.

1. Cancer Genome Atlas Network. Nature. 2015;517:576–582; 2. Abbas R, Larisch S. Cells. 2020;9(3):663; 3. Obexer P, Ausserlechner MJ. Front Oncol. 2014;4:197; 4. Zhao XY. Cells. 2020;9(4):1012; 5. Mohammad RM, et al. Semin Cancer Biol. 2015;35 Suppl(0):S78–S103; 6. Fulda S. Int J Cancer. 2009;124(3):511–515; 7. Nagata M, et al. Br J Cancer. 2011;105(9):1322–1330; 8. Yang X-H, et al. PLoS One. 2012;7:e31601; 9. Matzinger O, et al. Radiother Oncol. 2015;116(3):495–503; 10. Brunckhorst MK, et al. Cancer Biol Ther. 2012;13(9):804–811; 11. Gu L, et al. Cancer Cell. 2009;15(5):363–375.

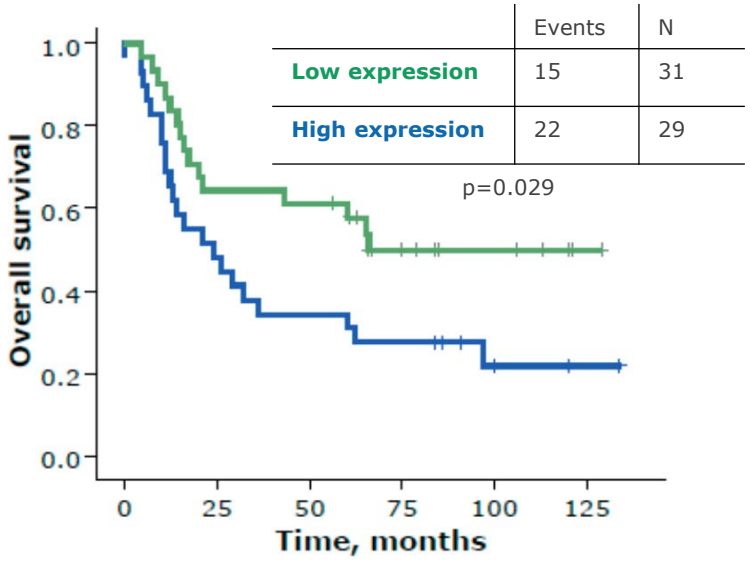
Mechanism of Disease Mediated by IAPs

XIAP was expressed in 17 of 60 samples from patients with locally advanced SCCHN; XIAP expression was significantly associated with cisplatin resistance (pre-treatment: p=0.036; post-treatment; p=0.005)[1]

OS by XIAP score pre-chemotherapy[1]



OS by XIAP score post-chemotherapy[1]



- XIAP expression levels increased in tumor samples from patients with SCCHN post-chemotherapy vs pre-chemotherapy (p=0.011) and XIAP levels in post-chemotherapy samples were significantly related to OS[1]
- In preclinical models of SCCHN, inhibition of survivin (an IAP family protein) decreased tumor cell proliferation and reversed cisplatin resistance[2]
- Silencing of XIAP gene expression in SCCHN cells increased sensitivity to cisplatin[1]

	Pre-chemotherapy			Post-chemotherapy		
Response to chemotherapy	**Low XIAP expression**	**High XIAP expression**	**P value**	**Low XIAP expression**	**High XIAP expression**	**P value**
SD + PD	15	11	0.036	8	18	0.005
CR + PR	28	6		23	11	

CR, complete response; IAP, inhibitor of apoptosis protein; OS, overall survival; PD, progressive disease; PR, partial response; SCCHN, squamous cell carcinoma of the head and neck; SD, stable disease; XIAP, X-linked inhibitor of apoptosis.

1. Yang XH, et al. PLoS One. 2012;7(3):e31601; 2. Kumar B, et al. Mol Cancer Ther. 2012;11:1988–1998.

Most patients with SCCHN are diagnosed at the locally advanced stage

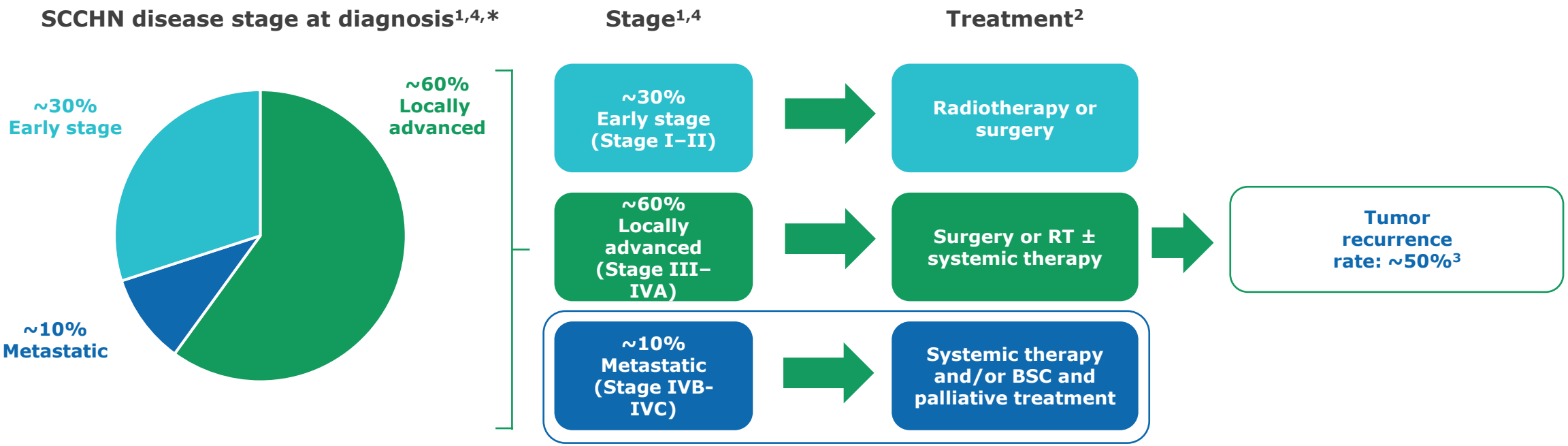
Staging for HPV-negative SCCHN (8th edition staging manual)[1]

	Stage	Approximate proportion of patients[2,3,*]		Prognosis[†]
		OC and pharyngeal cancer	Laryngeal cancer	
Early stage	I	28%	52%	60–90% disease-free survival[4]
	II			
Locoregionally advanced	III	50%	26%	**Potentially resectable (operable)** 40–50% 5-year OS[4] **Unresectable (non-operable)** 10–40% 5-year OS[4]
	III			
	IVA			
	IVB			
Metastatic	IVC	17%	18%	**Historically** ~10-month median OS[5] **New data with checkpoint inhibition** Up to 15 months median OS[6]

*Incidence data from oral cavity, pharynx and larynx (2012–2018); †Populations that are unselected for HPV status.
HPV, human papillomavirus; OS, overall survival; SCCHN, squamous cell carcinoma of the head and neck.

1. AJCC Cancer Staging Form Supplement, AJCC Cancer Staging Manual, 8th Edition. 2018; 2. Oropharyngeal Cancer. SEER Cancer Statistics Review. https://seer.cancer.gov/statfacts/html/oralcav.html (accessed October 2022); 3. Laryngeal Cancer. SEER Cancer Statistics Review. https://seer.cancer.gov/statfacts/html/laryn.html (accessed October 2022); 4. Ko C, et al. Oral Dis. 2009;15:121–132; 5. Vermorken JB, et al. N Engl J Med. 2008;359:1116–1127; 6. Burtness B, et al. Presented at ESMO 2018. Abstract No. LBA8_PR.

Most Patients Are Diagnosed With Locally Advanced SCCHN, but Nearly Half Will Experience Recurrence



*These data do not include the approximately 19% of patients with an unknown stage at diagnosis.

BSC, best supportive care; CRT, chemoradiotherapy; CT, chemotherapy; NCCN, National Comprehensive Cancer Network® (NCCN®); RT, radiotherapy; SCCHN, squamous cell carcinoma of the head and neck.

1. Corvò R. Radiother Oncol. 2007;85(1):156–170; 2. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Head and Neck Cancers V.2.2022. © 2022 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way; 3. Machiels JP, et al. Ann Oncol. 2020;31:1462–1475; 4. Bean MB, et al. Oncologist 2019;24(12):1562-1569.

Current Treatment Options for Locally Advanced SCCHN

Treatment of Locally Advanced SCCHN Generally Has Curative Intent, With a Long-term View to Quality of Survival[1–4]

Treatment goals for locally advanced SCCHN:

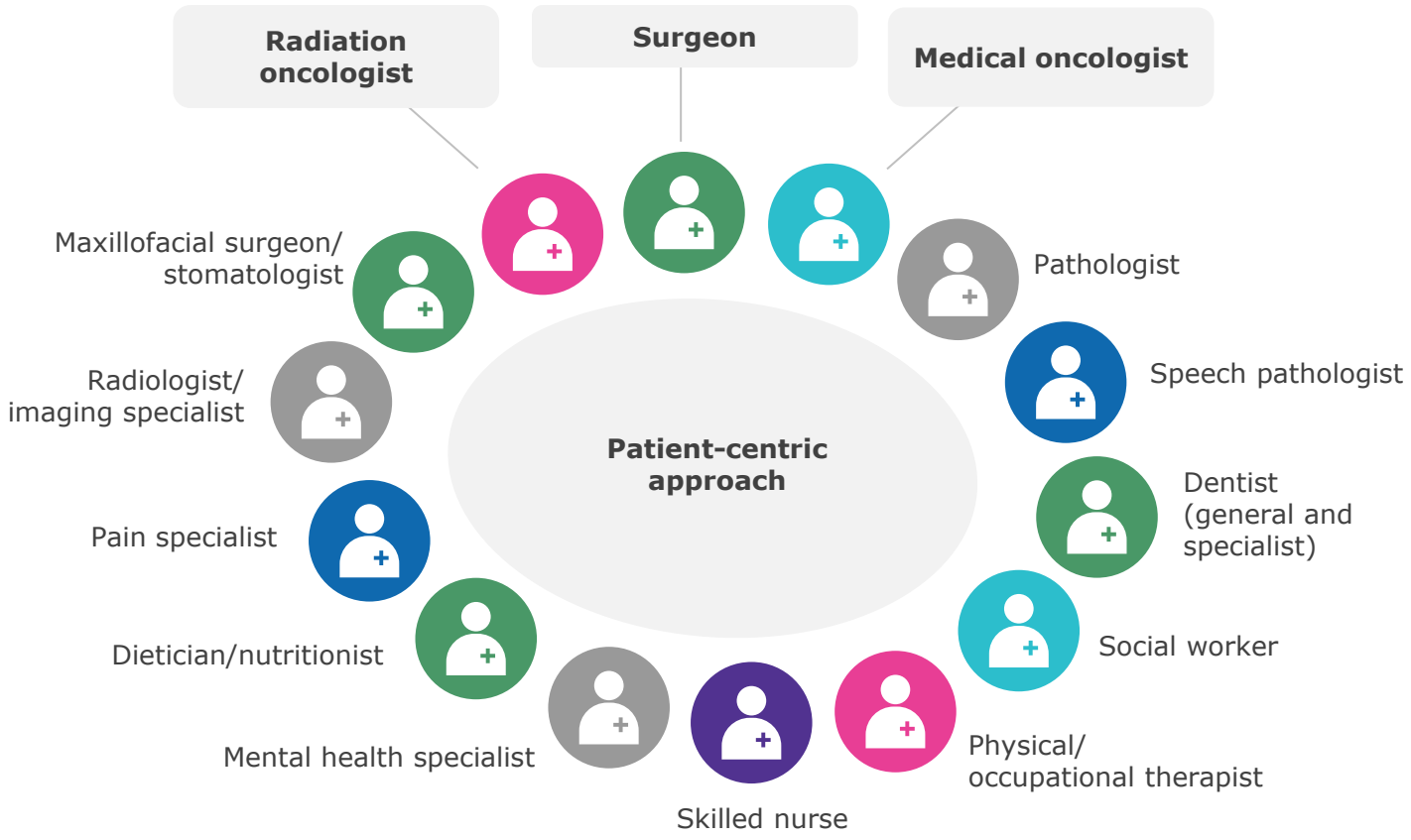
- **Reduced risk of recurrence[1,2]**
- **Organ preservation[1–4]**
- **Long-term survival[1,2]**
- **Quality of life[2,4]**
- **Locoregional control[3]**

Optimal management must take into account both clinical and psychosocial factors to optimize the future wellbeing of the patient[1]

SCCHN, squamous cell carcinoma of the head and neck.

1. Ang KK. Oncologist. 2008;13:899–910; 2. Haigentz M Jr, et al. Expert Opin Pharmacother. 2010;11:1305–1316; 3. Haddad RI, et al. Ann Oncol. 2018;29:1130–1140; 4. Lo Nigro C, et al. Cancer Manag Res. 2017;9:363–371.

MDT Management of SCCHN Is Recommended by International Guidelines to Optimize Outcomes in Patients With SCCHN[1,2]



- The key members of the MDT are the **radiation oncologist**, **surgeon** and **medical oncologist**[3,4]
- Patients with SCCHN often have additional needs, requiring input from other specialties to ensure a patient-centric approach[3,4]

A significant increase in survival has been observed in patients seen by an MDT vs patients who are not seen by one[5,*]:

- **Stages 0–IV, HR=0.79, p=0.024**
- **Stage IV, HR=0.69, p=0.004**

HR, hazard ratio; MDT, multidisciplinary team; NCCN, National Comprehensive Cancer Network® (NCCN®).

1. Machiels JP, et al. Ann Oncol 2020;31:1462–1475; 2. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Head and Neck Cancers V.2.2022. © 2022 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way; 3. Galloway T, Amdur RJ. http://www.uptodate.com/contents/management-and-prevention-of-complications-during-initial-treatment-of-head-and-neck-cancer (accessed October 2022); 4. Head and Neck Cancers. National Cancer Institute. https://www.cancer.gov/types/head-and-neck/head-neck-fact-sheet(accessed October 2022); 5. Friedland PL, et al. Br J Cancer. 2011;104:1246–1248.

Traditional Treatments for Locally Advanced SCCHN Include Surgery, Radiotherapy, Chemotherapy or Targeted Therapy

Local Treatment

Surgery

- Direct removal of tumors
- Risks include dysfunction or loss of function of vital organs, including those required for swallowing and speaking

Radiotherapy

- Can be used instead of surgery to reduce risk of injury to normal tissue
- Can be a single modality or combined with systemic therapy

Systemic Treatment

Platinum-based Chemotherapy

- Usually administered concomitantly with radiotherapy, either after surgery or in unresected (non-operated) disease

Targeted therapy

- May be administered without radiotherapy or in combination with radiotherapy

NCCN, National Comprehensive Cancer Network® (NCCN®); SCCHN, squamous cell carcinoma of head and neck.

Radiotherapy Is Used for Local Treatment of Locally Advanced SCCHN With Curative Intent[1]

Radiotherapy

- **Radiotherapy can be a single modality or combined with systemic therapy[1]**
- **Definitive radiation may be offered for "organ preservation" in cases where a tumor is resectable,** but there is risk of damage to anatomical structures critical for important functions, e.g., swallowing or communication[1,2]

IMRT

Radiotherapy techniques aim to minimize treatment-associated toxicities[3]:

- Currently IMRT is the standard radiotherapy technique[4]
- Linear-accelerators deliver high-precision radiation conforming to the 3D shape of the primary tumor, minimizing the exposure to surrounding tissues[3]

3D Radiotherapy

Treatment planner sets beam parameters to the shape of the tumor, minimizing exposure of surrounding tissues[3]

IMRT, intensity modulated radiotherapy; NCCN, National Comprehensive Cancer Network® (NCCN®); SCCHN, squamous cell carcinoma head and neck..

1. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Head and Neck Cancers V.2.2022. © 2022 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way; 2. Forastiere AA, et al. J Clin Oncol. 2018;36:1143–1169; 3. Nguyen LN, et al. Lancet Oncol. 2002;3:693–701; 4. Bucci MK, et al. CA Cancer J Clin. 2005;55:117–134.

Concurrent CRT Is an Option in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for the Treatment of Select Patients With Unresected Locally Advanced SCCHN

Non-nasopharyngeal* locally advanced SCCHN

Resectable†

Postoperative systemic therapy/RT

Preferred regimens

Cisplatin
(category 1 for high-risk non-OPCs)

Useful in certain circumstances

Docetaxel/cetuximab (category 2b) if cisplatin ineligible and positive margins and/or extranodal extension

Unresectable/ surgery not chosen

Primary systemic + concurrent RT

Preferred regimens

High-dose cisplatin‡
(category 1)

Carboplatin/infusional 5-FU
(category 1)

Other recommended regimens

Weekly cisplatin§
(category 2A)

Carboplatin/paclitaxel
(category 2B)

Useful in certain circumstances

5-FU/hydroxyurea (category 2B)

Cetuximab (category 2B)

Cisplatin/infusional 5-FU (category 2B)

Cisplatin/paclitaxel (category 2B)

*Non-nasopharyngeal cancers include lip, oral cavity, oropharynx, hypopharynx, glottic larynx, supraglottic larynx, ethmoid sinus, maxillary sinus, and occult primary. †Induction chemotherapy is also an option for these patients. Induction chemotherapy should only be administered at sites with expertise in these regimens because of challenges associated with appropriate patient selection and management of treatment related toxicities. ‡100 mg/m² cisplatin Q3W for 3 cycles. §40 mg/m² cisplatin QW.

5-FU, 5-fluorouracil; CRT, chemoradiotherapy; NCCN, National Comprehensive Cancer Network® (NCCN®); OPC, oropharyngeal cancer; Q3W, every 3 weeks; QW, weekly; RT, radiotherapy; SCCHN, squamous cell carcinoma of the head and neck.

Summary

Summary

SCCHN is a group of malignancies mainly derived from the oral cavity, oropharynx, hypopharynx and larynx that accounts for >90% of all head and neck cancers[1]

The incidence of SCCHN is increasing in Western countries, probably due to increasing rates of HPV infection[2]

Within 2 years of completing treatment, >50% patients have local recurrence or distant metastasis[3]

Treatment goals for locally advanced SCCHN are long-term survival, cure and locoregional control[4-7]; treatment options typically include surgery, RT and CT[8]

High-dose cisplatin + RT, and carboplatin/5-FU + RT are the preferred regimens for the treatment of unresectable locally advanced SCCHN when treating with chemoradiation; weekly cisplatin + RT, and carboplatin/paclitaxel + RT regimens are other recommendations; 5-FU/hydroxyurea + RT, cetuximab + RT, cisplatin/infusional 5-FU + RT and cisplatin/paclitaxel + RT regimens are treatments useful in certain circumstances[8]

5-FU, 5-fluorouracil; CT, chemotherapy; HPV, human papillomavirus; NCCN, National Comprehensive Cancer Network® (NCCN®) RT, radiotherapy; SCCHN, squamous cell carcinoma of the head and neck.

1. Bower M, Waxman J. Oncology Lecture Notes. 3rd ed. Wiley; 2015; 2. Chaturvedi AK, et al. J Clin Oncol. 2013;31:4550–4559; 3. Machiels JP, et al. Ann Oncol. 2020;31:1462–1475; 4. Lo Nigro C, et al. Cancer Manag Res. 2017;9:363–371; 5. Ang KK. Oncologist. 2008;13:899–910; 6. Haigentz M Jr, et al. Expert Opin Pharmacother. 2010;11:1305–1316; 7. Haddad RI, et al. Ann Oncol. 2018;29:1130–1140; 8. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Head and Neck Cancers V.2.2022.