Provincial Oropharyngeal Cancer Treatment Guidelines

Approved at the Provincial Head and Neck Cancer Guideline Meeting
May 8, 2015

Clinical practice guidelines have been developed after multi-disciplinary consensus based on best available literature. As the name suggests, these are to be used as a guide only. These guidelines do not replace physician judgment which is based on multiple factors including, but not limited to, the clinical and social scenario, comorbidities, performance status, age, available resources and funding considerations. The Saskatchewan Cancer Agency disclaims all liability for the use of guidelines except as expressly permitted by the Agency. No portion of these guidelines may be copied, displayed for redistribution to third parties for commercial purposes or any non-permitted use without the prior written permission from the Agency.

Recommendations for drug treatment presented in the Cancer Agency guidelines for a cancer site may not reflect provincial cancer drug funding. Please refer to the current Saskatchewan Cancer Agency drug formulary at www.saskcancer.ca for information on cancer drug listing and funding.

Benefits and risk of the proposed should be discussed with patient.

Participating in clinical trials is encouraged when available. Involvement of a multidisciplinary team is strongly recommended.

Content:

ANATOMICAL PARTS OF OROPHARYNX

Facial arch including soft palate, uvula and anterior tonsillar pillar
Glossotonsillar sulci and pharyngeal tonsils
Base of tongue
Pharyngeal wall including lateral and posterior walls and posterior tonsillar pillar

DIAGNOSIS AND WORK-UP

- History and clinical examination including Direct Fiberoptic Endoscopy
- Biopsy of either primary tumour or neck or both if clinically indicated.
- HPV testing using p16 expression reported
- CT scan with contrast of head and neck, chest.
- MRI, PET scan if clinically indicated
- Dental Consult mandatory; request for mouth guards if indicated
- Dietitian consult; Speech pathologist evaluation, swallowing assessment.
- If clinically indicated, examination under anesthesia (EUA), Panendoscopy and biopsies
- Multidisciplinary team consultation recommended
- Referral for prophylactic PEG tube may be considered for chemoradiation candidates, and for all others if clinically indicated.

STAGING

American Joint Committee on Cancer (AJCC) TNM Staging System (7th ed.,2010)

Primary tumour (T)

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour
Tis Carcinoma in situ
T1 Tumour 2cm or less in greatest dimension
T2 Tumour more than 2cm but not more than 4cm in greatest dimension
T3 Tumour more than 4cm in greatest dimension or extension to lingual surface of epiglottis
T4a Moderately advanced local disease. Tumour invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible*
T4b Very advanced local disease. Tumour invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery
* Mucosal extension to lingual surface of epiglottis from primary tumours of the base of the tongue and vallecula does not constitute invasion of larynx.

Regional lymph nodes (N)

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in a single ipsilateral lymph node, 3cm or less in greatest dimension
N2 Metastasis in a single ipsilateral lymph node, more than 3cm but not more than 6cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6cm in greatest dimension
N2a Metastasis in single ipsilateral lymph node more than 3cm but not more than 6cm in greatest dimension
N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6cm in greatest dimension
N3 Metastasis in a lymph node more than 6cm in greatest dimension

Distant metastases (M)
M0 No distant metastasis (no pathologic M0; use clinical M to complete stage group)
M1 Distant metastasis

Stage	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
III	T3 T1 T2 T3	N0 N1 N1 N1	M0 M0 M0 M0
IVA	T4a T4a T1 T2 T3 T4a	N0 N1 N2 N2 N2 N2	M0 M0 M0 M0 M0 M0
IVB	T4b Any T	Any N N3	M0 M0
IVC	Any T	Any N	M1

MANAGEMENT OF INVASIVE CARCINOMA OF OROPHARYNX:

Early stage:
T1-2, N0-1

Definitive Radiation Therapy. For T2N1 Concurrent ChemoRadiation may be considered.
Post radiation evaluation.
In case of incomplete response - salvage surgery

or

Surgical Resection of Primary tumour with or without ipsilateral or bilateral neck dissection
Adjuvant radiation or chemoradiation in case of adverse features.

Locally advanced resectable disease
T3-4a, N0-1

Concurrent ChemoRadiation
Post ChemoRadiation evaluation
In case of incomplete response - salvage surgery

Surgical or Trans-oral Resection of Primary site and Neck Dissection
Adjuvant radiation or chemoradiation in case of adverse features

As clinically indicated
Induction Chemotherapy followed by ChemoRadiation
Post ChemoRadiation evaluation
In case of incomplete response - salvage surgery

Any T, N2-3

Concurrent ChemoRadiation
Post ChemoRadiation evaluation
In case of incomplete response - salvage surgery

Surgical or Trans-oral Resection of Primary site and Neck Dissection
Adjuvant radiation or chemoradiation in case of adverse features

As clinically indicated
Induction Chemotherapy followed by ChemoRadiation
Post ChemoRadiation evaluation
In case of incomplete response - salvage surgery

De-escalation of treatment for HPV patients may be considered in clinical trial only.

POST-OPERATIVE ADJUVANT THERAPY INDICATIONS

High Risk features:

Combined ChemoRadiation
- Extracapsular nodal spread
or/and
- Positive surgical margins

Intermediate Risk Features:

Radiation therapy ± concurrent Chemotherapy may be considered in certain circumstances
- T3 or T4 primary
- N2-N3 nodal disease
- Lymphovascular invasion

The following features may be considered in making decision:
- Close surgical margin <5 mm as per RTOG 0920
- Nodal disease in levels IV or V as per NCCN guidelines

POSTCHEMORADIATION OR POST RADIATION EVALUATION

6 weeks since completing treatment:
Clinical assessment including complete head and neck exam with Direct Fiberoptic Examination

Progression or no response:
Metastatic work up to be considered (Imaging and biopsy at the discretion of multidisciplinary team)
If progression confirmed - salvage surgery

Response:
- Next follow up in 6 weeks

8 -12 weeks since completing treatment:
- Clinical assessment including complete head and neck exam with Direct Fiberoptic

Examination
- Imaging including MRI and CT with contrast
- PET at the discretion of the multidisciplinary team

Lymph nodes that are PET negative - continue follow up if continues to regress
Lymph node > 1 cm or PET positive - consider biopsy and Neck Dissection
Lymph node > 1 cm and PET positive – Neck Dissection
Primary persistent disease – biopsy and salvage resection

SALVAGE SURGERY

Primary Tumour:
Surgical removal *(salvage resection)* of the primary tumour should be performed if biopsy-proven cancer remains more than three months after completion of therapy

Neck dissection:
Biopsy should be considered before salvage neck dissection in case of incomplete response 12-20 weeks post treatment

A neck dissection irrespectively of response for patients with multiple neck nodes or with lymph nodes exceeding 3 cm in diameter *(N2a, N2b, N3)* is optional

Cervical lymphadenectomy should encompass the original levels of lymph node involvement. Preservation of the accessory nerve, jugular vein, and sternomastoid muscle is encouraged if consistent with complete removal of all residual nodal disease; however, the extent of the neck dissection will be at the discretion of the surgeon.

RADIATION THERAPY

Simultaneous Integrated Boost (SIM) Intensity Modulated Radiation Therapy (IMRT) is the preferable Radiation therapy technique.
The most common regimens that may be considered:

Definitive ChemoRadiation:

PTV primary and positive lymph nodes	PTV Intermediate risk	PTV Low Risk
7000cGy/35 fxs	6300cgy/35 fxs	5600cgy/35 fxs
7000cGy/33 fxs	5940cGy/33fxs	5400cGy/33fxs

Radiation Therapy without chemotherapy for small tumours T1-2, N0-1.
Unilateral neck radiation may be considered for wee lateralized tonsillar lesion.

6600cGy/30 fxs	60000cGy/30 fxs	5400cGy/30 fxs

Postoperative Radiation/ChemoRadiation

Postoperative bed	PTV Intermediate risk	PTV Low Risk
6000 cGy-6600cgy/30 fxs	6000cgy/30 fxs	5400cgy/30 fxs

CONCURRENT CHEMOTHERAPY

Cisplatin	100 mg/m sq days every 3 weeks for 2-3 cycles
Cisplatin	40 mg/m2 (max = 80) IV weekly for 5 - 6 cycles during EBRT
Cetuximab	400mg/m sq loading dose 7 days prior to radiation
	250 mg/m sq weeks 2 – 8 concurrently and week after radiation

MANAGEMENT OF RESIDUAL DISEASE, LOCO-REGIONAL RECURRENCE OR DISTANT METASTASES

Will be determined by multidisciplinary team and the clinical situation, and options are:

- surgical resection,
- re-irradiation,
- chemotherapy concurrent, neoadjuvant or palliative
- palliative care only

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39. RTOG 0129 A Phase III Trial of Concurrent Radiation and Chemotherapy (Followed By Surgery For Residual Primary/N2-3 Nodal Disease) for advanced Head and Neck Carcinomas
40. RTOG 0920 A phase III study of postoperative radiation therapy (IMRT) +/- cetuximab for locally-advanced resected head and neck cancer
41. RTOG 1216 Randomized phase II/III trial of surgery and postoperative radiation delivered with concurrent cisplatin versus docetaxel versus docetaxel and cetuximab for high-risk squamous cell cancer of the head and neck

Chairperson: Dr. Shazia Mahmood

Presenters: Dr. Shazia Mahmood, Dr. Evgeny Sadikov, Dr. Debra Korol, Dr. Ali El-Gayed, Dr. Derek Suderman, Dr. Rick Jaggi, Dr. Adnan Zaidi, Dr. Bryan Brunet, Dr. Wojciech Dolata, Dr. Kamal Haider

Attendees: Dr. Aisha Ahmed, Joe Andreas, Dr. Monica Behl, Dr. Janine Benoit, Dr. Bryan Brunet, Jennifer Cameron-Turley, Lorna Campbell, Dr. Peter Chang, Dr. Tineyi Chikukwa, Dena Colleaux, Dr. Wojciech Dolata, Dr. Ali El-Gayed, Lacey Fondrick, Christel Foord, Bertha Foote, Pauline Fox, Josh Giambattista, Dr. Kamal Haider, Dr. Rick Jaggi, Dr. Miroslav Jancewicz, Dr. Debra Korol, Lana Kruger, Dr. Shazia Mahmood, Courtney McKay, Dr. Mohamed Mohamed, Dr. William Moyer, Lori Muz, Dr. Mark Ogrady, Dr. Lenny Pillay, Dr. Florence Plaza Arnold, Dr. Evgeny Sadikov, Dr. Muhammad Salim, Judy Shaw, James Smetaniuk, Dr. Derek Suderman, Dr. Niranjan Venugopal, Brenda Wilde, Michelle Zahayko, Dr. Adnan Zaidi, Dr. Bill Ziegler