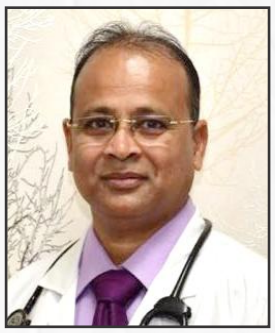
12th Issue
October, 2018

Onco News

Published by : Somex Research and Health Pvt. Ltd.
(A Clinical Research and Academic Organisation)
www.somexresearch.com

From the Desk of Editor



Dear Readers,

Happy festive season !

Head and neck cancer is the sixth most common cancer worldwide. According to Globcan 2018 statistics, squamous cell cancers of head and neck (SCCHN) are number one in Indian population. The disease complexity due to heterogeneity of organs and functions involved necessitates the need for a multi modality approach in the disease management and an individually tailored treatment plan in most patients. Furthermore, treatment goals which include cure, organ and function preservation, quality of life and palliation – must also be considered. A lot to be done for prevention, screening, treatment and rehabilitation of these patients.

With regards
Dr. Naresh Somani
M.D., D.M.
Senior Medical Oncologist

Introduction:

Malignancy of the head and neck cancer is the sixth most common cancer worldwide and the most common in central Asia. It encompasses a range of neoplasms arising from different anatomical sites:

- The oral cavity: Including the lips, gums, anterior tongue, floor or the mouth, hard plate, and buccal mucosa
- The pharynx: Including the nasopharynx, oropharynx, and hypopharynx
- The larynx: Including the supraglottic, glottis and subglottic regions
- The nasal cavity and paranasal sinuses: Maxillary, frontal, ethmoid and sphenoid
- The salivary glands

Although the term head and neck cancer includes many different disease, most of the skills required to assess and manage these patients are broadly similar.

Etiology: Smoking and alcohol use and chewing tobacco and pipe smoking are main . Human Papillomavir (HPV) infection is a risk factor for cancer of the larynx, pharynx and oral cavity. 40%-50% of squamous cell carcinomas of the orophyarynx are HPV related. The same high-risk strains that cause cervical cancer are implicated in etiology. Virally induced cancers may have a better prognosis than those attributable to smoking and alcohol use.

Screening and prevention: There is currently no national screening program; so the emphasis is on public health education to tackle the major modifiable risk factor of tobacco and alcohol use and to raise awareness of these cancers and their presenting symptoms. These efforts are to reduce the number of patients presenting with advanced-stage disease. Over 90% of cancers of the head and neck are squamous cell carcinomas, typically they invade adjacent structures, depending on the site of origin and spread via lymphatic to regional lymph nodes in the cervical chain.

Pre-malignant conditions:

- Leukoplakia • Erythroplakia • Dysplasia • Verrucos tumor

Contd.

Presentation:

Characteristic local symptoms depend on the site and size of the primary lesion and may not uncommonly present with painless cervical lymphadenopathy.

Laryngeal cancer: A hoarse voice and a persistent, irritating cough and dysphagia.

Cancer of the oral cavity: Persistent mouth ulcers, painful ulcerative lesion on lip or exophytic growth.

Nasopharyngeal cancer: Nasal symptoms, cervical lymphadenopathy, cranial nerve palsies due to base of skull invasion.

Oropharyngeal cancer: Sore throat or lump in the throat, pain referred to ear.

Hypopharyngeal cancer: Dysphagia and lump in the throat, odynophagia, pain referred to ear.

Investigations:

The aims of investigations include the following:

- Identifying the primary tumor site and extent, including cytological or histological confirmation.
- Staging the disease.
- Assessing the general fitness of patient.
- Clinical examination should be combined with appropriate imaging.
- CT scan/MRI is used to determine the extent of local tumor infiltration, particularly invasion of bone of cartilage.
- Obtain a biopsy if the primary tumor is identified and accessible.

Stating: Staging systems for head and neck cancers are based on the TNM**.**

Management:

Premalignant lesions: Treatment is usually be excision**.**

Malignant lesions: Investigation and management should be coordinated by a multidisciplinary team with expertise in the complex, psychological and functional issues. The aim of treatment is to combine optimal rates of cure with the best functional results. Most head and neck cancers are treated with surgery, radiotherapy or a combination of the two and chemotherapy. Generally, T1-2, N0, M0 disease can be treated with singe-modality treatment and retrospective data suggest that the results achieved by surgery or radiotherapy alone are equivalent. The modality of therapy that will give the best long-term quality of life should be chosen for stage I and II cancers. In more advanced disease, combined-modality regimes are frequently adopted, depending on the primary site.

Management of early stage disease:

Surgery alone: Potential advantages of surgery alone include the following:

- It provides complete pathological staging of the
- It provides quick local clearance of disease
- Treatment of metachronous head and neck tumors is not compromised
- It avoids the toxicity of radiotherapy

Radiotherapy alone: A typical radiotherapy regime might comprise 60-70 Gy administered to the primary site over 6-7 weeks. Intensity-modulated radiation therapy (IMRT) is an advanced from of conformal radiation therapy frequently used for head and neck cancer, in which a large number of treatment fields are used to maximize conformal radiation to the tumor and spare surrounding normal structures.

Advantages of primary radiotherapy include the following-

- Avoidance of operative mortality in patients who have significant comorbidities.
- Where surgical clearance is difficult or impossible.
- Organ conservation is more likely, including preservation of the voice and swallowing.
- The option of elective radiotherapy treatment of clinically occult regional lymph node disease has relatively little extra morbidity (compared with elected neck dissection)
- Surgery remains an option as salvage therapy in event of treatment failure.
- Radiotherapy enables treatment of multiple synchronous primaries.

Toxicity of radiotherapy includes the following-

- Mucositis and a dry mouth.
- Chronic ulceration of the mucosa and osteonecrosis are potential risks.

Surgery versus radiotherapy ?

Cure rates with primary radiotherapy are generally believed to be equivalent to those for surgery for early-stage disease of many head and neck tumors. In certain clinical situation, radiotherapy is clearly the first-line treatment of choice, e.g. in nasopharyngeal carcinoma when the use of surgery is limited to staging. In other clinical situations, surgery is the first choice if at all possible, e.g. tumors of the nasal cavity and paranasal sinuses.

Combined surgery and radiotherapy

Bulky tumors are generally best treated by a combination of surgery and radiotherapy, to minimize the risk of locoregional disease recurrence. The most important risk factors for prediction of recurrence and the need for postoperative radiotherapy are the following:

- Positive resection margins
- T3-T4 primary tumor
- Extracapsular lymph node spread
- ≥N2 disease
- Perineural or vascular invasion
- Poorly differentiated tumor

Contd.

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In Locally advanced SCCHN:

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- Erbitux+RT helps patients to complete the therapy[1]
- Erbitux+RT is the only weekly regimen with NCCN Category-1 recommendations[1,2#]

1. Curran D, et al. J Clin Oncol 2007;25:2191–2197 2. NCCN guidelines V2. 2018 Cetuximab (category 1 for oropharynx, hypopharynx, or larynx; category 2B for lip, oral cavity, ethmoid sinus, maxillary sinus, occult primary)
Non platinum based weekly regimen

Erbitux (Cetuximab) Abbreviated Prescribing Information:

SCHEDULE H PRESCRIPTION DRUG CAUTION Not to be sold by retail without the prescription of a Registered Medical Practitioner

Warning : To be sold by retail on the prescription of a Oncologist only

Before prescribing ERBITUX, please consult full prescribing information. **Presentation:** *ERBITUX 5 mg/mL solution for infusion. Excipients: sodium chloride, glycine, polysorbate 80, citric acid monohydrate, sodium hydroxide, water for injections. **Indications:** Epidermal growth factor receptor-expressing, RAS wild-type metastatic colorectal cancer (mCRC): in combination with irinotecan-based chemotherapy (CT), or in first-line in combination with FOLFOX, or as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan. Squamous cell carcinoma of the head and neck (SCCHN): in combination with radiation therapy (RT) for locally advanced (LA) disease or with platinum-based chemotherapy (pt-CT) for recurrent and/or metastatic (R/M) disease. **Dosage and administration:** Once a week, intravenously with an infusion pump, gravity drip or a syringe pump; separate infusion line. Initial dose 400 mg/m2 (should be given slowly with max. infusion rate: 5 mg/min; the recommended infusion period is over 120 mins); subsequent weekly doses 250 mg/m2 (Max. infusion rate: 10 mg/min; recommended over 60 mins). Supervision/monitoring by a physician experienced in antineoplastic therapy throughout infusion and for at least one hour afterwards is required. Resuscitation equipment must be ensured. Prior to first infusion: premedication with antihistamines and corticosteroids at least 1 hour prior to administration of ERBITUX; also recommended for all subsequent infusions. Administer CT not earlier than one hour after ERBITUX infusion. *mCRC:* administer ERBITUX until disease progression. Wild-type RAS tumor status must be verified prior to first infusion by an experienced laboratory using validated test methods. *LA SCCHN:* start ERBITUX therapy one week before RT and continue throughout treatment. *R/M SCCHN:* administer ERBITUX in combination with pt-CT and continue until disease progression**Special Populations:** *Elderly:* no dose adjustment required (limited experience in patients 75 years). *Pediatric patients* (<18 years): efficacy not established, no new safety signals. *Others:* only patients with adequate renal, hepatic and hematological parameters have been investigated. **Contraindications:** Known severe hypersensitivity reactions (grade 3/4 NCI CTCAE). In combination with oxaliplatin-containing CT if mutated/unknown RAS status. Contraindications for concomitantly used CT or RT must be considered. **Special warnings and precautions:** *Severe infusion-related reactions (IRRs) including anaphylactic reactions:* May commonly occur, in some cases with fatal outcome; immediate and permanent discontinuation of ERBITUX therapy; may necessitate emergency treatment. May be anaphylactic or anaphylactoid in nature or represent a cytokine release syndrome. Symptoms may occur during the first infusion and for up to several hours afterwards or with subsequent infusions and may include bronchospasm, urticaria, increase or decrease in blood pressure, loss of consciousness or shock. In rare cases, angina pectoris, myocardial infarction or cardiac arrest have been observed. The risk for anaphylactic reactions is much increased in patients with a history of allergy to red meat or tick bites or positive results of tests for IgE antibodies against Erbitux. *Mild/moderate IRRs:* decrease infusion rate, also for all subsequent infusions. Closely monitor patients with reduced performance status (PS) and pre-existing cardio-pulmonary disease. *Skin reactions:* oral tetracyclines and topical 1% hydrocortisone cream with moisturizer may be considered for prophylactic use and medium to high-potency topical corticosteroids or oral tetracyclines for treatment (acc. to clinical practice guidelines). *Severe skin reaction (grade):*interrupt treatment, only resume if reaction resolves to grade 2. Second or third occurrence of severe skin reactions: resume at lower dose (200 mg/m2 after second, 150 mg/m2 after third) only if reaction resolves to grade 2. Fourth occurrence or failure to resolve to grade 2 during interruption: permanent discontinuation. *Interstitial lung disease:* if diagnosed, discontinuation and appropriate treatment. *Electrolyte disturbances:* determination of serum electrolyte levels recommended prior to and periodically during treatment. Electrolyte repletion (e.g. hypomagnesaemia; hypokalaemia as a consequence of diarrhea; hypocalcemia, particularly in combination with pt-CT) is recommended. *Neutropenia and related infectious complications:* careful monitoring is recommended particularly in patients experiencing skin lesions, mucositis or diarrhea that may facilitate the occurrence of infections. *Severe and sometimes fatal cardiovascular events:* increased frequency associated with age 65 years or PS has been observed. Patient cardiovascular status, PS and concomitant administration of cardiotoxic compounds (e.g. fluoropyrimidines) should be taken into account. *Acute or worsening symptoms of keratitis:* refer promptly to an ophthalmologist, consider benefit/risk of continuing use. *Confirmed ulcerative keratitis:* interruption or discontinuation of ERBITUX. Use with caution in patients with history of keratitis, ulcerative keratitis or severe dry eye (e.g. use of contact lenses). *CRC patients with mutated/unknown RAS status:* ERBITUX should not be used since negative effects on PFS and OS as add-on to FOLFOX4 have been reported in RAS mutated tumors. There is limited experience in combination with RT in mCRC. **Fertility, pregnancy and lactation:** Only use during pregnancy or in women with inadequate contraception if potential benefits justify potential risks to fetus. Breast-feeding during treatment and 2 months later is not recommended. Effects on male/female fertility have not been evaluated. **Undesirable effects:** *Very common* (1/10): skin reactions (e.g. acne-like rash and/or pruritus, dry skin, desquamation, hypertrichosis, or nail disorders, single cases of skin necrosis), hypomagnesaemia, mild/moderate IRRs (e.g. fever, chills, dizziness, dyspnea), increased liver enzyme levels and mucositis, in some cases severe. Mucositis may lead to epistaxis. *Common* (1/100, <1/10): headache, conjunctivitis, diarrhea, nausea, vomiting, fatigue, dehydration, hypocalcemia, anorexia, weight loss, severe IRRs.*Uncommon* (1/1000, <1/100): blepharitis, keratitis, deep vein thrombosis, pulmonary embolism or interstitial lung disease. Very rare (<1/10,000): Stevens-Johnson syndrome/toxic epidermal necrolysis. *Frequency not known:* superinfection of skin lesions with subsequent complications (e.g. cellulitis, erysipelas, staphylococcal scalded skin syndrome, necrotising fasciitis, sepsis), aseptic meningitis. In combination with local RT in SCCHN: typical undesirable effects of RT (e.g. mucositis, radiation dermatitis, dysphagia or leukopenia, mainly as lymphocytopenia). In combination with ERBITUX: slightly higher rates of severe acute radiation dermatitis, mucositis and late RT-related events. **Interactions:** *Fluoropyrimidines:* increased frequency of hand-foot syndrome and cardiac ischaemia (e.g. myocardial infarction and congestive heart failure). *Capecitabine and oxaliplatin (XELOX):* frequency of severe diarrhoea may be increased. *pt-CT:* increased frequency of severe leukopenia/neutropenia, which may lead to a higher rate of febrile neutropenia, pneumonia and sepsis. Storage: Store in a refrigerator (2ºC – 8ºC) Shelf life: 48 months Date of revision: April 2015

For further information refer to full prescribing information or write to:

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Treatment of locally advanced unresectable disease

Chemoradiotherapy:

>60% of SCHNC have advanced locoregional disease at presentation (state III/IV M0). In some cases surgery remains an option and can result in 5 year survival rates of 20%-50% if combined with radiotherapy. In many cases surgery is either technically not possible or would be associated with unacceptable morbidity, e.g. base of tongue cancer requiring glossectomy and consequent loss of normal voice and swallow. The use of radiotherapy with concurrent chemotherapy has been demonstrated to be associated with a survival advantage over treatment with radiotherapy alone. Although
combined-modality therapy is associated with increased acute toxicity compared with radiation alone, concurrent full-dose platinum-based chemotherapy with radiation should be considered standard therapy to optimize the chance for organ preservation, locoregional control and survival in patients with good performance status, and relatively few comorbidities.

Role of targeted therapy in LAD-SCCHN: Patients not suitable to platinum based therapy Although the platinum based therapy is a preferred choice for treatment of fit patients LA-SCCHN, the toxic effects platinum ineligibility, replacing cisplatin with other (less toxic) cytotoxic agents or cetuximab may be taken into consideration.

Management of metastatic disease:

Chemotherapy: Certain chemotherapy agents, e.g. cisplatin, docetaxel, 5-fluorouracil, methotrexate and bleomycin have been shown to be active in advanced squamous cell carcinoma. The highest response rates appear to be achieved be combination regimes, although a survival advantage with this approach has not consistently been demonstrated. The EGFR-targeted monoclonal antibody**.** Cetuximab has shown significant clinical benefits in the treatment of both loco regionally advanced and recurrent and/or metastatic SCCHN. It has shown improvement in median survival from 7 to 10 months when it was added to platinum and 5-fluorouracil chemotherapy.

Recently immune-oncology drugs (e.g. nivolumab) have shown promising activities in relapse/refractory disease.

In last follow up, counseling for cessation of smoking, tobacco, chewing, alcohol consumption and rehabilitation and assessment of treatment related morbidities (e.g. radiation induced hypothyroidism) are equally important.

Upcoming conference of SoMex

2nd Annual Indian breast cancer conference (International meeting) on 5th to 7th October 2018. (Accrediated by RMC)

For details log on www.ibccindia.com

Recent Activities of SoMex

- **SoMex organized CME on "HCC" on 14 September 2018.**
- **SoMex organized CME on "CLL" on 5 September 2018 with International speaker.**
- **SoMex organized CME on "Lung Cancer" on 20 July 2018.**

BOOK - POST

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If undelivered please return to:
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Printed and Published by :
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