NHS
Kent and Medway
Cancer Collaborative

# Oncological Treatment of Head and Neck Cancer

## Pathway of Care

Kent & Medway Cancer Collaborative

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# 1.0 INTRODUCTION

## 1.1 Overview

This document has been written to provide guidance on the treatment of head and neck cancer in the Kent & Medway Cancer Collaborative.

Radiotherapy schedules are as defined in the Kent Oncology Centre Quality System Clinical Protocols (Disease Management and Radiotherapy Protocols).

See network chemotherapy prescribing proformas for details of chemotherapy / anti-cancer regimens.

All patients will be considered for entry into a clinical trial (see appendix A).

All patients should be discussed within a multidisciplinary team meeting before commencing initial treatment.

For skin cancers and sarcomas arising in the head and neck area, reference should be made to skin cancer and sarcoma treatment guidelines.

Please note, some of the drugs/doses recommended within this document are outside of the U.K. licensed marketing authorisation.

Patients with NTRK gene fusion may be considered for entrectinib or larotrectinib in line with commissioning criteria.

## 1.2 Guidelines on the Management of Drug-specific Toxicity

**DPD testing:**

Fluoropyridimines are rapidly degraded by dihyropyrimidine dehydrogenase (DPD). Therefore, DPD deficiency can lead to severe toxicity or death following treatment with, for example, 5-FU or capecitabine. Homozygotes to DPD are rare (but likely to have severe toxicity or die).
All patients, prior to commencing treatment with a fluoropyrimidine based therapy (5-fluorouracil, capecitabine) should be screened for four DPYD gene variants which have been associated with fluoropyrimidine-associated toxicity.
Patients only require this genomic test to be carried out once, at the start of their first fluoropyrimidine treatment, as the results remain applicable to subsequent fluoropyrimidine cycles and future treatment regimens containing a fluoropyrimidine.
Within the clinical pathway, the genomic test should be ordered for eligible patients at the point of consent for fluoropyrimidine chemotherapy or earlier if appropriate.
Clinicians should follow the UK Chemotherapy Board guidance on dosing adjustments for fluoropyrimidine therapy following detection of a DPYD variant.

**Uridine triacetate:**

Uridine triacetate (Vistoguard) is an antidote for management of early-onset severe or life-threatening toxicity, including diarrhoea, within 96 hours following 5FU or capecitabine administration. It is not licensed in the UK, but is available on an unlicensed basis via a 24/7 emergency ordering service, via tel 0207 8872235.
The policy statement (link below) from NHSE contains information on inclusion / exclusion criteria and also dosing information.
https://www.england.nhs.uk/wp-content/uploads/2020/03/1929_Policy_Statement_Final_v2.pdf

# 2.0 SQUAMOUS CARCINOMAS OF THE LIP AND ORAL CAVITY

This group includes cancers of the lip, anterior two-thirds of the tongue, floor of mouth, gum (alveolus) and hard palate.

## 2.1 Radical Treatment

Surgery is the preferred initial treatment.

Those with disease beyond the scope of surgery or those not sufficiently fit for surgery may be considered for radical radiotherapy +/- chemotherapy; neo-adjuvant chemotherapy can be considered for rare selective cases. For neo-adjuvant treatment options see section 3.2.

## 2.2 Adjuvant Treatment

Histology is reviewed in the H&N Multidisciplinary Meeting with emphasis on risk stratification. On this basis, patients may be grouped into those at high, intermediate or low risk of locoregional recurrence.

High risk features are:

- The presence of primary tumour at the resection margin
- Nodal involvement with extracapsular spread.

Intermediate risk features are:

- Resection margins <5mm
- Perineural infiltration
- Discohesive invasion front
- Vascular invasion
- Nodal involvement without extracapsular spread
- Adenoid cystic carcinoma

Those with high risk features are considered for postoperative concurrent chemoradiotherapy. Radiotherapy doses are governed by the respective Q Pulse Documents on radiotherapy protocols.

Concurrent chemotherapy options include:

| Drug | Dose | Duration | No. of Cycles |
|---|---|---|---|
| **Cisplatin** | 80-100mg/m$^2$ | Every 3-4 weeks during radiotherapy | 2- 3 cycles |
| **Cisplatin** | 40mg/m$^2$ | Every week during radiotherapy | 6 cycles |
| **Carboplatin*** | AUC 4-5 | Every 3-4 weeks during radiotherapy | 2- 3 cycles |
| **Carboplatin*** | AUC 1 – 1.5 | Every week during radiotherapy | 6 cycles |

*(if unable to use cisplatin)

Those with intermediate risk features are considered for postoperative radiotherapy alone.

## 2.3 Palliative Treatment

### 2.3.1 Palliative Radiotherapy

Palliative radiotherapy may be considered as initial treatment for those with locally advanced disease not amenable to radical treatment or patients with poor performance status.

Radiotherapy doses are governed by the respective Q Pulse Documents on radiotherapy protocols.

### 2.3.2 Palliative Systemic therapy

Systemic treatments may be considered for selected patients with metastatic disease.

Patients should have their PD-L1 status assessed.

Selected patients should have their NTRK status assessed.

Treatment options which can be considered are below.

| 1st Line | | | |
|---|---|---|---|
| **Regimen** | **Doses** | **Duration** | **Indication** |
| **Pembrolizumab Monotherapy** – previously untreated metastatic or unresectable recurrent disease; PD-L1 positive, CPS ≥1 | ▪ 200mg every 21d<br>**OR**<br>▪ 400mg every 42d where appropriate | Max 2 years treatment or disease progression (whichever comes earliest) | Non-bulky disease |
| **Cetuximab + Cisplatin + 5FU** Followed by maintenance Cetuximab | ▪ Cetuximab 400mg/m$^2$ loading dose, then 250mg/m$^2$ weekly<br>**&**<br>▪ Cisplatin 100mg/m$^2$ every 21d<br>**&**<br>▪ 5FU 1000mg/ m$^2$ day 1 – 4 every 21d<br><br>▪ Maintenance Cetuximab 500mg/m$^2$ | Cisplatin and 5FU with weekly Cetuximab x Max 6 cycles<br><br>Followed by<br><br>Maintenance cetuximab until disease progression. | For bulky or symptomatic disease. |
| **Cisplatin + 5FU** | ▪ Cisplatin 100mg/m$^2$ every 21d<br>**&**<br>▪ 5FU 1000mg/ m$^2$ day 1 – 4 every 21d | Max 6 cycles | |
| Carboplatin can be substituted for cisplatin; for those unlikely to tolerate large fluid loads or borderline renal function, performance status or ototoxicity.<br>Carboplatin AUC 4 - 5 | | | |
| **Subsequent lines** | | | |
| **Paclitaxel** | ▪ 80mg/ m$^2$ d1, d8, d15<br>▪ Every 28d | Max 6 cycles | Can be considered as first line in certain cases |
| **Nivolumab monotherapy** | ▪ 240mg every 2 weeks<br>**OR**<br>▪ 480mg every 4 weeks where appropriate | Until loss of clinical benefit or excessive toxicity or patient choice to discontinue therapy. | For SCC only after prior platinum-based chemotherapy.<br>**CANNOT BE USED** if received prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody. |

| | | | |
|---|---|---|---|
| **Gemcitabine + Cisplatin** | • Gemcitabine 1200mg/ $m^2$ d1 and d8<br>• Cisplatin 75mg/ $m^2$ d1<br>• Every 21d | Max 6 cycles | |
| **Gemcitabine + Carboplatin** | • Gemcitabine 1200mg/ $m^2$ d1 and d8<br>• Carboplatin AUC5 d1<br>• Every 21d | Max 6 cycles | |
| **Gemcitabine monotherapy** | • 1250mg/ $m^2$ d1, d8 every 21d | Max 6 cycles | |
| **Docetaxel** | • 75mg/ $m^2$, Every 21d | Max 6 cycles | |

Cetuximab is only licenced in oral cavity tumours in the palliative setting, as per NICE guidance August 2017.

# 3.0 SQUAMOUS CARCINOMAS OF THE OROPHARYNX, HYPOPHARYNX AND LARYNX

This group covers all oropharyngeal tumours (soft palate, tonsil, base of tongue, pharyngeal wall); hypopharynx (pharyngeal wall, pyriform fossa and postcricoid) and laryngeal tumours (supra, sub and trans glottis and epiglottis).

## 3.1 Radical Treatment

Primary radiotherapy +/- concurrent chemotherapy is the preferred treatment for such cases. Please refer to the higher operational policy for the specific indications for each tumour subgroup indication.

For concurrent chemo-radiotherapy regimens please refer to section 2.2.

Cetuximab can be given concurrently with radiotherapy for patients' PS 0-1, whom platinum based therapy is not appropriate.

Cetuximab 400mg/$m^2$ loading dose 1 week prior to radiotherapy, then 250mg/$m^2$ weekly during radiotherapy and 1 week after.

## 3.2 Neo-adjuvant Treatment

Neo-adjuvant (induction) chemotherapy is recommended for locally advanced squamous cancers, such as T3/T4 disease and bulky nodal disease, prior to concurrent chemo-radiotherapy. Patients must be PS0-1, and aged 70 or less. *Treatment can be offered to older patients, but based on individual case review, comorbidities and MDT discussion.*

Regimens include:

| Regimen | Doses | Duration | Indication |
|---|---|---|---|
| **TPF** (docetaxel, cisplatin and 5FU) | • Docetaxel 75mg/ $m^2$ d1<br>• Cisplatin 75mg/ $m^2$ d1<br>• 5FU 750mg/ $m^2$ d1-d5<br>• 21d | 2-4 cycles | Consider starting at 60mg/$m^2$ for docetaxel/cisplatin and 600mg/$m^2$ 5FU for patients with comorbidities |
| **T-Carbo-F** | • Docetaxel 75mg/ $m^2$ d1<br>• Carboplatin AUC5 d1<br>• 5FU 750mg/ $m^2$ d1-d5<br>• 21 d | 2-4 cycles | Consider starting docetaxel at 60mg/$m^2$ and carboplatin at AUC4 for selective cases with comorbidities |
| **TP or T-Carbo** | • Omitting 5FU; but as above | 2-4 cycles | As above |
| **Cisplatin + 5FU** | • Cisplatin 100mg/ $m^2$ d1<br>• 5FU 1000mg/m2 d1 – d4<br>• 21d | Up to max 6 cycles | |
| **Carboplatin +5FU** | • Carboplatin AUC5 d1<br>• 5FU 1000mg/ $m^2$ d1-d4<br>• 21d | Up to max 6 cycles | |

Surgery can be considered following chemotherapy for poor responders or based on individual cases as discussed in the MDT, with consideration for adjuvant radiotherapy+/-chemotherapy following surgery.

## 3.3 Palliative systemic therapy

Please see section 2.3.2 for the regimens which can be considered.

# 4.0 MALIGNANT SALIVARY GLAND TUMOURS

This group includes cancers of the parotid and submandibular glands and of minor salivary glands located within the oral cavity and pharynx.

## 4.1 Radical treatment

Surgery is the preferred initial treatment.

Those with disease beyond the scope of surgery or those not sufficiently fit for surgery may be considered for radical radiotherapy. There is no established role for concurrent chemoradiotherapy.

## 4.2 Adjuvant Treatment

Postoperative radiotherapy should be considered for those with high grade tumours or with tumour present at or close to resection margins.

## 4.3 Palliative Treatment

Palliative radiotherapy may be considered as initial treatment for those with locally advanced disease and poor performance status.

Chemotherapy may be considered for selected patients with metastatic disease and/or locally advanced locoregional disease beyond the scope of surgery and radiotherapy (excluding those with adenoid cystic carcinoma).

Chemotherapy regimens include:

| Regimen | Doses | Duration |
|---|---|---|
| **Carboplatin and paclitaxel** | ▪ Carboplatin AUC 5 D1<br>▪ Paclitaxel 175mg/ $m^2$ D1<br>▪ Every 21D | Max 6 cycles |
| **ECF** (epirubicin, cisplatin, 5FU) | ▪ Epirubicin 50mg/ $m^2$ D1<br>▪ Cisplatin 60mg/$m^2$ D1<br>▪ 5FU 1400mg/ $m^2$/7days D1, D8, D15<br>▪ Every 21D | 6 cycles |
| **ECX** (epirubicin, cisplatin, capecitabine) | ▪ Epirubicin 50mg/ $m^2$ D1<br>▪ Cisplatin 60mg/ $m^2$ D1<br>▪ Capecitabine 625mg/ $m^2$ BD continuously<br>▪ Every 21D | 6 cycles |
| **E-Carbo-F** (epirubicin, carboplatin, 5FU) | ▪ Epirubicin 50mg/ $m^2$ D1<br>▪ Carboplatin AUC 5 D1<br>▪ 5FU 1400mg/ $m^2$/7days D1, D8, D15<br>▪ Every 21D | 6 cycles |
| **E-Carbo-X** (epirubicin, carboplatin and capecitabine) | ▪ Epirubicin 50mg/ $m^2$ D1<br>▪ Carboplatin AUC 5 D1<br>▪ Capecitabine 625mg/ $m^2$ BD continuously | 6 cycles |
| **Paclitaxel** | ▪ 80mg/ $m^2$ D1, D8, D15<br>▪ Every 28D | Max 6 cycles |
| **Cisplatin and vinorelbine** | ▪ Cisplatin 75mg/$m^2$ D1 and vinorelbine 25mg/$m^2$ D1 and D8<br>▪ Every 21D | Max 6 cycles |

Adenoid Cystic Carcinomas:

**Patients should be considered for clinical trials where appropriate.**
Can consider cisplatin 75mg/$m^2$ D1 and vinorelbine 25mg/$m^2$ D1 and D8, 21D cycles, for max 6 cycles.

# 5.0 SINO-NASAL AND EAR CANCERS

This group includes cancers of the nasal cavity, maxillary or ethmoid sinuses (rarely frontal or sphenoidal sinuses), auditory canal and middle ear. Cancers of the pinna and nasal ala are considered as skin cancers (see skin cancer treatment guidelines).

## 5.1 Radical treatment

Surgery is the preferred initial treatment; followed by postoperative radiotherapy.

Those with disease beyond the scope of surgery or those not sufficiently fit for surgery may be considered for radical radiotherapy.

Concurrent chemoradiotherapy may be considered for those with locally advanced squamous sino-nasal cancer and a good response to induction chemotherapy.

Concurrent chemotherapy regimens use guidance in section 2.2.

## 5.2 Neo-adjuvant treatment.

This can be considered for certain exceptional cases deemed inoperable, as part of an MDT decision. If response is seen, then patients should be considered for surgery vs radical radiotherapy +/- chemotherapy.

Chemotherapy Regimens which can be considered are:

| Regimen | Doses | Duration |
|---|---|---|
| **TP** (docetaxel and cisplatin) | • Docetaxel 75mg/ $m^2$ D1<br>• Cisplatin 75mg/ $m^2$ D1<br>• Every 21d | 2- 4 cycles |
| **T-Carbo** (docetaxel and carboplatin) | • Docetaxel 75mg/ $m^2$ D1<br>• Carboplatin AUC 5 D1<br>• Every 21D | 2-4 cycles |
| **Cisplatin + 5FU** | • Cisplatin 100mg/ $m^2$ D1<br>• 1000mg/ $m^2$ D1 – D4<br>• Every 21D | Up to max 6 cycles |
| **Carboplatin +5FU** | • Carboplatin AUC5 D1<br>• 1000mg/ $m^2$ D1-D4<br>• Every 21D | Up to max 6 cycles |

## 5.3 Adjuvant treatment

Postoperative radiotherapy should be considered for those with high grade tumours or with tumour present at or close to resection margins.

Concurrent chemoradiotherapy may be considered for those with locally advanced squamous sino-nasal cancer with a good response to induction chemotherapy.

## 5.4 Palliative treatment

Please see section 2.3.2 for the regimens which can be considered.

# 6.0 NASOPHARYNGEAL CANCER

## 6.1 Radical Treatment

Radiotherapy can be offered alone for T1/T2 N0M0 disease. All other stages should be considered for radiotherapy +/- chemotherapy.

See section 2.2 for concurrent chemotherapy regimens.

## 6.2 Neo-adjuvant Treatment

Neo-adjuvant chemotherapy can be considered for selective cases.

Regimens include:

| Regimen | Doses | Duration | Indication |
|---|---|---|---|
| **Gemcitabine and cisplatin** | ▪ Gemcitabine 1000mg/ $m^2$ D1 and D8<br>▪ Cisplatin 80mg/ $m^2$ D1<br>▪ Every 21D | 2-4 cycles | This should be considered as 1st line option |
| Carboplatin can be substituted for cisplatin; for those unlikely to tolerate large fluid loads or borderline renal function, performance status or ototoxicity.<br>Carboplatin AUC 4 - 5 | | | |
| **TP** (docetaxel and cisplatin) | ▪ Docetaxel 75mg/ $m^2$ D1<br>▪ Cisplatin 75mg/ $m^2$ D1<br>▪ Every 21D | 2- 4 cycles | |
| **T-Carbo** (docetaxel and carboplatin) | ▪ Docetaxel 75mg/ $m^2$ D1<br>▪ Carboplatin AUC 5 D1<br>▪ Every 21D | 2-4 cycles | |

## 6.3 Palliative Treatment

Please see section 2.3.2 for the regimens which can be considered.

## 7.0 Miscellaneous Treatment

Based on particular pathological diagnoses, different chemotherapy regimens can be considered.

Regimens below

| | Regimen | Doses | Duration | Indication |
|---|---|---|---|---|
| Neuro-endocrine carcinomas or small cell variant | **Carboplatin and Etoposide** | ▪ Carboplatin AUC 5 D1<br>▪ Etoposide 100mg/ $m^2$ D1 IV<br>▪ 200mg/ $m^2$ D2 and 3 orally<br>▪ 21D cycle | 2 to 4 cycles if using as neoadjuvant<br>Max 6 cycles if using as palliative course | Can be used both neo-adjuvant or palliative |
| | **Cisplatin and Etoposide** | ▪ Cisplatin 75mg/ $m^2$ D1<br>▪ Etoposide 100mg/ $m^2$ D1 IV<br>▪ 200mg/ $m^2$ D2 and 3 orally<br>▪ 21D cycle | 2 to 4 cycles if using as neoadjuvant<br>Max 6 cycles if using as palliative course | Can be used both neo-adjuvant or palliative |
| ACE or CAV as 2nd line regimes<br>Consideration for clinical trials where appropriate | | | | |

Adenocarcinomas: see section 4.3 regimens, these can be used for all adenocarcinoma variants.
Consideration for clinical trials where appropriate.

Chemotherapy doses are based on the trial data which established these regimes. All chemotherapy doses should be considered in the context of the fitness and comorbidities of the patient and can be dose reduced at the clinician's discretion.

## 8.0 APPENDIX A: CLINICAL TRIALS

Refer to the local research team who will provide on request an orientation handbook, list of current trials and associated trial protocols and summaries.

**Contact numbers**

| | |
|---|---|
| **MTW – Clinical Trials Office** | 01622 225 033 |
| **Darent Valley Hospital – Clinical Trials Office** | 01322 428 100 ext. 4810 |
| **Medway Hospital – Clinical Trials Office** | 01634 825 094 |
| **East Kent Hospitals – Clinical Trials Office:** | |
| **Solid Tumours** | 01227 866 393 |

## 9.0 PERSONNEL AND CONTACT INFORMATION

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## 10.0 GLOSSARY

Acronyms in common usage throughout KMCC documentation

| | |
|---|---|
| BNF | British National Formulary |
| BOPA | British Oncology Pharmacist Association |
| CNB | Cancer Network Board |
| COSHH | Control of substances hazardous to health regulations. |
| CYP | Children & Young People (in relation to the IOG) |
| DCCAG | Diagnostic Cross Cutting Advisory Group |
| DOG | Disease Orientated Group (NSSG/TSSG/TWG) |
| DVH | Darent Valley Hospital |
| DGT | Dartford and Gravesham NHS Trust |
| EK | East Kent |
| EKHUFT | East Kent Hospitals University Foundation Trust |
| EPS | Electronic Prescribing System |
| FP10(HNC) | Prescriptions issued by hospital doctors for dispensing in the community |
| GP | General Practitioner |
| HoP | High Level Operational Policy |
| IOSC | Improving Outcomes: A Strategy for Cancer |
| IV | Intravenous |
| K&C | Kent & Canterbury Hospital, Canterbury, (EKHUFT) |
| KMCC | Kent & Medway Cancer Collaborative |
| KMCRN | Kent & Medway Cancer Research Network |
| KOMS | Kent Oncology Management System |
| LSESN | London & South East Sarcoma Network |
| MFT | Medway Foundation Trust |
| MTW | Maidstone & Tunbridge Wells NHS Trust |
| NHS | National Health Service |
| NMP | Non-medical prescriber |
| NPSA | National Patient Safety agency |
| NOG | Non-Surgical Oncology Group<br>*(Permanent oncologist sub group of the DOGs with a specific responsibility for chemo/rad pathways and advice to the DOG, Network and GEOGRAPHICAL LOCATIONs on new drugs)* |
| PoC | Pathway of Care<br>*(Network agreed disease site specific clinical guidelines)* |
| QEQM | Queen Elizabeth the Queen Mother Hospital, Margate (EKHUFT) |
| QoL | Quality of life |
| QSIS | Quality service information system |
| QST | Quality Surveillance Team |

| | |
|---|---|
| RAT | Research and Trial Group<br>*(Permanent sub-group of the DOGs with a specific responsibility for taking forward the clinical trials agenda)* |
| RMH | Royal Marsden Hospital |
| RNOH | Royal National Orthopaedic Hospital |
| SACT | Systemic Anti-Cancer therapy |
| SACT regimen | Systemic Anti-cancer prescription on the electronic prescribing system |
| SACT protocol | Systemic Anti-cancer protocol on KMCC website |
| TTO | Treatment to take home |
| QVH | Queen Victoria Foundation Trust Hospital East Grinstead |
| UCLH | University College Hospital London |
| WHH | William Harvey Hospital, Ashford (EKHUFT) |
| WK | West Kent |

## 11.0 DOCUMENT ADMINISTRATION

| | |
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| **Co-author(s)** | C. Waters / A. Zeniou |
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| April 2010 | 2 | Changes to palliative treatment gemcitabine regimens in section 2<br>Changes to radical treatment regimens in section 3.<br>(removal of carboplatin AUC 1.5 weekly and addition of carboplatin AUC 5 plus 5-fluorouracil 750mg/m$^2$) | Head and Neck NOG |

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| September 2022 | V10.1.1 | COVID interim funding link updated and CDF list referenced as resource. | M.Archer |
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