Kent and Medway Cancer Collaborative

Oncological Treatment of Skin Cancer

Pathway of Care

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1.0 ONCOLOGY PROVISION

1.1 Introduction

- This document has been written to provide guidance on the treatment of skin cancer in the Kent & Medway Cancer Collaborative. (NB: Treatment of cutaneous lymphoma is described within the Cutaneous Lymphoma Pathway of Care.)
- Radiotherapy schedules are as defined in the Kent Oncology Centre Quality System Clinical Protocols.
- All patients will be considered for entry into a clinical trial (see appendix A).
- See network chemotherapy prescribing proformas for details of chemotherapy / anti-cancer regimens.
- All chemotherapy regimes in these guidelines can be dose reduced at the consultant's discretion based on the patient factors.
- All patients should be discussed within a multidisciplinary team meeting before commencing initial treatment.
- Topical treatment will be discussed separately within the Skin Pathway of care documents.
- Patients with NTRK gene fusion may be considered for entrectinib or larotrectinib in line with commissioning criteria.

To allow for flexibility in the management of cancer during the COVID-19 pandemic, NHS England has endorsed interim treatment regimens for some cancer medicines. This is to reduce the need for direct patient contact for administration of drugs and to minimise potential side effects that make people more susceptible to viral infections and other ill-health effects that may add pressure to the health system. These interim treatment regimens can be access here:

https://www.nice.org.uk/guidance/ng161/chapter/7-Modifications-to-usual-service#interim-nhs-england-treatment-regimens

1.2 DPD Testing

All patients, prior to commencing treatment with a fluoropyrimidine based therapy (5-fluorouracil, capecitabine or tegafur) 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.

1.3 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

1.4 Genomic Testing

The National Genomic Test Directory specifies which genomic tests are commissioned by the NHS in England, the technology by which they are available, and the patients who will be eligible to access a test. Molecular testing for skin cancer in Kent will evolve in line with this guidance.

2.0 BASAL CELL CARCINOMA

2.1 Radical Treatment

The majority of cases can be treated either surgically or with radiotherapy.

2.2 Adjuvant Treatment

Where excision is incomplete adjuvant radiotherapy may be considered.

2.3 Palliative Treatment

For extensive basal cell carcinoma palliative radiotherapy may be beneficial.

2.3.1 Systemic Treatment

Vismodegib is available for sub group of patients with multiple BCCs and should be considered for;

- Adults with Gorlin syndrome with non-locally advanced, non-metastatic multiple (≥6) clinically evident lesions at the point of decision to treat of which 3 are at least 5mm
- Adults with non-locally advanced, non-metastatic multiple (≥6 clinically evident lesions) at the point of decision to treat of which 3 are at least 5mm
- Patients must be appropriate for surgery i.e. surgically eligible tumours.

The NOG approved dose of vismodegib is 150mg po od for 12 weeks followed by an 8 week break for a total of 72 weeks as per CDF funding.

3.0 CUTANEOUS SQUAMOUS CARCINOMA

3.1 Radical Treatment

The majority of cases can be treated either surgically or with radiotherapy.

3.2 Adjuvant Treatment

Where excision is incomplete and for cancers with high risk features, adjuvant radiotherapy should be considered. For very high risk cases, concurrent chemoradiotherapy may be considered as a treatment option.

3.2.1 Adjuvant Chemotherapy Schedules for Concurrent Use with Radiotherapy

Drug	Dose	Duration	No. of Cycles
Cisplatin	100mg/m^2	Every 3 weeks	2- 3 cycles
Carboplatin	AUC 5	Every 3 weeks	2- 3 cycles
Weekly Cisplatin	40mg/m^2 (max. 80mg)	Every 7 days for 4-6 weeks	
Weekly Carboplatin	AUC 1.5	Every 7 days for 4-6 weeks	

3.3 Palliative Treatment

Systemic treatment is indicated in patients with disease where surgery and/or radiotherapy is not an option, as well as the presence of metastatic disease where comorbidities and patient fitness allows safe use of systemic agents. For extensive squamous cancers, palliative radiotherapy may be beneficial.

3.3.1 Palliative Chemotherapy

Cemiplimab is licensed for metastatic or locally advanced cutaneous squamous cell carcinoma patients who are not candidates for curative surgery or curative radiation treatment, and have not 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 with a performance status 0-1. In the majority of eligible patients this will be the preferred first line treatment option.

Chemotherapy may be considered for selected patients with metastatic disease and/or locally advanced locoregional disease beyond the scope of surgery and radiotherapy.

First line treatment options include platinum based chemotherapy or cemiplimab.
Cemiplimab
• Cemiplimab 350mg day 1 every 3 weeks.
Platinum based chemotherapy
• Cisplatin 100mg/m2 plus 5-fluorouracil 1000mg/m2/day for 4 days every 3 weeks (up to 6 cycles) *
Carboplatin should be substituted for cisplatin in those unlikely to tolerate a large fluid load or those with borderline renal function, borderline performance status or ototoxicity from cisplatin:
• Carboplatin AUC=5 plus 5-fluorouracil 1000mg/m2/day for 4 days every 3 weeks (up to 6 cycles) *
Other palliative chemotherapy regimens which can be considered:
Platinum based chemotherapy second line.
• Gemcitabine 1250mg/m2 D1 and D8 on a 21 day cycle (up to 6 cycles) * • Paclitaxel 80mg/m2 D1, D8, D15 on a 28 day cycle (up to 6 cycles) *
Small cell tumours / neuroendocrine tumours should be treated with carboplatin & etoposide* first line and ACE as second line treatment.

*H&N protocols should be followed.

4.0 CUTANEOUS MELANOMA

4.1 Radical treatment

Radical treatment of melanoma is surgical. Surgery is the preferred treatment modality.

4.2 Adjuvant Treatment

BRAF V600 mutation positive
• Dabrafenib with trametinib • Pembrolizumab for completely resected stage III melanoma • Nivolumab for completely resected stage III or IV melanoma
BRAF Wild Type
• Nivolumab for completely resected stage III or IV melanoma • Pembrolizumab for completely resected stage III melanoma

Adjuvant radiotherapy treatment is not routinely recommended in the era of adjuvant targeted and immunotherapy treatments, but may be considered in selected cases where local control is important.

4.3 Palliative Treatment

4.3.1 Palliative Chemotherapy & Immunotherapy

4.3.1.1 First Line

BRAF Wild Type Unresectable or Metastatic Melanoma Patients
• Ipilimumab and Nivolumab, followed by nivolumab monotherapy • Ipilimumab monotherapy • Pembrolizumab monotherapy • Nivolumab monotherapy • Consider clinical trials • Best supportive care
BRAF Mutation Unresectable or Metastatic Melanoma Patients
• Dabrafenib in combination with Trametinib • Ipilimumab and Nivolumab, followed by nivolumab monotherapy • Encorafenib in combination with binimetinib • Vemurafenib and cobimetinib (funding approval required) • Ipilimumab monotherapy • Pembrolizumab or Nivolumab monotherapy • Consider clinical trials • Best supportive care

4.3.1.2 Second Line

BRAF Wild Type Unresectable or Metastatic Melanoma Patients 2nd Line
Depending on first line treatment • Ipilimumab in combination with Nivolumab • Ipilimumab monotherapy • Pembrolizumab or Nivolumab monotherapy • Consider clinical trials • Chemotherapy - Dacarbazine, Carboplatin/Paclitaxel, Temozolomide (esp for CNS disease) • Best supportive care
BRAF Mutation Unresectable or Metastatic Melanoma Patients 2nd Line
• Dabrafenib in combination with Trametinib • Ipilimumab and Nivolumab, followed by nivolumab monotherapy • Encorafenib in combination with binimetinib • Vemurafenib and cobimetinib (funding approval required) • Ipilimumab monotherapy • Pembrolizumab or Nivolumab monotherapy • Consider clinical trials • Best supportive care

4.3.1.3 Third Line

Depending on first and 2nd line combinations

- Ipilimumab (if not previously received)
- Clinical trials
- Chemotherapy
- Re challenge
- Best supportive care

Additional treatment strategies which can be considered

- Talimogene laherparepvec oncolytic virus
- Referral for electrochemotherapy
- Palliative radiotherapy for symptom control

Patients with CNS metastases should be discussed at the neuro-oncology MDT to consider local therapy options (surgery or stereotactic radiotherapy). Whole brain radiotherapy can be considered on an individual basis where surgery or stereotactic radiosurgery is not deemed possible or appropriate.

5.0 CHOROIDAL MELANOMA

5.1 Localised Disease

No role for adjuvant systemic therapy.

For 6 monthly follow up imaging with liver US or CT scan based on individual patient recurrence risk.

5.2 Metastatic Disease

All patients should be considered for a clinical trial where possible

- Consider surgical resection
- Ipilimumab and nivolumab
- Single agent PD-1 inhibitor – pembrolizumab or nivolumab
- Chemotherapy - Dacarbazine, Carboplatin/Paclitaxel, Temozolomide (esp for CNS disease)
- Best supportive care

6.0 MERKEL CELL CARCINOMA

6.1 Radical Treatment

Surgery is the preferred treatment modality but radical radiotherapy can be considered in patients where surgical resection is not possible for locoregional control.

6.2 Adjuvant Treatment

Adjuvant radiotherapy should be considered in all patients except those with small, low risk tumours (no lymphovascular invasion, <1cm, low risk site, completely excised)

Radiotherapy may be indicated as postoperative treatment where margins of excision of the primary tumours are close, or for nodal involvement.

6.3 Palliative Treatment

6.3.1 Palliative Chemotherapy

- Avelumab may be considered as first or second line treatment or for those intolerant to first line treatment, with MDT approval.
- Carboplatin and etoposide x 4-6 cycles
- Progression on to 3rd line treatment must be considered on an individual patient basis.

6.3.2 Palliative Radiotherapy

Palliative radiotherapy may be considered for symptom management

7.0 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

8.0 PERSONNEL AND CONTACT INFORMATION

A comprehensive, up to date list of MDM contact details can be found on the KMCC website via the following link: http://www.KMCC.nhs.uk/resource-library/

9.0 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 *(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 *(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 *(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

10.0 DOCUMENT ADMINISTRATION

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Revision History			
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April 2009	1	Published	N Rowell Head & Neck, Skin & Thyroid NOG
April 2011	1.1	Addition of section 4.4.2 – palliative radiotherapy as a treatment option for Merkel cell carcinoma	Nick Rowell
June 2011	2	Published	Nick Rowell
May 2012	2.1 – 2.2	Changes to palliative treatment gemcitabine regimens in section 2 Changes to radical treatment regimens in section 3. (removal of carboplatin AUC 1.5 weekly and addition of carboplatin AUC 5 plus 5-fluorouracil 750mg/m^2)	Head & Neck, Skin & Thyroid NOG
July 2012	3	Published	Head & Neck, Skin

			& Thyroid NOG
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