Oncological Treatment of Skin Cancer

Pathway of Care

Kent & Medway Cancer Collaborative

Publication date	Jan 2019
Expected review date	NOV 2019
Version number	10
Version status	Final

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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 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.

2.0 Basal Cell Carcinoma

2.1 Overview

Nodal or distant metastases of basal cell carcinoma are extremely rare and therefore treatment relates only to that of the primary tumour. Chemotherapy has no role in the treatment of basal cell carcinoma.

2.2 Radical treatment

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

2.3 Adjuvant treatment

Where excision is incomplete adjuvant radiotherapy may be considered.

2.4 Palliative treatment

For extensive basal cell carcinoma palliative radiotherapy may be beneficial.

3.0 Cutaneous squamous carcinoma

3.1 Overview

While the majority of squamous cancers remain localised, a small proportion does develop nodal metastases. A few patients develop distant metastases. Squamous cancers may be more aggressive in the presence of immunosuppression or haematological disorders such as CLL.

3.2 Radical treatment

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

3.3 Adjuvant treatment

Where excision is incomplete, adjuvant radiotherapy may be considered. For very high risk cases, concurrent chemoradiotherapy may be considered as a treatment option.

3.3.1 Adjuvant chemoradiotherapy

- Cisplatin 100mg/m^2 every 3 weeks for 2-3 cycles
- Carboplatin AUC 5 every 3 weeks for 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

3.4 Palliative treatment

For extensive squamous cancers, palliative radiotherapy may be beneficial. Chemotherapy is indicated in patients with disease which is too extensive for surgery and/or radiotherapy.

3.4.1 Palliative chemotherapy

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

Radiotherapy may be beneficial to those with metastatic disease, particularly in bones or brain.

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 should be with platinum based chemotherapy.

- cisplatin 100mg/m^2 *plus*

  5-fluorouracil 1000mg/m^2/day for 4 days every 3 weeks (up to 6 cycles)*

  Treatment can commence at 25% dose reduction for patients with co-morbidities (i.e 75mg/m2 and 750mg/m2)

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/m^2/day for 4 days every 3 weeks (up to 6 cycles)*
  (5FU can commence at 750mg/m2 for patients with co-morbidities)

Other palliative chemotherapy regimens which can be considered:

Gemcitabine 1250mg/m^2 D1 and D8 on a 21 day cycle (up to 6 cycles)*

Paclitaxel 80mg/m^2 D1, D8, D15 on a 28 day cycle (up to 6 cycles)*

Small cell 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

Surgery is the preferred treatment modality.

4.2 Adjuvant treatment

BRAF V600 mutation positive

- Dabrafenib with trametinib

BRAF Wild Type

- Nivolumab (access scheme)

Radiotherapy may be indicated as post operative treatment following nodal dissection.

4.3 Palliative treatment

4.3.1 Palliative chemotherapy & immunotherapy

Chemotherapy see section 3.4.1

4.3.1.1 First line

Unresectable IIIb, IIIc or stage IVM1a malignant melanoma

- Talimogene laherparepvec oncolytic virus

BRAF Wild Type unresectable or metastatic melanoma patients

- Ipilimumab and Nivolumab
- Ipilimumab monotherapy
- Pembrolizumab or Nivolumab monotherapy
- Consider clinical trials
- Best supportive care

BRAF mutation unresectable or metastatic melanoma patients

- Dabrafenib in combination with Trametinib
- Ipilimumab in combination with Nivolumab
- Vemurafenib or Dabrafenib. Vemurafenib may be used for patients who are intolerant to dabrafenib (necessitating discontinuation of dabrafenib within first 2 months of treatment) and vice versa 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
- Best supportive care

BRAF mutation unresectable or metastatic melanoma patients 2nd line

Depending on first line combination

- Dabrafenib in combination with trametinib
- Ipilimumab in combination with Nivolumab
- Vemurafenib or Dabrafenib. Vemurafenib may be used for patients who are intolerant to dabrafenib (necessitating discontinuation of dabrafenib within first 2 months of treatment) and vice versa
- 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
- Clinical trials
- Chemotherapy
- Re challenge
- Best supportive care

4.3.2 Palliative radiotherapy

Radiotherapy may be considered for the control of symptoms caused by metastases particularly those to the bone, skin, lymph nodes or brain.

5.0 Merkel cell carcinoma

5.1 Overview

While the majority of Merkel cell tumours are localised, some patients present with nodal metastases and a few with distant metastases. Typically this disease presents in older patients for whom treatment decisions will be determined by performance status.
Merkel cell carcinomas will be treated within the cancer centre.

5.2 Radical treatment

Surgery is the preferred treatment modality.

5.3 Adjuvant treatment

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

5.3.1 Adjuvant chemotherapy

Adjuvant chemotherapy may be considered for those with nodal involvement

- **Carboplatin and etoposide x 4-6 cycles**

5.4 Palliative treatment

5.4.1 Palliative chemotherapy

See section 3.4.1

- Avelumab may be considered as first or second line treatment or for those intolerant to first line treatment, with MDT approval.

5.4.2 Palliative radiotherapy

Radiotherapy may be considered for the control of symptoms caused by metastases particularly those to the bone, skin, lymph nodes or brain.

6.0 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 Maritime Hospital – Clinical Trials Office	01634 825 094

East Kent Hospitals – Clinical Trials Office:

Solid Tumours (excluding Gynae)	01227 866 393

7.0 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

8.0 Glossary

Acronyms in common usage throughout KMCC documentation

CNB	Cancer Network Board
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
EK	East Kent
EKHUFT	East Kent Hospitals University Foundation Trust
HoP	High Level Operational Policy
IOSC	Improving Outcomes: A Strategy for Cancer
K&C	Kent & Canterbury Hospital, Canterbury, (EKHUFT)
KMCC	Kent & Medway Cancer Collaborative
KMCRN	Kent & Medway Cancer Research Network
LSESN	London & South East Sarcoma Network
MFT	Medway Foundation Trust
MTW	Maidstone & Tunbridge Wells NHS Trust
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
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
QVH	Queen Victoria Foundation Trust Hospital East Grinstead
UCLH	University College Hospital London
WHH	William Harvey Hospital, Ashford (EKHUFT)
WK	West Kent

9.0 Document Administration

Document Title	Oncological Treatment of skin cancer
Principle author	Nick Rowell
Co-author(s)	Caroline Waters
Current version number	9
Current status	Final
Agreed as “Fit for Publication” by	K Nathan
Original publication date	May 2018
Expected review date by	June 2019

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Revision History			
Date of revision	New Version Number	Nature of Revision	Confirmation of Accuracy by
April 2009	1	Published	Nick 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	Addition of Vemurafenib & Ipilumamab as treatment options for metastatic cutaneous melanoma reworking of section 3.3.1.2	Head & Neck, Skin & Thyroid NOG
July 2012	3	Published	Head & Neck, Skin & Thyroid NOG
January 2013	3.1	Draft – removal of funding approval required for both ipilimimab and vemurafenib following published NICE guidance.	
March 2013	4	Published	
October 2013	4.1	Draft – addition of vismodegib for basal cell carcinoma- section 2.4 Addition of dabrafenib (CDF list)	Nick Rowell
February 2014	5	Published	

August - December 2014	5.1- 5.2	Section 4.3.1.1 addition of ipilimumab 1st line Section 4.3.1.1 and 4.3.1.2. – removal of alpha interferon as a treatment option. Dabrafenib as per NICE TA 321 added	
January 2015	6	Published	N Rowell
November 2015	6.1	Addition of pembrolizumab for metastatic melanoma that has progressed following ipilimumab. Addition of first line pembrolizumab for metastatic melanoma.	
February 2016	6.2	Addition of Nivolumab	N Rowell/ A Clarke
April 2016	7	Published	
August 2016	7.1	Updated in line with NICE TA 396 and 400	
October 2016	7.2	Review at the H& N NOG. Addition of Carboplatin to section 3.3.1 Removal of cytotoxic chemotherapy options as first line treatment section 4.3.3.1 and added to third line setting. Section 4 reviewed by A Clarke	
June 2017	8	Published	H&N NOG
April 2018	8.1-8.5	Addition of Avelumab to section 5.4.1 Palliative chemotherapy & immunotherapy updated information section 3.4.1 Section 2.4 Vismodegib removed from guidance. 4.3.1 Palliative chemotherapy & immunotherapy updated information 5.4.1 updated 7.0 Updated web link added Sections in 4 numbering corrected Section 3.3.1 updated	H&N NOG
May 2018	V9	Published	K Nathan
NOV 2018	V9.1	Update to section 5.4 avalumab Update to section 4.2 adjuvant treatment 4.3.1 Palliative chemotherapy & immunotherapy: confirmed all protocols	H&N NOG