North of Scotland Clinical Management Guideline (CMG): Oesophageal Cancer (Squamous and Adenocarcinoma)

Last Updated 07/09/2023

Lead Group: North Cancer Upper GI Pathway Board (NCGPB) **File Reference:** NCA-CMG-OES V4
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For symptoms of suspected Upper GI cancer, please refer to the Scottish Referral Guidelines for Suspected Cancer

Contents

Staging

All patients with a confirmed diagnosis of Oesophageal cancer will have their cancer staged using the TNM staging system as documented on Page 6 of this CMG.

Cancer staging will allow a clinical decision on treatment options to be made in accordance with the guidance provided by this CMG in the management of patients aged 18 years and older with Oesophageal cancer.

General Principles

- Referrals should be vetted in accordance with the Scottish Referral Guidelines for Suspected Cancer.
- All patients must be discussed at MDT Meetings throughout their patient journey as required.
- Where available, clinical trials should always be considered as the preferred option for all eligible patients and consideration given to referral to other centres in Scotland.
- Patients must be involved in all decision-making relating to their care with informed consent required for patients undergoing treatment.
- A list of SACT regimens is provided (Page 7).
- All patients should be identified to the Clinical Nurse Specialist at the earliest opportunity for assessment and ongoing specialist advice, education, co-ordination of care and psychological/emotional/social support for both the patient and their relatives throughout the treatment pathway.
- At all stages through the treatment pathway, any treatment plans should be discussed with the patients during their preparation and subsequent review, patients should be provided with written information and/ or signposted to accredited resources. Primary |Care should be notified and kept updated of patients' pathway progress.

All Patients: Initial Investigations

- Full medical history
- Clinical examination
- Routine blood profile (Full Blood Count, U+E, LFT, CA + HER2* status)
- Endoscopic visualisation of oesophagus
- Biopsy
- CT Thorax, Abdomen and Pelvis
- Performance Status (ECOG and/or ASA or other)
- Nutritional screening (MUST score and referral to dietitian if MUST ≥2)

**HER2 status should be undertaken on all patients being considered for palliative systemic treatment.*

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Pathology

For Biopsy (Site, Type, Differentiation)

For Resection (in addition to above) - Margin Status, nodal involvement, local invasion, background abnormalities

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All Patients: Further Investigations (if indicated)

- Formal fitness assessment (may include CPEX after MDT discussion)
- EUS
- PET-CT
- HER2 status*
- PDL1 CPS*

**HER2 status should be undertaken on all patients being considered for palliative systemic treatment.*

North Cancer Alliance

North of Scotland Clinical Management Guideline (CMG): Oesophageal Cancer Treatment Overview

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Evaluation	Treatment	Follow-Up

Nutritional Screening – all patients identified as 'at risk' by MUST screening tool will be referred for assessment and nutritional care planning/support.

<u>Clinical Assessment</u>
History
Physical Examination
Performance Status
Nutritional Screening #

<u>Investigations</u>
OGD and Biopsy
CT of Chest, Abdomen & Pelvis
HER 2 status *

*HER2 status should be undertaken on all patients being considered for palliative systemic treatment.

**For any palliative patient to be considered for SACT, PDL1 should be tested in the HER2 negative group of adenocarcinomas

MDTM Discussion

CURABLE OR POTENTIALLY CURATIVE DISEASE

<u>Additional Assessments</u>
Formal fitness assessment (may include CPEX)

<u>Additional Investigations as required</u>
EUS
PET CT
HER 2 status *
MRI Liver
Laparoscopy including peritoneal cytology

Small mucosal lesion T1a N0 → Endoscopic Mucosal Resection → MDTM → Follow-up (see page 5)

MDTM Review Curative

For a few carefully selected patients only

Pre-operative chemotherapy or pre-operative chemoradiotherapy → Surgery → MDTM → Further chemotherapy if given pre-operatively → Follow-up (see page 5)

Definitive Chemoradiotherapy Or Radical Radiotherapy → Follow-up (see page 5)

INCURABLE DISEASE → Non Curative Treatment (see page 4)**

North of Scotland Clinical Management Guideline (CMG): Oesophageal Cancer – Relapse disease

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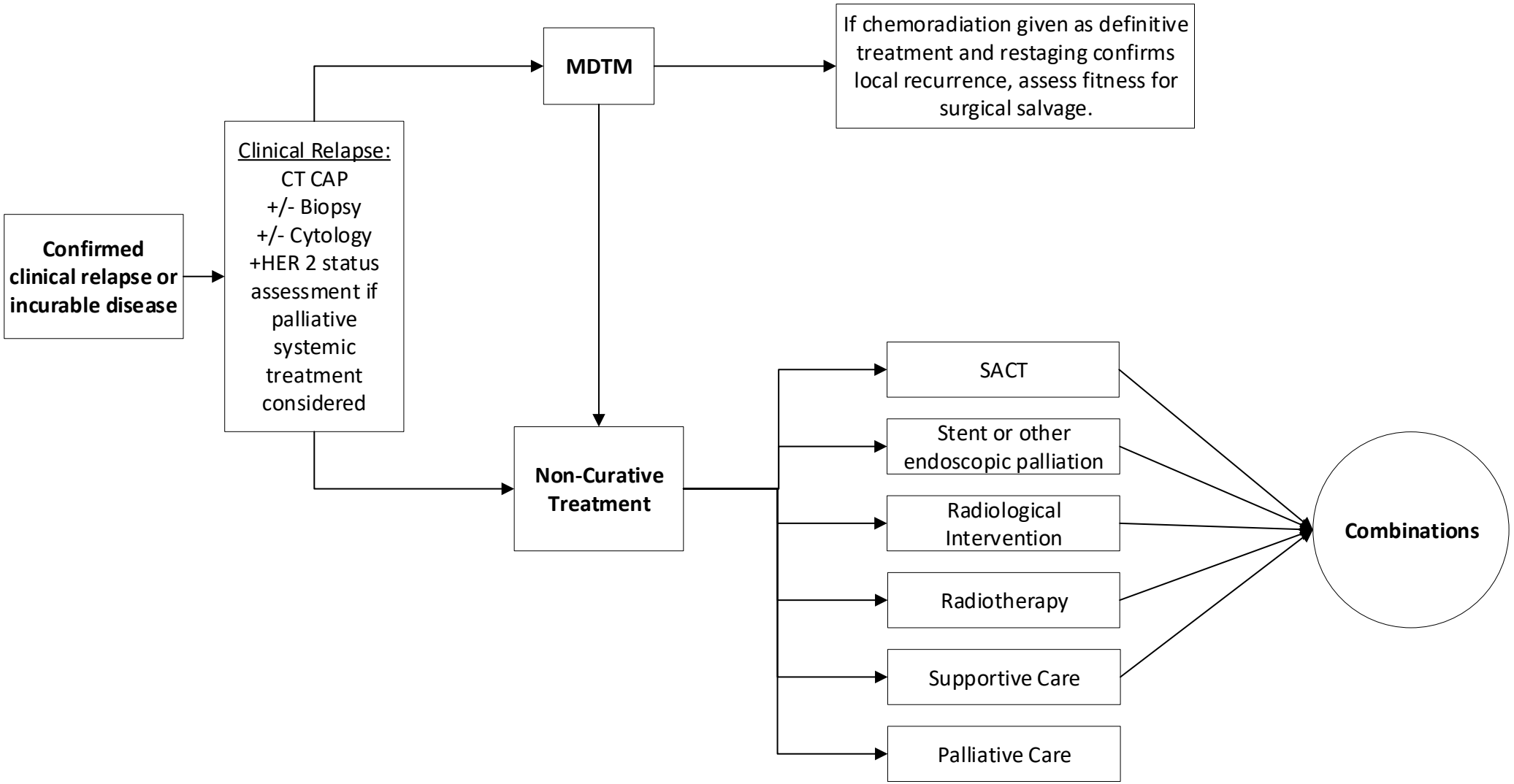
Evaluation	Treatment	Follow-Up



There continues to be a lack of clinical evidence or definitive guidance to support a regional recommendation on post-treatment follow up.

Consequently (and excepting for patients who are participating in a clinical trial and who should thereafter be followed up according to the applicable trial protocol), it is recommended that:

- All patients should have Holistic Needs Assessment (HNA) completed as part of their discharge planning
- Any post treatment follow-up should be determined on an individual patient basis and according to local policies currently in place

Stage	Definition
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	High Grade Dysplasia, defined as malignant cells confined by the basement membrane
T1	Tumour invades lamina propria, muscularis mucosae, or submucosa
T1 a	Tumour invades the lamina propria or muscularis mucosae
T1 b	Tumour invades submucosa
T2	Tumour invades muscularis propria
T3	Tumour penetrates the adventitia
T4	Tumour invades adjacent structures
T4 a	Tumour the pleura, pericardium, azygos vein, diaphragm or peritoneum
T4 b	Tumour invades other adjacent structures, such as the aorta, vertebral body, or trachea
Nodal Involvement	
NX	Regional lymph node(s) cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 to 2 regional lymph nodes
N2	Metastasis in 3 to 6 regional lymph nodes
N3	Metastasis in 7 or more regional lymph nodes
Metastasis	
M0	No distant metastases
M1	Distant metastases

- The classification applies only to carcinomas and include adenocarcinomas of the oesphagogastric/gastroesophageal junction
- There should be histological confirmation of the disease and division of cases by topographic localisation and histological t ype
- A tumour, the epicentre of which is within 2cm of the oesophagogastric junction and also extends into the oesophagus, is classified and staged using the oesophageal scheme
- Cancer involving the oesophagogastric junction whose epicentre is within the proximal 2cm cardia (Siewert types I/II) are to be staged as oesophageal cancers.
- In patients who receive neoadjuvant chemotherapy and then have a resection, this classification (whether is it gastric or oesophageal based on the epicentre) should be made according to the clinical endoscopic findings before treatment and should not be changed after chemotherapy

North of Scotland Clinical Management Guideline (CMG): SACT regimens for Oesophageal Cancer

Last Updated 07/09/2023

Neoadjuvant and adjuvant treatment / Resectable adenocarcinoma - stomach, OGJ, lower oesophagus				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
1	**FLOT**	5-Fluorouracil 2600mg/m2 IV Day 1 (over 24 hours) Oxaliplatin 85mg/m2 IV Day 1 Docetaxel 50mg/m2 IV Day 1 Folinic acid 350mg IV Day 1 Every 14 days for 8 cycles (peri-operative - 4 pre / 4 post)		Curable
2	**mFOLFOX** (Alternative to FLOT)	Oxaliplatin 85mg/m2 IV Day 1 5-Fluorouracil 400mg/m2 IV Day 1 Folinic acid 350mg IV Day 1 5-Fluorouracil 2400 mg/m2 IV over 46 hours Every 14 days for 8 cycles (peri-operative - 4 pre / 4 post)		Curable
3	**ECX** (Alternative to FLOT)	Epirubicin 50mg/m2 IV Day 1 Cisplatin 60mg/m2 IV Day 1 Capecitabine 625mg/m2 Oral/Twice daily Days 1-21 Every 21 days for 6 cycles (peri-operative - 3 pre / 3 post)		Curable
4	**ECF (21 DAY 5FU)** (Alternative to FLOT)	Epirubicin 50mg/m2 IV Day 1 Cisplatin 60mg/m2 IV Day 1 5-Fluorouracil 200mg/m2/day IV continuous Days 1-21 Every 21 days for 6 cycles (peri-operative - 3 pre / 3 post)		Curable
5	**ECF (4 DAY 5FU)** (Alternative to FLOT)	Epirubicin 50mg/m2 IV Day 1 Cisplatin 60mg/m2 IV Day 1 5-Fluorouracil 1000mg/m2/day IV continuous Days 1-4 Every 21 days for 6 cycles (peri-operative) - 3 pre / 3 post)		Curable
6	**Nivolumab** **(SMC 2429)**	Nivolumab 240mg every 2 weeks (or 480mg every 4 weeks) After 16 weeks, 480mg every 4 weeks Maximum of 12 months	Adjuvant treatment (completely resected oesophageal or GOJ cancer if residual pathologic disease following prior neoadjuvant chemoradiotherapy)	Curable

Neoadjuvant treatment of oesophageal adenocarcinoma or squamous cell carcinoma				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
7	**Carboplatin + paclitaxel (+ RT)**	Carboplatin AUC 2 IV Day 1 Paclitaxel 50mg/m2 IV Day 1 Every 7 days for 5 weeks		Curable

8. Neoadjuvant treatment of resectable oesophageal or GOJ adenocarcinoma or oesophageal squamous cell carcinoma 9. Metastatic squamous cell carcinoma of oesophagus				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
8/9	**CX(75/625)**	Cisplatin 75mg/m2 IV Day 1 Capecitabine 625mg/m2 Oral/Twice daily Days 1-21 8. Every 21 days for 2 cycles 9. Every 21 days for 6 cycles		8. Curable 9. Non-curable

Definitive concurrent chemoradiotherapy for oesophageal adenocarcinoma and squamous cell carcinoma				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
10	**Cisplatin + capecitabine + RT**	Cisplatin 75mg/m2 IV Day 1 Capecitabine 625mg/m2 Oral/Twice daily Days 1-21 Every 21 days for 2 cycles	Two induction cycles followed by concurrent chemoradiation (cycles 3 and 4 with continuous capecitabine and cisplatin on days 1 and 29)	Curable
11	**Cisplatin + 5-FU + RT (1000)** (on Chemocare as CIS+5FU(1000)+RT)	Cisplatin 80mg/m2 IV Day 1 5-Fluorouracil 1000mg/m2/day IV continuous Days 1-4 Every 21 days for 1-2 cycles	Then two further cycles concurrent with weeks 1 and 5 of RT	Curable
12	**Cisplatin + 5-FU + RT (750)** (on Chemocare as CIS+5FU(750)+RT)	Cisplatin 80mg/m2 IV Day 1 5-Fluorouracil 750mg/m2/day IV continuous Days 1-4 Every 21 days for 1-2 cycles	Then two further cycles concurrent with weeks 1 and 5 of RT	Curable
13	**Cisplatin + 5FU + RT (5 weeks)**	Cisplatin 20 mg/m2 IV Day 1 5-Fluorouracil 200mg/m2/day IV continuous Days 1-7 (i.e. 1400mg/m2/week) Every 7 days for 5 weeks (RT given Monday-Friday for 5 weeks)		Curable

Inoperable gastric, oesophageal, OGJ (locally advanced and metastatic)				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
14	**Pembrolizumab** **(with CapOX every 3 weeks, maximum 6 cycles)** **(SMC 2420)**	Pembrolizumab 200mg IV Day 1 Oxaliplatin 130mg/m2 IV Day 1 Capecitabine 1000mg/m2 Oral/Twice daily Days 1-14 Every 21 days Can continue immunotherapy for up to 2 years i.e. Pembrolizumab 200mg IV every 3 weeks or 400mg every 6 weeks	As per SMC 2420, first-line treatment (HER2-negative). In summary:- -squamous or undifferentiated -if CPS>10 -not gastric Adenocarcinoma/oesophageal /CPS >10 - prescribe either pembrolizumab or nivolumab	Non-curable
15	**Nivolumab** **(with mFOLFOX, every 2 weeks, maximum 9 cycles)** **(SMC 2458)**	Nivolumab 240mg IV Day 1 Oxaliplatin 85mg/m2 IV Day 1 5-Fluorouracil 400mg/m2 IV Day 1 5-Fluorouracil 2400mg/m2 IV over 46 hours Every 14 days Can continue immunotherapy for up to 2 years i.e. Nivolumab 360mg every 3 weeks or 240mg every 2 weeks	As per SMC 2420, first-line treatment (HER2-negative). In summary:- -includes gastric -adenocarcinoma only, CPS>5 -the only option if CPS >5 and <10 Adenocarcinoma/oesophageal /CPS >10 - prescribe either pembrolizumab or nivolumab	Non-curable
16	**Pembrolizumab** **(with Cisplatin/5FU every 3 weeks, maximum 6 cycles)** **(SMC 2420)**	Pembrolizumab 200mg IV Day 1 Cisplatin 80mg/m2 IV Day 1 5FU 1000mg/m2/day IV Days 1-4 Every 21 days Can continue immunotherapy for up to 2 years i.e. Pembrolizumab 200mg IV every 3 weeks or 400mg every 6 weeks	As per indications above and for use when oxaliplatin may be contra-indicated (e.g. neurotoxicity). (5FU may be given via either a 4-day pump or 2 x 2-day pumps)	Non-curable

Inoperable gastric, oesophageal, OGJ (locally advanced and metastatic)				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
17	**CX(75/625)**	Cisplatin 75mg/m2 IV Day 1 Capecitabine 625mg/m2 Oral/Twice daily Days 1-21 Every 21 days for 6-8 cycles		Non-curable
18	**CF**	Cisplatin 80mg/m2 IV Day 1 5-Fluorouracil 1000mg/m2/day IV continuous Days 1-4 Every 21 days for 6-8 cycles		Non-curable
19	**CAPOX**	Oxaliplatin 130mg/m2 IV Day 1 Capecitabine 1000mg/m2 Oral/Twice daily Days 1-14 Every 21 days for 6-8 cycles		Non-curable
20	**OXCAP**	Oxaliplatin 130mg/m2 IV Day 1 Capecitabine 625mg/m2 Oral/Twice daily Days 1-21 Every 21 days for 6-8 cycles		Non-curable
21	**G02 OXCAP**	Oxaliplatin 78mg/m2 IV Day 1 Capecitabine 375mg/m2 Oral/Twice daily Days 1-21 Every 21 days for 6-8 cycles	Lower doses (60%) for frail or older patients	Non-curable
22	**Teysuno (tegafur/gimeracil/oteracil) + Cisplatin**	Cisplatin 75mg/m2 IV Day 1 Teysuno 25* mg/m2 Oral/Twice daily Days 1-21 *expressed as tegafur Every 28 days for 6 cycles (can continue beyond 6 cycles until disease progression or toxicities)	Prescribed rarely in coronovasospasm (alternatively give paclitaxel/carboplatin)	Non-curable
23	**mFOLFOX**	Oxaliplatin 85mg/m2 IV Day 1 5-Fluorouracil 400mg/m2 IV Day 1 Folinic acid 350mg on Day 1 5-Fluorouracil 2400mg/m2 IV over 46 hours Every 14 days for 8 cycles	If unable to swallow capecitabine	Non-curable

Inoperable gastric, oesophageal, OGJ - progressed on or after 1st line treatment				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
24	**Docetaxel**	Docetaxel 75mg/m2 IV Day 1 Every 21 days for 6 cycles		Non-curable
25	**Paclitaxel**	Paclitaxel 80mg/m2 IV Days 1, 8, 15 Every 28 days for 6 cycles		Non-curable
26	**Irinotecan**	Irinotecan 180mg/m2 IV Day 1 Every 14 days for 12 cycles	If neuropathy with taxanes. Can apply a dose reduction to 150mg/m2 if required	Non-curable
27	**Nivolumab** **(SMC 2362)**	Nivolumab 240mg IV Day 1 14 days until disease progression or toxicities	2nd line, unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based combination chemotherapy	Non-curable

1st line treatment of HER-2 positive metastatic or locally advanced adenocarcinoma of stomach or OGJ				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
28	**Trastuzumab + cisplatin + capecitabine (T-CX)**	Trastuzumab 6mg/kg IV Day 1 (Cycle 1 Loading = 8mg/kg) Cisplatin 80mg/m2 IV Day 1 Capecitabine 1000mg/m2 Oral/Twice daily Days 1-14 Every 21 days for 6 cycles (trastuzumab continued beyond 6 cycles until disease progression)	Primary option	Non-curable
29	**Trastuzumab + cisplatin + 5-FU**	Trastuzumab 6mg/kg IV Day 1 (Cycle 1 Loading = 8mg/kg) Cisplatin 80mg/m2 IV Day 1 5-Fluorouracil 800mg/m2/day Continuous IV over 5 days (Days 1-5) Every 21 days for 6 cycles (trastuzumab continued beyond 6 cycles until disease progression)	Primary option	Non-curable
30	**Trastuzumab + CAPOX**	Trastuzumab 6mg/kg IV Day 1 (Cycle 1 Loading = 8mg/kg) Oxaliplatin 130mg/m2 IV Day 1 Capecitabine 1000mg/m2 Oral/Twice daily Days 1-14 Every 21 days for 6 cycles (trastuzumab continued beyond 6 cycles until disease progression)	If not suitable for cisplatin	Non-curable
31	**Trastuzumab + GO2 OXCAP**	Trastuzumab 6mg/kg IV Day 1 (Cycle 1 Loading = 8mg/kg) Oxaliplatin 78mg/m2 IV Day 1 Capecitabine 375mg/m2 Oral/Twice daily Days 1-21 Every 21 days for 6 cycles (trastuzumab continued beyond 6 cycles until disease progression)	If not suitable for cisplatin or CAPOX, i.e. frail or older patients	Non-curable

1st line treatment of HER-2 negative metastatic or locally advanced adenocarcinoma of stomach or OGJ				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
32	**Cisplatin + Capecitabine**	Cisplatin 80mg/m2 IV Day 1 Capecitabine 1000 mg/m2 Oral/Twice daily Days 1-14 Every 21 days for 6 cycles	Primary option Select CAPOX or OXCAP alone, if cisplatin contra-indicated (see regimens 19 and 20)	Non-curable

Metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
33	**Lonsurf (trifluidine/tipiracil)** **(SMC 2329)**	Lonsurf 35mg/m2 orally TWICE daily on days 1-5 and days 8-12 (based on trifluridine content) (maximum 80mg per dose) Every 28 days until disease progression or toxicities	3rd line and beyond, i.e. previously treated with at least two prior systemic treatment regimens for advanced disease	Non-curable

Other regimens - LA or metastatic squamous or adenocarcinoma of oesophagus - Neo-adjuvant, adjuvant or metastatic gastric or OGJ cancer				
No.	**Regimen name**	**Regimen details**	**Other information**	**Treatment intent**
34	**Carboplatin + Paclitaxel**	Carboplatin AUC 5 IV Day 1 Paclitaxel 175mg/m2 IV Day 1 Every 21 days for 6 cycles	If 5-FU contraindicated (e.g. due to cardiac toxicity)	Non-curable

Definitions

ASA – American Society of Anesthesiologists
CPEX – Cardio-Pulmonary Exercise Testing
ECOG – East Coast Oncology Group
MDTM – Multidisciplinary Team Meeting
MUST – Malnutrition Universal Screening Tool
OGD – Oesophago-Gastric-Dueodenoscopy