10.0 EM Upper GI NSSG Clinical and Referral Guidelines
(Demonstrating Compliance with Measures 11-1C-103f, 104f, 105f)

The East Midlands Upper GI Cancer NSSG has agreed that the referral guidelines for Upper Gastrointestinal Cancer are those contained in the NICE Guidance on Referral of Suspected Cancer. The website for these guidelines is as follows:
www.nice.org.uk/CG027

The point of contact for Referral for Suspected Cancer has been agreed in each Trust as follows:

Trust	Named Contact	Telephone/Email
Kettering General Hospital	▪ 2 ww Office team	01536 493303
Northampton General Hospital	▪ Laura Grant & Elaine Bateley (2ww Office Co-ordinators)	01604 544235
UHL	2ww team	0116 250 2543
Derby Hospitals	• 2ww Office Team • Choose and book	Tel:- 01322 788395 Fax:- 01332 785842
Burton	Patient Access Centre	Tel:- 01283 593200 Fax:- 01283 593090
Kings Mill	Choose and Book	01623 622515
NUH	Helen Andrews	0115 9691169
United Lincoln	Julie Miller	Tel:- 01522 512512 Ext 2660 Fax:- 01522 573351

These serve as the 'Named Teams' in respect of '11-1A-203f'
The policy for onward referral to another MDT within or out with the Network is included in Appendix D.

Measure 11-1C- 103f: The East Midlands Upper GI NSSG Clinical Guidelines, which included Imaging Guidelines and Pathology Guidelines, were reviewed collectively and ratified by the Chair on 12.06.09 and the Chair of The Network on 15.06.09. and reviewed on 22 June 2012.

Measure 11-1c-105f: The East Midlands Upper GI Cancer NSSG Guidelines for Histopathology were accepted as:

- Royal College of Pathologists Upper GI Cancer Data Sets

Dataset for the histopathological reporting of gastric carcinoma (2nd Edition) January 2007
http://www.rcpath.org/resources/pdf/G013GastricDatasetFINALJan07.pdf

- Dataset for the histopathological reporting of oesophageal carcinoma (2nd Edition) February 2007

http://www.rcpath.org/resources/pdf/G006OesophagealDatasetFINALFeb07.pdf

Measure 11-1C-104f & 105f: The East Midlands Upper GI Cancer NSSG Imaging Guidelines were accepted as:

- Royal College of Radiologists: Recommendations for Cross Sectional Imaging in Cancer Management (RCR(06)1)
  www.rcr.ac.uk/publications.aspx?PageID=310
- UK PET CT Advisory Board Revision January 2009 (Included in Appendix E)
- Standards for communication of critical, urgent and unexpected significant radiological findings
  www.rcr.ac.uk/publications.aspx?PageID=310

This demonstrates compliance with measure 11-1C-104f and 11-1C-105f.

Non-surgical oncology guidelines will be reviewed as part of the NSSG Work Plan by the Oncology Subgroup.

East Midlands Cancer Network Upper GI NSSG Agreed Referral Guidelines to other MDTs

(Demonstrating Compliance with Measures11-1A-205f)

All new Upper GI patients must be discussed at an Upper GI MDT. This will, in the first instance, almost always be in the Trust receiving the first referral. These will be the diagnostic & local teams (including specialist teams acting as local teams) as outlined in 11-1A-203f and 11-1A-204f) (See Constitution)

Referrals from first local/diagnostic MDT to second specialist MDT within or out with the East Midlands Cancer Network by reason of referral as follows:

1. Consideration of a complex case in line with the IOG agreed configuration for specialised care as outlined in Measures 11-1A-204, 205f (specialist Upper GI and HPB Teams) (Constitution Pages 7 & 8)

(e.g. management decision to be within the agreed specialist MDT as per network guidelines and operational policies, borderline decision for surgery due to extensive co-morbidity, resection agreed at SMDT, rare tumour, diagnostic uncertainty, etc.)

All cases in this category must be discussed by the second 'specialist' MDT in line with guidelines and operational policies. The second specialist MDT decisions would usually supersede the decisions of the first local/diagnostic MDT. The second specialist MDT will take lead responsibility in this case

2. Second opinion requested by patient or first local/diagnostic MDT or specialist MDT

All such cases will be discussed at the second specialist MDT. The two sets of views will be considered in the decision making with the patient.

3. Referral to another specialist MDT for further tests/treatment

Many staff participate in more than one MDT. It is not therefore necessary to discuss straightforward cases again at a second MDT (e.g. CHART radiotherapy, brachytherapy, mediastinoscopy, uncomplicated surgery, etc.) However these patients may be discussed if the referral does not follow the agreed care pathway, the clinician receiving the referral feels it would be of advantage or it is second specialist MDT policy.

Lead responsibility will remain with the referring MDT whether this be local/diagnostic or specialist

4. Referrals to and from non-upper GI MDTs

These will be referred on to the most appropriate MDT by the Upper GI MDT at which the case is discussed initially. The Upper GI MDT will offer advice as necessary on cases referred from other site specific MDTs as necessary. In this situation the appropriate site-specific MDT will take lead responsibility.

5. Communication and waiting times

Good and rapid communication between the MDTs involved is vital. The MDT co-ordinator for each Upper GI MDT should have a list of all fax numbers for MDT co-ordinators across the network(s). Referrals should be secure faxed in the first instance.

East Midlands
Strategic Clinical Network

UPPER GI
NETWORK SITE SPECIFIC GROUP

CLINICAL GUIDELINES FOR THE MANAGEMENT OF OESOPHAGEAL & GASTRIC CANCER & GI STROMAL TUMOURS

11-1C-103f

Status: Draft

Ratified by: Mr Simon Parsons, NSSG Chair & Members 12 June 201209

Endorsed by: C Kelly, Chair of the Network on 5 September 2012

Updated:

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Distributed to:

Contents

Epidemiology and Aetiology

- There has been an increase in the incidence of adenocarcinoma of the lower third of the oesophagus and gastro-oesophageal junction in the past two decades with a corresponding decrease in incidence of distal gastric cancer.

- Oesophageal and gastric cancer rates may be decreased by measures to reduce smoking and alcohol intake and to increase dietary intake of fresh fruit and vegetables.

- Oesophageal cancer may be influenced by a reduction in the duration and severity of gastro-oesophageal reflux and by a reduction in the incidence of obesity.

- Eradication of *Helicobacter* may decrease gastric cancer incidence.

Referral Guidelines

The referral guidelines are in line with the recommended NICE Guidelines published in June 2005.

- An urgent referral for endoscopy or to a specialist with expertise in upper gastrointestinal cancer should be made for patients of any age with dyspepsia who present with any of the following:

    - Chronic gastrointestinal bleeding
    - Dysphagia
    - Progressive unintentional weight loss
    - Persistent vomiting
    - Iron deficiency anaemia
    - Epigastria mass
    - Suspicious barium meal result

- In patients aged 55 years and older with unexplained and persistent recent-onset dyspepsia alone, an urgent referral for endoscopy should be made.
- In patients aged less than 55 years, endoscopic investigation of dyspepsia is not necessary in the absence of alarm symptoms.
- In patients presenting with dysphagia (interference with the swallowing mechanism that occurs within 5 seconds of having commenced the swallowing process), an urgent referral should be made.
- *Helicobacter pylori* status should not affect the decision to refer for suspected cancer.
- In patients without dyspepsia, but with unexplained weight loss or iron deficiency anaemia, the possibility of upper gastrointestinal cancer should be recognised and an urgent referral for further investigation considered.

- In patients with persistent vomiting and weight loss in the absence of dyspepsia, upper gastro-oesopohageal cancer should be considered and, if appropriate, an urgent referral should be made.
- An urgent referral should be made for patients presenting with either:
    - Unexplained upper abdominal pain and weight loss, with or without back pain, or
    - An upper abdominal mass without dyspepsia.

Risk Factors

In patients with unexplained worsening of their dyspepsia an urgent referral should be considered if they have any of the following known risk factors:

- Barrett's oesophagus
- Known dysplasia, atrophic gastritis or intestinal metaplasia

Investigations

- Patients being referred urgently for endoscopy should ideally be free from acid suppression medication, including proton pump inhibitors or H2 receptor antagonists, for a minimum of 2 weeks.
- In patients where the decision to refer has been made a full blood count may assist specialist assessment in the outpatient clinic. This should be carried out in accordance with local arrangements.
- All patients with new-onset dyspepsia should be considered for a full blood count in order to detect iron deficiency anaemia.

Patients must be referred back for clinical specialist review whenever sinister symptoms arise.

Hospital follow up for patients suspected of having neoplasm at endoscopy should be arranged from the Endoscopy Unit to allow joint review of histology and endoscopic findings, ideally within 7 days (maximum 14 days).

Diagnosis

- The index of suspicion for cancer is high when vague dyspeptic symptoms are combined with alarm symptoms (e.g. weight loss, vomiting, and anaemia). General practitioners should be encouraged to refer patients as early as possible.
- Rapid access gastroscopy is the investigation of choice with appropriate biopsy for those with risk symptoms.

- Patients with longstanding history of reflux and/or dysphagia should not be assumed to be suffering from benign stricture or simple oesophagitis until endoscopy and biopsy has been performed.

- High grade dysplasia of the oesophagus should precipitate urgent repeat endoscopy and biopsy as a significant number of patients will already have or develop intramucosal cancer.

- Anti-secretory therapy should be ideally withheld until after endoscopy to avoid misdiagnosis.

- In patients with Barrett's Oesophagus and dysplasia biopsies should be repeated with the patient established on anti-secretory therapy to avoid confusion with regenerative changes.

- The diagnosis of gastric cancer should be suspected in all patients with recent onset "dyspepsia" over the age of 55 years.

- Gastric ulcers should be followed up to healing with repeat biopsy.

Patient Information

- The management of all patients who are diagnosed with gastric or oesophageal cancer should be discussed within a multidisciplinary forum.

- Information relating to local and national support services should be made available to both patients and carers.

- Patients with oesophageal or gastric cancer should be offered written information at the time of diagnosis detailing the possible sequence of events and providing them with a named contact on the multidisciplinary team.

- Patients should be given clear information relating to the potential risks and benefits of treatment.

- All patients newly diagnosed with oesophageal or gastric cancer should have access to a clinical nurse specialist for support, advice and information and to facilitate timely communication with primary care.

Staging

- Staging needs to be thorough and accurate for all patients in order to plan optimal therapeutic options.

- Accurate staging is achieved by a combination of techniques interpreted by dedicated staff in a timely fashion.

- Initial staging assessment should include spiral computed tomography (CT) of the thorax and abdomen to determine the presence or absence of metastatic disease. Estimated TNM stage of the tumour should be recorded.

- In the absence of metastatic disease assessment of operability is best made by endoscopic ultrasound.

- PET-CT should be used in staging oesophageal cancers that are being considered for radical treatment.

- The role of PET-CT in gastric cancer is less clear and should be used at the discretion of the MDT

- Adjuncts to staging include magnetic resonance imaging (MRI), bronchoscopy, laparoscopy and transabdominal ultrasound.

Pathology

- Diagnosis of high grade dysplasia both in Barrett's oesophagus and in the stomach should be made by an experienced histopathologist and corroborated by a pathologist with a special interest in gastrointestinal disease.

- Reports should comply with the Royal College of Pathologists minimum datasets for oesophageal and gastric carcinoma.

- Reports on oesophageal resection specimens should include, as a minimum, type of tumour, depth of invasion, involvement of the resection margins, vascular invasion, the presence of Barrett's metaplasia and the number of lymph nodes resected and the number containing metastatic tumour. The report should include the TNM stage.

- Reports on gastric resection specimens should include, as a minimum, type of tumour, depth of invasion, involvement of the resection margins, nodal disease (including number of involved lymph nodes) and metastatic spread. The report should include the TNM stage.

- Oesophageo-gastric junctional tumours should be classified as Type I (distal oesophagus), Type II (cardia) and Type III (proximal stomach). Siewert Classification.

Imaging

Oesophageal cancer

The incidence of oesophageal cancer is increasing and represents the third most common gastrointestinal malignancy. The majority of patients with adenocarcinoma of the oesophagus receive combined modality treatment in the form of either combination chemotherapy followed by surgery, or chemoradiotherapy followed by surgery. For patients presenting with squamous carcinoma of the oesophagus, there is less UK consensus in optimal management. Neoadjuvant chemotherapy, neoadjuvant chemoradiotherapy andsurgery, and definitve chemoradiation should all be considered.

Primary oesophageal adenocarcinoma most commonly presents in the lower third of the oesophagus, and much less commonly in the mid- and upper-oesophagus, and is strongly associated with a hiatus hernia and reflux disease. Mediastinal, subcarinal, peri-oesophageal and perigastric nodal disease constitutes regional lymphadenopathy. For all oesophageal tumours, nodal disease at or below the level of the coeliac axis constitutes metastatic disease, however in selected patients this does not preclude surgical intervention. For tumours arising above the thoracic inlet, namely in the cervical oesophagus, local regional lymph nodes are considered to be present in the peri-oesophageal, supraclavicular, cervical, internal jugular and the scalene territories.

Who should be imaged?

All patients with oesophageal cancer diagnosed at endoscopy or suspected following an upper gastrointestinal barium examination using fluoroscopy who are potentially suitable for radical therapy.

Staging objectives

- To define tumour position and estimate the proximal and distal extent of the tumour and length of tumour.
- To identify local invasion, particularly with respect to the trachea, main bronchi, aorta, pericardium, pleura, diaphragmatic hiatus and crura.
- To identify lymph node enlargement, particularly peri-oesophageal, mediastinal and perigastric regions.
- To identify metastases in retroperitoneal lymph nodes, in the liver and peritoneal cavity.
- To determine the degree of oesophageal obstruction and to identify the presence of complications such as localised perforation or fistulation.

Staging

CT of the thorax and abdomen is the primary imaging investigation.

CT

- Oral administration of 1 litre of water or iodinated contrast medium (see Tips).
- 100-150 ml of intravenous iodinated contrast medium injected at 3-4 ml/sec.
- MDCT is commenced at 20-25 seconds (chest) and 70-80 seconds (abdomen) post-injection.
- Using MDCT, slice thickness will depend on scanner capability.

Values of CTDIvol should normally be below the relevant national reference dose for the region of scan and patient group.

PET-CT

18FDG PET-CT is increasingly being used for primary tumour staging as oesophageal carcinoma is intensely 18FDG avid and the technique is helpful for delineating the craniocaudal extent of oesophageal disease and also for detecting involved regional and distant nodes, and metastases when feasible.

Follow-up

Clinical follow up with imaging or endoscopic examination as indicated.
Patients who have undergone radical chemoradiation and would be fit for salvage surgery should be considered for routine reinvestigation at an interval post treatment. CT is the primary imaging modality for follow-up. Further imaging will depend on disease status and patient symptoms.

Tips

- 200 ml of water given orally immediately before the patient is scanned may help to maximise oesophageal distension and visualisation of the endoluminal component of the tumour.
- Laparoscopy is required in all sub-diaphragmatic tumours in order to detect small volume peritoneal disease that may not be seen by imaging.

Stomach cancer

Clinical background

In patients presenting with symptoms of gastric cancer, approximately one-third will have metastatic disease with an associated 2% relative survival rate. Patients presenting with early stage disease may be curable with surgery, with survival varying from 50% to 15%. Patients receive perioperative chemotherapy in addition to surgery for this disease.

The objective of gastric resection is to achieve clear histological margins and total gastrectomy is not necessary for all patients with gastric adenocarcinoma. The extent of nodal dissection is defined as a major factor in staging and can influence outcome by stage. Although there is no benefit in routinely performing extended lymph node dissection in gastric cancer, a more extended dissection may be of benefit in selected patients. Imaging is also essential to rule out metastatic disease in patients considered suitable for surgery. Currently, nodal staging is not sufficiently accurate to enable selection between patients who will require limited versus extended surgical lymph node dissection.

Who should be imaged?

All patients with gastric carcinoma.

Staging objectives

- To identify metastatic disease in the liver and peritoneum including ovarian deposits.
- To determine the proportion of stomach involved by tumour to assist with decision making with regard to the extent of surgery to be performed.
- To identify the presence or absence of peritoneal nodules and nodal enlargement (peri-gastric, coeliac axis nodes versus metastatic nodal disease in retroperitoneum).
- To document the degree of outflow obstruction in order to guide the clinical management of obstructive symptoms.

Staging

CT of the thorax, abdomen and pelvis is the primary imaging investigation.

CT

- Oral administration of 1 litre of water as a contrast agent, of which 400 ml is to be drunk immediately prior to going onto the scanner (see Tips).
- To ensure maximum gastric distension (an anti-peristaltic agent is, in general, not required).
- MDCT is commenced at 20-25 seconds (chest) and 70-80 seconds (abdomen and pelvis) post-injection.
- Using MDCT, slice thickness will depend on scanner capability.

Values of CTDIvol should normally be below the relevant national reference dose for the region of scan and patient group.

PET-CT

Although 18FDG PET-CT can be a useful modality for the assessment of gastric carcinomas, the value of the technique in this disease appears to be less than that observed with oesophageal carcinoma. This is because the stomach often shows low to moderate grade physiological 18FDG uptake and small local involved nodes may not demonstrate significant 18FDG uptake.

Follow-up

Primary follow up (5 years) is clinical with imaging as appropriate.
CT is the primary imaging modality for follow-up with the same protocol if indicated.

Treatment

- Treatment and management of all patients should be undertaken in the context of a multidisciplinary team which plans and performs staging, treatment selection (radical and palliative) treatment provision, post-treatment care and follow up.

- Careful evaluation of the patient's pre-treatment health must be made, particular attention being made to the cardiovascular and respiratory systems and performance status.

Preoperative Assessment

- Routine investigations should include haematological and biochemical profiles, a resting ECG, chest X-ray, pulmonary function tests and where appropriate exercise testing

- Optimising the patient's fitness for surgery is a multidisciplinary process and all available expertise should be utilised.

- Patients should be encouraged to stop smoking immediately.

- Nutritional status should be assessed and, as far as possible, corrected before surgery. The patient's weight and height should be recorded so that a body mass index is calculated.

- All patients should have antithrombotic and antibiotic prophylaxis instituted at an appropriate time in relation to their surgery and postoperative recovery.

- Anaesthesia for oesophageal surgery should only be conducted by anaesthetists familiar with one lung ventilation and epidural analgesia.

- Quality of life at presentation should be assessed and taken into consideration in treatment planning.

Treatment: Endoscopic

- Endoscopic Mucosal Resection and Endoscopic Ablation should be considered in high grade dysplasia and early (Tis, T1) tumours of the oesophagus and stomach.

Treatment: Oesophageal Resection

- Oesophagectomy should be undertaken only in centres capable of carrying out careful case selection, with a large case volume and sufficient surgical and intensive care experience.

- There is no evidence favouring one method of oesophageal resection over another.

The operative strategy should ensure that adequate longitudinal and radial resection margins are achieved whenever possible. The extent of lymphadenectomy should be tailored to the age and fitness of the patient together with the location and stage of the cancer.

- Single layer manual or stapled anastomoses can be used.

- Clinical anastomotic leakage should not exceed 10%.

- Curative (R0) resection rates should exceed 30%.

- In hospital and 30 day mortality combined should be less than 10%.

- Post-operative nutritional support by the enteral route should be considered in all patients.

Treatment: Gastric Resection

- The test results are likely to be produced by experienced surgeons operating in specialised units as part of a multidisciplinary team.

- Distal (antral) tumours should be treated by subtotal gastrectomy and proximal tumours by total gastrectomy.

- Limited gastric resections should presently only be used for palliation or in the very elderly.

- The extent of lymphadenectomy should be tailored to the age and fitness of the patient together with the location and stage of the cancer.

- The distal pancreas and spleen should not be removed as part of a resection for a cancer in the distal two thirds of the stomach.

- The distal pancreas should be removed only when there is direct invasion and still a chance of a curative procedure in patients with carcinoma of the proximal stomach.

- Resection of the spleen and splenic hilar nodes should only be considered in patients with tumours of the proximal stomach located on the greater curvature/posterior wall of the stomach close to the splenic hilum where the incidence of splenic hilar nodal involvement is likely to be high.

- Curative (R0) resection rates should exceed 30%.

- In hospital mortality should be less than 10% for total gastrectomy and less than 5% for subtotal/partial gastrectomy.

- Post-operative nutritional support by the enteral route should be considered.

Treatment: Chemotherapy and Radiotherapy

Oesophageal Cancer

- There is no evidence for a role of adjuvant chemotherapy in oesophageal cancer.

- Neoadjuvant chemotherapy with cisplatin and 5-fluouracil (5-FU) improves short term survival over surgery alone.

- Peri operative Epirubicin, cisplatin and 5 Fluorouracil (Magic Regimen) has a survival benefit compared to surgery alone in adenocarcinoma of lower oesophagus and GOJ. Capecitabine has been shown to be aseffective as 5-FU.

- Preoperative chemoradiation may improve long term survival. And is the subject of NeoSCOPE, a UK trial opening 2013. The CROSS study demonstrated benefit of chemoradiation neoadjuantly for both squamous and adenocarcinomas using a carboplatin and pacliatxel regimen.

- Post operative chemotherapy should be offered to GOJ and gastric adenocarcinomas if fitness allow, with the exception of early tumours.
  The role of chemoradiation is unclear post-operatively in the absence of defined involved resection margins, although can be considered as salvage therapy in local recurrences individually.

Gastric Cancer

- 5-FU is the most active chemotherapeutic agent. A combination of 5-FU with other agents is superior to single agent treatment. The combination of epirubicin, cisplatin and continuous infusion of 5-FU (ECF) appears to be one of the most active regimens. Oral 5-FU may be substituted for infusional 5FU in appropriate patients.

- Adjuvant chemotherapy should be considered in fit patients with high risk gastric cancers. Chemoradiation being considered in specific patients with defined R1 margins'

- Neoadjuvant chemotherapy has been shown to improve resection rates, progression free and overall survival.

Palliative Treatment

- Palliative treatment should be planned by the multidisciplinary team with direct involvement of the palliative care team and the clinical nurse specialist.

Oesophageal Cancer

- Dilation alone should be reserved for patients who are considered to have a very short lifespan

- Palliative radiotherapy should be considered for palliation of dysphagia unless the patient has total or near total dysphagia when an oesophageal stent should be considered.

- Oesophageal intubation is the treatment of choice for firm stenosing tumours (capable of retaining an endoprosthesis), more than 2cm from the cricopharyngeus, where rapid relief of dysphagia in a one stage procedure is desirable.

- Expandable metal stents are preferable to plastic tubes in view of the lower complication rate at insertion and shorter hospital stay.

- Covered expandable metal stents or cuffed plastic tubes are the treatment of choice for malignant tracheo-oesophageal fistulation or following oesophageal perforation sustained during dilatation of a malignant stricture.

- Injection of tumour with 0.5-1ml aliquots of 100% alcohol should be considered in the following situations:-

    - For eccentric or soft exophytic tumours, unsuitable for endoscopic intubation.
    - Tumours too close to the cricopharyngeus for endoscopic intubation
    - For treatment of tumour overgrowth at the ends of an oesophageal prosthesis.

- Laser treatment is effective for relief of dysphagia in exophytic tumours of the oesophagus and gastric cardia and in treating tumour overgrowth following intubation.

- For patients whose dysphagia is palliated using laser therapy, the effect can be prolonged substantially by using adjunctive external beam radiotherapy or brachytherapy.

- Chemoradiation provides a survival benefit over radiotherapy alone.

- Radiotherapy or chemotherapy alone palliate dysphagia more slowly than intubation or laser treatment.

- Photodynamic therapy (PDT) is experimental and not universally available.

- Argon plasma coagulation (APC) may be used for relief of dysphagia in exophytic tumours of the oesophagus and gastric cardia and in treatment tumour overgrowth following intubation.

- Palliative radiotherapy should be considered for patients with mainly local disease. Salvage stenting should be used in patients whose dysphagia does not improve or recurs after palliative radiotherapy.

- Palliative chemotherapy should be considered for patients with mainly systemic disease. Salvage radiotherapy or stenting could be used if dysphagia does not improve or recurs after palliative chemotherapy.

Gastric Cancer

- Palliative chemotherapy for locally advanced and/or metastatic disease provides quality of life and survival benefit.

- For a small group of patients second line chemotherapy may be helpful to provide symptomatic benefit.

- Downstaging of locally advanced disease with chemotherapy is possible in individual cases with anecdotal reports of prolonged survival following complete surgical resection. However, no randomised trials have been conducted to demonstrate a survival advantage from addition of surgery following palliative chemotherapy.

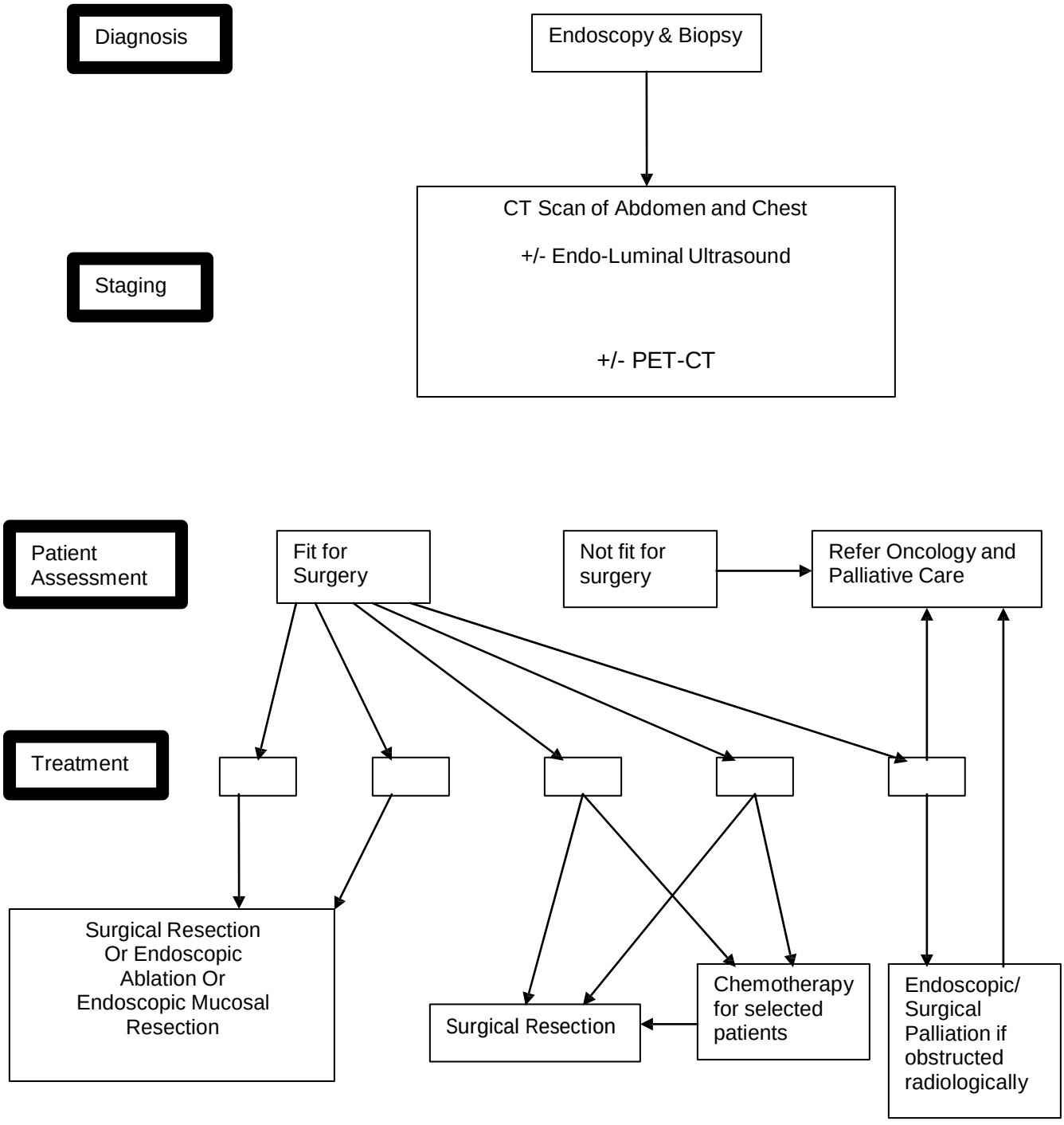
- Outflow Obstruction should be treated with gastro-duodenal stenting or palliative surgery

Follow up

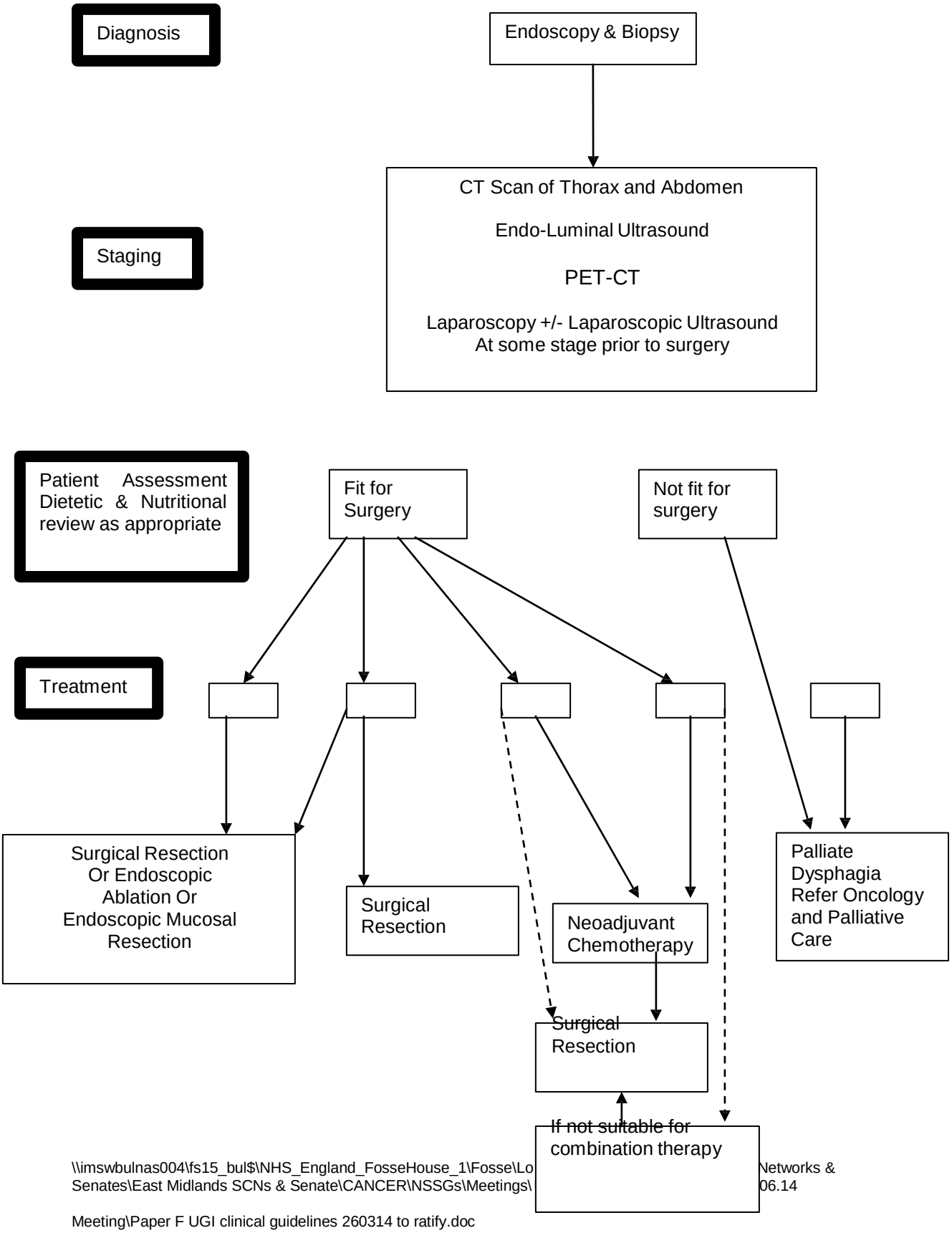
- In the absence of randomised controlled trials the most persuasive arguments for follow up are patient support and audit. Audit should be structured with particular reference to outcome measures and should be regarded as a routine part of the work of the multidisciplinary team.

- Patients should receive on going nutritional support and advice.

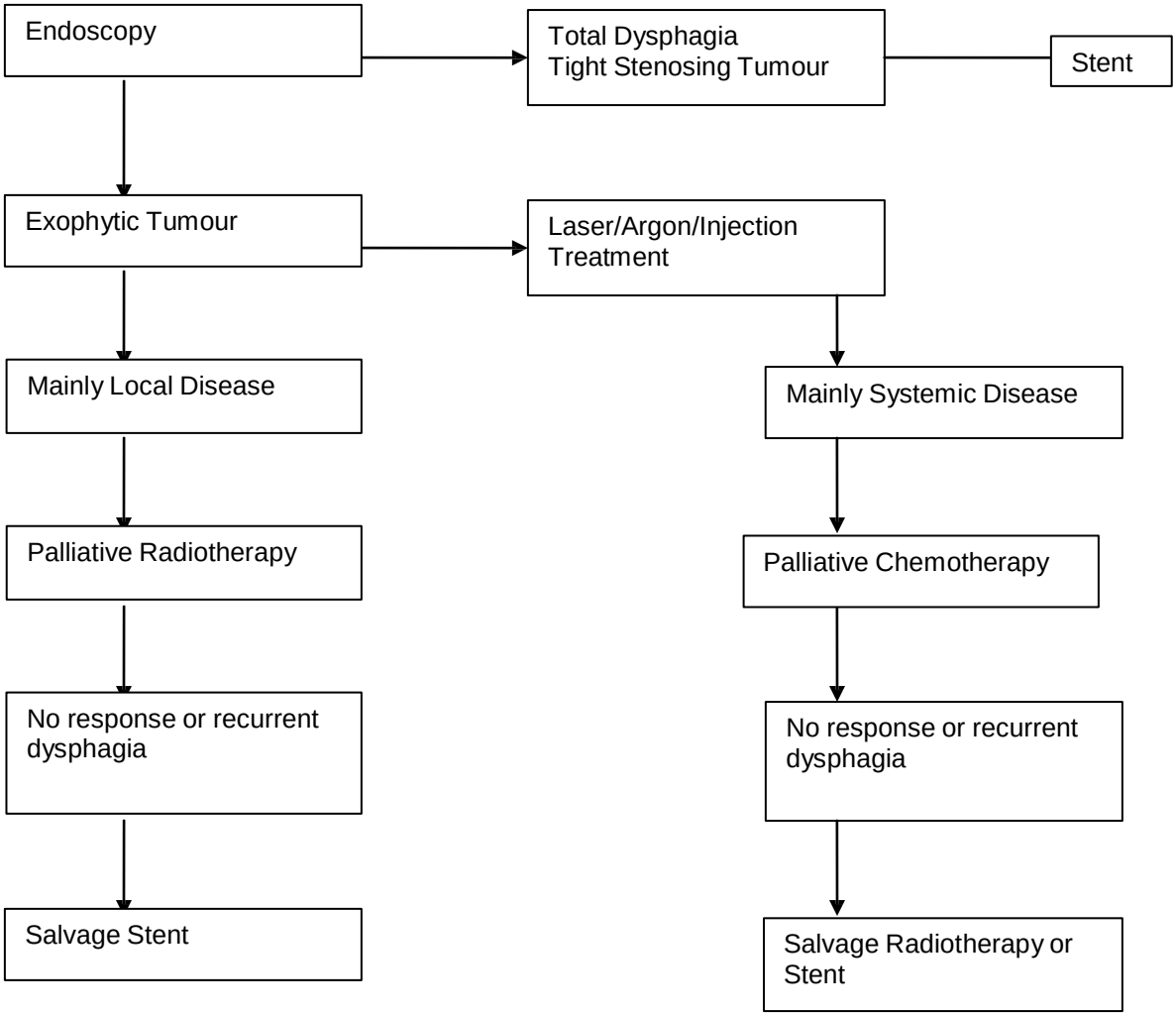
Guidelines for the Management of Gastric and Type III GOJ Cancers



Guidelines for the Management of Oesophageal and Gastro-oesophageal Cancers Type I and II



Palliative Therapy
(Any stage; poor performance status; unfit for surgery or chemoradiotherapy)



Protocol for the Management of Patients with High Risk Gastric Cancer

Summary

The outcome of patients with gastric cancer remains unacceptable with 5 year survival figures of only 10-15% for apparently localised proximal tumours and 50% for distally localised tumour[1]. These figures are of particular concern with the rise in number of gastro-oesophageal junction tumours. A number of approaches have been attempted to improve these figures including improvement in surgical lymphadenectomy, neoadjuvant chemotherapy and postoperative chemoradiation protocols.

The MAGIC study randomised patients to 3 cycles of epirubicin, cisplatin and 5-fluorouracil chemotherapy prior to surgery and then 3 further cycles after surgery[2]. Results demonstrated a 10% of improvement in curative resection rates in the chemotherapy arm with an improvement in progression free survival. Although this did not result in an improvement in overall survival, this may be due to the study being underpowered.

We propose that patients with stage I gastric or Siewert type III gastro-oesophageal cancer should go directly to surgery. Fit patients with stage II or more gastric or type III gastro-oesophageal cancer should receive 3 cycles of ECF chemotherapy prior to surgical resection followed by 3 cycles of ECF after resection.

Patients who did not receive chemotherapy prior to surgery and are then found to have more advanced disease than anticipated should be re-discussed at the MDT. For a limited few adjuvant therapy with ECF chemotherapy may be appropriate.

Background

Gastric cancer remains one of the most important causes of cancer death worldwide. While the incidence of distal gastric cancer is falling, the incidence of gastro-oesophageal junction tumours is increasing. As a group these tumours are much more challenging to treat which is evident from the 5 year survival figures of only 10-15% for apparently localised proximal tumours and 50% for distally localised tumours. Surgery remains the only potentially curative modality of treatment, but despite improvements in staging and techniques, these 5 year survival figures remains unacceptable.

Epirubicin, cisplatin and infused 5-fluorouracil have been shown to achieve high response rates in locally advanced and metastatic gastro-oesophageal cancer and are the standard of care when treating these tumours[3]. The REAL-2 study has demonstrated that oral capecitabine can be substituted for the 5FU infusion pump[4]. The MAGIC study explored the effect of neoadjuvant administration of these drugs on the operability and survival of patients with gastric cancer.

The MAGIC study randomised patients to 3 cycles of epirubicin, cisplatin and 5-fluorouracil chemotherapy prior to surgery and then 3 further cycles after surgery. All patients had histologically proven adenocarcinomas of the stomach or lower third of the oesophagus and WHO performance status of 0 or 1. Patients were stage II or greater with non-metastatic disease. The study was powered to demonstrate a 15% increase in

5-year survival from 23% to 38% with 5% significance and 90% power (85% power for a 10% difference). 503 patients were randomised with 250 in the experimental arm and 253 in the surgical arm. 100 patients received all the planned therapy i.e. 6 cycles of chemotherapy. 79% of patients had curative surgery in the chemotherapy arm compared with 69% in the surgery alone arm. Progression free survival was statistically significantly better in the chemotherapy arm although significance was not reached for overall survival. 2 year survival was 48% compared with 40% and median survival 24 months compared with 19 months.

Protocol for Perioperative ECF Chemotherapy

Investigations

All patients will undergo upper GI endoscopy followed by staging CT thorax, abdomen and pelvis. Where appropriate patients will undergo laparoscopy and EUS.

For gastro-oesophageal tumours, the endoscopist will need to decide whether the bulk of the tumour is in the cardia, if so the patient should be treated on this protocol, if not the patient should be treated with the oesophageal neoadjuvant chemotherapy protocol.

The performance status of the patient should be established. Only patients with PS 0 or 1 should be considered.

Other co-morbid conditions should be known to assess the suitability of the patient for chemotherapy.

All patients with any cardiac history require an echo prior to chemotherapy. If this demonstrates any reduction in LV function it should be repeated prior to surgery.

FBC and clinical chemistry blood tests are required prior to each cycle of chemotherapy and surgery.

All patients must have a nutritional assessment pre-treatment and close liaison with the dietician will be necessary while the patient is on treatment.

Treatment

Chemotherapy

Epirubicin 50 mg/m^2 IV bolus day 1
Cisplatin 60 mg/m^2 4-hour infusion day 1
5-FU 200 mg/m^2/day, continuous infusion days 1-21 or Capecitabine 625 mg/m^2 continuously

Cycles repeated every 3 weeks

If 5FU is administered as a pump, this should be through a PICC line or if not feasible a Hickman line. Standard anti-emetic and hydration protocol as per ECF protocol.

Surgery

The CT scan should be repeated and the patient re-discussed at the MDT after the third cycle of chemotherapy. Surgery should be carried out no longer than 4-6 weeks after the third cycle of chemotherapy and not before the patient has fully recovered from the side effects of chemotherapy. The anaesthetist should be aware that the patient has received chemotherapy.

Post-operative chemotherapy

3 cycles of post-operative ECF should commence 6-12 weeks after surgery.
Any dose reductions from the first three cycles should continue. The BSA should be recalculated.

Expected toxicity rates from MAGIC data	
Grade 3/4 neutropenia	24%
Grade 3/4 PPE	4%
Grade 3/4 nausea and vomiting postop	12%*
Post operative deaths	6%

* identified as in the study the postoperative nausea and vomiting was worse than the pre-operative

References:

1. National Cancer Institute (www.nci.nih.gov) Gastric Cancer PDQ summaries
2. Allum W et al., 2003 Proc ASCO Abstract 998
3. Webb A et al., 1997 Randomised trial comparing ECF versus FAMTX in advanced oesophagogastric cancer. Journal of Clinical Oncology 15(1); 261-267
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APPENDIX 1:
Staging of Gastric and oesophageal cancers

TMN definitions

Rules for Classification

A tumour the epicentre of which is within 5cm of OGJ and which involves the oesophagus is classified and staged as oesophageal.

Tumour with epicentre greater than 5cm from OGJ or those within 5cm of OGJ but do not involve oesophagus are classified and staged as gastric.

Primary tumour (T) Oesophagus

- Tx: Primary tumour cannot be assessed
- T0: No evidence of primary tumour
- Tis: Carcinoma in situ: intraepithelial tumour without invasion of the lamina propria
- T1: Tumour invades lamina propria or submucosa
- T1a Tumour invades lamina propria or muscularis mucosae
- T1b Tumour invades submucosa
- T2: Tumour invades the muscularis propria
- T3:~~*~~ Tumour invades adventitia
- T4a~~3~~: Tumour invades pleura, pericardium, or diaphragm
- T4b: Tumour invades other adjacent structures such as aorta, trachea, vertebra.

Regional Lymph Nodes (N) Oesophagus

Nodes in oesophageal drainage area including celiac axis and paraoesophageal nodes in neck but not supraclavicular nodes.

- 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 3-6 regional lymph nodes
- N3: Metastasis in 7 or more regional lymph nodes

pN0 A regional lymphadenectomy specimen will ordinarily contain at least 6 lymph nodes. If the lymph nodes are negative but the number ordinarily examined is not met, still classify as pN0.

Primary tumour (T) Stomach

- Tx: Primary tumour cannot be assessed
- T0: No evidence of primary tumour
- Tis: Carcinoma in situ: intraepithelial tumour without invasion of the lamina propria
- T1: Tumour invades lamina propria or submucosa
- T1a Tumour invades lamina propria or muscularis mucosae
- T1b Tumour invades submucosa
- T2: Tumour invades the muscularis propria
- T3:Tumour invades subserosa
- T4a: Tumour perforates serosa

T4b: Tumour invades adjacent structures** * [*Note: A tumour may penetrate the muscularis propria with extension into the gastrocolic or gastrohepatic ligaments, or into the greater or lesser omentum, without perforation of the visceral peritoneum covering these structures. In this case, the tumour is classified T3~~2~~. If there is perforation of the visceral peritoneum covering the gastric ligaments or the omentum, the tumour should be classified T4a~~3~~.*]

** [*Note: The adjacent structures of the stomach include the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum.*]

*** [*Note: Intramural extension to the duodenum or oesophagus is classified by the depth of greatest invasion in any of these sites, including stomach.*]

Regional lymph nodes (N) Stomach

Gastric

The regional lymph nodes are the perigastric nodes, found along the lesser and greater curvatures, and the nodes located along the left gastric, common hepatic, splenic, hepatoduodenal and celiac arteries. Involvement of other intra-abdominal lymph nodes, such as the , retropancreatic, mesenteric, and para-aortic, is classified as distant metastasis.

- 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 3-6 regional lymph nodes
- N3: Metastasis in 7 or more regional lymph nodes
- N3a 7-15 nodes
- N3b 16 or more nodes

pN0 A regional lymphadenectomy specimen will ordinarily contain at least 16 lymph nodes. If the lymph nodes are negative but the number ordinarily examined is not met, still classify as pN0.

Distant metastasis (M)

- MX: Distant metastasis cannot be assessed
- M0: No distant metastasis
- M1: Distant metastasis
- Note: Distant metastasis includes peritoneal seedlings, positive peritoneal cytology, and omental tumour not part of primary extension.

AJCC Stage Groupings

Stage 1

- T1 N0 M0
- T1 N1 M0
- T2 N0 M0

Stage 2

- T1 N2 M0
- T2 N1 M0
- T3 N0 M0

Stage 3

- T2 N2 M0
- T3 N1 M0
- T3 N2 M0
- T4 N0 M0

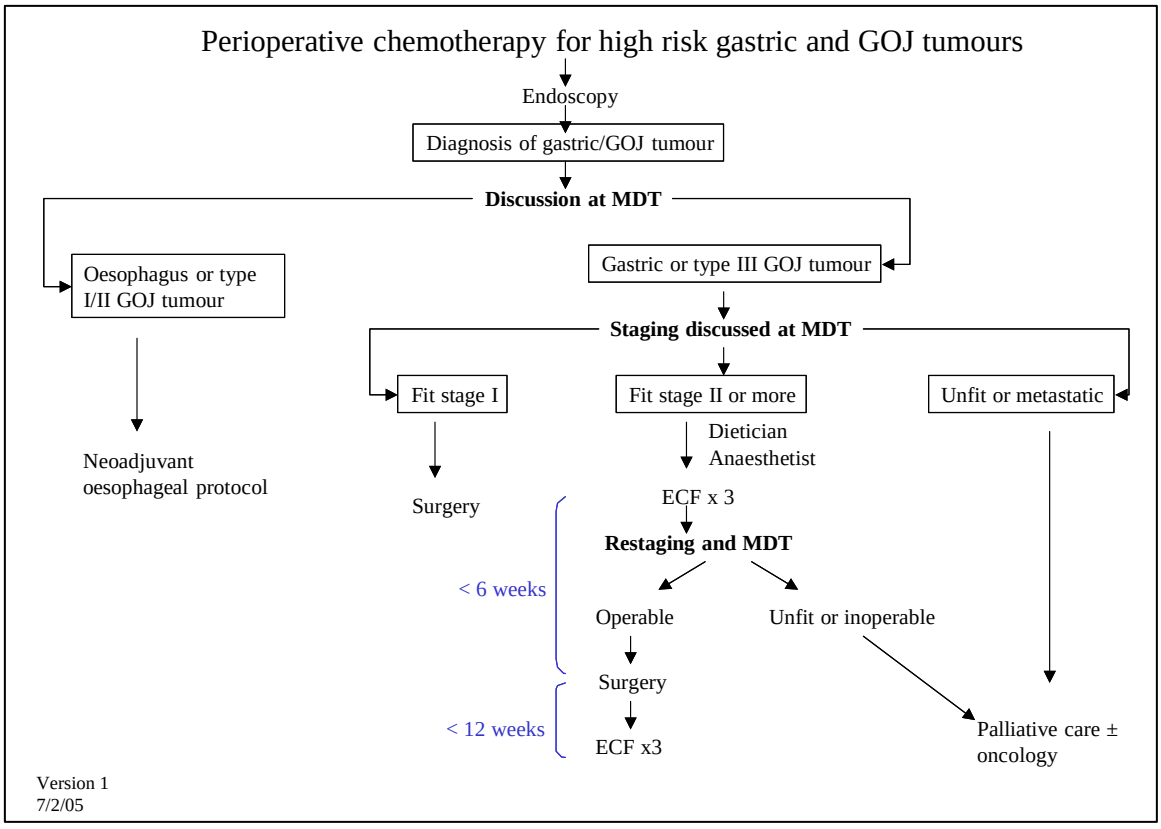
Stage 4

- T4 N1 M0
- T4 N2 M0
- T4 N3 M0
- T1 N3 M0
- T2 N3 M0
- T3 N3 M0

- Any T and N, M1

APPENDIX 2: Who Performance Status

Grade	Performance Status
0	Able to carry out all normal activity without restriction
1	Restricted in strenuous physical activity but ambulatory and able to carry out light work
2	Ambulatory and capable of all self-care but unable to carry out any work; up and about more than 50% of waking hours
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours
4	Completely disable; cannot carry out any self-care; totally confined to bed or a chair



Key Recommendations for the Management of GI Stromal Tumours

These recommendations will be reviewed with the updated national guidelines are published

Management

- The management of GISTs should be undertaken by a multidisciplinary team (MDT) with experience in this disease.

Diagnosis

- Pathological review of all cases should be made by a pathologist experienced in this tumour type.
- For resectable tumours a definitive diagnosis is usually made after surgery.
- For patients with unresectable and/or metastatic tumours a biopsy should be taken and a definitive diagnosis made.

Imaging Studies

- Endoscopic ultrasonography (EUS) especially of the oesophagus, stomach, duodenum and the anorectum can confirm the diagnosis of small incidental GISTs <2cms.
- For large tumours computed tomography (CT) of chest, abdomen and pelvis is recommended to assess primary tumour extension and to stage for metastases.

Histopathology and immunochemistry

- Macroscopic examination of the tumour with adequate sampling should be performed.
- The diagnosis of GIST is supported by positive CD117 staining as part of an immunohistochemical panel in a spindle cell tumour of the GI tract when morphologic and clinical features of the tumour are consistent with GIST.

Prediction of tumour behaviour

- All GISTs have malignant potential
- It is recommended that the National Institutes of Health workshop assessment criteria should be used to assess prognosis.

Treatment – Resectable Disease

- Surgery is the principal treatment for GISTs and suitability for resection should be explored by an appropriate sub-specialist surgeon.

- Patients should be considered for inclusion in clinical trials of neoadjuvant and adjuvant therapy.

Preoperative assessment

- A chest, abdominal and pelvic CT should be included in the preoperative assessment.

- Percutaneous biopsies should not be used if the tumour is considered resectable.

Principles of surgery

- A wide local resection with macroscopic and microscopic removal of the entire tumour is recommended (R0).

- Surgeon should aim to preserve function but not at the expense of an R0 resection

- Extended lymphadenectomy is normally not required.

- Some small tumours may be resected laparoscopically.

- Where adjacent organs are involved *en bloc* resection is recommended whenever possible – input from other specialist surgeons should be considered prior to embarking on a resection.

- Endoscopic resection is not recommended.

Follow up following resection

- All patients following resection should be discussed in an MDT.

- All patients should be followed up by clinicians linked to MDT.

- CT is the prim modality for detecting recurrence.

Treatment – Unresectable and/or metastatic disease

Prior to treatment

Baseline assessment should include:-

- Full history and clinical examination
- WHO performance status
- Concomitant medication

- Pregnancy or breast feeding
- Liver function tests
- Full blood count
- Weight
- The patient should be staged fully by CT

Treatment

- Conventional cytotoxic chemotherapy and radiotherapy are not recommended.

- Glivec (imatinib) should be used as treatment for unresectable and/or metastatic GISTs.

- The recommended starting dose of Glived is 400mg/day.

Follow up

- Patients should be seen weekly for the first month, then monthly for 2 months, then every 3 months thereafter, depending on response and tolerability.

- LFTs should be monitored at each visit.

- Toxicities should be monitored at each visit.

- A CT examination should be performed at 3 monthly intervals.

- Surgical resection should be performed if the tumour becomes operable.

- Treatment should be continued until there is radiological and symptomatic progression
    - Conventional criteria for measuring response should not be used in isolation upon which to base treatment decisions.
    - An increase in tumour size does not always indicate that treatment should be stopped.
    - In progressive disease, consider escalating dose of Glivec.

Other points to consider

- Role of PET-CT. This may help to determine the duration of neoadjuvant imatinib treatment and, therefore, should be considered as part of base line staging.

- Mutational analysis at a recognised laboratory may be useful in optimising a patients treatment in the metastatic setting.

- Adjuvant imatinib should be considered according to license.

- Second line sutent therapy should be considered especially in patients intolerant or resistant to imatinib with exon 13 or 14 mutation.

Management after Glivec

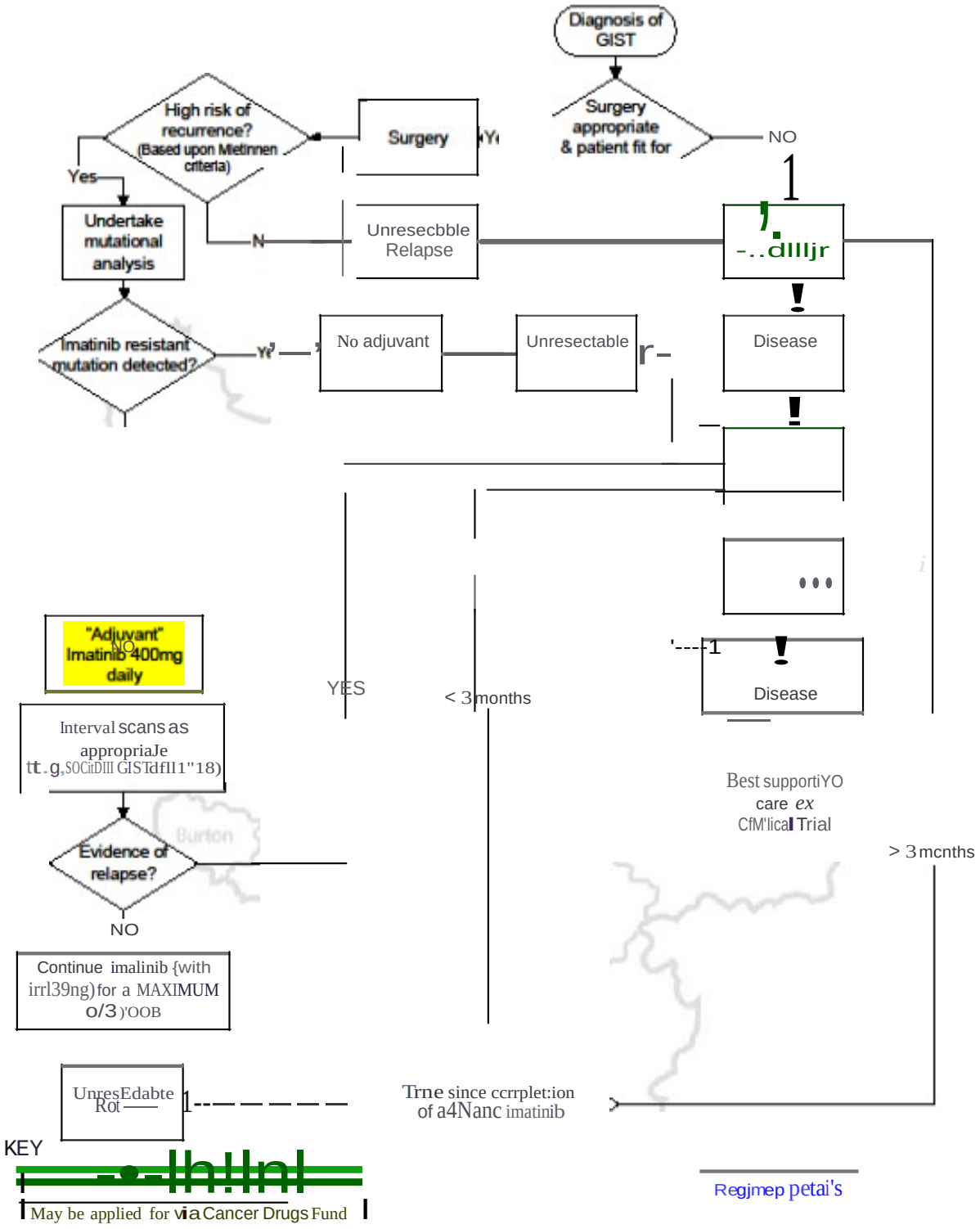
- The MDT should discuss and decide the treatment approach on a case-by-case basis.

- Surgery may have a role at any stage in management.

- Other interventional procedures may be beneficial such as stenting, radiofrequency ablation, embolism and local endoscopic treatment.

- Patients should be considered for appropriate clinical trials.

Chemotherapy Algorithm for Gastro Intestinal Stromal Tumours (GIST)



Wherever possible, eligible patients should be offered access to treatment as part of clinical trials

Guidelines for the use of adjuvant imatinib in the treatment of GI Stromal Tumours - Dr Anne L Thomas on behalf of the EMCN Upper GI NSSG

Summary

Imatinib is now approved for the adjuvant treatment of adult patients who are at significant risk of relapse following resection of c-KIT-positive GIST [1]. Patients who have a low or very low risk of recurrence should not receive adjuvant treatment. These guidelines are written in conjunction with the National Guidelines for the management of GI Stromal tumours. It is anticipated that they will need to be reviewed regularly and updated in light of the emerging data in this area

Patients will be identified from the Upper GI MDT at UHL. Adjuvant imatinib will be considered for patients with:

- Successful R0 resection of tumour
- High risk of relapse
- No significant co-morbidities
- PS 0-2
- C-kit Exon 11 mutation
- Treatment starts within 90 days of surgery

Background

Imatinib is well-established as a palliative treatment for patients with unresectable or metastatic GIST [2,3]. DeMatteo *et al* have demonstrated that adjuvant imatinib at 400 mg daily for one year, is safe and improves recurrence-free survival compared to placebo [4]. In a randomised phase III, double blind, placebo –controlled study, 713 patients were enrolled. 359 were randomised to imatinib 400 mg daily and 354 to placebo. Imatinib significantly improved recurrence-free survival compared with placebo (98% CI96-100) vs (83% CI 73-88) at 1 year; hazard ratio 0.35 [0.22-0.53]. On the basis of this data we recommend the use of adjuvant imatinib. On the basis of this study, imatinib was approved for the adjuvant treatment of adult patients who are at significant risk of relapse following resection of c-KIT-positive GIST.

Not all patients with resected GIST require adjuvant imatinib. It is known that patients with c-kit exon 11 mutation, have a better response to imatinib in the metastatic disease population and exon 9 mutations harbour resistance [5]. Data suggest that the presence of c-kit exon 11 mutation in patients treated adjuvantly with imatinib also confers a survival benefit [6,7]. In addition disease site, mitotic index and size of tumour are also important [8]. In general GISTs occurring in the stomach tend to have a more favourable prognosis than those of comparable size and mitotic rate occurring in the small intestine Gastric GISTs ≤10 cm in diameter and ≤5 mitoses per 50 HPFs have a low risk for metastasis; in contrast, those >5 cm in diameter and with >5 mitoses per 50 HPFs have a high risk for

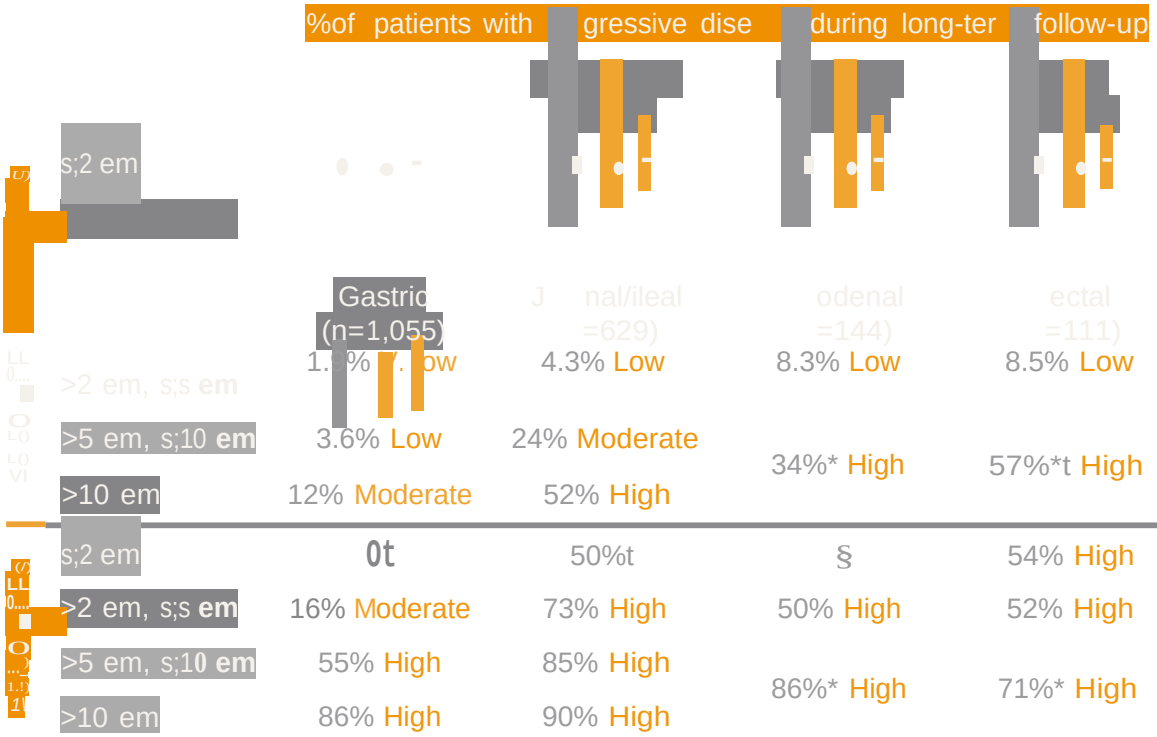
metastasis. All small intestinal GISTs >5 cm carry at least a moderate risk for metastasis, regardless of mitotic rate, while all with a mitotic rate >5 per 50 HPFs have a high risk for metastasis.

Proposal details
All patients who have had an R0 resection of GIST will be considered. Mutational analysis should be carried out in a recognised laboratory (eg. Dr Taniere at Birmingham). Only those with exon 11 mutation will be considered. Patients must have PS of 0-2 with no significant co-morbidities. Only patients deemed high risk will be treated – see table 1.

Treatment
Imatinib 400 mg daily which should commence within 90 days of surgery and continue for 1 year unless there are unacceptable toxicities or progression of disease

Follow up
Patients receiving adjuvant imatinib should have a CT at 3 months after surgery, then 6 monthly for 2 years, then annually to five years.

Table 1


%of patients with gressive dise during long-ter follow-up
s;2 em
Gastric (n=1,055)
J nal/ileal =629)
odenal =144)
ectal =111)
>2 em, s;s em
4.3% Low
8.3% Low
8.5% Low
>5 em, s;10 em
3.6% Low
24% Moderate
34%* High
57%*t High
>10 em
12% Moderate
52% High
s;2 em
0t
50%t
§
54% High
>2 em, s;s em
16% Moderate
73% High
50% High
52% High
>5 em, s;10 em
55% High
85% High
86%* High
71%* High
>10 em
86% High
90% High

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1. Novartis Pharmaceuticals UK Ltd (29 April 2009). Glivec summary of product characteristics. Novartis Pharmaceuticals UK Ltd; Frimley, Surrey.
2. Demetri GD, von Mehren M, Blanke CD *et al.* N Engl J Med 2002; 347(7): 472–480.
3. Blanke CD, Demetri GD, von Mehren M *et al*. J Clin Oncol 2008; 26(4): 620–625.
4. DeMatteo RP *et al*. Lancet 2009; 373(9669): 1097–1104.
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6. Li *et al* Proc ASCO 2009; 27: Abs 10556
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NOTE

There is a great deal of emerging data in this area and therefore it is anticipated that these guidelines may change before their formal 12 month review.

Chemotherapy Clinical Guidelines - Dr Anne L Thomas on behalf of the EMCN Upper GI NSSG

Introduction

This document has been written to provide guidance on the oncological treatment of Upper GI cancer in the East Midlands Cancer Network (EMCN). It should be read in conjunction with the EMCN Upper GI Network Site Specific Group (NSSG) Clinical Guidelines and EMCN Upper GI NSSG Radiotherapy Clinical Guidelines.

See Network website for approved chemotherapy protocols including dosing schedules and suggested dose modifications:

http://www.lnrcancernetwork.nhs.uk/healthcareprofessionals/medicinesmanagement/protocols/uppergi/default.aspx

All patients will be considered for entry into a clinical trial (see Clinical Trials contacts below).

All patients should be discussed within a Multidisciplinary Team (MDT) meeting before commencing initial treatment.

General Guidance Regarding Chemotherapy

Prior to commencing chemotherapy all patients should undergo standard oncological assessment. This should include but not be restricted to:

- Performance status
- Cardiac history
- Renal function
- Comorbidities (e.g. diabetes)

If patient has renal impairment (GFR 30-60 mls/min consider appropriate dose modification for Cisplatin)

Cisplatin is contraindicated if GFR is less than 30, consider substituting with Oxaliplatin or Carboplatin

If patient has cardiac history with reduced LV function omit Epirubicin

If patient has a significant history of uncontrolled angina avoid 5FU /Capecitabine

Please see below (Table 1) a summary of approved regimens:

Table 1

Regimen	Drug	Dose	Derby	Burton	Nottingham	Nottingham & Sherwood Forest Comments	Sherwood Forest	Lincoln	Lincoln comments	Kettering	Northampton	Leicester	Leicester comments
						UPPER GI							
ECF **Gastric** *dose per day* ***Day 8*** ***Day 15***	Epirubicin Cisplatin Infusor 5FU Infusor 5FU Infusor 5FU	50 60 200 200 200	Y	Y	y		N	Y		N	y	n	Only used of specifically want to give 5FU due to compliance issues
ECX **Gastric** *BD*	Epirubicin Cisplatin Capecitabine	50 60 625	Y	Y	y		N	Y		N	y	n	Now replaced by EOX
FAM **Gastric**	5FU Doxorubicin Mitomycin C	500 30 10	N	N	n		N	N		N	?	Y	2nd line or frail/compliance issues
IRINOTECAN **Gastric**	Atropine Irinotecan	250ug 350	N	N	n		N	N		N	?	n	Not funded
EOX **Gastric**	Epirubicin Oxaliplatin Capecitabine	50 130 625 round to	Y	Y	y		N	Y	also EOF	Y	y	Y	
5-FU + Carboplatin 48hr infusor (Day 1) 48hr infusor (Day 3)	Carboplatin 5-FU 5-FU	AUC 2000 2000	Y	Y	n		N	Y		N	?	y	AUC=5 5
5-FU + Cisplatin Day 1 Day 2 Day 3 Day 4 In-patient regimen	Cisplatin 5-FU 5-FU 5-FU 5-FU	80 1000 1000 1000 1000	Y	N	y	oesophagus	N	Y		N	y	y	
5-FU + Cisplatin 48hr infusor (Day 1) 48hr infusor (Day 3) Day case regimen	Cisplatin 5-FU 5-FU	80 2000 2000	Y	Y	n		N	Y		N	?	y	
Capecitabine + Cisplatin For 21 days	Cisplatin Capecitabine	60 625 (BD)	Y	Y	y	4-weekly with RT	N	N		N	?	y	
Continuous Infusional 5-FU 7-day infusor	5-FU	2100	Y	Y	n		N	N		N	?	n	
MF **Gastric** *dose per day* ***Day 8*** ***Day 15***	MMC Infusor 5FU Infusor 5FU Infusor 5FU	7 300 300 300	Y	Y	y		N	?		N	?	?	
Docetaxel **Gastric**	Docetaxel	75	?	?	?		?	Y		?	?	?	
Capecitabine + Cisplatin For 21 days **Gastric**	Cisplatin Capecitabine	80 1000 bd for 14 d	?	?	?		?	Y		?	?	?	
Sunitinib	Sunitinib PO	50mg OD 28 days	?	?	?		?	?		?	Y	?	
E-Carbo-X **Gastric** *BD*	Epirubicin Carboplatin Capecitabine	50 AUC5 625	?	?	?		?	?		?	Y	?	
E-Carbo-F **Gastric** *dose per day* ***Day 8*** ***Day 15***	Epirubicin Carboplatin Infusor 5FU Infusor 5FU Infusor 5FU	50 AUC5 200 200 200	?	?	?		?	?		?	Y	?	
Carboplatin	Carboplatin	AUC	?	?	?		?	?		?	?	Y	Single agent for Gastro-oesophageal jn. Rare but occasional use

1.0 **Oesophageal Cancer** (including Type I/II Gastro-Oesophageal Tumours)

1.1 Neoadjuvant Chemotherapy

Indications:
T2-3N0M0
T1-3N1M0
T1-3N0-1M1a

Treatment:
Either a doublet or triplet chemotherapy regimen is acceptable and the choice is at the oncologist's discretion once the patient has been reviewed.

- 2 cycles CF (as OE02 trial)
- 3 cycles of ECX or ECF

Tumour Assessment:
OGD, CT scan, EUS, PET/CT scan and laparoscopy (if tumour has sub-diaphragmatic component) pre-chemotherapy.
CT scan after 2-3 cycles of chemotherapy.
(Laparoscopy pre-surgery if not performed pre-chemotherapy).

Surgery:
To be performed 4-6 weeks following chemotherapy.

1.2 Adjuvant Chemotherapy

Indications:
Patients with lower third oesophageal or oesophago-gastric junction adenocarcinoma who underwent pre-operative chemotherapy with 3 cycles of ECX (or ECF) may be considered for 3 cycles of the same chemotherapy postoperatively on the basis of the MRC MAGIC trial which demonstrated a 13% absolute survival benefit at 5 years for peri-operative chemotherapy.

For patients undergoing surgery for oesophageal carcinoma without pre-operative chemotherapy, there is no proven role for adjuvant chemotherapy. However, in the presence of adverse risk factors (nodal involvement, positive surgical excision margins), adjuvant chemotherapy with up to 6 cycles of ECX (or ECF) may be considered on an individual case basis. Patients with positive surgical margins may also benefit from postoperative chemoradiation (see EMCN Upper GI NSSG Radiotherapy Clinical Guidelines).

Treatment:

- Up to 6 cycles of ECX or ECF
- Patients with positive proximal or distal surgical margins may also benefit from postoperative chemoradiation (see EMCN Upper GI NSSG

Radiotherapy Clinical Guidelines)

1.3 Radical Chemoradiotherapy (see EMCN Upper GI NSSG Radiotherapy Clinical Guidelines)

See EMCN Upper GI NSSG Radiotherapy Clinical Guidelines.

1.4 First Line Palliative Chemotherapy

Indications:
Metastatic disease
Localised or locally advanced disease and patient unsuitable for or unwilling to receive surgery or radical chemoradiation
Performance status 0-2

Treatment:

- 6-8 cycles of EOX or one of the regimens listed in table 1 (where contraindications exist see introduction paragraph)
- For patients with cardiac history single agent carboplatin is suggested or carboplatin/paclitaxel

1.5 Palliative Radiotherapy

Palliative external beam radiotherapy to the oesophagus can be offered for symptom control (see EMCN Upper GI NSSG Radiotherapy Clinical Guidelines).

Tumour Assessment:
CT scan pre-treatment
CT scan post 3-4 cycles (consider suitability for surgery if locally advanced disease down-staged)
CT scan post 6-8 cycles

1.6 Second Line Palliative Chemotherapy

Indications:
Patients remaining of good performance status (0-1) following disease progression after first line palliative chemotherapy or radical chemoradiation where surgical salvage is not appropriate.

Treatment:

(i) Disease-free interval from completion of previous chemotherapy > 6 months; consider rechallenge with EOX/ECF/ECX as appropriate
(ii) Disease-free interval < 6 months; No standard treatment options. Single agent Docetaxel. Consider referral for phase I/II clinical trials.
(iii) Cardiac Hx – Carbo-taxol (funding approval required)

Tumour Assessment:
CT scan every 2-3 months

2.0 Gastric Cancer (including Type III Gastro-Oesophageal Tumours)

2.1 Peri-operative Chemotherapy

Indications:
Gastric or oesophago-gastric junction adenocarcinoma considered suitable for curative resection (as per MRC MAGIC study):
T1, N1-3, M0
T2a, N0-3, M0
T2b, N0-3, M0
T3, N0-3, M0

Treatment:
ECX or ECF x 3 cycles preoperative and 3 cycles postoperative.

Tumour Assessment:
OGD, CT scan, laparoscopy pre-treatment. EUS for tumours involving oesophago-gastric junction
CT scan post 3 cycles

Surgery:
Surgery should be performed 4-6 weeks after completion of the third cycle of chemotherapy

2.2 Adjuvant Chemoradiation

Indications:
The Intergroup 0116 study demonstrated a survival benefit for patients who had undergone a microscopically complete surgical resection of gastric adenocarcinoma who received adjuvant chemoradiation therapy compared with no adjuvant treatment. although subsequent European studies failed to demonstrate this so clearly.

Adjuvant chemoradiation should therefore be considered a treatment option for these patients, particularly if there is considered to be a high risk of local failure (e.g. no/ limited lymphadenectomy performed, close or microscopically involved surgical excision margins). See EMCN Upper GI NSSG Radiotherapy Clinical Guidelines.

2.3 Adjuvant Chemotherapy

Indications:

The role of adjuvant postoperative chemotherapy following resection of gastric cancer remains unclear. A large number of clinical trials have addressed this question, the majority of which have not demonstrated a benefit from treatment. However, many of these trials were of poor methodologic quality, were underpowered to demonstrate a small but clinically relevant survival advantage, and employed chemotherapy regimens with limited activity in the advanced disease setting. Several meta-analyses of these data have been undertaken, which demonstrate a small benefit for adjuvant chemotherapy over no post-operative treatment, with a hazard ratio for survival between 0.72 and 0.88. However, when analysed separately, the positive effect of chemotherapy on survival was confined to Asian trials, with no benefit observed in Western studies.

Therefore at present, adjuvant chemotherapy should not be recommended routinely. However, in the presence of adverse risk factors (nodal involvement, positive surgical excision margins), or where patients proceeded directly to surgery for gastric outlet obstruction, adjuvant chemotherapy may be considered on an individual case basis.

Treatment:
Up to 6 cycles ECX or ECF

2.4 First Line Palliative Chemotherapy

Indications:
Metastatic disease
Locally advanced disease
Localised disease and patient unsuitable for or unwilling to receive surgery
Performance status 0-2

Treatment:

- 6-8 cycles of EOX or one of the regimens listed in Table 1 (where contraindications exist see introduction paragraph)
- For HER-2 positive patients (IHC3+ or FISH amplified) CX or CF x 6 cycles + Trastuzumab until progressive disease. ~~.)~~

Tumour Assessment:
CT scan pre-treatment
CT scan post 3-4 cycles (consider suitability for surgery if locally advanced disease down-staged)
CT scan post 6-8 cycles

2.5 Second Line Palliative Chemotherapy

Indications:
Patients remaining of good performance status (0-2) following disease progression after first line palliative chemotherapy or peri-operative

chemotherapy.

Treatment:

(i) Disease-free interval from completion of previous chemotherapy > 6 months; consider rechallenge with EOX/ECX/ECF

(ii) Disease-free interval < 6 months; no standard treatment options. FAM is approved. Single agent Docetaxel. Consider referral for phase I/II clinical trials.

Tumour Assessment:
CT scan every 2-3 months

2.6 Palliative Radiotherapy

Palliative radiotherapy to the stomach can be offered for haemostasis if surgery is not indicated, or for pain management.

3.0 Gastrointestinal Stromal Tumours (see national guidance)

3.1 Adjuvant Therapy

Imatinib 400mg od for 1 year is licensed for the adjuvant treatment of high risk GIST (funding approval required). Please see NSSG agreed Guidelines for the use of adjuvant imatinib in the treatment of GI Stromal Tumours.

3.2 First Line Metastatic Therapy

Patients presenting with advanced inoperable disease should have tumour sent for mutational analysis as this may aid further treatment.

Imatinib 400mg daily is currently considered standard therapy for all patients. However, for patients with exon-9 c-kit mutations or wild type, there is emerging evidence for a benefit from higher initial Imatinib doses e.g. 600-800mg daily (funding approval required).

<u>Monitoring for patients receiving Imatinib</u>
The occurrence of toxicity following institution of Imatinib is unpredictable. The following schedule of assessments should be undertaken, with clinical assessment, FBC, U+E and LFT performed at each of 2 weeks, 4 weeks, 8 weeks, 12 weeks then 3 monthly thereafter.

Tumour assessment should be performed with CT every 12 weeks during Imatinib therapy.

3.3 Second Line Metastatic Therapy

Options for second line treatment include high dose Imatinib 800mg daily (funding approval required) or Sunitinib 50mg daily for 4 of every 6 weeks.

Treatment can be decided on the basis of testing for exon-9 mutation, for example:

- If the patient is exon-9 +ve then high dose Imatinib 800mg daily is the option of choice (funding approval required)
- If the patient is exon-9 –ve (or if funding is not available exon-9 +ve patient) then Sunitinib 50mg daily for 4 of every 6 weeks will be the option of choice.

Clinical Trials Contacts

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 details

Burton Hospitals NHS Foundation Trust – Clinical Trials Office:
01283511511 extension 5764

Derby Hospitals NHS Foundation Trust – Clinical Trials Office:
01332 783095

Kettering General Hospital NHS Foundation Trust – Clinical Trials Office:
01536 492588

Northampton General Hospital NHS Trust – Clinical Trials Office:
01604 545911

Nottingham University Hospitals NHS Trust – Clinical Trials Office:
City Hospital – 01159691169 x54676

Sherwood Forest Hospitals NHS Foundation Trust – Clinical Trials Office:
King's Mill Hospital – 01623 622515 extension 6304

United Lincolnshire Hospitals NHS Trust – Clinical Trials Office:
Lincoln County Hospital– 01522 573202
Pilgrim Hospital, Boston – 01205 364801 extension 6031
Grantham & District Hospital – 01476 464535

University Hospitals of Leicester NHS Trust – Clinical Trials Office:
0116 2586318

Radiotherapy Clinical Guidelines – Dr S Mukherjee on behalf of the EMCN Upper GI NSSG

PURPOSE:
To ensure that there is a documented protocol for the treatment of oesophago-gastric and pancreatic cancer which is clearly defined within a consistent and standard process.

SCOPE:
Oesophagus
Pre-and Post-Operative Chemo-Radiotherapy
Definitive Radiotherapy (+/- chemotherapy)
Palliative Radiotherapy
Brachytherapy

Stomach
Palliative Radiotherapy

Pancreas
Pre-operative chemo-radiotherapy
Definitive chemoradiotherapy
Palliative Radiotherapy

AUTHORISED PERSONNEL:
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Oesophagus

ANATOMY [ref: Crosby et al]

The oesophagus is usually measured from central incisors (usually 15-40cm) at endoscopy. It is often divided into thirds.

Cervical oesophagus	Starts below cricopharyngeus to thoracic inlet	15-18cm	C6 to T2/3
Thoracic oesophagus			

Upper	To tracheal bifurcation	18-24cm	T3 ~T 4/5
Middle	To ½ way to OG junction	24-32cm	T5 ~ T8.
Lower	To OG junction	32-40cm	T8~T10

The sterna notch is at 18cm and the carina is usually at 25cm but this can vary significantly between patients [Roberts SA, Clin Onc]

GOJ tumours are defined as tumours that have their centre within 5cm proximal or distal of the anatomic cardia. Siewert describes a system to further sub-classify tumours involving the GO junction. Type I tumours are predominantly oesophageal and Type III predominantly gastric. In Type 11 tumours the disease equally straddles the junction.

PRIMARY/LYMPHATIC SPREAD TO BE CONSIDERED FOR RT PLANNING:

PRIMARY:

Submucosal [can have skip lesions], peri-neural and local adjacent structures [pleura, mediastinum, trachea, aorta]

LYMPHATIC.

The first station lymph nodes of the oesophagus are para-oesophageal, para-tracheal, subcarinal, supraclavicular, deep cervical, left gastric and coeliac.

SUMMARY OF INDICATIONS FOR RT/CRT:

Palliative RT	Definitive CRT [Cervical, Thoracic, GOJ Type I and II, total disease length <10cm]	Pre-operative and Post-operative CRT
• Advanced +/- metastatic disease with prominent local symptoms [use as primary therapy or adjunct to palliative chemotherapy] • Patients not considered suitable for radical treatment	• Localised disease considered by MDT to be at high risk of R1 or R2 resection where the expected total cranio-caudal length of tumour plus nodes will be encompassable in a radical fields (<8-10cm) • Medical co-morbidities that are likely to cause unacceptable peri-operative morbidity/mortality • As an alternative to surgery in advanced operable disease where the expected survival is likely to be less than 2 years* and in patients with SCC	*In selected cases the MDT may offer triple modality therapy in fit patients with:* • Advanced inoperable disease with aim to downstage prior to surgery • Positive resection margins or tumour perforation where the risk of local recurrence is considered very high • In the context of a clinical trial *The increased peri-operative risks of triple modality therapy must be carefully weighed against its benefits and implications fully discussed with the patient but the CROSS data indicates potential benefits to selected patients*

* As patients who relapse within 2 years never regain their Quality Of Life [Blazeby, Cancer 88(8), 2000]

Radiotherapy/chemo-radiotherapy: indications and dose schedules:

PALLIATIVE RADIOTHERAPY:

Indication: dysphagia, odynophagia, bleeding

20Gy in 5# or 30Gy in 10# to tumour with 2-3 cm margin, using 6-10MV photons, anterior-posterior parallel opposed fields.

Patients with localized disease, of good performance status [WHO PS 0-1], who are otherwise considered unfit for radical radiotherapy/chemoradiotherapy due to

co-morbidity may be offered high dose palliative radiotherapy [40Gy in 15# to a planned volume] to maximize local control.

Single fraction 8-10Gy using 6-10MV photons, anterior-posterior parallel opposed fields may be used to treat bleeding, non-obstructive tumours

Intra-luminal brachytherapy [ILBT]: 12 Gy to a depth of 1cm, preferably under endoscopic guidance can be used as primary therapy for dysphagia or recurrence of dysphagia following EBRT. Dysphagia scores at 3 months following ILBT has been shown to be superior to stenting [ref] although no randomized data exists comparing ILBT to short course palliative RT. Local expertise, patient choice, invasive procedure vs multiple visits must be taken into consideration when offering either modality to patients. Departments offering ILBT should have their own SOPs in place.

DEFINITIVE CRT [dCRT]:

Indications:

- Deemed unsuitable for surgery [or at high risk of R1 /R2 resection] because of local infiltration, co-morbidity or age
- Patient choice of CXRT over radical surgery
- Advanced operable disease with life-expectancy <2years or patients with Squamous cell carcinoma as an alternative to surgical-based therapy.

Patients being considered for CRT should satisfy all of the criteria below:

- Localised disease [T1-4, N0-1, M1a (coeliac nodes)],
- WHO PFS 0-1,
- Maximum disease [ie tumour + lymphadenopathy] length ≤10cm
- Adequate cardiac [EF >40%, no IHD*], respiratory [FEV1>1L], renal [GFR>50*], haematological and liver function to tolerate multi-modality treatment.
  *In presence of renal or cardiac dysfunction consider modified regimens [see below]

Rationale, evidence and caveats:

- Updated results from the MRC OE02 study indicate that 5 year survivals for patients treated with surgery [S] and chemotherapy/surgery [C+S] are 17.1% and 23% respectively. Patients with R0, R1 and R2 have a 3-year survival of 42.4%, 18% and 8.6% respectively [Allum, JCO 27(30), Oct 2009]. Given the poor survival in patients with positive margins, dCRT should be offered as alternative to surgery in advanced tumours where pre-operative investigations indicate a high likelihood of positive margins
- Although no randomised studies exists comparing C+S v dCRT in operable oesophageal cancer, retrospective series of dCRT and

randomised studies of CRT +/- surgery indicate similar efficacy of dCRT compared to surgical-based treatment. 3-month post treatment mortality is low with dCRT [0.8%] although there is higher requirement for oesophageal stent (32% v 5%) [Bedenne, JCO, 2007].

Selected studies of dCRT:

Author, year	N	Treatment	SCC[%]	2-year OS [%]	3-year OS [%]	5-year OS [%]	Median OS [mo]	p
Adams[series] 2007	118	dCRT		50		27		
	65	C+S		37		27		
	57	CRT+S		57		40		
Crosby[series] 2004	90	dCRT	48%	51	44	25		
Stahl 2001	177	dCRT v CRT+S	100%	35 v 38	24 v 31%	-	15 v 16	NS
Bedenne 2007	444 [randomised =259]	dCRT v CRT+S	90%	40 v 34	-	-	19.3 v 17.7	NS

Recommended CRT regimen(s):

	Induction phase	Concurrent phase	RT prescription
Standard	Cisplatin 60mg/m^2 D1 and capecitabine 625mg/m^2 D1-21 x 2 cycles	Cisplatin 60mg/m^2 D1 and capecitabine 625mg/m^2 D1-21 x 2 cycles Note: stop capecitabine on the last day of RT	dCRT: 50Gy in 25 fractions pre-OP and Post-op: 45 Gy in 25 fractions
Cisplatin contraindicated [Renal impairment**, low cardiac ejection fraction or sensori-neural deafness]	Replace cisplatin with carboplatin AUC 5	Replace cisplatin with carboplatin AUC 5	As above
Capecitabine contraindicated [renal impairment** or dysphagia]	Replace with infusional 5FU 200 mg/m^2	Replace with infusional 5FU 200 mg/m^2	As above
Ischemic heart disease [adapted from phII study of cis/docetaxel in pre-op CRT] [Ruhstaller, 2009]	Carboplatin AUC5 & Paclitaxel 175mg/m^2 D1 x 2 cycles OR Cisplatin 75mg/m2 & docetaxel 75mg/m^2 Day 1, 22	Carboplatin AUC5 & Paclitaxel 175mg/m^2 D1 x 2 cycles OR Cisplatin 25mg/m2 & docetaxel 20mg/m^2 weekly x 5 weeks	As above As above
Elderly patients/ not	Options [pragmatic regimens, modified from published literature]:		

considered fit for full dose CRT	• Cisplatin 25-35 mg/m2/week + RT [40Gy/15# or 50Gy/25#][adapted from Kumar, Acta Oncologica, 2001] • Docetaxel 20 mg/m2/week + RT [40Gy/15# or 50Gy/25#] [adapted from Font, Clin Trans Oncol, 2007] • Cis 60mg/m^2 Day 1+cap 625mg/m2 D1-21 + RT[40Gy/15#] with/without 1 cycle CisCap as induction chemotherapy. [adapted from Walsh, NEJM, 1996] • Radical radiotherapy alone [upto 64Gy in 32 #, depending on tolerance]

****** Chemotherapy dose modification for renal impairment [adopted from SCOPE protocol]. Formal 24 hour urine collection or EDTA GFR should be performed if baseline calculated GFR <60ml/min. Formal GFR should be repeated and chemotherapy dose adjusted if calculated GFR drops by >25% during treatment.

Baseline & prior to day 1 Action
60mls/min - Continue full dose
50-59 mls/min - Cisplatin 50% dose
40-49mls/min - Cisplatin 50% dose; Capecitabine 75% dose
30-39 mls/min - Stop cisplatin, use carboplatin AUC 5; Capecitabine 50%
< 30mls/min - Stop cisplatin + capecitabine, use carboplatin AUC 5+ 5FU
Consider dose reduction of 5FU in cases of severe renal impairment (GFR<10)

PRACTICAL GUIDE FOR PLANNING

For clinical management purposes upper third can be treated like H + N eg post cricoid, (eg. need immobilisation shell for planning, and treatment with anterior and ant oblique fields, combined modality therapy as part of H + N team approach). Not discussed further here.

Localisation

Patients should be planned and treated in the supine position with their arms above their heads. Wherever possible the planning CT scan should be performed within 2 weeks of starting the Neo-adjuvant phase of chemotherapy AND within 6 weeks of the staging spiral CT scan.

In most cases the GTV (extent of primary and nodal disease) is defined by the EUS taking into account information from the diagnostic spiral CT scan, barium studies and 18-FDG PET scan. The target volumes are localised on axial slices of the planning CT scan using EUS to define a reference point (carina or arch of aorta) as well as the superior and inferior extent of the GTV. The GTV is marked on axial images and PTV grown with appropriate lateral margins. The PTV for the superior and inferior margins should be drawn manually to follow the axis of

oesophagus, ie not generated automatically in the sup-inf direction by the planning system.

Planning Target Volume (PTV)

The target volume is;

superiorly and inferiorly	the EUS defined extent of tumour (primary or nodal) with a 3cm margin along the axis of the oesophagus (see above)
laterally and anteriorly	1.5margin around the tumour defined by the planning CT scan
posteriorly	1-1.5cm margin around the tumour defined by the planning CT scan

The maximum treatment field length is 17cm, ie maximum EUS disease length (primary tumour and lymph nodes) 10cm assuming 1cm extension from PTV to field length.

Lower 1/3rd tumours

If the tumour involves the GO junction, ie Siewert Type 1, the inferior margins to define the PTV should be 3 cm below the EUS defined GTV. However the inferior volume should be grown manually to cover the lymph node stations along the lesser curve to include the para-cardial, and left gastric lymph nodes. Once again, **the maximum treatment field length is 17cm.**

Treatment delivery

All treatment will be delivered in a single 3D (conformal) CT planned phase ie treatment cannot start following conventional simulation. Given the target volume described above and the normal tissue dose constraints below, it is up to individual centres to decide the field arrangements. It is recommended however that a single 3 or 4 field technique is usually satisfactory, with anterior-posterior parallel opposed and two posterior oblique or lateral fields. 4DCT planning for GOJ tumours may be used in centres where this has been passed through QA.

The total dose is 45-50Gy delivered in 25 fractions, treating each field daily Mon-Fri and prescribed to the ICRU 50 reference point, usually the point of intersection of the central axes. The PTV min should be no less than 93% and the PTV max should be no more than 107% of the dose prescribed to the ICRU 50 reference point. No point outside the PTV should receive >105%.

Normal Tissue Tolerance

The following normal tissue tolerance doses should be observed and recorded for each patient plan;

Spinal cord	less than 5% of the spinal cord within the target volume should receive more than 40Gy and none should receive more than 45Gy ie D 40Gy<5%, D45Gy<0

Heart	less than 40% of the total volume of heart should receive more than 30Gy ie V30Gy < 40%
Lung	less than 25% of the total lung volume should receive more than 20Gy ie V20Gy < 25%
Liver	less than 60% of the total liver volume should receive more than 30Gy ie V30Gy<60%

Gaps in treatment should be managed according to usual Centre practice. Squamous cell carcinomas should be Category 1, ie unscheduled breaks in treatment should not lead to prolonged overall treatment time where possible eg by delivering 2 fractions per day (more than 6 hours apart).

Pre- treatment and on-treatment verification:
Centres should follow their local protocols as regards pre-treatment verification. This may include a simulator check using barium prior to start of the treatment where any adjustments required should also be made according to local practice. An alternative system verifies the positional accuracy on the first fraction of treatment by generation of 'dummy' isocentre fields in the treatment planning system. As such the treatment is verified on set and a pre-treatment simulator check is not performed. On-treatment verification would be as per centre protocols but it would be reasonable to obtain portal images on first 3 fractions of treatment and weekly thereafter. Images are verified using anatomical matching using vertebral bodies for anterior image and vertebral bodies and sternum for lateral image.

The SCOPE Trial 'treatment planning and delivery' document provides useful guidance on RT planning although the ultimate responsibility lies with the individual clinician/department.

Explanation to patient
Procedure plus side effects:
Acute – tiredness, oesophagitis, pain or difficulty swallowing, myelosuppresion, nausea, diarrhoea, painful sore eyes (5FU) palmar plantar syndrome, renal and neurotoxicity.
Late – pnuemonitis, oesophageal stricture, fistula.

Supportive treatment during treatment
Dietician assessment [all patients], PEG feeding if required
Weekly review clinic
Mucaine, loperamide, antiemetics, pyridoxine(?), treat infection, transfuse as necessary

N.B. All patients undergoing radiotherapy/chemoradiation should undergo transfusion to maintain their Hb above 12g/dl.

Stomach

The use of radiotherapy in gastric cancer is less frequent

Palliative Radiotherapy:
Indications: Bleeding, dysphagia, pain.

Technique
Single anterior-posterior field arrangement

Localisation
CT simulation with water load [or barium contrast] to define stomach and tumour location is preferable. Endoscopy and diagnostic CT information regarding tumour location must be available. The field is defined by the whole stomach or if it can be identified, by the tumour with a 2cm margin. Field sizes usually 10 x 10–12 x 12 cm.

Dose

Haemostasis	8Gy in single #
Other palliation	20Gy in 5# or 30Gy in 10#

Post-operative chemoradiation:

The benefit of post-operative chemoradiation for gastric cancer has been suggested following the outcome of a single US Intergroup trial, Int 0116. However this treatment is not common practice in the UK where MAGIC style peri-operative chemotherapy is used. The decision to give post-operative CXRT may be made at the MDT in exceptional cases in fit patients with R1/R2 resection or heavy node positivity. If this treatment is used it is suggested that the protocol described in this study is followed carefully. The RT technique is outside the remit of this document.

East Midlands Cancer Network

East Midlands Upper G I Pathway for patients aged 13-24 years

All patients suspected with cancer between the ages of **13-18 years** living within the East Midlands (East Midlands region as part of the East Midlands Cancer Network boundaries) must be referred to the East Midlands Children's and Young Persons' Integrated Cancer Service *(Principal Treatment Centre at Nottingham University Hospitals, Queen's Medical Centre Campus (Nottingham Children's Hospital) and University Hospitals of Leicester, Leicester Royal Infirmary site)*. This service is accessed by contacting the Paediatric Oncology Consultant on-call at Queens Medical Centre in Nottingham when a patient is judged likely to have cancer. The contact number for this service is 0115 849 3302.

- The paediatric pathway requires the centralisation of diagnostic investigations, surgery and the most intensive chemotherapy to QMC, but most patients from Leicestershire, Rutland and Northamptonshire will receive most or all of their treatment in Leicester. There is also a shared care arrangement with the paediatric team at Northampton General Hospital.

- The Paediatric team welcomes discussions about patients in this age group with local and regional site specific teams in case a specific patient needs individualisation of their pathway.

Patients aged **18 years (but <19y)** are to be treated in an age-appropriate cancer facility, but depending on education/employment/diagnosis/trial availability etc it may be appropriate for them to be treated by the Paediatric or the Adult site-specific pathway (in age-appropriate facilities). A discussion between the

Paediatric Team and the Site-specific Consultant about patients in this age group helps to ensure that patient's needs are best served. This decision will be made on a patient-by-patient basis, but the location of care should be in an age-appropriate environment.

- The *East Midlands Children's and Young Persons' Integrated Cancer Service* currently provides this service within a predominantly paediatric setting in the Leicester Royal Infirmary and at Queens Medical Centre in Nottingham. This is being upgraded in order to enhance the teenage age-appropriate cancer facilities.

All patients aged **19-24 years** will be offered the choice:

- to be referred to a young adult age-appropriate cancer facility
- access local adult cancer services
- It is good practice for patients to be seen at the PTC TYA team prior to making the choice with regards to treatment location

The East Midlands will have young adult (19 – 24y) age-appropriate cancer facilities at the following sites:

- Leicester Royal Infirmary, University Hospitals of Leicester (13-24 years)
- Nottingham City Hospital, Nottingham University Hospitals (19-24 years)
- *(Nottingham Children's Hospital, Queen's Medical Centre Campus – Nottingham University Hospitals (13-18 years)*

Choice regarding place of care will also be offered as appropriate at relapse, palliative and end of life care and for long term follow up.

The young adult age-appropriate inpatient, day care and outpatient facility is under development and until this is in place the additional age-appropriate support that these patients will be able to access in Leicester and Nottingham will be limited to an on-site teenage and Young Adult Activity Coordinator/Development Officer, Social Worker and TYA Clinical Nurse Specialist. As soon as the facilities are completed all Site - Specific MDT's will be informed.

All patients diagnosed with cancer between the ages of 13-24, living within the East Midlands (East Midlands region as part of the East Midlands Cancer Network boundaries) must be discussed at the TYA MDT and relevant Site Specific MDT or Paediatric Cancer MDTs. The TYA MDT will discuss the treatment plan forwarded from the (Site Specific MDT/Paediatric Cancer MDT) and discuss the patients psychosocial care needs. Please refer to the East Midlands TYA Multidisciplinary Operational Policy for the referral process *(referral information outlined in brief below)*

- Referrals to the TYA MDT will need to made via the referral form, this referral form can be obtained from your trust Cancer Centre, East Midlands Cancer Network website www.eastmidlandscancernetwork.nhs.uk or the Principal Treatment Centre.
- The following referral routes have been identified:
  - Site Specific MDTs (MDT Coordinator) 19-24 years
  - Paediatric Cancer MDTs (MDT Coordinator)
  - Surgeon at Biopsy stage of the pathway
  - Childrens and Young Persons' Integrated Cancer Service 13-18 years
  - Via Pathology Department
  - Via Alert System

- Via Clic Sargent Social Workers
- In exceptional circumstances trusts/Departments i.e. other medical departments or psychosocial/psychological service providers
- In exceptional circumstances by GP/Dentist referral

All patients should be referred back to the TYA MDT on completion of treatment, at relapse, and when commencing palliative and end of life care.

Responsibility for making the referral will lie with local MDT Coordinators, Consultants, Cancer Centres and Clinical Nurse Specialists. All referral forms accompanied with relevant information relating to the patient will either be faxed to the Principal Treatment Centre or electronically using the nhs.net email address or (via post is discouraged due to the inherent delay). Contact details can be found by telephoning UHL 0116 2586721 and NUH 0115 9691169 ext 54550 and asking for assistance relating to the TYA MDT.

All patients aged 15-24 years will need to be registered with the TYAC Registration Process; this will be completed via the TYA MDT.

Chemotherapy Algorithms

UGI Chemotherapy Algorithms can be viewed at:

http:www/eastmidlandscancernetwork.nhs.uk/_HealthProfressionals-Chemotherapy-oncology-UGIcancer.aspx