Barts Health NHS
NHS Trust

LONDON CANCER
NORTH AND EAST

NHS
Royal Free London
NHS Foundation Trust

London Cancer

HEPATIC PANCREATIC AND BILIARY (HPB)

FACULTY CLINICAL GUIDELINE

Management of Patients with Colorectal Liver Metastases

SEPTEMBER 2014

This operational policy is agreed and accepted by:

Designated individuals	**Signed**	**Date**
HPB Pathway Director		
Dr Andrew Millar		15/09/2014
Colorectal Tumour Specific Group		
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Contents

1. Background

In April 2011, NHS London published outline specification for an Integrated Cancer System (ICS) for the capital to delivery seamless cancer care. The North Central London & West Essex Cancer Network and North East *London Cancer* Network merged to become the *London Cancer* ICS.

London Cancer ICS began operation on 1 April 2012. It is designed to empower our dedicated and talented clinicians to drive improvements by implementing a coordinated cancer service via integrated patient pathways. It also brings together providers from across the health community, academia and the voluntary sector to drive step change improvements in outcomes and experience for the patients and population we serve.

There are two HPB Specialist MDTs (SMDT) in *London Cancer*, based at the Royal London Hospital (part of Barts Health NHS Trust) and Royal Free Hampstead NHS Foundation Trust.

1.1. Introduction

Recent advances in liver surgery and new chemotherapeutic agents have altered the approach to colorectal liver metastases (CLM) dramatically. Of the 50-60% of patients with colorectal cancer who develop liver secondaries up to 40% will be amenable to resection, more than doubling the historic resection rate of 10-15%, and more than 40% of these patients will be alive and disease free at 5 years post-resection (compared to an untreated 5 year survival rate of less than 1%). Radiofrequency ablation (RFA), stereotactic radiotherapy (cyberknife) has a developing role in patients with liver alone metastases and may be suitable for patients who would not withstand major liver surgery due to co-morbid disease. The imaging of all patients with CLM should be assessed by a specialist HPB MDT and patients who may benefit from surgical or radiological intervention should undergo clinical review. UK National Guidelines on the assessment and indications for liver surgery in patients with colorectal metastases have been prepared by the surgical section of the British Society of Gastroenterologists and were published in 2006.

(O J Garden, M Rees, G J Poston, D Mirza, M Saunders, J Ledermann, J N Primrose and R W Parks *Gut 2006*; **55** (Suppl III): iii1–iii8).

1.2. Royal Free Hampstead (RFH) SMDT

The Royal Free HPB SMDT receives referral from the Mount Vernon Cancer Network and the North Central part of *London Cancer*, serving a population of over 3.4 million.

CCG name	ADS registered population adjusted to new ONS13 projections
NHS Barnet CCG	374,434
NHS Camden CCG	243,707
NHS Enfield CCG	306,891
NHS Haringey CCG	274,286
NHS Islington CCG	211,870
NHS West Essex CCG	280,158
NHS Bedfordshire CCG	429,384
NHS Luton CCG	206,245
NHS East and North Hertfordshire CCG	560,129
NHS Herts Valleys CCG	577,721
Total	**3,464,825**

The referring MDTs are:

- Hemel Hempstead Hospital (West Hertfordshire Hospitals NHS Trust)
- Luton and Dunstable Hospital (Luton and Dunstable Hospital NHS Foundation Trust)
- Lister Hospital (East &North Hertfordshire NHS Trust)
- Watford General Hospital (West Hertfordshire Hospitals NHS Trust)
- QEII (East &North Hertfordshire NHS Trust)
- Barnet General Hospital (Barnet & Chase Farm Hospitals NHS Trust)
- Chase Farm Hospital (Barnet & Chase Farm Hospitals NHS Trust)
- North Middlesex University Hospital (North Middlesex Hospital NHS Trust)
- Princess Alexandra Hospital (Princess Alexandra Hospital NHS Trust)
- Whittington Hospital (Whittington Hospital NHS Trust)
- University College Hospital (University College London Hospitals NHS Foundation Trust)
- Royal Free Hospital (Royal Free Hampstead NHS Foundation Trust)

1.3. Royal London Hospital SMDT

The Royal London Hospital HPB SMDT receives referral from North East part of *London Cancer*, South Essex and East Sussex, serving a population of 3.4 million.

CCG name	ADS registered population adjusted to new ONS13 projections
NHS Barking & Dagenham CCG	193,736
NHS City and Hackney CCG	261,712
NHS Havering CCG	252,238
NHS Newham CCG	320,748
NHS Redbridge CCG	277,717
NHS Tower Hamlets CCG	265,181
NHS Waltham Forest CCG	272,648
NHS Basildon and Brentwood CCG	255,603
NHS Castle Point, Rayleigh and Rochford CCG	171,942
NHS Southend CCG	178,029
NHS Thurrock CCG	163,848
NHS Brighton & Hove CCG	282,892
NHS Eastbourne, Hailsham and Seaford CCG	181,704
NHS Hastings & Rother CCG	180,258
NHS High Weald Lewes Havens CCG	162,714
Total	**3,420,970**

The referring MDTs are:

- The Royal London Hospital (Barts Health NHS Trust)
- Newham Hopsital (Barts Health NHS Trust)
- Whipps Cross Hospital (Barts Health NHS Trust)
- Homerton Hospital (Homerton University Hospital NHS Trust)
- Queen's Hospital (Barking, Havering and Redbridge University Hospitals NHS Trust)
- Southend Hospital (Southend University Hospital NHS Foundation Trust)
- Basildon Hospital (Basildon and Thurrock University Hospitals NHS Foundation Trust)
- Colchester Hospital (Colchester Hospital University NHS Foundation Trust)
- Royal Sussex County Hospital (Brighton and Sussex University Hospitals NHS Trust)
- Conquest Hospital (East Sussex Healthcare NHS Trust)
- Eastbourne District General Hospital (East Sussex Healthcare NHS Trust)

2. Referral Guideline

See also Chapter 4

Referrals should be made using the *London Cancer*& MVCN Liver Resection for Colorectal Metastases Proforma *(Appendix 1)* and sent to the Royal Free Hospital HPB Office or the Royal London Office as appropriate (fax number and address on proforma).

HPB SMDT	**MDT Co-ordinator**
Royal Free	**Scott Green** **Tel** 0207 794 0500 **ext:** 31409 **Bleep**: 71-2159 **Email:**scotgreen@nhs.net **Referral to be sent to Rfh.hpbsmdt@nhs.net**
Royal London	Sally Howe or Emma Rothwell Fax 020 3594 3255 Tel 020 3594 0762 or 020 3594 0763 E-mails for sending referrals (best copied to all 3): sally.howe@bartshealth.nhs.uk; emma.rothwell@bartshealth.nhs.uk; karen.mawire@bartshealth.nhs.uk

2.1. HPB MDT Meetings

All patients with known or suspected colorectal liver metastases will be reviewed at the regional HPB MDT.

HPB SMDT	**MDT Co-ordinator**
Royal Free	Every Tuesday 0800-1230 Mount Vernon Oncologists participate in the NLCN Hepatobiliary MDT Meeting at the Royal Free on Tuesday morning via video-conferencing facilities at Mount Vernon Cancer Centre at 0800-0900.
Royal London	The SMDT is held every Wednesday 0800-1100 There are separate video-linked discussions between the RLH HPB surgeons and the local MDTs at Colchester, Southend, and Basildon (on Mondays, Thursdays and Fridays) and the Queen's MDT is attended by a RLH HPB surgeon

All patients with liver alone metastases will be offered:

- Review by a GI oncologist dealing with colorectal metastases.
- Review by an HPB surgeon with experience in managing liver metastases.
- Conclusions from the HPB MDT are recorded in real time into MDT Information System (Infoflex or Somerset) during the HPB SMDT.
- Copies of MDT discussions will be emailed to managing/referring Consultants within 1 working day detailing the discussion and plan/decision.
- Information regarding appointments will also be sent to the managing/referring Consultant as well as the patients.

- The correspondence will be filed in the electronic patient record.
- The responsible consultant is responsible for ensuring clinic review to discuss the outcome of the MDT with the patient.
- The patient will be offered copies of all correspondence.

3. HPB CNS and Key Worker policy

The HPB CNS will review all new patients referred for consideration of liver resection for colorectal metastases. Contact details will be provided to the patient and family. Information sheets on liver resection will be provided.

4. Screen for liver metastases in patients with colorectal cancer

Point to consider:

Follow-up protocol after resection of a primary colorectal cancer within our Centre is as follows, as far as detection of liver metastases is concerned:

- Month 6 LFTs, CEA, Ultrasound (or CT abdomen & pelvis)
- Month 12 LFTs, CEA, Ultrasound (or CT abdomen & pelvis)
- Month 18 LFTs, CEA, CT chest, abdomen, pelvis (or failing that MR)
- Month 24 LFTs, CEA, Ultrasound (or CT abdomen & pelvis)
- Month 30 LFTs, CEA, Ultrasound (or CT abdomen & pelvis)
- Month 36 LFTs, CEA, Ultrasound (or CT abdomen & pelvis)
- Month 48 LFTs, CEA, Ultrasound (or CT abdomen & pelvis)
- Month 60 LFTs, CEA, Ultrasound (or CT abdomen & pelvis), & **Colonoscopy**

This protocol takes into account the UK recommendations that a CT should happen at least once in the first 2 years and that a colonoscopy should be repeated after 5 years.

5. Imaging guidelines

Contrast enhanced CT of chest; abdomen and pelvis should be the standard form of staging. Baseline LFTs and CEA should also be part of the initial investigations. At the time of treatment for CLM, the latest axial staging imaging must not be more than 6 weeks old.

Further axial imaging in the form of MRI will occasionally be used after review of the initial CT at the HPB MDM. This is mainly indicated where the nature of liver lesions is uncertain or additional information is required prior to planning surgery (i.e. vascular and/or biliary anatomy considerations).

The role of PET scanning is under evaluation worldwide and definitive results are awaited. Current policy is the use of PET where extra-hepatic disease is suspected but cannot be confirmed on CT or

MRI. It may be of particular value in patients at high risk of local or peritoneal recurrence e.g. ruptured or advanced stage primary cancer or for high-risk groups needing extended or complicated surgical procedures.

Other investigative measures such as EUS, image guided biopsy and laparoscopic biopsy can also be used under individual circumstances.

Avoid biopsy of liver lesions unless discussed with HPB team.

6. Indications for resection

6.1. Patients to be considered for resection

All patients who are considered fit to undergo major surgery and in whom all disease sites can be treated with curative intent should be considered for resection.

6.2. Inclusions

- No age cut off
- Solitary liver metastases
- Multiple unilobar liver metastases
- Bilobar resectable liver metastases
- Multiple bilobar liver metastases amenable to down-staging
- Synchronous resectable primary and metastatic liver disease
- Liver and localised resectable or ablatable lung metastases

6.3. Exclusions

- Unfit for major surgery (e.g. IHD, COAD)
- Unresectable primary disease (not amenable to down-staging)
- Pelvic local residual disease
- Peritoneal disease
- Bony or unresectable lung metastases

7. Pre-operative evaluation

Any liver resection irrespective of the extent or the mode (laparoscopic or open) should be considered as major surgery. In addition, the majority of these patients would have undergone various periods of systemic chemotherapy. Therefore, appropriate cardiovascular, respiratory and nutritional assessment is mandatory.

These patients should undergo consultant anaesthetist led pre-operative assessment.

7.1. Baseline investigations at out-patient review

FBC, U&Es, clotting profile, LFTs, tumour markers (CEA and CA19.9), chest x-ray, ECG, cross-match of appropriate amount of blood, screen for nosocomial pathogens and the first stage of consent taken by a member of the surgical team.

8. Surgical planning

The appropriateness of liver resection should be discussed at the HPB SMDT but the nature and extent of procedure, the risks involved and the likely outcome should be discussed with the patient and family by a consultant HPB surgeon. The CNS Keyworker will be present to counsel the patient and their family further. All patients receiving a diagnosis of cancer will be told by an appropriately trained MDT member (i.e. a Consultant) in the presence of a CNS.

The following principles should be observed:

I. Complete tumour clearance with clear resection margins; when anatomically feasible the rule of 1cm should be observed.
II. Full evaluation of the liver with intra-operative USS
III. Planning for resection should (if possible) take into account the extent of the disease at the time of presentation, prior to chemotherapy.
IV. Relative contraindications for liver resection at the time of surgery are the presence of peritoneal spread and porta-hepatis nodal involvement
V. Where the liver resection is following a course of chemotherapy at least 4 weeks should be allowed for liver recovery between the completion of chemotherapy and surgery.

9. Strategies to increase resectability

London Cancer has been at the forefront of strategies to facilitate resection of colorectal liver metastases. The rationale, technique and outcome of these strategies are outlined in the following review:

Fusai K., Davidson B.R.,

Strategies to increase the resectability of liver metastases from colorectal cancer. *Dig Surge* 2003; **20(6):** 481-496

The main techniques which have wide application in the management of colorectal liver metastases are:

9.1. Portal vein embolisation (PVE)

When, on volumetric studies, the expected remnant functional liver mass after the proposed hepatectomy would be inadequate (<30% of normal liver or 40% with steatotic or post chemotherapy liver), percutaneous right portal vein embolisation should be explored as a mode to induce compensatory hypertrophy of the unaffected part of the liver, thus facilitating an extended right hepatectomy. If satisfactory response is achieved then resection is scheduled no later than 6-8 weeks after the PVE.

9.2. Two-stage hepatectomy

For patients with bi-lobar disease when complete removal of all tumours is thought not possible with a single procedure a two-stage approach can be adopted by first resecting the most tumour-laden lobe. Allowing for a period of 6 weeks for regeneration of the remnant liver, resection is then completed with removal of part of the remaining liver lobe. This approach can be combined with PVE prior to the first stage and/or RFA of the remnant tumours at either stage.

10.Laparoscopic Liver Resection

In recent years there has been an expansion in the application of laparoscopic techniques in HPB surgery. There is now enough data to support the role for laparoscopic resection in the treatment of patients with CLM. Although almost any type of liver resection can be performed laparoscopically there is a lack of long-term survival data. At RFH and RLH all patients who require resection of a single anterior segment or resection of the left lateral segments of the liver are offered a laparoscopic approach unless there is a specific contra-indication.

11.Radio-Frequency Ablation (RFA)

Resection is the gold standard for treatment of CLM. However RFA may be a useful treatment options for patients who:

I. Are not candidates for liver resection due to poor performance status.

II. Have multi-focal disease that cannot be resected (even after the implementation of the previously discussed pre-operative strategies).

III. Have recurrent disease in their liver remnant that will not tolerate further resection

IV. Are not willing to undergo liver resection, but would accept a less invasive mode of treatment

V. Require consideration of RFA in combination with liver resection when parenchyma sparing is required as means of control of otherwise irresectable disease

VI. Finally, as a part of a two-stage hepatectomy, as outlined above

- RFA can be delivered either percutaneously or intra-operatively (laparoscopic or open) based on individual patient needs.
- All patients being considered for RFA of colorectal liver metastases will be discussed at the HPB SMDT.
- Treatment will only be carried out by a surgeon or radiologist experienced with RFA at the specialist centre
- Data on treated patients will be collected and follow up arranged as outlined in the UK RF users Group.
- Audit data on RFA treatments will be presented annually to the Tumour Board by the RFA team.

12.Synchronous liver metastases

There is some data to suggest that it may be safe and effective to resect right-sided colonic cancer at the same time as small and isolated liver metastases. Most centres avoid combining a major liver resection (more than 3 liver segments) with left-sided or pelvic colectomies due to increased risk for post-operative liver failure and/or septic complications from anastomotic leaks. Patients at RFH are considered for synchronous laparoscopic resection of right colon cancers and solitary metastases in the anterior segments. In the same context major liver resections should not be combined with other major GI tract procedures (i.e. reversal of covering stomas).

12.1. Recurrent metastatic liver disease

Patients who have undergone a liver resection for their CLM and present with recurrent disease in their liver remnant should be assessed for repeat hepatectomy in the same way as for their first resection. Repeat hepatectomies for CLM in high volume centres follow the same pattern of morbidity and mortality as the primary liver resections. Furthermore, the prognosis for these patients seems to be unaffected by the number of liver resections, but rather by the ability to remove all measurable disease with enough remnant functional liver.

13.Liver and pulmonary metastatic disease

The simultaneous presence of liver and lung colorectal metastases does not preclude the surgical treatment of both sites. Long term survival in the current literature following resection of pulmonary metastases is almost entirely in patients who have developed pulmonary metastases on follow up after a liver resection for metastatic disease. If, however, by thoracic criteria the pulmonary disease is resectable then the CLM should be assessed for treatment and this should be completed prior to the lung resection(s). The advent of RFA for pulmonary metastases can further enhance the therapeutic options for this group of patients.

14.Neo-adjuvant chemotherapy

Chemotherapy has transformed the treatment of CLM as neoadjuvant therapy can increase the resectability rate.

All patients with CRC liver metastases should be reviewed by an appropriate GI oncologist prior to considering liver resection.

Results of the recent EORTC/GITCCG trial 40983 (pre and post op Oxaloplatin/5FU vs control) showed an improvement in 3 yr. progression free survival with this regime.

A staggered approach (chemotherapy-surgery-chemotherapy) may offer the best results for patients treated for their CLM for the first time.

It has been agreed that any chemotherapy for patients given as combination treatment with metastatectomy, should be managed by an oncologist from the referring colorectal MDT, who should discuss the patient's care (face-to-face or via video-conferencing facilities, personally or via a designated deputy), with members of the liver resection team.

15.Follow-up after liver resection for colorectal metastases

Following a liver resection all patients will be reviewed at the surgical clinic to ensure:

- They have made a full clinical recovery.
- They are fully informed of the surgical and radiological findings.
- A full discharge summary has been sent to the referring consultant, copied to the GP and has been filed in the notes.
- All clinicians involved in the patient management have been informed.
- The final histology report has been discussed with the patient, copied to the referring consultant and GP and has been filed in the notes.
- The follow up protocol has been discussed and the site of follow up investigations has been established.
- Arrangements have been made for Oncology review.

The follow up protocol will involve 3 monthly CT and tumour markers for the first two years and 6 monthly for the subsequent 3 years. Follow up will normally be under the care of the oncology team but can be carried out if necessary by the HPB or GI surgical team.

Month 6 LFTs, CEA, CT abdomen & pelvis
Month 12 LFTs, CEA, CT abdomen & pelvis
Month 18 LFTs, CEA, CT abdomen & pelvis
Month 24 LFTs, CEA, CT abdomen & pelvis
Month 30 LFTs, CEA, CT abdomen & pelvis
Month 36 LFTs, CEA, CT abdomen & pelvis
Month 48 LFTs, CEA, CT abdomen & pelvis
Month 60 LFTs, CEA, CT abdomen & pelvis

16.Key worker transfer

If the follow up is transferred from the HPB surgical; team to the Oncology team the key worker for the patient will automatically transfer from the HPB CNS to the GI Oncology CNS. If the patient proves unresectable and is not suitable for chemotherapy then the HPB CNS may transfer key worker responsibility to the palliative care CNS in the community.

17.Research

17.1. *London Cancer* Research Priorities

A. Ensure all those involved in the HPB Cancer Pathway are kept updated as to active trials and research – via the HPB website, email bulletins and direct communication with local and specialist CNS staff

B. Ensure patients are educated from an early point in their care about the importance of taking part in clinical research

C. Research program for earlier diagnosis of abdominal symptoms (EDAS) developed following the symposium on the 12th November

D. *London Cancer* to act as advocate and support mechanism to set up and fund research

E. HPB Tumour specific groups to report on research activity to Board and to present results of Faculty research at four monthly meetings with an Annual HPB Faculty Meeting set up which will be open to external clinicians and combine local and international speakers.

17.2. GI trials *London Cancer* October 2013

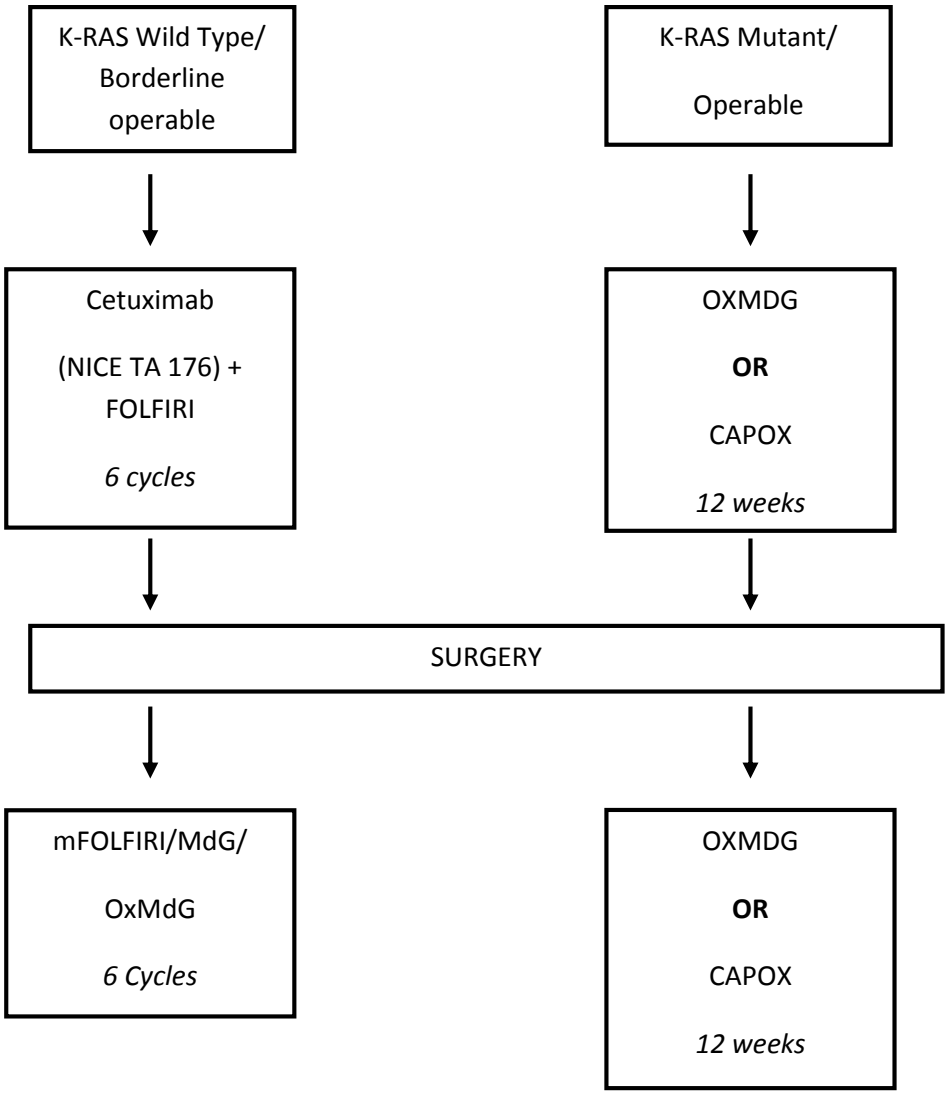
Trial		
SCOT	Adjuvant colorectal cancer	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=3817
BILCAP	Adjuvant biliary tract cancer	
STO3	Neoadjuvant oesophagogastric cancer	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=1752
Streamline C	Imaging study colorectal	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=12770
ARISTOTLE	Neoadjuvant rectal	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=7890
BACCHUS	Neoadjuvant rectal	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=12897
PULMICC	Lung resection	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=9018
FOXTROT	Neoadjuvant study colorectal	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=3771
NSCGG	Genetics study colorectal	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=1269
PANTHER	Advanced colorectal	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=13526
FOXFIRE	Advanced colorectal	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=5174
CUP One	Translational study CUP	
AMGEN 2007	Advanced oesophagogastric	
BIL QOL	QL study biliary	
DARECK	Advanced disease colorectal	
LEO	Neoadjuvant oesophagogastric	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=9848
ESPAC-4	Adjuvant pancreas (RFH only)	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=4307
VIP	Advanced pancreas	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=9908

MK-0752	Advanced pancreas (SBH only)	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=8449
TACE-2	Inoperable HCC	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=5347
TUMOUR ANGIOGENESIS	Colorectal	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=7116
NEO-SCOPE	Neoadjuvant oesophagus	http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=13764

See http://www.ncri.org.uk for further details.

Appendix 1 Chemotherapy Algorithms for Liver Resection for Colorectal Metastases

Colorectal – Metastatic Operable



Key to chemotherapy regimens:

OXMDG = oxaliplatin + 5-fluorouracil/folinic acid (modified de Gramont)

CAPOX = capecitabine + oxaliplatin

NB patients >70 or with renal impairment default to OXMDG

FOLFIRI = irintoecan + 5-fluorouracil/folinic acid (modified de Gramont)