Cetuximab in combination with Modified De Gramont plus Irinotecan (IrMdG) (GIWOS-010/1)

**Indication**

The use of Cetuximab within first-line chemotherapy regimens can be considered for patients with EGFR expressing K-ras wild-type metastatic colorectal cancer with inoperable, liver-only, metastatic disease who may be suitable for potentially curative resection in the event of tumour regression.

Note: this regimen is not included as part of the cetuximab patient access scheme for this indication. This regimen is for patients where Cetuximab in combination with OXMdG is contraindicated.

**Case selection**

CONSIDER ENTRY INTO CLINICAL TRIAL IF AVAILABLE/APPROPRIATE

**Eligibility**

**Inclusion**

- Histologically proven colorectal cancer with features of metastatic disease restricted to the liver, which is felt to be inoperable, but in whom potentially curative liver metastasis resection would be undertaken if the lesions became resectable after treatment with chemotherapy and cetuximab. This should be agreed after MDT discussion.
- No previous chemotherapy for metastatic disease
- The tumour should be K-ras wild-type as demonstrated by laboratory genotyping
- PS 0 - 2 (Karnofsky ≥ 60%)
- No major abnormality of haematological or biochemical baseline parameters, eg absolute neutrophil count ≥ 1.5 x 10^9/l, Platelets ≥ 75 x 10^9/l, Creatinine clearance ≥ 30ml/min, bilirubin ≤ 3 times upper limit of normal (ULN).
- Men and women who are fertile must use a medically acceptable contraceptive throughout the treatment period and for 6 months following cessation of treatment.
- Written informed consent
- Patients may have their primary tumour still in situ providing symptoms are modest and non-obstructive in nature

**Exclusion**

- Patients who are not candidates for liver resection due to medical co-morbidity
- Patients who are not suitable for chemotherapy due to medical co-morbidity, eg clinically significant / uncontrolled cardiac disease
- Known or suspected DPD deficiency
- Known hypersensitivity to irinotecan based therapy
- Pregnant or lactating females / women of child bearing potential not using a contraceptive method
- History of significant psychiatric disorder
- It is advised patients who have significant symptoms (particularly any symptoms suggestive of obstruction) from their primary tumour should undergo resection of the lesion prior to receiving chemotherapy & cetuximab
- Clinically significant cardiac disease – uncontrolled CHF, unstable angina or MI within last 6 months
- Interstitial pneumonia or extensive symptomatic lung fibrosis
- Peripheral neuropathy of CTC (Version 3) grade ≥1
- Other intercurrent serious illness which in the opinion of the treating consultant would render patient at risk of severe toxicity

**Treatment Intent is curative**

**Pre-treatment evaluation**

1. Histological confirmation of colorectal adenocarcinoma
2. Radiologic staging using CT, PET-CT +/- MRI of liver
3. MDT review with consensus of non-resectable liver metastatic disease, with no evidence of extra-hepatic metastatic disease
4. Confirmation of K-ras wild type tumour (see below)
5. Informed consent
7. Assessment of performance status
8. Height, weight and BSA
9. Baseline haematological / biochemical assessment and calculated creatinine clearance, LFTs and CEA. It is recommended serum magnesium be documented at baseline.
10. Medical history and examination

**K-ras analysis**

Samples required for K-ras analysis comprise tumour tissue blocks and a single H&E slide.

Details of sample requirements are described in Appendix A
K-ras analysis request form is in Appendix B.

Samples should be sent to the Molecular Pathology Service at the following address:

**Dept of Pathology / Molecular Genetics Laboratory,**
**Level 6, Ninewells Hospital**
**Dundee DD1 9SY.**

It is important there is clear labelling of samples with patient’s details together with contact details for the referring pathologist.

**Contact details for the Dundee Molecular Genetics Laboratory**

Tel 01382 632548 or 01382 496261.
Fax 01382 640966 or 01382 496382
E-mail tay-uhb.moleculargenetics@nhs.net
**Regimen**

All patients should receive pre-medication with an antihistamine and corticosteroid prior to each infusion of cetuximab.

**Cetuximab / IrMdG regimen**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Administration</th>
<th>Infusion fluid</th>
<th>Day to be given</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetuximab*</td>
<td>400mg/m² initial dose, then 250mg/m² used weekly thereafter</td>
<td>IV</td>
<td>Initial dose given over 2 hours, subsequent doses given over 1 hour. Patients must be closely observed during the infusion and for 1 hour after the end of the infusion.</td>
<td>0.9% Sodium Chloride 500ml</td>
<td>Day 1 and day 8</td>
</tr>
<tr>
<td>Irinotecan</td>
<td>180mg/m²</td>
<td>IV</td>
<td>Over 30 minutes starting 1 hour after cetuximab</td>
<td>5% Glucose or 0.9% Sodium Chloride 250ml</td>
<td>Day 1</td>
</tr>
<tr>
<td>Folinic Acid</td>
<td>350mg</td>
<td>IV</td>
<td>Over 2 hours</td>
<td>5% Glucose or 0.9% Sodium Chloride 250ml</td>
<td>Day 1</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>400mg/m²</td>
<td>IV</td>
<td>Over 10 minutes</td>
<td>0.9% Sodium Chloride 100ml</td>
<td>Day 1</td>
</tr>
<tr>
<td>Fluorouracil**</td>
<td>2400mg/m²</td>
<td>IV</td>
<td>Over 46 hours</td>
<td>1000ml 0.9% Sodium Chloride or via ambulatory infusion device</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

* Flush line with sodium chloride at the end of infusion. Chemotherapy must not be administered earlier than 1 hour after the end of cetuximab infusion.

**Regimen given as day case treatment if patient has PICC/Hickman line in situ

Re-load cetuximab at 400mg/m² if there has been a break in treatment for more than 4 weeks.

Repeat every 14 days for 8 cycles

Cap BSA AT 2.2m²

Loperamid supplied with each cycle of chemotherapy (see ‘Precautions’) – clear verbal and written instructions supplied on how to use loperamide as below:

“If diarrhoea occurs start Loperamide immediately. Take TWO tablets initially then ONE every 2 hours until 12 hours after the last liquid stool up to a maximum of 48 hours. If symptoms persist beyond 48 hours seek medical advice immediately”.

**Emetogenic Risk: Moderate** – refer to local anti-emetic policy

**Is GCSF indicated?**

- **Primary prophylaxis** - Not recommended
- **Secondary prophylaxis**. Not routinely recommended. Consider dose reduction.
Adverse effects – for both Irinotecan and Fluorouracil

<table>
<thead>
<tr>
<th>Very Common</th>
<th>Common</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastrointestinal:</strong> severe diarrhoea, nausea and vomiting</td>
<td><strong>Gastrointestinal:</strong> dehydration as a result of diarrhoea/vomiting, constipation as a result of loperamide use with Irinotecan</td>
</tr>
<tr>
<td><strong>Blood disorders:</strong> neutropenia, anaemia</td>
<td><strong>Blood disorders:</strong> febrile neutropenia, thrombocytopenia</td>
</tr>
<tr>
<td><strong>General Disorders &amp; infusion site reactions:</strong> Acute cholinergic syndrome*</td>
<td><strong>Infection &amp; Infestation:</strong> infrequent cases of renal insufficiency, hypotension or cardio-circulatory failure observed in patients who experienced sepsis</td>
</tr>
<tr>
<td><strong>Skin &amp; subcutaneous tissue disorders:</strong> alopecia (reversible), thrombophlebitis/vein tracking</td>
<td><strong>Respiratory disorders:</strong> dyspnoea*</td>
</tr>
<tr>
<td></td>
<td><strong>Laboratory tests:</strong> mild to moderate increases in AST, ALT, Bilirubin or Creatinine</td>
</tr>
<tr>
<td></td>
<td><strong>Skin &amp; subcutaneous tissue disorders:</strong> dermatitis, pigmentation, changes in the nails, palmer-plantar erythrodysesthesia</td>
</tr>
<tr>
<td></td>
<td><strong>Cardiovascular:</strong> chest pain, tachycardia*</td>
</tr>
<tr>
<td></td>
<td>Other: increased lacrimation, dacryostenosis, visual changes &amp; photophobia,</td>
</tr>
</tbody>
</table>

*see ‘Precautions’

Uncommon

For more detailed information regarding Irinotecan and Fluorouracil please refer to the full current summary of product characteristics (SPC) 6,7.

Cetuximab

Cetuximab can be associated with a number of acute toxicities, with a proportion of patients experiencing acute hypersensitivity reactions. For some patients these symptoms are modest (rash, flushing, urticaria and dyspnoea) but in severe cases shock and acute anaphylaxis can occur. The incidence of severe anaphylactic reactions is estimated at 3% and for this reason all patients must initially receive prophylactic corticosteroids and antihistamines. It is recommended these are given with each subsequent cycle of cetuximab Other infusion related side-effects include dizziness, chills and fever.

Up to 80% of patients will develop skin rash due to cetuximab, the occurrence of which is associated with tumour response. It tends to evolve within 1-3 weeks of the start of treatment and takes the form of a papulo-pustular eruption, with subsequent crusting. Affected areas often exhibit residual erythema. The grading of the skin rash is problematic and although CTC grading has been used in many clinical trials, this grading relies heavily on the surface area of skin affected rather than the intensity / severity of the eruption.

Less common cutaneous side effects can include dry skin, pruritus, skin fissures, palmar–plantar rash, hyperkeratosis, telangiectasia, hyperpigmentation, blisters, mucositis, and pyogenic granuloma. Changes may also occur to the hair (for example, alopecia or trichomegaly of the eyelashes) and nails (usually periungual manifestations such as paronychia)

Hypomagnesaemia is reported to occur in patients undergoing treatment with cetuximab and it is recommended regular monitoring of serum magnesium is undertaken, with supplementation / replacement if significantly low levels are identified.

Extravasation Risk Category

<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irinotecan</td>
<td>Irritant</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Inflammatory Agent</td>
</tr>
</tbody>
</table>

In the event of an extravasation occurring refer to local extravasation policy
Contraindications

- A known history of hypersensitivity to any of the drugs
- Chronic Inflammatory bowel disease and/or bowel obstruction
- Pregnancy and lactation
- Severe bone marrow failure
- Severe hepatic impairment, Bilirubin > 3 times ULN
- Concomitant use of St Johns Wort
- WHO performance status > 2

Precautions

- **Delayed diarrhoea**
  - Patients should be made aware of the risk of delayed diarrhoea more than 24 hours after administration of Irinotecan and at any time within each chemotherapy cycle. Patients should be advised on initiation of antidiarrhoeal therapy (*see 'Regimen'*) and the need to drink large quantities of electrolyte containing beverages as soon as the first liquid stool occurs.
  - Patients with a higher risk of suffering delayed diarrhoea include: females, those with pelvic tumours and/or those receiving pelvic radiotherapy.
  - There is an increased risk of infections and haematological toxicity in patients with severe diarrhoea. FBC should always be performed in patients with severe diarrhoea.

- **Acute cholinergic syndrome** -
  - Defined as early diarrhoea, sweating, abdominal cramping, lacrimation, myosis and salivation. Atropine Sulphate 0.25mg should be administered subcutaneously unless contraindicated (caution in those with asthma. Prophylactic atropine should be given in subsequent cycles of Irinotecan in those who experience an acute and severe cholinergic syndrome.

- **Interstitial pulmonary disease**
  - Presenting as pulmonary infiltrates is uncommon during irinotecan therapy, however it can be potentially fatal patients with risk factors which include those receiving pneumotoxic drugs, radiation therapy and/or colony stimulating factors should be closely monitored for respiratory symptoms before and during treatment.

- Chest pain, tachycardia, breathlessness and ECG changes may occur with 5fluorouracil therefore careful monitoring should be performed in those patients with a history of heart disease or those who develop chest pain during treatment.
Drug Interactions

Irinotecan

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interaction</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST JOHNS WORT</td>
<td>SIGNIFICANTLY DECREASES THE ACTIVE METABOLITE OF IRINOTECAN</td>
<td>AVOID CONCOMITANT USE - CONTRAINDICATED</td>
</tr>
<tr>
<td>CYP3A4-inducing (e.g rifampicin, carbamazepine, Phenobarbital, phenytoin) or inhibiting (e.g ketoconazole) drugs</td>
<td>Metabolism of Irinotecan altered</td>
<td>Avoid concomitant use where possible</td>
</tr>
<tr>
<td>Neuromuscular blocking agents e.g suxamethonium and the neuromuscular blockade of non-depolarising drugs</td>
<td>Prolongation of neuromuscular blocking effects due to anticholinesterase activity of irinotecan may occur – theoretical interaction</td>
<td>Risk versus benefit assessment</td>
</tr>
</tbody>
</table>

- Various agents have been reported to biochemically modulate the antitumour efficacy or toxicity of 5FU, common drugs include Methotrexate, Metronidazole, Leucovorin as well as Allopurinol and Cimetidine which can affect the availability of the active drug – obtain advice from pharmacy.

Investigations prior to subsequent cycles

- Medical review (or review by nurse/pharmacist in appropriate clinic) at each cycle with clinical assessment, repeat FBC, U&Es, LFTs and toxicity assessment documented by CTCAE Version 3.
- Monitor serum Magnesium (cetuximab may produce hypomagnesaemia)
- Monitor CEA and LFTS for disease progression at each cycle visit.
- Monitor patients weight

Dose modifications

General Recommendations

Treatment should be delayed until Neutrophils ≥ 1.5 x 10⁹/l and/or platelets ≥ 75 x 10⁹/l

Treatment should be delayed until any non-haematological toxicity has improved to CTC grade 0-1 (except alopecia).

Treatment delayed for more than one week should trigger a 20% dose reduction.

Grade 4 toxicity of any sort should prompt consideration as to treatment discontinuation. Dose Modifications for any grade 4 toxicity to be made at the discretion of the responsible consultant, if continuation of treatment is felt appropriate.

No dose adjustments are required for anaemia, treatable by transfusion if required.

For recurrent Grade 3 cetuximab induced skin reactions, dose reduction can be considered if topical remedies and treatment interruption fail to provide improvement.
Haematological Toxicity

Treatment should be delayed until Neutrophils $\geq 1.5 \times 10^9/l$ and/or platelets $\geq 75 \times 10^9/l$

Treatment delayed for more than one week should trigger a 20% dose reduction

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>CTC Grade</th>
<th>Bolus 5-FU</th>
<th>Infus 5-FU</th>
<th>Irinotecan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>1-2</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>80%</td>
<td>80%</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider discontinuing treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>1-2</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>80%</td>
<td>80%</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider discontinuing treatment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dose Modifications for grade 4 neutropenia, febrile neutropenia and/or grade 4 thrombocytopenia should be made at the discretion of the responsible consultant if continuation of treatment is felt appropriate

Non-haematological toxicity

Treatment should be delayed until non-haematological toxicity has improved to CTC grade 0-1 (except alopecia).

Treatment delayed for more than one week should trigger a 20% dose reduction

<table>
<thead>
<tr>
<th>Toxic Non-haematological effect in previous cycle</th>
<th>Grade (CTC v3)</th>
<th>Dose modification for subsequent cycles</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Bolus 5-FU</td>
</tr>
<tr>
<td>Delayed diarrhoea</td>
<td>1 or 2</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>80%</td>
</tr>
<tr>
<td>Stomatitis, oral</td>
<td>1 or 2</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>80%</td>
</tr>
<tr>
<td>Skin (Hand Foot synd)</td>
<td>3</td>
<td>80%</td>
</tr>
<tr>
<td>Other events</td>
<td>3</td>
<td>80%</td>
</tr>
</tbody>
</table>

Renal Function

Irinotecan studies in renal impairment have not been performed and Irinotecan should be used with caution in this setting

Fluorouracil SPC advises to use fluorouracil with caution in patients with renal impairment. If CrCl is < 30ml/min discuss with responsible consultant.

Hepatic Function

Irinotecan Dose reduction should be considered if bilirubin between 1.5 and 3 x ULN. Irinotecan is contra-indicated if bilirubin is 3 x ULN.

Fluorouracil SPC advises to use fluorouracil with caution in patients with hepatic impairment.
Cetuximab and skin toxicity

The management of cetuximab skin toxicity is largely based on qualitative evidence and anecdotal experience rather than robust clinical evidence.

In general patients should be advised to avoid sun exposure as this may exacerbate the severity of the rash on unprotected areas. Patients should also be counselled to avoid activities and skin care products that dry the skin. Examples include long, hot showers; alcohol-based or perfumed products; and over-the-counter acne medication. Greasy ointments should also be avoided in favour of frequent moisturizing with alcohol-free emollient creams. In general creams are more effective than lotions, and when kept cool (for example, refrigerated), can provide symptomatic benefit – emollient based soap substitutes and urea based creams particularly.

Specific treatments including topical clindamycin, fucidic acid cream and a low- to medium-potency topical steroid such as 1% hydrocortisone can be considered. Systemic anti-biotics such as doxycycline are often preferred to topical agents. Maintainence of full treatment dosing should be attempted however dose modification or discontinuation (see below) should be considered if the patient is severely symptomatic (for example, if necrosis, blistering, or petechial or purpuric lesions are present) or if multiple hair, nail, and skin issues emerge. (8).

<table>
<thead>
<tr>
<th>≥ Grade 3 Skin toxicity</th>
<th>On resolution to ≤ grade 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st occurrence</td>
<td>Interrupt</td>
</tr>
<tr>
<td></td>
<td>Resume at previous dose</td>
</tr>
<tr>
<td>2nd occurrence</td>
<td>Interrupt</td>
</tr>
<tr>
<td></td>
<td>Resume at 200mg/m2 weekly</td>
</tr>
<tr>
<td>3rd occurrence</td>
<td>Interrupt</td>
</tr>
<tr>
<td></td>
<td>Resume at 150mg/m2 weekly</td>
</tr>
<tr>
<td>4th occurrence</td>
<td>Stop</td>
</tr>
</tbody>
</table>

If skin toxicity has not resolved to ≤ grade 2 after three consecutive weeks then treatment should be discontinued.

Allergic Reactions

Cetuximab – For grade 1-2 infusion-related reaction (symptoms such as fever, chills, dizziness or dyspnoea), the infusion rate may be decreased. It is recommended the infusion remains at the lower rate for all subsequent treatments. For patients who experience a severe infusion-related reaction (grade 3 = urticaria, angioedema, hypotension, bronchospasm, grade 4 = anaphylaxis) emergency treatment with adrenaline, steroids and anti-histamines will be necessary. In such events immediate and permanent discontinuation of cetuximab is required.

Evaluation of response to treatment

Patients should undergo radiological re-assessment after 12 weeks (ie 6 cycles of treatment) using CT, MRI of liver and / or CT-PET scans may be required in addition. In the event of responding disease a further 2 cycles of treatment can be administered to allow time for MDT consideration of possible resection.

It is recommended individual MDTs formulate protocols detailing optimal time to resection after treatment discontinuation. In general it is suggested there is at least a 6 week interval between cetuximab-containing chemotherapy and liver resection.
References


2. Van Cutsem E, Köhne CH, Hitre E et al. Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer. NEJM. 2009 Apr 2;360(14):1408-17


Document control

<table>
<thead>
<tr>
<th>Prepeared by</th>
<th>Dr AC McDonald &amp; Mr J Milne</th>
</tr>
</thead>
<tbody>
<tr>
<td>Checked by</td>
<td>Prof J Cassidy &amp; Dr A Waterston</td>
</tr>
<tr>
<td>Approved by</td>
<td>RCAG Prescribing Advisory Subgroup</td>
</tr>
<tr>
<td>Issue date</td>
<td>September 2010</td>
</tr>
<tr>
<td>Review date</td>
<td>September 2012</td>
</tr>
<tr>
<td>Reference/version no.</td>
<td>GIWOS-010/1</td>
</tr>
<tr>
<td>Replaces</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
APPENDIX A – K-ras testing protocol

TESTING FOR COMMON KRAS MUTATIONS

SAMPLE REQUIREMENTS

- Tumour tissue blocks, together with a single H&E slide should be sent to the Molecular Pathology Service, Department of Pathology at the above address.

- Where possible, the referring Pathologist should ensure that the tumour tissue represents at least 40% of the sample.

- Details of the referring Pathologist together with the referring centre address must be included for reporting and return of the tumour block and slide.

TESTING PROTOCOL

- Tissue specimens will be booked in by the Department of Pathology

- The single H&E slide will be examined by Prof F Carey / Dr S Walsh.

- If the area of the tumour is <40% of the total section, a report will be issued to the referring Pathologist requesting an additional tissue sample. No KRAS testing will be undertaken, since a minimum of 40% tumour tissue is required for optimum mutation detection.

- If the proportion of tumour is >40%, the sample is suitable for KRAS mutation testing and 6x10μm tissue sections will be cut and passed to Molecular Genetics

- DNA will be extracted from the tissue sections and the quantity and quality assessed by Nanodrop 100 spectrophotometry.

- The KRAS mutation status (codons 12, 13 and 61) will be determined in triplicate using the Qiagen PyroMark Q24 KRASv2.0 kit (standard operating procedure MGM177)

- Reports detailing the KRAS mutation status and confirming the presence of tumour in the section will to sent to the referring Pathologist within 7 working days from specimen receipt. The tissue block and H&E slide will be returned along with the reports.
# REQUEST FOR KRAS MUTATION TESTING

**Molecular Pathology Service**  
Pathology, Level 6, Ninewells Hospital, Dundee, DD1 9SY  
Phone/FAX: Tel 01382 496304 / Fax 01382 496352  
E-mail: Tay-Hill.molecular Genetics@nhs.net

## PATIENT DETAILS (printed label preferred)
- **Family Name:**  
- **First Name(s):**  
- **DOB:**  
- **Sex:** M / F  
- **NHS Number:**  
- **Hospital Number:**  
- **Address:**  
- **Postcode:**

## REQUESTING CONSULTANT (ONCOLOGIST)
- **Consultant Name:**  
- **Address for Report:**  
- **Date of Request:**  
- **Phone:**  
- **Fax:**  
- **Contact / Address for Invoice:**

## CLINICAL DETAILS (TO BE COMPLETED BY REQUESTING CONSULTANT)
- **Does the patient meet NICE (541/09) criteria:** Yes / No  
- **Is the patient being considered for 1st line treatment:** Yes / No  
- **Is the patient being considered for 2nd / 3rd line treatment:** Yes / No  
- **Other reason for referral (please state):**

## SPECIMEN DETAILS (TO BE COMPLETED BY CONSULTANT PATHOLOGIST)
- **Name of Pathologist:**  
- **Address of Pathology Department (for return of blocks):**  
- **Block Reference Number:**  

A paraffin block of suitable tumour material and an accompanying H&E slide should be sent to the Molecular Pathology Service at the address above. Samples should be dispatched as soon as possible since treatment is dependent on the results of KRAS testing. The block and copy of the Molecular Genetic test report will be returned to the referring Pathology department as soon as analysis is complete.

## MOLECULAR PATHOLOGY LAB USE ONLY
- **Block Received by and Date:**  
- **Pathology Sample Number:**  
- **Consultant Pathologist:**  
- **Please estimate what proportion of the tissue section is tumour:**  
- **Date sections sent to Molecular Genetics:**

## MOLECULAR GENETIC LAB USE ONLY
- **Sections Received by and Date:**  
- **MG Number:**  

Please note unless otherwise requested, following testing, all DNA samples will be stored in the laboratory.

Incomplete or illegible forms will cause delay or rejection of samples.