Manchester Cancer

RAS mutation testing policy

Greater Manchester Cancer Services Colorectal Cancer Pathway Board and Clinical Subgroup

Start date: June 2014

Review date: May 2017

RAS mutation testing

Background

In metastatic colorectal cancer the presence of mutations in the RAS genes, KRAS and NRAS, are of prognostic value with patients having shorter Overall Survival (OS) compared with patients in whom no mutations are detected (termed wild-type). The presence of RAS gene mutations also predicts lack of benefit from treatment targeting the Epidermal Growth Factor Receptor (EGFR) e.g. Cetuximab and Panitumumab. RAS mutation testing is listed in the drug license and/ or NICE guidance as a pre-requisite for patients with colorectal cancer being considered for treatment with these drugs.

Mutations in codons 12 and 13 of KRAS gene are the most commonly observed in approximately 40% of patients with metastatic colorectal cancer. Data from recently completed clinical trials has demonstrated that additional mutations in the KRAS gene (codons 61 and 146) and the NRAS gene (codons 12, 13, 59, 61, 117 and 146) also result in lack of benefit from anti-EGFR mAb treatment. These mutations in the KRAS and NRAS genes are present in approximately 50% of patients diagnosed with metastatic colorectal cancer and are an important determinant of treatment options.

Funding RAS mutation testing

From April 2016 funding for RAS mutation testing is by NHS England.

RAS testing pathway

1. Material
   a. Biopsy - endoscopic from primary or from metastasis
   b. Resection specimen - if RAS testing has not already been performed send a representative tumour block conforming with the genetic laboratories guidelines.
   c. If radiotherapy or chemotherapy treatment is planned as initial treatment, and adenocarcinoma occupies >10% of the biopsy, RAS testing is preferred on this sample.
2. Requests
   a. General points
      i. RAS mutations status can be requested following initial MDT review, at which metastatic disease has been identified, or after a new patient appointment in Oncology clinic.
      ii. Request following MDT review is the preferred option so that RAS mutation status is available at the time of new patient appointment with an oncologist.
      iii. The Medical or Clinical Oncologist supporting an MDT will be the lead for the process of RAS mutation testing. The MDT can agree to delegate completion of the request form to another individual e.g. specialist nurse, etc.
      iv. The RAS mutation testing form should be completed ticking the appropriate box dependent on patient details - "other NHS patient diagnosed with colorectal cancer" or "meets NICE guidelines (TA176)".
      v. The referrer details on the RAS testing request should be the Medical or Clinical Oncologist, based at the Christie, who supports the MDT.
      vi. **COMPLETED FORMS SHOULD BE E-MAILED TO JANE McKEOWN** (jane.mckeown3@nhs.net) at The Genomic Diagnostic Laboratory.
      vii. **Janet GALLAGHER** (Contracts Manager, Christie Hospital, 01614463807, janet.gallagher1@nhs.net) **should be copied into the request**. If this process is not followed significant issues with the invoicing and payment for RAS testing will arise.
   b. Genetic laboratory
      i. A number of laboratories are funded nationally to undertake RAS testing.
      ii. The Regional Genetics Service based at St. Mary's Hospital, Manchester is the local provider and the preferred laboratory for samples to be sent to. The current version of the RAS request form is available at: http://www.mangen.org.uk/useful-forms.php
      iii. All samples should conform with the standards set out by the receiving Genetic laboratory.
3. Results

a. The Genetics laboratory will produce a RAS mutation testing report which should be filed in the patient's notes.
b. An addendum should be made to the original histopathology report to include RAS mutation testing results.

4. Interpretation of results and treatment

a. RAS mutation testing influences the treatment options for a patient with metastatic colorectal cancer. Discussion of RAS mutation results with patients will be undertaken by the treating oncologist.