

## Clinical Genomics (The Royal Marsden)

**Head: Dr Lisa Thompson; Dörte Wren (Senior Clinical Scientist, SIHMDS lead (molecular)); Dr Suzanne MacMahon, Dr Tosin Taiwo, Dr Yiwen Liu**

Clinical Genomics, The Centre for Molecular Pathology, The Royal Marsden NHS Foundation Trust 15 Cotswold Road Sutton SM2 5NG

Tel: 02089156565 Fax: 02089156566 Email: [rmh-tr.moleculardiagnosics@nhs.net](mailto:rmh-tr.moleculardiagnosics@nhs.net)

### **TP53 testing of CLL referrals to the RMH SIHMDS Clinical Genomics Laboratory**

*(Please note there must be a contract in place with Janssen in order to access free TP53 mutation testing; please contact Peter Hillan, Health Economy Liaison Manager; email: [phillan@its.jnj.com](mailto:phillan@its.jnj.com) for further information)*

#### **Download the appropriate referral form:**

1. Click on the following link: <https://www.royalmarsden.nhs.uk/our-consultants-units-and-wards/clinical-departments/cancer-diagnostics/haematology-diagnostics>
2. Scroll down to the “**Downloads**” section for our pdf TP53 mutation/ deletion request form

#### **Samples:**

- Please send samples for TP53 testing of patients who are approaching the need for *any* line of treatment as per BSH guidelines (Oscier et al, British Journal of Haematology, 2012)
- Guidelines (ESMO, BSH and ERIC) suggest CLL patients at point of treatment intent should be tested for deletion 17p and TP53 mutation (Ladetto et al, Annals of Oncology, 2016; Oscier et al, British Journal of Haematology, 2012 and Malcikova et al, Leukemia, 2017)
- 8ml anti-coagulated blood required (2 tubes, one EDTA for NGS, one Lithium heparin for FISH)
- Please indicate on the referral form whether TP53 mutation NGS or both TP53 mutation NGS and TP53 deletion FISH are required.

#### **Test:**

TP53 testing will assess:

1. TP53 gene sequence for mutations – by next generation sequencing (NGS) covering exons 2-11.
  2. Deletion of the short arm of chromosome 17 (17p), where the TP53 gene is located, by interphase fluorescence in situ hybridisation (FISH). The test performed also detects deletion of the ATM gene on chromosome 11.
- Both TP53 NGS and FISH are recommended in order to investigate different mechanisms of TP53 gene disruption. However, either test can be ordered separately.
  - **TP53 mutation testing by NGS is free** (supported by Janssen – see above). FISH analysis will not be reimbursed by Janssen and will be invoiced for separately.
  - An integrated report on the results of the FISH and TP53 NGS test will be provided when both tests are ordered.
  - The 17p/TP53 deletion analysis by FISH has a detection sensitivity of 10%.
  - The NGS TP53 mutation sequencing has a validated sensitivity of >3%.
  - Patients with a low level of cells with TP53 dysfunction due to deletion or mutation have an equally poor prognosis compared to those with a higher level of cells with abnormal TP53 (Rossi et al, Blood, 2014, Malcikova et al, Leukemia, 2017)

#### **Results and turnaround time:**

- Any TP53 variants will be evaluated utilising the recommended databases and clinical relevance will be assigned as appropriate by clinical scientists at RMH
- Target turn-around time is 15 days following sample receipt.

#### **Reporting results:**

- A report will be issued to the referring clinician in printed form **via RMH Specialist Pathology Order & View web based portal** – see website above for more details **or** by e-mailed pdf.
- E-mail reporting will require set up of e-mail reporting facility with an appropriate nhs.net account