OXFORD Molecular Diagnostics Centre
Transforming patient healthcare, pioneering tomorrow's technology

Oxford University Hospitals NHS
NHS Foundation Trust

UNIVERSITY OF OXFORD

Janssen TP53 Testing for CLL Oxford MDC Information and Specification:

Samples:

- Please send samples for TP53 testing of ALL patients who are approaching the need for *any* line of treatment as per BCSH guidelines (Oscier et al, British Journal of Haematology, 2012 and new guidelines, in preparation)
- A lymphocyte count of >25x10^9/l is ideal and at levels less than this sensitivity may be affected (as is the case with Sanger)
- 8ml of EDTA anticoagulated blood is required (2x4 ml tubes)

Test:

- TP53 testing should assess 1. The sequence of DNA in the TP53 gene – by either Sanger sequencing or next generation sequencing (NGS) 2. Loss of the short arm of chromosome 17 (17p) where the TP53 gene by fluorescence in situ hybridisation (FISH). These tests are complementary.
- Oxford Regional Genetics Laboratory can provide either FISH for 17p deletion and NGS for TP53 mutation testing together, or just NGS for TP53 mutation testing alone using the blood samples submitted. If both tests are requested the cost of the 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 if both tests are requested. In the box on the OBRCHMDS request form labelled, 'Lymphoma/Leukemia Requests' clearly write: TP53 only OR TP53 + FISH according to the tests required.
- Sanger sequencing is the technique most commonly used to look for mutations in the sequence of the DNA
- Sanger sequencing has a sensitivity down to a level of approximately 20% and may fail to detect TP53 mutations at lower levels
- The Oxford MDC TP53 NGS test has a validated sensitivity of 5%
- Data indicates that patients with a low level of TP53 mutation have an equally poor prognosis compared to those with a higher level of TP53 mutation (Rossi et al, Blood, 2014)
- NGS technology may struggle to pick up large deletions (>10bp) but these make up a very small proportion of TP53 mutations (0.2% of 848 Oxford patients) in those who previously had Sanger sequencing

Results and TAT:

- The TP53 NGS assay is UKAS accredited to ISO 15189 standard
- Any positive result in the TP53 NGS test is repeated at the Oxford MDC to ensure accurate reporting
- All detected TP53 variants undergo a rigorous assessment by clinical scientists to determine pathogenicity
- The TP53 NGS test result is accessible by an online portal and one report will be issued to the relevant contact on the referring documentation
- Turn-around time is approximately 4 weeks