Quantitative and Qualitative BCR-ABL1 and ABL1 kinase mutation screening in ALL

Clinical Background and Genetics
- Acute lymphocytic leukaemia (ALL) is a malignant disorder of haematopoietic cells of the lymphocyte cell lineage, which mainly affects lymphocytes and lymphocyte producing cells in the bone marrow.
- The presence of a reciprocal translocation between chromosomes 9 and 22 resulting in the formation of a derivative chromosome 22 (the Philadelphia chromosome) and subsequent formation of the BCR-ABL1 fusion gene is found in approximately 20-30% of adult ALL and 3-5% of childhood ALL.
- The predominant BCR-ABL1 rearrangement noted in ALL occurs within the minor breakpoint cluster region arising from the fusion of the BCR gene with the ABL1 gene within exons e1 and a2, respectively. However, the e13a2 and e14a2 transcripts more commonly identified in patients with CML can also be present.
- The molecular monitoring of ALL via BCR-ABL1 RQ-PCR can aid in the disease management in patient’s receiving tyrosine kinase inhibitor (TKI) therapy.

Service offered
- BGL is part of the Bristol Haematology-oncology Diagnostic Service (BHODs) and has access to a full range of complementary pathology services.
- Alongside conventional cytogenetic analysis and fluorescent in situ hybridisation using BCR-ABL1 break apart probes, this laboratory offers a range of molecular services for the diagnosis and subsequent monitoring of patients with BCR-ABL1 positive ALL including qualitative reverse transcriptase PCR (RT-PCR), real time quantitative PCR (RQ-PCR) and ABL1 kinase domain mutation screening.
- RT-PCR is performed on the diagnostic sample and allows for the detection of the BCR-ABL1 transcripts to identify whether the patient is suitable for RQ-PCR analysis in the laboratory.
- RQ-PCR allows for the molecular monitoring of ALL in patients with the common e12a2/e13a2/e14a2 transcripts using the Europe Against Cancer probes and primers described in Gabert et al., (2003).
- ABL1 kinase domain mutation screening is offered when a patient is either not optimally responding to therapy or when disease levels begin to rise suggesting a loss of response to therapy.
- Patients are monitored according to BCSH guidelines.
- The main objective of molecular monitoring is to assess the patient response to TKI therapy and to recognise the early signs of relapse. However, it is also important that cytogenetic studies are retained to confirm molecular findings and to help identify disease progression.

Referrals
- Diagnostic testing and disease monitoring

Clinical Advice: If clinical discussion is required, we would recommend contact with a local consultant haematologist

Target reporting Times
- Target Reporting Time (calendar days) TRT
  - Qualitative diagnostic screen 3 days
  - Quantitative molecular monitoring 14 days
  - ABL1 kinase domain mutation screen 28 days

Quality
- BGL participates in the UK NEQAS LI EQA programme for BCR-ABL1 quantitation and the pilot scheme for BCR-ABL1 kinase domain mutation status.

References