Bristol Genetics Laboratory is a UKAS accredited medical laboratory No.9307.

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

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Sample Required:
See Sample requirements page at www.nbt.nhs.uk/genetics **for full details**

5-10ml blood in EDTA. It is important that these samples reach the laboratory within 72 hours of being taken. Any samples received after this time will not be processed as RNA quality cannot be guaranteed.

Samples should be accompanied by a FULLY completed request form (available as download at www.nbt.nhs.uk/genetics or from the laboratory).

Please include details of the test required, family history, address and POSTCODE, NHS number, referring clinician and centre.

Consent and Storage:
All genetic testing requires consent. **It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.**

DNA is stored from **ALL** patients undergoing DNA testing, unless consent for this is specifically denied.

Stored material from all referrals may be retained for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

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 Haemato-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 e1a2/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

- Gabert *et al.,* (2003) Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia – A Europe Against Cancer program. I, 17: 2318–2357.

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