BRAF V600E Mutation in Hairy Cell Leukemia

Indications for Ordering

- Confirm diagnosis of hairy cell leukemia (HCL)
- Monitor tumor burden

Test Description

- Genomic DNA is extracted
- Polymerase chain reaction (PCR) amplification of fragment spanning the *BRAF* V600 codon with allele-specific primers for the wild type and the *BRAF* V600E mutant allele
- Quantitation using hydrolysis probe
- Relative percentages of the wild type of *BRAF* V600 and V600E mutant alleles are calculated using a heterozygous calibrator plasmid

Tests to Consider

Primary test

BRAF V600E Mutation Detection in Hairy Cell Leukemia by Real-Time PCR, Quantitative 2007132

- Diagnosis/monitoring of HCL

Related test

Leukemia/Lymphoma Phenotyping by Flow Cytometry 2008003

- Initial testing to establish tumor lineage

Disease Overview

Prevalence – rare lymphoproliferative disorder

Diagnostic issues

BRAF V600E is a reliable molecular marker to confirm diagnosis of HCL

- Mutations detected in nearly all cases of HCL but rarely in other lymphoproliferative disorders (Tiacci E, 2011)

Treatment issues

Quantitation of allele burden allows monitoring of response to therapy

Genetics

Gene – *BRAF*

Structure/function

- BRAF protein kinase acts in the RAS/mitogen-activated protein kinase-signaling pathway
- Major role in cell proliferation, survival, and neoplastic transformation

Mutations

Most mutations occur at codon V600

- Mutation results in V600E change

Test Interpretation

Analytical sensitivity – 0.2% mutant allele

Results

- Positive – *BRAF* V600E allele detected and quantified
- Weakly positive, nonquantifiable – *BRAF* V600E mutation detected at 0.2-0.4% mutant allele

Limitations

Limit of detection is 0.2% mutant allele