**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