- **Detection of Variance of Uncertain Significance:** RUNX1 (9) p.Ser369Trp (c.1106C>G) with 20.19% VAF.

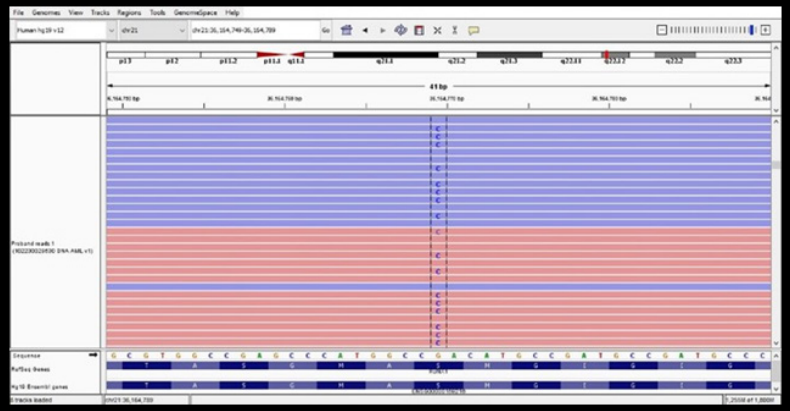

Figure 5: RUNX1 (9) p.S369W VUS.

DIFFERENTIAL DIAGNOSIS

Acute leukemia

FINAL DIAGNOSIS GIVEN

ACUTE MYELOID LEUKEMIA

DISCUSSION:

A. BCR(14) - ABL1(2)

Variant Annotation: The identified BCR-ABL fusion, arises from the fusion of 5′ region (exon 1 to 14) of BCR to the 3′ region (exon 2 to 11) of ABL1 gene and has been reported to result in aberrant over-expression of BCR-ABL fusion transcript.(3)

Gene Summary: A reciprocal translocation between chromosomes 22 and 9 produces the Philadelphia chromosome, which is often found in patients with chronic myelogenous leukemia. The chromosome 22 breakpoint for this translocation is located within the BCR gene. The translocation produces a fusion protein which is encoded by sequence from both BCR and ABL, the gene at the chromosome 9 breakpoint. Although the BCR-ABL fusion protein has been extensively studied, the function of the normal BCR gene product is not clear. The unregulated tyrosine kinase activity of BCR-ABL1 contributes to the immortality of leukemic cells. The BCR protein has serine/threonine kinase activity and is a GTPase-activating protein for p21rac and other kinases.(4)

Variant Incidence: BCR-ABL1 Fusion is present in 0.21% of AACR GENIE cases, with chronic myeloid leukemia, breast invasive ductal carcinoma, unknown, B-cell lymphoblastic leukemia/lymphoma, and acute myeloid leukemia having the greatest prevalence.(5)