«TableStart:Samples»

Sample: «sample» Name: «patient» DOB: «dob» URN: «urn»

**SOLID TUMOUR MUTATION ANALYSIS** «isdraft»

**SPECIMEN**

Skin, Squamous cell carcinoma, 80%

**INDICATION**

**FHx of melanoma, PHx of non-melanoma skin cancer, excised sebaceoma, abnormal MLH1 & PMS2 IHC staining, ? mutation to inform personalised therapeutic options**

«TableStart:Variants»

**RESULT**

**Gene Reference Variant Protein Frequency Clinical Significance**

«gene» «refseq» «hgvsc» «hgvsp» «afpct»% Unknown

«TableEnd:Variants»

**INTERPRETATION**

«TableStart:Variants»«mut»

«TableEnd:Variants»

**THERAPUTIC SIGNIFICANCE**

The predictive significance of this variant is currently unknown in the somatic context; resistance to anti-EGFR antibody targeted therapies has been reported in HRAS-mutated head and neck squamous cell carcinoma [3]. Preclinical data indicates HRAS activation predicts sensitivity to MEK inhibition in cultured squamous cell carcinoma cell lines (ref).

If other clinic-pathologic features are suggestive, germline testing to exclude Costello Syndrome may be indicated [4, 5]. In addition, since this assay does not detect mutations in mismatch repair genes, MSI testing or MMR gene analysis may be indicated to exclude Muir Torre syndrome.

**TEST DESCRIPTION**

Tumour DNA was tested in duplicate for mutations in exons 2, 3 and 4 of the KRAS gene, exons 2, 3 and 4 of the NRAS gene, and exon 15 of the BRAF gene using massively parallel sequencing. This test detects single nucleotide variants and indels in the target exons only. At 1000x coverage, the limit of detection of this assay has been determined to be X%. At 500x coverage the limit of detection has been determined to be X%. The sample was sequenced to an average «ampReads» aligned reads per amplicon with «ampPct»% uniformity. Regions with less than 100x coverage have not been analysed. These are listed below.

**REFERENCES**

1. Gripp, K.W., et al., Costello syndrome associated with novel germline HRAS mutations: an attenuated phenotype? Am J Med Genet A, 2008. 146A(6): p. 683-90.

2. Aslam, A., et al., Naevus sebaceus: a mosaic RASopathy. Clin Exp Dermatol, 2014. 39(1): p. 1-6.

3. Rampias, T., et al., RAS/PI3K crosstalk and cetuximab resistance in head and neck squamous cell carcinoma. Clin Cancer Res, 2014. 20(11): p. 2933-46.

4. Aoki, Y., et al., The RAS/MAPK syndromes: novel roles of the RAS pathway in human genetic disorders. Hum Mutat, 2008. 29(8): p. 992-1006.

5. Gripp, K.W., Tumor predisposition in Costello syndrome. Am J Med Genet C Semin Med Genet, 2005. 137C(1): p. 72-7.

Low coverage amplicons:

«lowAmps»

Assay region of interest coverage:

«rois»

*«TableEnd:Samples»*