Sample: 16K1500-1 Name: Moore,Terrence DOB: 28-Jan-1955 URN: 16/11/67462

COLORECTAL CANCER MUTATION ANALYSIS DRAFT

SPECIMEN
extref

PATHOLOGY
Histological typing: .....
The sample was reviewed by a pathologist and was considered to have ....% tumour cells within the area selected for analysis. Please note: This is not a formal pathology review and is based solely on an H&E of the tissue provided and not on ancillary clinical or pathology information that may be available elsewhere.

RESULT

Gene	NRAS
Reference	NM_002524.4
cDNA Change	c.298A>G
Protein Change	NP_002515.1:p.(Ile100Val)
Read Depth	87/2797 3.1%

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 2832 aligned reads per amplicon with 96.38% uniformity. Regions with less than 100x coverage have not been analysed. These are listed below.

INTERPRETATION
NRAS: CurVariant chr1:g.115252342T>C not yet curated.

COMMENTS
Activating RAS mutations are common in colorectal cancer and occur most frequently at codons 12, 13 and 61 of KRAS and NRAS. RAS mutations cause constitutive activation resulting in a continual proliferative signal downstream of EGFR (1). Mutant RAS colorectal cancer is therefore insensitive to anti-EGFR therapies (2). In RAS wild type colorectal cancer, RAF mutations are associated with a poorer therapeutic response (3). RAS/RAF mutation status should be determined for colorectal cancer patients prior to the administration of anti-EGFR therapies.

Note: Testing of tissue treated with chemo and/or radiotherapy reduces the cellularity of the neoplastic element and reduces the sensitivity of the assay. Where possible tissue derived from untreated tumour should be tested.

REFERENCES
1. Karapetis, C.S., et al., K-ras Mutations and Benefit from Cetuximab in Advanced Colorectal Cancer. N Engl J Med, 2008. 359(17): p. 1757-1765.
2. Douillard, J.Y., et al., Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer. N Engl J Med, 2013. 369(11): p. 1023-34.
3. Di Nicolantonio, F., et al., Wild-type BRAF is required for response to panitumumab or cetuximab in metastatic colorectal cancer. J Clin Oncol, 2008. 26(35): p. 5705-12.

Low coverage amplicons:
There were 0 low read amplicons with <100 aligned reads:
not listed

Assay region of interest coverage:
BRAF_Ex11_444 (coverage 3897)
BRAF_Ex11_460-470 (coverage 3897)
BRAF_Ex15_594-603 (coverage 10285)

KRAS_Ex2_12-13 (coverage 4193)
KRAS_Ex3_59-61 (coverage 6355)
KRAS_Ex4_117 (coverage 7753)
KRAS_Ex4_146 (coverage 4366)
NRAS_Ex2_12-13 (coverage 6661)
NRAS_Ex3_59-61 (coverage 9796)
NRAS_Ex4_117 (coverage 12029)
NRAS_Ex4_146 (coverage 12029)
PIK3CA_Ex10_540-550 (coverage 2903)
PIK3CA_Ex21_1020-1050 (coverage 1871)
RNF43_Ex3_117 (coverage 5189)
RNF43_Ex9_659 (coverage 4160)