Metastatic melanoma – urgent BRAF testing on ctDNA

Background

Melanoma is a type of skin cancer and is one of the most common forms of cancer in the UK. Genomic testing of melanomas informs diagnosis, prognosis and treatment options, with particular emphasis on genes that can be targeted by specific inhibitors such as BRAF. While early stage melanoma generally confers a very good five-year survival rate, stage IV melanoma has a poor prognosis and can present acutely with urgent need for treatment.

BRAF variants are detected in approximately 50% of malignant melanomas, with over 90% of these BRAF variants being the most common BRAF variant, c.1799T>A p.(Val600Glu) (often referred to as V600E). NICE guidelines recommend the use of BRAF-targeted therapies for locally advanced or metastatic melanoma patients with the BRAF V600E variant; this is the best possible treatment for extending life in such patients and needs to be commenced as soon as possible following diagnosis/progression of disease.

The standard pathway for the melanoma testing service in the AWGL involves NGS analysis of FFPE-derived DNA for hotspot regions in the BRAF, KIT and NRAS genes (see PD-GEN-MelanNGSInfo), and/or pyrosequencing of FFPE-derived DNA for BRAF codons 599, 600 and 601. The NGS service has a 14 calendar day turnaround time, while the pyrosequencing service has a 7 calendar day TAT.

Pyrosequencing using ctDNA derived from a blood sample is available for exceptionally urgent cases (Stage IV or rapidly deteriorating) when a suitable FFPE sample is not available.

PLEASE NOTE THAT IT IS NOT CURRENTLY POSSIBLE TO ASSESS THE LEVEL OF CTDNA EXTRACTED FROM BLOOD SAMPLES AND THEREFORE FOLLOW-UP TISSUE TESTING IS VERY STRONGLY RECOMMENDED FOR ANY PATIENTS WITHOUT A VARIANT DETECTED USING CTDNA.

Molecular analysis

- Pyrosequencing of codons 599, 600 and 601 of exon 15 of the BRAF gene, to detect the c.1799T>A p.(Val600Glu) (V600E) variant
- The analysis can detect variants down to a level of 5% in a background of wild-type genomic DNA.

Prices and TAT

- Funded by WHSSC for Welsh patients
- Prices available on request
- 7CD TAT (but we will expedite as much as possible)

Sample requirements

- 10-20ml of whole blood in Streck Cell-Free DNA BCT® or Janssen CellSave Preservative Tubes. NB: Streck tubes are available on request from the laboratory

- Samples must reach the laboratory within 96 hours of blood draw
- Samples should not be sent to the lab on Fridays unless extremely urgent and/or by prior arrangement
- Please label samples with three identifiers and date of collection; all samples must be accompanied by a completed request form
- Consent for testing and DNA storage is assumed when the testing request is received
- For full details on how to collect and handle blood samples for ctDNA analysis, please refer to PD-GEN-ctDNAinstructions

Contact details

Samples and completed request forms (PD-GEN-ReqctDNABRAFPyro) to be sent to:

All Wales Genomics Laboratory
Institute of Medical Genetics
University Hospital of Wales
Heath Park
Cardiff CF14 4XW

Laboratory email address (queries and Streck tube requests): lab.genetics.cav@wales.nhs.uk
Rachel Dodds (Principal Clinical Scientist, ctDNA Section): Rachel.Dodds@wales.nhs.uk
Holly Lewis (Principal Clinical Scientist, melanoma service): holly.lewis2@wales.nhs.uk

AWMGS website: http://www.medicalgenomicswales.co.uk/

Streck blood tubes: Cell-Free DNA BCT RUO & CE - Streck
CellSave blood tubes: CELLSEARCH® | Product and Systems Overview | CellSave Preservative Tubes (cellsearchctc.com)