Release Notes for v1.6:

1. We are now releasing cancer WGS analyses that contain Tier 3 germline analysis.

The criteria for Tier 3 analysis were evolved by the NHSE V&R working subgroup on cancer germline findings.  We shall be reporting all non-synonymous low frequency variants in a broad panel of genes that confer susceptibility to cancer.  Variants in genes on the germline panel for the relevant tumour type will be placed at the top of the list.  Variants will be annotated, including by a link to ClinVar (where variant exists in ClinVar). Technical details can be found at [https://www.genomicsengland.co.uk/information-for-gmc-staff/cancer-programme/cancer-genome-analysis/](https://www.genomicsengland.co.uk/information-for-gmc-staff/cancer-programme/cancer-genome-analysis/%22%20%5Ct%20%22_blank). The gene panels used for Tier 3 calling can be found at [https://panelapp.genomicsengland.co.uk](https://panelapp.genomicsengland.co.uk/%22%20%5Ct%20%22_blank). The version of each panel used for the analysis will be provided in HTML report, and each version can be downloaded or queried from PanelApp.

As you are likely aware, the criteria by which we report Tier 1 germline variants are (i) on-tumour association (ii) truncating (in LOF gene) and/or 2 star pathogenic/likely pathogenic classification on ClinVar.

It is not anticipated or required that Tier 3 will be reviewed for all patients, but it may be appropriate to review if (i) the likely susceptibility gene is less well reported on ClinVar such that bone fide pathogenic missense/splicing variants have not achieved 2 stars (ii) there is a high index of suspicion of germline susceptibility in the individual and/or (iii) a strong family history of other cancers.

As per Tier 1 variants, if a variant is deemed relevant, it is recommended that you review the variant in the IGV provided and assess via ACMG criteria. Variants should be technically validated locally.  Variants returned to the patient should be reported in the feedback form.

2. We now display the tumour mutational burden (TMB) of the patient plotted against the range of TMB values for the respective tumour type and alongside different tumour types that have been sequenced in the 100,000 Genomes Project.

3. We also would like to remind you that the variant's genomic coordinates in HTML report are linked to IGV view. You can also use 'Download batch script' functionality to review the variant in IGV viewer on your local machine. Please find details in the 'Access to genomic data for GMCs – User guide' available at https://www.networks.nhs.uk/nhs-networks/gmc-network/documents/access-to-genomic-data-for-nhs-gmcs-2013-user-guide/view