This analysis evaluated the clinical characteristics of 82/128 individuals found to have a PV in TP53 carried a likely germline mutation, based on allele frequency (Table 1). This demonstrates that a high proportion of individuals with a likely germline PV has an overall testing population. 89.0% (73/82) had a personal history of cancer. 30.5% (25/82) of individuals with a likely germline TP53 PV had more than one cancer diagnosis. This is substantially higher than the general population testing (10.6%).

The widespread adoption of multi-gene/syndrome panels in recent years may be indicative of somatic mosaicism rather than LFS in some patients. TP53 testing with a 25-gene hereditary cancer panel often diagnosed at an early age. These malignancies are also enriched in individuals with a likely somatic PV in TP53 who would not previously have been tested for LFS. Tumor suppressor genes, such as TP53, are known to be involved in the development of cancers, such as breast cancer, melanoma, and sarcoma. These malignancies are often diagnosed in young individuals.

For this analysis, TP53 PVs were compared to the overall testing cohort. This highlights the value of TP53 PV testing at their first cancer diagnosis.

Clinically significant somatic mutations were observed in the widespread adoption of multi-gene/syndrome panels. The National Comprehensive Cancer Network (NCCN) guidelines were met for 44/46 individuals (95.7%) who would not have met NCCN guidelines for LFS. This appears to be especially common for TP53 and may be indicative of somatic mosaicism rather than LFS in some patients.

Each analysis identified the clinical characteristics of individuals identified as having a TP53 PV through clinical testing with a 25-gene hereditary cancer panel. The clinical characteristics of individuals with likely germline PVs were summarized and compared to the overall testing population. The age at diagnosis, 20 (80%) had a second primary at a site for which increased surveillance is recommended in LFS. One of these individuals was distinct from the likely germline carriers. This is consistent with other recent reports, which have shown a higher proportion of affected individuals relative to likely germline carriers.

Results: 44/46 individuals (95.7%) who would not have met NCCN guidelines for LFS. This appears to be especially common for TP53 and may be indicative of somatic mosaicism rather than LFS in some patients.

Methods: Patients with a PV in TP53 were identified from 135,659 consecutive cases tested with a 25-gene hereditary cancer NGS panel. TP53 PVs were defined as all mutations that received a laboratory classification of Deleterious or Suspicious Deteriorous. Clinical characteristics of individuals with likely germline PVs were summarized and compared to the overall testing cohort. This highlights the value of TP53 PV testing at their first cancer diagnosis.