Tempus xG Sample Report Guide

Germline testing identifies potential hereditary cancer risk factors that may affect patients and their family members.

By combining both somatic and germline results, Tempus provides a more comprehensive view of your patient's molecular profile.

**xG Sample Report: Page 1**

**xG+ (extended hereditary cancers) or xG (common hereditary cancers)**

xG report dates may vary from somatic tests (xT and xF). They follow separate testing timelines and can be ordered at different time points.

88 (xG+) or 52 (xG) genes associated with hereditary cancer risk

**Positive Result:**
Pathogenic variant in BRCA2 and variant of uncertain significance in PMS2 identified by germline sequencing.

NCCN Guidelines for management are available for pathogenic/likely pathogenic variants. Testing may also be considered for at-risk relatives for these findings.

Due to unclear clinical significance of variants of uncertain significance, management guidelines are not available.

---

**Result:** Positive

Pathogenic variant in BRCA2 and variant of uncertain significance in PMS2 identified by germline sequencing.

NCCN Guidelines for management are available for pathogenic/likely pathogenic variants. Testing may also be considered for at-risk relatives for these findings.

Due to unclear clinical significance of variants of uncertain significance, management guidelines are not available.

---

**Interpretation**
This individual is heterozygous for a pathogenic variant in BRCA2, consistent with Hereditary Breast and Ovarian Cancer syndrome and associated with the following lifetime cancer risks: female breast 38-84%, second primary breast 62%, ovarian 16.5-27%, pancreatic 2-7%, prostate 20%, male breast 8.9%.

**Recommendation(s)**
- Genetic counseling is recommended.

---

**Laboratory Directed by Sean Hofherr, Ph.D., FACMG**
207 Perry Parkway, Gaithersburg, MD 20877
GeneDx.com
T: (888) 729-1206
E: zebras@gendx.com

---

**xG Powered by GeneDx**
Learn more at TEMPUS.COM
Gene specific summaries are included with gene function and information about associated syndromes and cancers.

Information utilized to classify variant(s) is included for all pathogenic/likely pathogenic variants and variants of uncertain significance.

**BRCA2**

**GENE SUMMARY**

BRCA2 encodes a tumor suppressor protein with an important role in DNA double-stranded break repair and regulation of RAD51 (PMID: 11447276, 11239456). Heterozygous pathogenic variants in BRCA2 cause autosomal dominant hereditary breast and ovarian cancer syndrome (HBOC) which predisposes to early onset female breast, ovarian, and other cancers, including melanoma, male breast, pancreatic, and prostate cancers (PMID: 20301425). Two pathogenic variants on opposite alleles of BRCA2 cause the rare autosomal recessive condition Fanconi anemia (FA), complementation group D1. FA is disorder of genomic instability which may present with some or all of the following features: skeletal abnormalities, microcephaly, short stature, renal and urogenital anomalies, hearing loss, heart defects, intellectual disability, progressive bone marrow failure, and cancer susceptibility (PMID: 20301575).

**c.4456_4459delGTTA:p.(V1486Nfs*5)** in exon 11 of the BRCA2 gene (NM_000059.3). The sequence with the altered base(s) in brackets is: CATA[delGTTA]AACA

Frameshift variant predicted to result in protein truncation or nonsense mediated decay in a gene for which loss-of-function is a known mechanism of disease

Observed in individuals with a personal or family history consistent with pathogenic variants in this gene (Verhoog 1999, Churpek 2015, Susswein 2016, Pritzlaff 2017)

Not observed at a significant frequency in large population cohorts (Lek 2016)

Truncating variants in this gene are considered pathogenic by a well-established clinical consortium and/or database

Also known as 4684_4687delGTTA or 4454_4457delTAGT

We interpret this as a Pathogenic Variant.