Table S2. Annotation of germline variants in 27 cancer-predisposing genes defined by ClinVar and SnpEff

		[a]SnpEff version 4.3t			Total
		HIGH	MODERATE	LOW+MODIFIER	
ClinVar (ver. 2022-03-06)	Pathogenic	**157**	**28**	**1**	186
	Benign	0	105	763	868
	Uncertain significance	**23**	1,992	117	2,132
	Not registered	**100**	1,145	419	1,664
Total		280	3,270	1,300	4,850

We defined “pathogenic variants” in this study as either loss-of-function variants determined by the SnpEff ver 4.3t.,[1] or pathogenic/likely pathogenic variants identified by ClinVar (ver. 2022-03-06).[2] Variants that are considered pathogenic in this study are highlighted in boldface and underlined.

[a]Variants impacts were classified into "HIGH", "MODERATE", and "LOW+MODIFIER", accordance to SnpEff.

HIGH; the variants are assumed to have high impact in the protein, probably causing protein truncation, loss of function or triggering nonsense mediated decay. MODERATE; non-disruptive variants that might change protein effectiveness. LOW; the variants assumed to be mostly harmless or unlikely to change protein behavior. MODIFIER; usually non-coding variants or variants affecting non-coding genes, where predictions are difficult, or there is no evidence of impact.

1. Cingolani P, Platts A, Wang lL, et al. A program for annotating and predicting the effects of single nucleotide polymorphisms, SnpEff: SNPs in the genome of

Drosophila melanogaster strain w1118; iso-2; iso-3. Fly (Austin). 2012; 6: 80-92.

2. Landrum MJ, Lee JM, Benson M, et al. ClinVar: public archive of interpretations of clinically relevant variants. Nucleic Acids Res. 2016; 44: D862-868.