**Supplementary Table 1.** Breakdown of study population according to phenotype and number of mutations identified in the whole 135-gene panel.

|  |  |  |  |
| --- | --- | --- | --- |
| Phenotype | Patients | Pathogenic/likely pathogenic mutation | % |
| Hereditary breast-ovarian cancer syndrome | 633 | 132 | 20.85 |
| Hereditary nonpolyposis colorectal cancer | 210 | 63 | 30.00 |
| (Attenuated) Familial adenomatous polyposis | 77 | 9 | 11.69 |
| Li-Fraumeni syndrome | 15 | 3 | 20.00 |
| Other | 88 | 20 | 22.73 |
| TOTAL | 1023 | 227 | 22.19 |

**Supplementary Table 2.** Published cancer risk for the genes mutated in our cohort of MINAS patients

|  |  |  |  |
| --- | --- | --- | --- |
| Gene | Cancer risk | Associated risk | Cancer risk / age |
| *APC* | Colorectal cancer | Very high | <50 years: 93%[1] |
| *ATM* | Female breast cancer  Pancreatic cancer | Moderate  Low | >50 years:4.94%[2]  Lifetime risk: 2.41%[2] |
| *BARD1* | Female breast cancer | Moderate\* [3], [4],[5] | NA |
| *BRCA1* | Female breast cancer  Ovarian cancer  Prostate cancer  Male breast cancer | High  High  Low  Low | <70 years: 60-66%[6], [7]  <70 years: 41-59%[6], [7]  <65 years: 8.6%[8]  <70 years: 1.2%[9] |
| *CHEK2* | Female breast cancer  Prostate cancer  Colorectal cancer | Moderate  Moderate  Low | <80 years: 23-48%[10], [11], [12], [13].  Lifetime risk: 24-44%[14]  Lifetime risk: 7.2-9.5%[15] |
| *ERCC3* | Breast Cancer | Moderate\* [16] | NA |
| *EXO1* | Female breast cancer  Lung cancer  Glioma  Gastric cancer | Low\*[17]  Low\*[17]  Low\*[17]  Low\*[17] | NA  NA  NA  NA |
| *FANCA* | Female breast cancer | Low\* [18], [19], [20] | NA |
| *FLCN* | Renal cancer  Colorectal cancer | Moderate [21]  Low\*[22] | Lifetime risk: 16% [21]  NA |
| *FH* | Hereditary leiomyomatosis Renal cell carcinoma  Female breast cancer | High[23]  Moderate[23] [24]  Low[23] | NA  Lifetime risk: 15% [24]  NA |
| *MEN1* | Endocrine tumors | High[25] | NA |
| *MLH1* | Colorectal cancer  Endometrial cancer  Upper GI cancer  Ovarian cancer  Urinary tract | High  High  Moderate  Moderate  Low | <70 years: 46%[26]  <70 years: 34%[26]  <70 years: 18%[26]  <70 years: 11%[26]  <70 years: 2%[26] |
| *PALB2* | Female breast cancer  Pancreatic cancer | High  Low [27], [28] | <70 years:35%[29]  NA |
| *RAD51D* | Ovarian cancer | Moderate | <80 years: 10%[30] |
| *SDHB* | Paraganglioma  Pheochromocytoma | Moderate[31]  Moderate[31] | 30 years: 29%[32]  NA |
| *TP53* | Female breast cancer  Overall cancer risk | High  Very High | <70 years: 54%[33]  <70 years: ~100%[33] |
| *TSC2* | Hamartomas | High[34] | NA |
| *XPA* | Bladder cancer  Lung cancer  Breast cancer | Low\*[35]  Low\*[36]  Low\*[37] | NA |

GI includes gastric, pancreatic biliary tract and duodenal cancers

\* More evidence needed

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