

## Germline mutations in cancer-predisposition genes in patients with biliary tract cancer

### SUPPLEMENTARY MATERIALS

**Supplementary Table 1: Germline mutation classified as benign or variants of unknown significance and clinical characteristics of the patients with those mutations in this study.** See Supplementary Table 1

**Supplementary Table 2: Inclusion criteria for hereditary breast and/or ovarian cancer related cancer used in this study**

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- Individual from a family with a known deleterious *BRCA1/BRCA2* gene mutation
  - Personal history of breast cancer + one or more of the following:
    - » Diagnosed  $\leq 45$  years old
    - » Diagnosed  $\leq 50$  years old with:
      - An additional breast cancer primary
      - $\geq 1$  close blood relative with breast cancer at any age
      - $\geq 1$  close blood relative with pancreatic cancer
      - $\geq 1$  relative with prostate cancer (Gleason score  $\geq 7$ )
      - $\geq 1$  relative with biliary tract cancer
      - An unknown or limited family history
    - » Diagnosed  $\leq 60$  years old with:
      - Triple negative breast cancer
    - » Diagnosed at any age with:
      - $\geq 2$  close blood relatives with breast cancer, pancreatic cancer, prostate cancer (Gleason score  $\geq 7$ ), or biliary tract cancer at any age
      - $\geq 1$  close blood relative with breast cancer diagnosed  $\leq 50$  years old
      - $\geq 1$  close blood relative with ovarian carcinoma
      - A close male blood relative with breast cancer
      - For an individual of ethnicity associated with higher mutation frequency no additional family history may be required
  - Personal history of ovarian carcinoma
  - Personal history of male breast cancer
  - Personal history of prostate cancer (Gleason score  $\geq 7$ ) at any age with  $\geq 1$  close blood relative with ovarian carcinoma at any age or breast cancer diagnosed  $\leq 50$  years old or two relatives with breast, pancreatic, prostate cancer (Gleason score  $\geq 7$ ), or biliary tract cancer at any age
  - Personal history of pancreatic cancer at any age with  $\geq 1$  close blood relative with ovarian carcinoma at any age or breast cancer diagnosed  $\leq 50$  years old or two relatives with breast, pancreatic, prostate cancer (Gleason score  $\geq 7$ ), or biliary tract cancer at any age
  - Personal history of biliary tract cancer at any age with  $\geq 1$  close blood relative with ovarian carcinoma at any age or breast cancer diagnosed  $\leq 50$  years old or two relatives with breast, pancreatic, prostate cancer (Gleason score  $\geq 7$ ), or biliary tract cancer at any age
  - Personal history of pancreatic cancer and Ashkenazi Jewish ancestry
  - *BRCA1/2* mutation detected by tumor profiling in the absence of germline mutation analysis
  - Family history only (significant limitations of interpreting test results for an unaffected individual should be discussed):
    - » First- or second-degree blood relative meeting any of the above criteria
    - » Third-degree blood relative who has breast cancer and/or ovarian carcinoma and who has  $\geq 2$  close blood relatives with breast cancer (at least one with breast cancer diagnosed  $\leq 50$  years old) and/or ovarian carcinoma
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**Supplementary Table 3: Inclusion criteria for Lynch syndrome related cancer used in this study**

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- Colorectal cancer or biliary tract cancer diagnosed in a patient who is less than 50 years of age.
  - Presence of synchronous, metachronous colorectal, or other hereditary nonpolyposis colorectal cancer-associated tumors, regardless of age.
  - Colorectal cancer or biliary tract cancer with the microsatellite instability-high histology diagnosed in a patient who is less than 60 years of age.
  - Colorectal cancer or biliary tract cancer diagnosed in one or more first-degree relatives with a hereditary nonpolyposis colorectal cancer-associated tumors, with one of the cancers being diagnosed under age 50 years.
  - Colorectal cancer or biliary tract cancer diagnosed in two or more first- or second-degrees relatives with hereditary nonpolyposis colorectal cancer-associated tumors, regardless of age.
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