**Supplementary Tables and Figures**

### Supplementary Table 1: Distribution of the 40 PGV by penetrance status

|  |  |  |
| --- | --- | --- |
|  | **PGM** | **Total (n=40)** |
| **High Penetrance** | BRCA1 | 1 (2.5%) |
| BRCA2 | 9 (22.5%) |
| CDKN2A | 1 (2.5%) |
| MSH6 | 1 (2.5%) |
| PALB2 | 2 (5.0%) |
| SDHA | 2 (5.0%) |
| TP53 | 1 (2.5%) |
| **Moderate Penetrance** | ATM | 7 (17.5%) |
| CHEK2 | 4 (10.0%) |
| HOXB13 | 1 (2.5%) |
| NBN | 2 (5.0%) |
| RAD51C | 1 (2.5%) |
| **Low Penetrance** | APC (I1307K) | 1 (2.5%) |
| MUTYH-monoallelic | 3 (7.5%) |
| **Recessive** | FH | 1 (2.5%) |
| MSH3 | 1 (2.5%) |
| NTHL1 | 2 (5.0%) |

### Supplementary Table 2: Predictors of Positive Germline variant, Univariate unadjusted

|  |  |  |  |
| --- | --- | --- | --- |
|  | OR | 95% CI | p.value |
| Gender  Female (vs Male) | 0.71 | 0.34-1.42 | 0.336 |
| Age Group Age <60 Years (vs >60 years) | 1.36 | 0.61-2.87 | 0.439 |
| Staging AJCC 8th edition  Late Stage (3-4) vs Early Stage (1-2) Stage 4 vs Other stages (1-3) | 1.011.55 | 0.50-2.140.77-3.12 | 0.9790.212 |
| Family History of cancer in a first degree relative Yes (vs No) | **2.36** | **1.14-5.20** | **0.025** |
| Tumor Location  Body (vs Head) Tail (vs Head) | 1.042.27 | 0.36-2.610.94-5.22 | 0.9360.058 |
| Smoking  No (vs Yes) | 0.60 | 0.30-1.19 | 0.146 |
| Diabetes Mellitus  No (vs Yes) | 1.11 | 0.52-2.52 | 0.802 |
| Obese  No (vs Yes) | 1.35 | 0.49-4.78 | 0.591 |
| CA19-9  >37 (vs <37) >300 (vs <300) | 1.010.64 | 0.47-2.300.30-1.31 | 0.9930.231 |

**Supplementary Table 3: Hazards ratio for survival and Median overall survival of the groups**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | HR | 95% CI | P value | Median overall survival |
| Gender Male Female | 1.01.15 | 0.76-1.73 | 0.52 | 16.5 vs. 16.4 months |
| Age > 60 years < 60 years | 1.01.28 | 0.80-2.03 | 0.30 | 16.4 vs. 16.7 months |
| PGV (carriers vs. non-carriers) Non-carrier Carrier | 1.00.51 | 0.25-1.01 | 0.049 | 16.8 vs. 16.5 months |
| BRCAness PGV  No Yes | 1.00.46 | 0.20-1.05 | 0.057 | 16.4 vs 21.1 months |
| CA 19-9  >300 <300 | 1.0**0.48** | **0.31-0.73** | **<0.001** | 19.1 vs. 13.5 months |
| Disease Stage Early Stage (1-2) Late stage (3-4) | 1.0**3.75** | **2.15-6.54** | **<0.001** | 16.8 vs. 16.5 months |
| Tumor location (Body vs. Tail) Head Body Tail | 1.01.490.68 | 0.90-2.470.33-1.37 | 0.11 | 17.0 vs. 13.8 vs. 15.9 months |

### Supplementary Table 4: Systemic treatments for pathogenic germline carriers

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Case** | **Gene** | **Clinical effect** | **Stage** | **NEOTT** | **RES** |  **ADJ** | **MTX 1** | **RES** | **MTX 2** | **RES** |  **MTX 3** | **RES** | **MTX 4** | **RES** |
| 1 | BRCA2 | Splice acceptor | 1 | FF-> Cap + RDT | PR | No | No | NA | No | NA | No | NA | No | NA |
| 2 | NBN | p.Ser292Valfs\*12 | 2 | No | NA | FF | Gem | SD | No | NA | No | NA | No | NA |
| 3 | MUTYH (monoallelic) | p.Gln338\* | 4 | No | NA | No | FF | SD | GNAB | SD | NAL-IRI + 5-FU | SD | No | NA |
| 4 | MUTYH (monoallelic) | p.Gly396Asp | 4 | No | NA | No | GNAB | PR | No | NA | No | NA | No | NA |
| 5 | ATM | p.Phe2958\* | 4 | No | NA | No | FF | PR | NAL-IRI + 5-FU | PR | No | NA | No | NA |
| 6 | PALB2 | p.Arg975Glufs\*4 | 3 | FF-> Cap+ RDT | PR | No | No | NA | No | NA | No | NA | No | NA |
| MSH3 | p.Asp767Glyfs\*2 |
| 7 | BRCA2 | p.Ser3147Cysfs\*2 | 2 | FF | PR | Gem-> Cap + RDT | No | NA | No | NA | No | NA | No | NA |
| 8 | BRCA2 | p.Thr1378\* | 2 | GNAB | PR | Cap + RDT | No | NA | No | NA | No | NA | No | NA |
| 9 | PALB2 | p.Ser254Ilefs\*3 | 3 | Cis + Gem | PR | No | No | NA | No | NA | No | NA | No | NA |
| 10 | ATM | Silent | 4 | No | NA | No | GNAB | DP | FOX | SD | NAL-IRI + 5-FU | DP | FOX | PR |
| 11 | NBN | p.Lys219Asnfs\*16 | 4 | No | NA | No | FF | PR | GNAB | DP | Cap | SD | No | NA |
| 12 | MSH6 | Deletion (Exon 2) | 4 | No | NA | No | GNAB | PR | Pem | SD | No | NA | No | NA |
| 13 | BRCA2 | p.Phe1182\* | 4 | No | NA | No | GNAB | PR | FF | NON | No | NA | No | NA |
| 14 | TP53 | p.Tyr234Cys | 3 | No | NA | No | GNAB | DP | No | NA | No | NA | No | NA |
| CHEK2 | p.Ser428Phe |
| 15 | SDHA | p.Arg31\* | 3 | No | NA | No | GNAB | PR | GNAB | SD | No | NA | No | NA |
| 16 | ATM | p.Lys79Asnfs\*37 | 4 | No | NA | No | GNAB | SD | NAL-IRI + 5-FU | SD | No | NA | No | NA |
| 17 | SDHA | p.Arg31\* | 3 | No | NA | No | GNAB | PR | No | NA | No | NA | No | NA |
| 18 | ATM | Splice acceptor | 4 | No | NA | No | GNAB | PR | NAL-IRI + 5-FU | PR | No | NA | No | NA |
| 19 | BRCA2 | p.Lys1025\_Lys1026delinsAsn\* | 4 | No | NA | No | FF | PR | NAL-IRI + 5-FU | SD | No | NA | No | NA |
| 20 | ATM | p.Met1? | 4 | No | NA | No | FF | PR | GNAB | PR | No | NA | No | NA |
| 21 | BRCA1 | Deletion (Exon 15) | 4 | No | NA | No | FF | PR | GNAB | DP | No | NA | No | NA |
| 22 | MUTYH (monoallelic) | p.Gly396Asp | 1 | FF -> Cap + RDT | PR | No | No | NA | No | NA | No | NA | No | NA |
| 23 | FH | p.Lys477dup | 2 | No | NA | FF | No | NA | No | NA | No | NA | No | NA |
| 24 | RAD51C | Deletion (Exons 4-9) | 4 | No | NA | No | FF | PR | GNAB | SD | No | NA | No | NA |
| 25 | ATM | p.Ala2067Asp | 2 | GNAB | PR | No | No | NA | No | NA | No | NA | No | NA |
| 26 | CHEK2 | p.Arg117Gly | 3 | No | NA | No | GNAB | PR | Gem | SD | No | NA | No | NA |
| 27 | NTHL1 | p.Gln90\* | 4 | No | NA | No | GNAB | DP | NAL-IRI + 5-FU | PR | No | NA | No | NA |
| 28 | BRCA2 | p.Leu2865Phefs\*4 | 2 | No | NA | Gem | No | NA | No | NA | No | NA | No | NA |
| 29 | CDKN2A | p.Met53Ile | 1 | No | NA | FF | No | NA | No | NA | No | NA | No | NA |
| 30 | CHEK2 | p.Thr367Metfs\*15 | 4 | No | NA | No | GNAB | PR | No | NA | No | NA | No | NA |
| 31 | NTHL1 | p.Gln90\* | 1 | No | NA | FF | No | NA | No | NA | No | NA | No | NA |
| 32 | BRCA2 | p.Arg2318\* | 4 | No | NA | No | FF | PR | OLP\* | PR | No | NA | No | NA |
| 33 | BRCA2 | p.Tyr1762\* | 4 | No | NA | No | Gem + Carb | SD | NAL-IRI + 5-FU + RUC | PR | No | NA | No | NA |
| 34 | CHEK2 | p.Ser428Phe | 4 | FF -> Cap + RDT | PR | No | No | NA | No | NA | No | NA | No | NA |
| 35 | ATM | Silent | 4 | No | NA | No | No | NA | No | NA | No | NA | No | NA |
| 36 | HOXB13 | p.Gly84Glu | 1 | FF -> Cap + RDT | PR | No | No | NA | No | NA | No | NA | No | NA |
| 37 | APC (I1307K) | p.Ile1307Lys | 1 | FF -> Niv + RDT | SD | No | No | NA | No | NA | No | NA | No | NA |
| 38 | BRCA2 | p.Glu2198Asnfs\*4 | 2 | FF -> Cap + RDT | PR | No | No | NA | No | NA | No | NA | No | NA |
| Legend: NEOTT: neoadjuvant treatment, ADJ: adjuvant treatment, RES: best response, MTX1: first-line systemic treatment for metastatic disease, MTX2: second-line systemic treatment for metastatic disease, MTX3: third-line systemic treatment for metastatic disease, MTX4: fourth-line systemic treatment for metastatic disease, NA: not applicable, FF: FOLFIRINOX, Cap: capecitabine, Gem: Gemcitabine, RDT: radiotherapy, GNAB: gemcitabine + nab-paclitaxel, Niv: nivolumab, SD: stable disease, PR: partial response, DP: disease progression, FOX: FOLFOX, OLP: Olaparib, RUC: Rucaparib, Carb: Carboplatin, NAL-IRI: liposomal irinotecan, 5-FU: fluorouracil, Pem: Pembrolizumab, Cis: Cisplatin, NON: Not available (ongoing treatment- no response assessment).\*: Maintenance treatment |

### Supplementary Table 5: Overall systemic treatments

|  |  |  |  |
| --- | --- | --- | --- |
|  | Positive (N=38) | VUS/Negative (N=212) | Total (N=250) |
| **Stage of Cancer** |  |  |  |
|    1 | 6 (15.8%) | 30 (14.2%) | 36 (14.4%) |
|    2 | 7 (18.4%) | 43 (20.3%) | 50 (20.0%) |
|    3 | 6 (15.8%) | 56 (26.4%) | 62 (24.8%) |
|    4 | 19 (50.0%) | 83 (39.2%) | 102 (40.8%) |
| **Surgery** |  |  |  |
|    Yes | 18 (47.4%) | 83 (39.2%) | 101 (40.4%) |
|    No | 20 (52.6%) | 129 (60.8%) | 149 (59.6%) |
| **Neoadjuvant treatment** |  |  |  |
|    Yes | 11 (28.9%) | 61 (28.8%) | 72 (28.8%) |
|    No | 27 (71.1%) | 151 (71.2%) | 178 (71.2%) |
| **Neoadjuvant type** |  |  |  |
|    Capecitabine + (Gemcitabine + Radiotherapy) | 0 (0.0%) | 1 (1.6%) | 1 (1.4%) |
|    Capecitabine + Radiotherapy | 0 (0.0%) | 1 (1.6%) | 1 (1.4%) |
|    Cisplatin + Gemcitabine | 1 (9.1%) | 0 (0.0%) | 1 (1.4%) |
|    mFOLFIRINOX | 1 (9.1%) | 14 (22.9%) | 15 (20.8%) |
|    mFOLFIRINOX (switch Gemcitabine + Nab-paclitaxel) + (Capecitabine + radiotherapy) | 0 (0.0%) | 4 (6.5%) | 4 (5.6%) |
|    mFOLFIRINOX (switch Gemcitabine + Nab-paclitaxel) | 0 (0.0%) | 1 (1.6%) | 1 (1.4%) |
|    mFOLFIRINOX + (Capecitabine + Radiotherapy) | 6 (54.6%) | 18 (29.4%) | 24 (33.4%) |
|    mFOLFIRINOX + (Gemcitabine + Radiotherapy) | 0 (0.0%) | 2 (3.3%) | 2 (2.8%) |
|    mFOLFIRINOX + Nivolumab + Radiotherapy | 1 (9.1%) | 0 (0.0%) | 1 (1.4%) |
|    Gemcitabine + Nab-paclitaxel (switch mFOLFIRINOX) + (Capecitabine + Radiotherapy) | 0 (0.0%) | 1 (1.6%) | 1 (1.4%) |
|    Gemcitabine + Capecitabine | 0 (0.0%) | 1 (1.6%) | 1 (1.4%) |
|    Gemcitabine + Nab-paclitaxel | 2 (18.2%) | 5 (8.2%) | 7 (9.7%) |
|    Gemcitabine + Nab-paclitaxel + (Capecitabine + Radiotherapy) | 0 (0.0%) | 7 (11.4%) | 7 (9.7%) |
|    Gemcitabine + Nab-paclitaxel + (Gemcitabine + Radiotherapy) | 0 (0.0%) | 2 (3.3%) | 2 (2.8%) |
|    Gemcitabine + Nab-paclitaxel + Radiotherapy | 0 (0.0%) | 3 (4.9%) | 3 (4.2%) |
|    Gemcitabine + Radiotherapy | 0 (0.0%) | 1 (1.6%) | 1 (1.4%) |
|    No neoadjuvant treatment | 27 | 151 | 178 |
| **Best response to neoadjuvant treatment** |  |  |  |
|    CR | 0 (0.0%) | 2 (3.3%) | 2 (2.8%) |
|    PR | 10 (90.9%) | 45 (73.8%) | 55 (76.4%) |
|    SD | 0 (0.0%) | 7 (11.5%) | 7 (9.7%) |
|    No Response | 1 (9.1%) | 7 (11.5%) | 8 (11.1%) |
|    No neoadjuvant treatment | 27 | 151 | 178 |
| **Adjuvant chemotherapy** |  |  |  |
|    Yes | 7 (18.4%) | 47 (22.2%) | 54 (21.6%) |
|    No | 31 (81.6%) | 165 (77.8%) | 196 (78.4%) |
| **Adjuvant chemotherapy type** |  |  |  |
|    Capecitabine + Radiotherapy | 1 (14.3%) | 1 (2.1%) | 2 (3.8%) |
|    Fluorouracil + Gemcitabine + Radiotherapy | 0 (0.0%) | 1 (2.1%) | 1 (1.9%) |
|    Fluorouracil + Radiotherapy | 0 (0.0%) | 1 (2.1%) | 1 (1.9%) |
|    FOLFIRI | 0 (0.0%) | 1 (2.1%) | 1 (1.9%) |
|    mFOLFIRINOX | 4 (57.1%) | 15 (31.9%) | 19 (35.2%) |
|    mFOLFIRINOX (switch to Gemcitabine [toxicity]) | 0 (0.0%) | 1 (2.1%) | 1 (1.9%) |
|    mFOLFIRINOX + (Capecitabine + Radiotherapy) | 0 (0.0%) | 3 (6.4%) | 3 (5.6%) |
|    Gemcitabine + Capecitabine | 0 (0.0%) | 11 (23.4%) | 11 (20.4%) |
|    Gemcitabine | 1 (14.3%) | 7 (14.9%) | 8 (14.8%) |
|    Gemcitabine + (Capecitabine + Radiotherapy) | 1 (14.3%) | 3 (6.4%) | 4 (7.5%) |
|    Gemcitabine + Nab-paclitaxel | 0 (0.0%) | 2 (4.3%) | 2 (3.7%) |
|    Gemcitabine + Radiotherapy | 0 (0.0%) | 1 (2.1%) | 1 (1.9%) |
|    No adjuvant treatment | 31 | 165 | 196 |
| **First-line treatment for advanced/recurrent disease** |  |  |  |
|    Yes | 22 (57.9%) | 147 (69.3%) | 169 (67.6%) |
|    No | 16 (42.1%) | 65 (30.7%) | 81 (32.4%) |
| **First-line chemotherapy name** |  |  |  |
|    Carboplatin + Paclitaxel | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
|    Dabrafenib + Trametinib | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
|    FOFIRINOX + CPI-613 | 0 (0.0%) | 2 (1.4%) | 2 (1.2%) |
|    mFOLFIRINOX | 8 (36.4%) | 62 (42.2%) | 70 (41.5%) |
|    FOLFOX | 0 (0.0%) | 2 (1.4%) | 2 (1.2%) |
|    Gemcitabine + Nab-paclitaxel + FOLFIRI (alternating) | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
|    Gemcitabine | 1 (4.5%) | 1 (0.7%) | 2 (1.2%) |
|    Gemcitabine + Anetumab | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
|    Gemcitabine + Carboplatin | 1 (4.5%) | 0 (0.0%) | 1 (0.6%) |
|    Gemcitabine + Cisplatin | 0 (0.0%) | 2 (1.4%) | 2 (1.2%) |
|    Gemcitabine + Cisplatin + Nab-paclitaxel | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
|    Gemcitabine + Nab-paclitaxel | 12 (54.5%) | 57 (38.8%) | 69 (40.8%) |
|    Gemcitabine + Nab-paclitaxel + APX005M | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
|    Gemcitabine + Nab-paclitaxel + BMS-813160 + Nivolumab | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
|    Gemcitabine + Nab-paclitaxel + Cisplatin + Paricalcitol | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
|    Gemcitabine + Nab-paclitaxel + Napabucasin | 0 (0.0%) | 6 (4.1%) | 6 (3.6%) |
|    Gemcitabine + Nab-Paclitaxel + Nivolumab | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
|    NaL-IRI + 5-FU | 0 (0.0%) | 4 (2.7%) | 4 (2.4%) |
|    NaL-IRI + 5FU | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
|    TIL + IL-2 | 0 (0.0%) | 1 (0.7%) | 1 (0.6%) |
| **Best response to first-line treatment** |  |  |  |
|    CR | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
|    PR | 15 (68.2%) | 79 (54.5%) | 94 (56.3%) |
|    SD | 4 (18.2%) | 34 (23.4%) | 38 (22.8%) |
|    No Response | 3 (13.6%) | 32 (22.1%) | 35 (21.0%) |
| **Second-line treatment** |  |  |  |
|    Yes | 17 (44.7%) | 86 (40.6%) | 103 (41.2%) |
|    No | 21 (55.3%) | 126 (59.4%) | 147 (58.8%) |
| **Second-line chemotherapy name** |  |  |  |
|    5FU + NaL-IRI +CXCR4i +Pembrolizumab | 0 (0.0%) | 1 (1.2%) | 1 (1.0%) |
|    Cabiralizumab + Nivolumab | 0 (0.0%) | 1 (1.2%) | 1 (1.0%) |
|    Capecitabine | 0 (0.0%) | 3 (3.5%) | 3 (2.9%) |
|    FOLFIRI | 2 (11.8%) | 3 (3.5%) | 5 (4.9%) |
|    mFOLFIRINOX | 1 (5.9%) | 10 (11.6%) | 11 (10.7%) |
|    mFOLFOX | 1 (5.9%) | 1 (1.2%) | 2 (1.9%) |
|    mFOLFOX + Nivolumab + Cabiralizumab | 0 (0.0%) | 1 (1.2%) | 1 (1.0%) |
|    Gemcitabine | 1 (5.9%) | 1 (1.2%) | 2 (2.0%) |
|    Gemcitabine + Capecitabine | 0 (0.0%) | 1 (1.2%) | 1 (1.0%) |
|    Gemcitabine + Cisplatin | 0 (0.0%) | 1 (1.2%) | 1 (1.0%) |
|    Gemcitabine + Nab-paclitaxel | 6 (35.3%) | 39 (45.3%) | 45 (43.7%) |
|    Gemcitabine + Nab-paclitaxel + Nivolumab + Cabiralizumab | 0 (0.0%) | 2 (2.4%) | 2 (2.0%) |
|    HPN 536 | 0 (0.0%) | 1 (1.2%) | 1 (1.0%) |
|    NaL-IRI + 5-FU | 3 (17.7%) | 20 (23.3%) | 23 (22.3%) |
|    NaL-IRI + 5-FU + Rucaparib | 1 (5.9%) | 0 (0.0%) | 1 (1.0%) |
|    Olaparib | 1 (5.9%) | 0 (0.0%) | 1 (1.0%) |
|    Pembrolizumab | 1 (5.9%) | 1 (1.2%) | 2 (1.9%) |
| **Second-line response** |  |  |  |
|    CR | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
|    PR | 6 (37.5%) | 24 (29.3%) | 30 (30.6%) |
|    SD | 8 (50.0%) | 26 (31.7%) | 34 (34.7%) |
|    No Response | 2 (12.5%) | 32 (39.0%) | 34 (34.7%) |
| **Third-line treatment** |  |  |  |
|    Yes | 3 (7.9%) | 35 (16.5%) | 38 (15.2%) |
|    No | 35 (92.1%) | 177 (83.5%) | 212 (84.8%) |
| **Third-line chemotherapy name** |  |  |  |
|    Avelumab + PF-04518600 | 0 (0.0%) | 1 (2.9%) | 1 (2.6%) |
|    Capecitabine | 1 (33.3%) | 2 (5.7%) | 3 (7.9%) |
|    CapeOx | 0 (0.0%) | 2 (5.7%) | 2 (5.3%) |
|    FOLFIRI | 1 (33.3%) | 3 (8.6%) | 4 (10.5%) |
|    mFOLFIRINOX | 0 (0.0%) | 1 (2.9%) | 1 (2.6%) |
|    FOLFOX | 0 (0.0%) | 3 (8.6%) | 3 (7.9%) |
|    Gemcitabine + Capecitabine | 0 (0.0%) | 1 (2.9%) | 1 (2.6%) |
|    Gemcitabine + Cisplatin | 0 (0.0%) | 1 (2.9%) | 1 (2.6%) |
|    Gemcitabine + Nab-paclitaxel | 0 (0.0%) | 6 (17.2%) | 6 (15.8%) |
|    Gemcitabine + Nab-paclitaxel + Cisplatin | 0 (0.0%) | 2 (5.7%) | 2 (5.3%) |
|    NaL-IRI + 5-FU | 1 (33.3%) | 12 (34.5%) | 13 (34.1%) |
|    TAS 102 | 0 (0.0%) | 1 (2.9%) | 1 (2.6%) |
| **Third-line response** |  |  |  |
|    CR | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
|    PR | 0 (0.0%) | 9 (26.5%) | 9 (24.3%) |
|    SD | 2 (66.7%) | 6 (17.6%) | 8 (21.6%) |
|    No Response | 1 (33.3%) | 19 (55.9%) | 20 (54.1%) |
| **Fourth-line treatment** |  |  |  |
|    Yes | 1 (2.6%) | 7 (3.3%) | 8 (3.2%) |
|    No | 37 (97.4%) | 205 (96.7%) | 242 (96.8%) |
| **Fourth-line chemotherapy name** |  |  |  |
|    Atezolizumab + KY1044 | 0 (0.0%) | 1 (14.3%) | 1 (12.5%) |
|    mFOLFIRINOX | 0 (0.0%) | 1 (14.3%) | 1 (12.5%) |
|    FOLFOX | 1 (100.0%) | 1 (14.3%) | 2 (25.0%) |
|    NaL-IRI + 5FU | 0 (0.0%) | 2 (28.6%) | 2 (25.0%) |
|    Nivolumab | 0 (0.0%) | 1 (14.3%) | 1 (12.5%) |
|    Oradoxel | 0 (0.0%) | 1 (14.3%) | 1 (12.5%) |
| **Fourth-line response** |  |  |  |
|    CR | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
|    PR | 1 (100.0%) | 0 (0.0%) | 1 (12.5%) |
|    SD | 0 (0.0%) | 1 (14.3%) | 1 (12.5%) |
|    No Response | 0 (0.0%) | 6 (85.7%) | 6 (75.0%) |

### Supplementary Table 6: Screening Guidelines met by patients with and without PGV

|  |  |  |  |
| --- | --- | --- | --- |
|  | 2018 (N=38) | 2020 (N=38) | p value |
| **Did they meet NCCN/NSGC/ACMG testing guidelines?** |  |  | < 0.001 |
|    Yes | 26 (68.4%) | 38 (100.0%) |  |
|    No | 12 (31.6%) | 0 (0.0%) |  |
| **Did they meet guidelines based on family history regardless of personal history?** |  |  | 0.889 |
|    Yes | 15 (39.5%) | 17 (44.7%) |  |
|    No | 19 (50.0%) | 17 (44.7%) |  |
|    Not available | 4 (10.5%) | 4 (10.5%) |  |

**Supplementary Figure 1: Kaplan Meier curves for overall survival of HRR gene PGV carriers vs Negative/VUS**

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**Supplementary Figure 2: Kaplan Meier curves for overall survival AJCC 8th Edition Early versus Late Stage**



**Supplementary Figure 3: Kaplan Meier curves for overall survival with**

**CA19-9 >300 vs. < 300**

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