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<th>ARX-negative, n = 30 (22%)</th>
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<th>PDX1-negative, n = 61 (45%)</th>
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Abbreviations: ALT, alternative lengthening of telomeres; NF-PanNET, non-functional pancreatic neuroendocrine tumor; WHO, World Health Organization
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<tr>
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<td>70 (86%)</td>
<td>55 (63%)</td>
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<td>11 (14%)</td>
<td>32 (37%)</td>
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<td>43 (26%)</td>
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<td>11 (14%)</td>
<td>32 (37%)</td>
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<td>32 (37%)</td>
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</table>

**Abbreviations:** ALT, alternative lengthening of telomeres; NF-PanNET, non-functional pancreatic neuroendocrine tumor; WHO, World Health Organization
<table>
<thead>
<tr>
<th>Patient or Tumor Characteristics</th>
<th>Total, n = 256</th>
<th>ARX-positive, n = 167 (65%)</th>
<th>ARX-negative, n = 89 (35%)</th>
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<th>PDX1-positive, n = 142 (56%)</th>
<th>PDX1-negative, n = 114 (44%)</th>
<th>p</th>
<th>ALT-positive, n = 151 (60%)</th>
<th>ALT-negative, n = 105 (40%)</th>
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<td>97 (56%)</td>
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<td>47 (68%)</td>
<td>90 (48%)</td>
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<tr>
<td>Mean age (range), years</td>
<td>59.1 (22 - 93)</td>
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<td>16 (20%)</td>
<td>46 (28%)</td>
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<td>27 (41%)</td>
<td>46 (30%)</td>
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<td>36 (53%)</td>
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<td>174 (68%)</td>
<td>149 (89%)</td>
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<td>64 (78%)</td>
<td>149 (86%)</td>
<td>0.001</td>
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<td>82 (32%)</td>
<td>18 (11%)</td>
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<td>18 (22%)</td>
<td>149 (86%)</td>
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<td>56 (81%)</td>
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<td>8 (12%)</td>
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</tr>
<tr>
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<td>64 (25%)</td>
<td>50 (30%)</td>
<td>14 (16%)</td>
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<td>14 (17%)</td>
<td>50 (29%)</td>
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<td>61 (88%)</td>
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<tr>
<td>Negative</td>
<td>187 (73%)</td>
<td>111 (66%)</td>
<td>76 (85%)</td>
<td>0.001</td>
<td>69 (84%)</td>
<td>118 (68%)</td>
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<td>13 (16%)</td>
<td>56 (32%)</td>
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</tbody>
</table>

**Abbreviations:** AL, alternative lengthening of telomeres; NF-PanNET, non-functional pancreatic neuroendocrine tumor; WHO, World Health Organization; UPMC, University of Pittsburgh Medical Center; WHO, World Health Organization
### Clinical and pathologic comparison of 561 primary NF-PanNETs based on the status of ARX and PDX1

<table>
<thead>
<tr>
<th>Patient or Tumor Characteristics</th>
<th>ARX-positive/PDX1-negative, n = 280 (50%)</th>
<th>ARX-negative/PDX1-positive, n = 113 (20%)</th>
<th>ARX-positive/PDX1-positive (DP), n = 126 (22%)</th>
<th>ARX-negative/PDX1-negative (DN), n = 42 (8%)</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td><strong>Gender</strong></td>
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<tr>
<td>Male</td>
<td>160 (57%)</td>
<td>53 (47%)</td>
<td>55 (44%)</td>
<td>18 (43%)</td>
<td>0.031</td>
</tr>
<tr>
<td>Female</td>
<td>120 (43%)</td>
<td>60 (53%)</td>
<td>71 (56%)</td>
<td>24 (57%)</td>
<td></td>
</tr>
<tr>
<td><strong>Mean age (range), years</strong></td>
<td>57.5 (26 - 83)</td>
<td>58.2 (20 - 93)</td>
<td>54.2 (23 - 76)</td>
<td>56.9 (22 - 85)</td>
<td>0.050</td>
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<td><strong>Mean tumor size (range), cm</strong></td>
<td>3.5 (0.7 - 15.5)</td>
<td>2.8 (0.6 - 9.5)</td>
<td>3.2 (0.7 - 18.0)</td>
<td>3.2 (0.7 - 10.0)</td>
<td>0.049</td>
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<td><strong>Location</strong></td>
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<tr>
<td>Head, neck and uncinate</td>
<td>91 (33%)</td>
<td>55 (49%)</td>
<td>62 (49%)</td>
<td>25 (60%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Body and tail</td>
<td>188 (67%)</td>
<td>58 (51%)</td>
<td>62 (49%)</td>
<td>17 (40%)</td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>1 (&lt;1%)</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
<td>0 (0%)</td>
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</tr>
<tr>
<td><strong>WHO grade</strong></td>
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<tr>
<td>Low (G1)</td>
<td>175 (63%)</td>
<td>82 (73%)</td>
<td>81 (64%)</td>
<td>24 (57%)</td>
<td>0.003</td>
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<tr>
<td>Intermediate (G2)</td>
<td>101 (36%)</td>
<td>30 (26%)</td>
<td>45 (36%)</td>
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<tr>
<td>High (G3)</td>
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<td>0 (0%)</td>
<td>5 (12%)</td>
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<td><strong>Primary tumor (pT) stage</strong></td>
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</tr>
<tr>
<td>T1</td>
<td>88 (31%)</td>
<td>47 (42%)</td>
<td>32 (25%)</td>
<td>12 (29%)</td>
<td>0.065</td>
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<tr>
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<td>106 (38%)</td>
<td>41 (36%)</td>
<td>62 (49%)</td>
<td>19 (43%)</td>
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</tr>
<tr>
<td>T3</td>
<td>81 (29%)</td>
<td>25 (22%)</td>
<td>30 (24%)</td>
<td>11 (26%)</td>
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</tr>
<tr>
<td>T4</td>
<td>5 (2%)</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
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<tr>
<td><strong>Regional node (pN) stage</strong></td>
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<td>93 (74%)</td>
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<td>101 (89%)</td>
<td>96 (76%)</td>
<td>35 (83%)</td>
<td>&lt; 0.001</td>
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<tr>
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<td>171 (61%)</td>
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<td>93 (74%)</td>
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<td>&lt; 0.001</td>
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<td>6 (14%)</td>
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Abbreviations: ALT, alternative lengthening of telomeres; DN, double negative for ARX and PDX1; DP, double positive for ARX and PDX1; NF-PanNET, non-functional pancreatic neuroendocrine tumor; WHO, World Health Organization
<table>
<thead>
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<th>Patient or Tumor Characteristics</th>
<th>ARX⁺/DN, n = 322 (57%)</th>
<th>PDX1⁺/DP, n = 239 (43%)</th>
<th>P</th>
<th>Loss of ATRX/DAXX, n = 142 (25%)</th>
<th>Preserved ATRX/DAXX, n = 419 (75%)</th>
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<td>2.8 (0.6 - 10.0)</td>
<td>&lt; 0.001</td>
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<td>50 (35%)</td>
<td>183 (44%)</td>
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<td>1 (1%)</td>
<td>2 (&lt;1%)</td>
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<tr>
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<tr>
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<td>81 (57%)</td>
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<td>&lt; 0.001</td>
<td>19 (13%)</td>
<td>136 (32%)</td>
<td>&lt; 0.001</td>
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<td>126 (53%)</td>
<td>123 (87%)</td>
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<td>0 (0%)</td>
<td>&lt; 0.001</td>
<td>100 (70%)</td>
<td>222 (53%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Positive</td>
<td>0 (0%)</td>
<td>239 (100%)</td>
<td>42 (30%)</td>
<td>197 (47%)</td>
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<td>197 (82%)</td>
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<td>18 (7%)</td>
<td>391 (93%)</td>
<td>&lt; 0.001</td>
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<tr>
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<td>42 (18%)</td>
<td>31 (12%)</td>
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<td>207 (64%)</td>
<td>194 (81%)</td>
<td>&lt; 0.001</td>
<td>10 (7%)</td>
<td>391 (93%)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Positive</td>
<td>115 (36%)</td>
<td>45 (19%)</td>
<td>132 (93%)</td>
<td>28 (7%)</td>
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</table>

**Abbreviations.** ALT, alternative lengthening of telomeres; DN, double negative for ARX and PDX1; DP, double positive for ARX and PDX1; NF-PanNET, non-functional pancreatic neuroendocrine tumor; WHO, World Health Organization
**Supplementary Table 6. Clinical and pathologic comparison of ATRX and DAXX status in 561 non-syndromic, primary NF-PanNETs.**

<table>
<thead>
<tr>
<th>Patient or Tumor Characteristics</th>
<th>Total, n = 561</th>
<th>Loss of ATRX, n = 70 (12%)</th>
<th>Preserved ATRX, n = 491 (88%)</th>
<th>p</th>
<th>Loss of DAXX, n = 47 (8%)</th>
<th>Preserved DAXX, n = 414 (92%)</th>
<th>p</th>
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<tbody>
<tr>
<td><strong>Gender</strong></td>
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<tr>
<td>Female</td>
<td>275 (49%)</td>
<td>27 (39%)</td>
<td>248 (50%)</td>
<td>0.073</td>
<td>39 (45%)</td>
<td>236 (50%)</td>
<td>0.416</td>
</tr>
<tr>
<td>Male</td>
<td>286 (51%)</td>
<td>43 (61%)</td>
<td>243 (50%)</td>
<td>0.073</td>
<td>48 (55%)</td>
<td>238 (50%)</td>
<td>0.416</td>
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<td><strong>Mean age (range), years</strong></td>
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<tr>
<td>56.9 (20 - 93)</td>
<td>56.8 (29 - 93)</td>
<td>56.9 (20 - 85)</td>
<td>0.064</td>
<td>59.7 (26 - 82)</td>
<td>56.4 (20 - 93)</td>
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<td><strong>Mean tumor size (range), cm</strong></td>
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<td>3.3 (0.6 - 18.0)</td>
<td>4.9 (1.1 - 15.5)</td>
<td>3.0 (0.6 - 18.0)</td>
<td>&lt;0.001</td>
<td>4.7 (0.9 - 18.0)</td>
<td>3.0 (0.6 - 15.5)</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Location</strong></td>
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<tr>
<td>Head, neck and uncinate</td>
<td>233 (41%)</td>
<td>28 (40%)</td>
<td>205 (42%)</td>
<td>0.864</td>
<td>30 (35%)</td>
<td>203 (43%)</td>
<td>0.174</td>
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<td>Body and tail</td>
<td>325 (58%)</td>
<td>42 (60%)</td>
<td>283 (57%)</td>
<td>0.864</td>
<td>56 (64%)</td>
<td>269 (56%)</td>
<td>0.864</td>
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<tr>
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<td>0.001</td>
<td>38 (44%)</td>
<td>324 (68%)</td>
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<tr>
<td>Intermediate (G2)</td>
<td>189 (33%)</td>
<td>47 (67%)</td>
<td>142 (29%)</td>
<td>0.001</td>
<td>47 (54%)</td>
<td>142 (30%)</td>
<td>0.001</td>
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<tr>
<td>High (G3)</td>
<td>10 (2%)</td>
<td>2 (3%)</td>
<td>8 (2%)</td>
<td>0.001</td>
<td>2 (2%)</td>
<td>8 (2%)</td>
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<tr>
<td><strong>Lymphovascular invasion</strong></td>
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<td>n = 51</td>
<td>n = 173</td>
<td>n = 62</td>
<td>n = 162</td>
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<td><strong>Perineural invasion</strong></td>
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<td>n = 424</td>
<td>n = 51</td>
<td>n = 373</td>
<td>n = 62</td>
<td>n = 362</td>
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<td><strong>Primary tumor (pT) stage</strong></td>
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<tr>
<td>T1</td>
<td>179 (32%)</td>
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<td>0.001</td>
<td>4 (5%)</td>
<td>175 (37%)</td>
<td>0.001</td>
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<tr>
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<td>42 (48%)</td>
<td>186 (39%)</td>
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<tr>
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<td>39 (45%)</td>
<td>108 (23%)</td>
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<tr>
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<td>2 (2%)</td>
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<tr>
<td><strong>Regional node (pN) stage</strong></td>
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<td>n = 86</td>
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<td>385 (81%)</td>
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<td>49 (56%)</td>
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<td>418 (88%)</td>
<td>0.289</td>
<td>73 (84%)</td>
<td>418 (88%)</td>
<td>0.289</td>
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<td>14 (16%)</td>
<td>56 (12%)</td>
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<td>73 (84%)</td>
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<tr>
<td>Loss</td>
<td>87 (16%)</td>
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<td>73 (15%)</td>
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<td>14 (16%)</td>
<td>56 (12%)</td>
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**Abbreviations:** ALT, alternative lengthening of telomeres; NF-PanNET, non-functional pancreatic neuroendocrine tumor; WHO, World Health Organization
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<th>Total, n = 196</th>
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<th>ARX-negative, n = 63 (32%)</th>
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<th>PDX1-positive, n = 107 (54%)</th>
<th>PDX1-negative, n = 89 (46%)</th>
<th>p</th>
<th>ALT-positive, n = 17 (9%)</th>
<th>ALT-negative, n = 179 (91%)</th>
<th>p</th>
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<tbody>
<tr>
<td>Gender</td>
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<td></td>
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</tr>
<tr>
<td>Female</td>
<td>104 (53%)</td>
<td>64 (48%)</td>
<td>40 (63%)</td>
<td>0.048</td>
<td>57 (66%)</td>
<td>47 (43%)</td>
<td>0.002</td>
<td>9 (53%)</td>
<td>95 (53%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Male</td>
<td>92 (47%)</td>
<td>69 (52%)</td>
<td>23 (37%)</td>
<td>30 (48%)</td>
<td>62 (57%)</td>
<td>84 (47%)</td>
<td>0.047</td>
<td>8 (47%)</td>
<td>84 (47%)</td>
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</tr>
<tr>
<td>Mean age (range), years</td>
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<td>57.1 (23 - 82)</td>
<td>57.3 (33 - 83)</td>
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<td>56.8 (23 - 83)</td>
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<td>1.4 (0.7 - 2.0)</td>
<td>1.4 (0.6 - 2.0)</td>
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<td>1.6 (0.7 - 2.0)</td>
<td>1.4 (0.6 - 2.0)</td>
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</tr>
<tr>
<td>Head, neck and uncinate</td>
<td>68 (35%)</td>
<td>45 (34%)</td>
<td>23 (37%)</td>
<td>0.749</td>
<td>37 (34%)</td>
<td>31 (28%)</td>
<td>0.050</td>
<td>7 (41%)</td>
<td>61 (34%)</td>
<td>0.999</td>
</tr>
<tr>
<td>Body and tail</td>
<td>128 (65%)</td>
<td>88 (66%)</td>
<td>40 (63%)</td>
<td>50 (57%)</td>
<td>78 (72%)</td>
<td>10 (59%)</td>
<td>118 (66%)</td>
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<tr>
<td>WHO grade</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Low (G1)</td>
<td>162 (83%)</td>
<td>110 (83%)</td>
<td>52 (83%)</td>
<td>1.000</td>
<td>70 (80%)</td>
<td>92 (84%)</td>
<td>0.570</td>
<td>8 (47%)</td>
<td>154 (86%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Intermediate (G2)</td>
<td>34 (17%)</td>
<td>23 (17%)</td>
<td>11 (17%)</td>
<td>17 (20%)</td>
<td>17 (16%)</td>
<td>9 (53%)</td>
<td>25 (14%)</td>
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<tr>
<td>Lymphovascular invasion</td>
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</tr>
<tr>
<td>n = 159</td>
<td>n = 104</td>
<td>n = 55</td>
<td>n = 67</td>
<td>0.001</td>
<td>62 (95%)</td>
<td>46 (95%)</td>
<td>1.000</td>
<td>8 (74%)</td>
<td>141 (95%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Absent</td>
<td>148 (93%)</td>
<td>93 (91%)</td>
<td>55 (100%)</td>
<td>0.017</td>
<td>62 (95%)</td>
<td>46 (95%)</td>
<td>1.000</td>
<td>8 (74%)</td>
<td>141 (95%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Present</td>
<td>11 (7%)</td>
<td>11 (11%)</td>
<td>0 (0%)</td>
<td>5 (7%)</td>
<td>6 (7%)</td>
<td>4 (36%)</td>
<td>7 (55%)</td>
<td></td>
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</tr>
<tr>
<td>Perineural invasion</td>
<td>n = 159</td>
<td>n = 104</td>
<td>n = 55</td>
<td>1.000</td>
<td>62 (95%)</td>
<td>46 (95%)</td>
<td>1.000</td>
<td>10 (91%)</td>
<td>136 (92%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Absent</td>
<td>146 (92%)</td>
<td>91 (91%)</td>
<td>55 (95%)</td>
<td>0.001</td>
<td>62 (95%)</td>
<td>46 (95%)</td>
<td>1.000</td>
<td>10 (91%)</td>
<td>136 (92%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Present</td>
<td>13 (8%)</td>
<td>9 (9%)</td>
<td>4 (7%)</td>
<td>5 (7%)</td>
<td>8 (9%)</td>
<td>1 (9%)</td>
<td>12 (8%)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Metachronous metastases/recurrences</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Absent</td>
<td>178 (91%)</td>
<td>118 (89%)</td>
<td>60 (99%)</td>
<td>0.018</td>
<td>79 (91%)</td>
<td>99 (91%)</td>
<td>1.000</td>
<td>10 (59%)</td>
<td>168 (94%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Present</td>
<td>18 (9%)</td>
<td>15 (11%)</td>
<td>3 (5%)</td>
<td>8 (9%)</td>
<td>10 (9%)</td>
<td>7 (41%)</td>
<td>11 (60%)</td>
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<tr>
<td>ARX Expression</td>
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</tr>
<tr>
<td>Negative</td>
<td>63 (32%)</td>
<td>47 (54%)</td>
<td>16 (15%)</td>
<td>0.017</td>
<td>16 (6%)</td>
<td>62 (35%)</td>
<td>0.014</td>
<td>16 (94%)</td>
<td>117 (65%)</td>
<td>0.014</td>
</tr>
<tr>
<td>Positive</td>
<td>133 (68%)</td>
<td>40 (46%)</td>
<td>93 (85%)</td>
<td>16 (94%)</td>
<td>117 (65%)</td>
<td>97 (54%)</td>
<td>0.214</td>
<td></td>
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<tr>
<td>PDX1 Expression</td>
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<td></td>
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</tr>
<tr>
<td>Negative</td>
<td>109 (56%)</td>
<td>93 (70%)</td>
<td>16 (25%)</td>
<td>&lt; 0.001</td>
<td>12 (71%)</td>
<td>97 (54%)</td>
<td>0.214</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Positive</td>
<td>87 (44%)</td>
<td>40 (31%)</td>
<td>47 (25%)</td>
<td>5 (29%)</td>
<td>82 (46%)</td>
<td>82 (46%)</td>
<td>0.014</td>
<td></td>
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<tr>
<td>ATRX/DAXX Expression</td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preserved</td>
<td>183 (93%)</td>
<td>121 (91%)</td>
<td>62 (98%)</td>
<td>0.065</td>
<td>82 (94%)</td>
<td>101 (93%)</td>
<td>0.777</td>
<td>5 (29%)</td>
<td>178 (99%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Loss</td>
<td>13 (7%)</td>
<td>12 (9%)</td>
<td>1 (2%)</td>
<td>5 (4%)</td>
<td>8 (7%)</td>
<td>12 (11%)</td>
<td>1 (1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT status</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>179 (91%)</td>
<td>117 (68%)</td>
<td>62 (98%)</td>
<td>0.014</td>
<td>82 (94%)</td>
<td>97 (90%)</td>
<td>0.214</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>17 (9%)</td>
<td>16 (12%)</td>
<td>1 (2%)</td>
<td>5 (6%)</td>
<td>12 (11%)</td>
<td>12 (11%)</td>
<td>1 (1%)</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** ARX, alternative splicing isoform; ALT, alternative lengthening of telomeres; NF-PanNET, non-functional pancreatic neuroendocrine tumor; WHO, World Health Organization
### Supplementary Table 8. RFS rates based on tumor size thresholds for NF-PanNETs of ≤2.0 cm and without lymph node metastases.

<table>
<thead>
<tr>
<th>Tumor size threshold</th>
<th>1, 5 and 10-year RFS rates, below and equal to (≤) tumor size threshold</th>
<th>1, 5 and 10-year RFS rates, above (&gt; ) tumor size threshold</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.7 cm</td>
<td>92%, 92% and 92%</td>
<td>97%, 89% and 78%</td>
<td>0.883</td>
</tr>
<tr>
<td>0.8 cm</td>
<td>95%, 95% and 95%</td>
<td>97%, 89% and 78%</td>
<td>0.529</td>
</tr>
<tr>
<td>0.9 cm</td>
<td>96%, 96% and 96%</td>
<td>97%, 89% and 77%</td>
<td>0.394</td>
</tr>
<tr>
<td>1.0 cm</td>
<td>98%, 98% and 98%</td>
<td>96%, 87% and 75%</td>
<td>0.099</td>
</tr>
<tr>
<td>1.1 cm</td>
<td>98%, 94% and 94%</td>
<td>96%, 88% and 75%</td>
<td>0.150</td>
</tr>
<tr>
<td>1.2 cm</td>
<td>99%, 95% and 95%</td>
<td>96%, 87% and 74%</td>
<td>0.059</td>
</tr>
<tr>
<td>1.3 cm</td>
<td>97%, 95% and 95%</td>
<td>96%, 86% and 72%</td>
<td>0.054</td>
</tr>
<tr>
<td>1.4 cm</td>
<td>97%, 95% and 95%</td>
<td>96%, 86% and 72%</td>
<td>0.042</td>
</tr>
<tr>
<td>1.5 cm</td>
<td>97%, 91% and 91%</td>
<td>96%, 86% and 65%</td>
<td>0.046</td>
</tr>
<tr>
<td>1.6 cm</td>
<td>98%, 92% and 92%</td>
<td>95%, 85% and 61%</td>
<td>0.017</td>
</tr>
<tr>
<td>1.7 cm</td>
<td>97%, 90% and 90%</td>
<td>96%, 88% and 58%</td>
<td>0.040</td>
</tr>
<tr>
<td>1.8 cm</td>
<td>97%, 89% and 89%</td>
<td>97%, 92% and 58%</td>
<td>0.095</td>
</tr>
<tr>
<td>1.9 cm</td>
<td>97%, 89% and 89%</td>
<td>97%, 91% and 58%</td>
<td>0.074</td>
</tr>
</tbody>
</table>

Abbreviations: N/A, not available; NF-PanNET, non-functional pancreatic neuroendocrine tumor; RFS, relapse-free survival.
### Table 5. Clinical and pathologic comparison of ARX, PDX1, ATRX/DAXX, and ALT status in 107 patients with NF-PanNET metastases.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ARX-positive, n = 85 (79%)</th>
<th>ARX-negative, n = 22 (21%)</th>
<th>P Value</th>
<th>PDX1-positive, n = 36 (34%)</th>
<th>PDX1-negative, n = 71 (66%)</th>
<th>P Value</th>
<th>Loss of ATRX/DAXX, n = 66 (62%)</th>
<th>Preserved ATRX/DAXX, n = 41 (38%)</th>
<th>P Value</th>
<th>ALT-positive, n = 76 (71%)</th>
<th>ALT-negative, n = 31 (29%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Female 53 (63%) 38 (61%) 15 (68%) 0.059</td>
<td>Male 54 (51%) 47 (55%) 7 (32%) 0.004</td>
<td>25 (69%) 28 (39%) 0.003</td>
<td>25 (38%) 28 (68%) 0.003</td>
<td>30 (39%) 23 (74%) 0.001</td>
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</tr>
<tr>
<td>Mean age at initial presentation, years</td>
<td>60.2 (31 - 85) 60.8 (32 - 85) 58.1 (31 - 78) 0.414</td>
<td>58.1 (31 - 85) 61.3 (36 - 83) 0.203</td>
<td>61.3 (31 - 85) 58.6 (31 - 82) 0.290</td>
<td>60.6 (31 - 85) 59.3 (31 - 82) 0.734</td>
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</tr>
<tr>
<td>Mean primary tumor size, cm</td>
<td>5.3 (1.0 - 18.0) 5.6 (1.5 - 18.0) 4.2 (1.0 - 13.0) 0.079</td>
<td>5.3 (1.0 - 18.0) 5.0 (1.5 - 18.0) 0.280</td>
<td>5.1 (1.0 - 18.0) 5.6 (1.5 - 18.0) 0.197</td>
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</tr>
<tr>
<td>Primary tumor location</td>
<td>Head, neck and uncinate 43 (40%) 31 (36%) 12 (55%) 0.147</td>
<td>Body and tail 64 (60%) 54 (64%) 10 (45%) 0.024</td>
<td>20 (56%) 23 (32%) 0.004</td>
<td>19 (29%) 24 (59%) 0.003</td>
<td>30 (39%) 23 (74%) 0.001</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Primary tumor, WHO grade</td>
<td>Low (G1) 29 (27%) 20 (24%) 9 (41%) 0.024</td>
<td>Intermediate (G2) 72 (67%) 62 (73%) 10 (45%) 0.145</td>
<td>11 (31%) 18 (25%) 0.145</td>
<td>17 (29%) 29 (44%) 0.056</td>
<td>20 (26%) 9 (29%) 0.001</td>
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</tr>
<tr>
<td>Metastatic tumor(s), highest WHO grade</td>
<td>Low (G1) 20 (19%) 14 (16%) 6 (27%) 0.177</td>
<td>Intermediate (G2) 79 (74%) 66 (78%) 13 (59%) 0.234</td>
<td>11 (31%) 18 (25%) 0.234</td>
<td>11 (14%) 19 (26%) 0.225</td>
<td>20 (26%) 9 (29%) 0.001</td>
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</tr>
<tr>
<td>ARX expression</td>
<td>Negative 22 (21%) 22 (61%) 0 (0%) &lt; 0.001</td>
<td>Positive 85 (79%) 14 (39%) 71 (100%) 58 (88%) 27 (66%) 67 (88%) 18 (58%) 0.001</td>
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</tr>
<tr>
<td>PDX1 expression</td>
<td>Negative 71 (66%) 71 (84%) 0 (0%) &lt; 0.001</td>
<td>Positive 36 (35%) 14 (39%) 22 (61%) 54 (82%) 17 (29%) &lt; 0.001 62 (82%) 9 (29%) &lt; 0.001</td>
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<td></td>
</tr>
<tr>
<td>ATRX/DAXX expression</td>
<td>Preserved 61 (55%) 27 (62%) 14 (48%) 0.013</td>
<td>ATRX/DAXX expression 61 (67%) 14 (39%) 8 (33%) 0.004 10 (15%) 31 (50%) &lt; 0.001</td>
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</tr>
<tr>
<td>ALT status</td>
<td>Negative 31 (29%) 18 (27%) 13 (59%) 0.003</td>
<td>Positive 30 (39%) 16 (22%) 9 (30%) 0.003</td>
<td>13 (19%) 24 (24%) 0.004</td>
<td>6 (8%) 9 (29%) 0.225</td>
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<td></td>
</tr>
<tr>
<td>Timing of metastatic tumor(s)</td>
<td>Synchronous 14 (13%) 10 (12%) 4 (18%) 0.567</td>
<td>Metachronous 45 (42%) 35 (41%) 10 (46%) 0.038</td>
<td>6 (9%) 8 (20%) 0.138 32 (42%) 13 (39%)</td>
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</tr>
</tbody>
</table>

Abbreviations: ALT, alternative lengthening of telomeres; NF-PanNET, non-functional pancreatic neuroendocrine tumor; WHO, World Health Organization.
## Supplemental Table 10. Clinical and pathologic comparison of ARX and PDX1 among primary gastric, duodenal, rectal and appendiceal NETs.

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>ARX Expression</th>
<th>PDX1 Expression</th>
<th>p</th>
<th>ARX Expression</th>
<th>PDX1 Expression</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumor (pT) stage</td>
<td>T1</td>
<td>12 (43%)</td>
<td>8 (93%)</td>
<td>0.066</td>
<td>15 (42%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>Regional node (pN) stage</td>
<td>N0</td>
<td>24 (86%)</td>
<td>3 (75%)</td>
<td>0.512</td>
<td>3 (75%)</td>
<td>24 (86%)</td>
</tr>
<tr>
<td>Metachronous metastases/recurrences</td>
<td>Present</td>
<td>6 (21%)</td>
<td>0 (0%)</td>
<td>0.066</td>
<td>6 (21%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>14 (50%)</td>
<td>1 (25%)</td>
<td>1.000</td>
<td>3 (100%)</td>
<td>3 (100%)</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>15 (50%)</td>
<td>4 (75%)</td>
<td>0.066</td>
<td>2 (25%)</td>
<td>3 (42%)</td>
</tr>
<tr>
<td>Mean age (range), years</td>
<td>57.4 (35 - 82)</td>
<td>45.8 (17 - 62)</td>
<td>0.392</td>
<td>46.0 (17 - 62)</td>
<td>57.3 (35 - 82)</td>
<td>0.424</td>
</tr>
<tr>
<td>Mean tumor size (range), cm</td>
<td>1.6 (0.3 - 3.0)</td>
<td>1.7 (1.2 - 2.3)</td>
<td>0.721</td>
<td>1.5 (1.0 - 2.3)</td>
<td>1.6 (0.3 - 3.0)</td>
<td>0.891</td>
</tr>
<tr>
<td>WHO grade</td>
<td>Low (G1)</td>
<td>20 (72%)</td>
<td>2 (50%)</td>
<td>0.454</td>
<td>20 (72%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td></td>
<td>Intermediate (G2)</td>
<td>6 (21%)</td>
<td>2 (50%)</td>
<td>0.217</td>
<td>6 (21%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td></td>
<td>High (G3)</td>
<td>2 (7%)</td>
<td>0 (0%)</td>
<td>0.217</td>
<td>2 (7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Lymphvascular invasion</td>
<td>Absent</td>
<td>23 (82%)</td>
<td>3 (75%)</td>
<td>1.000</td>
<td>23 (82%)</td>
<td>3 (75%)</td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>5 (18%)</td>
<td>1 (25%)</td>
<td>1.000</td>
<td>5 (18%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>Absent</td>
<td>24 (86%)</td>
<td>4 (100%)</td>
<td>1.000</td>
<td>24 (86%)</td>
<td>4 (100%)</td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>4 (14%)</td>
<td>0 (0%)</td>
<td>1.000</td>
<td>4 (14%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Tumor Site</td>
<td>Gastric NETs (n = 32)</td>
<td>Duodenal NETs (n = 41)</td>
<td>Rectal NETs (n = 17)</td>
<td>Appendiceal NETs (n = 28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abbreviations: N/A, not applicable; NET, neuroendocrine tumor; WHO, World Health Organization</td>
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</table>

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