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**Supplementary information for:**

**Safety and activity of anti-mesothelin antibody–drug conjugate anetumab  
ravtansine in combination with pegylated-liposomal doxorubicin in platinum-  
resistant ovarian cancer: Multicenter, phase Ib dose escalation and expansion  
study**

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Ana Oaknin, Ignacio Romero, Sami Diab, Larry J. Copeland, Bradley J. Monk,  
Robert L. Coleman, Thomas J. Herzog, Jonathan Siegel, Linda Kasten, Andreas  
Schlicker, Anke Schulz, Karl Köchert, Annette O. Walter, Barrett H. Childs, Cem Elbi,  
Iurie Bulat

19 **SUPPLEMENTARY TABLES**20 **Supplementary Table S1. FoundationOne (Foundation Medicine) targeted gene**21 **panel used in next-generation sequencing of tumor tissue samples.**

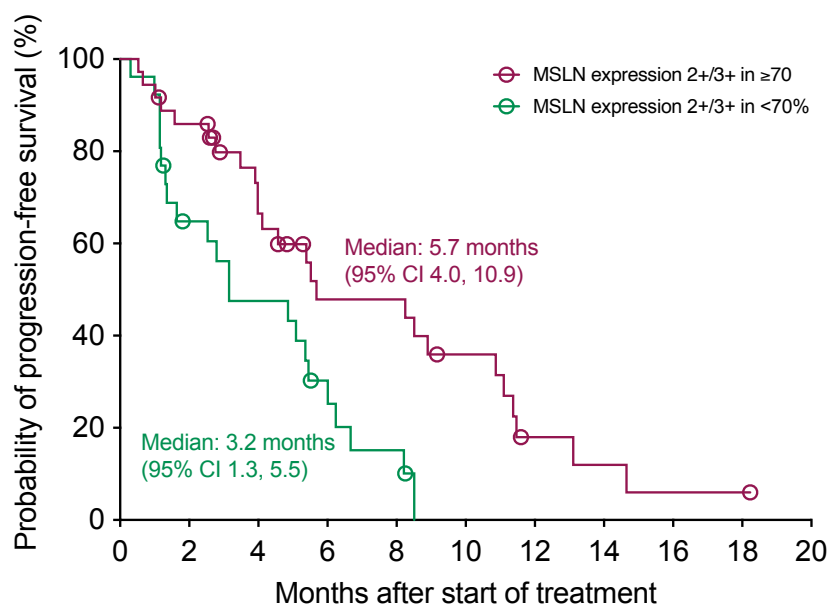
Genes included in the panel							
<i>ABL1</i>	<i>CASP8</i>	<i>DIS3</i>	<i>FGFR4</i>	<i>KEAP1</i>	<i>MYC</i>	<i>PIM1</i>	<i>SLC34A2</i>
<i>ACVR1B</i>	<i>CBFB</i>	<i>DNMT3A</i>	<i>FH</i>	<i>KEL</i>	<i>MYCL</i>	<i>PMS2</i>	<i>SMAD2</i>
<i>AKT1</i>	<i>CBL</i>	<i>DOT1L</i>	<i>FLCN</i>	<i>KIT</i>	<i>MYCL1</i>	<i>POLD1</i>	<i>SMAD4</i>
<i>AKT2</i>	<i>CCND1</i>	<i>EED</i>	<i>FLT1</i>	<i>KLHL6</i>	<i>MYCN</i>	<i>POLE</i>	<i>SMARCA4</i>
<i>AKT3</i>	<i>CCND2</i>	<i>EGFR</i>	<i>FLT3</i>	<i>KMT2A</i>	<i>MYD88</i>	<i>PPARG</i>	<i>SMARCB1</i>
<i>ALK</i>	<i>CCND3</i>	<i>EMSY</i>	<i>FOXL2</i>	<i>KMT2D</i>	<i>NBN</i>	<i>PPP2R1A</i>	<i>SMO</i>
<i>ALOX12B</i>	<i>CCNE1</i>	<i>EP300</i>	<i>FUBP1</i>	<i>KRAS</i>	<i>NF1</i>	<i>PPP2R2A</i>	<i>SNCAIP</i>
<i>AMER1</i>	<i>CD22</i>	<i>EPHA3</i>	<i>GABRA6</i>	<i>LTK</i>	<i>NF2</i>	<i>PRDM1</i>	<i>SOCS1</i>
<i>APC</i>	<i>CD274</i>	<i>EPHB1</i>	<i>GATA3</i>	<i>LYN</i>	<i>NFE2L2</i>	<i>PRKAR1A</i>	<i>SOX2</i>
<i>AR</i>	<i>CD70</i>	<i>EPHB4</i>	<i>GATA4</i>	<i>MAF</i>	<i>NFKBIA</i>	<i>PRKCI</i>	<i>SOX9</i>
<i>ARAF</i>	<i>CD74</i>	<i>ERBB2</i>	<i>GATA6</i>	<i>MAP2K1</i>	<i>NKX2-1</i>	<i>PTCH1</i>	<i>SPEN</i>
<i>ARFRP1</i>	<i>CD79A</i>	<i>ERBB3</i>	<i>GID4</i>	<i>MAP2K2</i>	<i>NOTCH1</i>	<i>PTEN</i>	<i>SPOP</i>
<i>ARID1A</i>	<i>CD79B</i>	<i>ERBB4</i>	<i>GNA11</i>	<i>MAP2K4</i>	<i>NOTCH2</i>	<i>PTPN11</i>	<i>SRC</i>
<i>ASXL1</i>	<i>CDC73</i>	<i>ERCC4</i>	<i>GNA13</i>	<i>MAP3K1</i>	<i>NOTCH3</i>	<i>PTPRO</i>	<i>STAG2</i>
<i>ATM</i>	<i>CDH1</i>	<i>ERG</i>	<i>GNAQ</i>	<i>MAP3K13</i>	<i>NPM1</i>	<i>QKI</i>	<i>STAT3</i>
<i>ATR</i>	<i>CDK12</i>	<i>ERRFI1</i>	<i>GNAS</i>	<i>MAPK1</i>	<i>NRAS</i>	<i>RAC1</i>	<i>STK11</i>
<i>ATRX</i>	<i>CDK4</i>	<i>ESR1</i>	<i>GRM3</i>	<i>MCL1</i>	<i>NT5C2</i>	<i>RAD21</i>	<i>SUFU</i>
<i>AURKA</i>	<i>CDK6</i>	<i>ETV4</i>	<i>GSK3B</i>	<i>MDM2</i>	<i>NTRK1</i>	<i>RAD51</i>	<i>SYK</i>
<i>AURKB</i>	<i>CDK8</i>	<i>ETV5</i>	<i>H3F3A</i>	<i>MDM4</i>	<i>NTRK2</i>	<i>RAD51B</i>	<i>TBX3</i>
<i>AXIN1</i>	<i>CDKN1A</i>	<i>ETV6</i>	<i>HDAC1</i>	<i>MED12</i>	<i>NTRK3</i>	<i>RAD51C</i>	<i>TEK</i>
<i>AXL</i>	<i>CDKN1B</i>	<i>EWSR1</i>	<i>HGF</i>	<i>MEF2B</i>	<i>NUTM1</i>	<i>RAD51D</i>	<i>TERC</i>
<i>BAP1</i>	<i>CDKN2A</i>	<i>EZH2</i>	<i>HNF1A</i>	<i>MEK1</i>	<i>P2RY8</i>	<i>RAD52</i>	<i>TERT</i>
<i>BARD1</i>	<i>CDKN2B</i>	<i>EZR</i>	<i>HRAS</i>	<i>MEK2</i>	<i>PALB2</i>	<i>RAD54L</i>	<i>TET2</i>
<i>BCL2</i>	<i>CDKN2C</i>	<i>FAM123B</i>	<i>HSD3B1</i>	<i>MEN1</i>	<i>PARK2</i>	<i>RAF1</i>	<i>TGFBR2</i>
<i>BCL2L1</i>	<i>CEBPA</i>	<i>FAM46C</i>	<i>ID3</i>	<i>MERTK</i>	<i>PARP1</i>	<i>RARA</i>	<i>TIPARP</i>
<i>BCL2L2</i>	<i>CHEK1</i>	<i>FANCA</i>	<i>IDH1</i>	<i>MET</i>	<i>PARP2</i>	<i>RB1</i>	<i>TMPRSS2</i>
<i>BCL6</i>	<i>CHEK2</i>	<i>FANCC</i>	<i>IDH2</i>	<i>MITF</i>	<i>PARP3</i>	<i>RBM10</i>	<i>TNFAIP3</i>
<i>BCOR</i>	<i>CIC</i>	<i>FANCG</i>	<i>IGF1R</i>	<i>MKNK1</i>	<i>PAX5</i>	<i>REL</i>	<i>TNFRSF14</i>
<i>BCORL1</i>	<i>CREBBP</i>	<i>FANCL</i>	<i>IKBKE</i>	<i>MLH1</i>	<i>PBRM1</i>	<i>RET</i>	<i>TP53</i>
<i>BCR</i>	<i>CRKL</i>	<i>FAS</i>	<i>IKZF1</i>	<i>MLL</i>	<i>PD1</i>	<i>RICTOR</i>	<i>TSC1</i>
<i>BRAF</i>	<i>CSF1R</i>	<i>FBXW7</i>	<i>INPP4B</i>	<i>MLL2</i>	<i>PDCD1</i>	<i>RNF43</i>	<i>TSC2</i>
<i>BRCA1</i>	<i>CSF3R</i>	<i>FGF10</i>	<i>IRF2</i>	<i>MMSET</i>	<i>PDCD1LG2</i>	<i>ROS1</i>	<i>TYRO3</i>
<i>BRCA2</i>	<i>CTCF</i>	<i>FGF12</i>	<i>IRF4</i>	<i>MPL</i>	<i>PDGFRA</i>	<i>RPTOR</i>	<i>U2AF1</i>
<i>BRD4</i>	<i>CTNNA1</i>	<i>FGF14</i>	<i>IRS2</i>	<i>MRE11A</i>	<i>PDGFRB</i>	<i>RSPO2</i>	<i>VEGFA</i>
<i>BRIP1</i>	<i>CTNNB1</i>	<i>FGF19</i>	<i>JAK1</i>	<i>MSH2</i>	<i>PDK1</i>	<i>SDC4</i>	<i>VHL</i>
<i>BTG1</i>	<i>CUL3</i>	<i>FGF23</i>	<i>JAK2</i>	<i>MSH3</i>	<i>PDL1</i>	<i>SDHA</i>	<i>WHSC1</i>
<i>BTG2</i>	<i>CUL4A</i>	<i>FGF3</i>	<i>JAK3</i>	<i>MSH6</i>	<i>PDL2</i>	<i>SDHB</i>	<i>WHSC1L1</i>
<i>BTK</i>	<i>CXCR4</i>	<i>FGF4</i>	<i>JUN</i>	<i>MST1R</i>	<i>PIK3C2B</i>	<i>SDHC</i>	<i>WT1</i>
<i>C11orf30</i>	<i>CYP17A1</i>	<i>FGF6</i>	<i>KDM5A</i>	<i>MTAP</i>	<i>PIK3C2G</i>	<i>SDHD</i>	<i>XPO1</i>
<i>C17orf39</i>	<i>DAXX</i>	<i>FGFR1</i>	<i>KDM5C</i>	<i>MTOR</i>	<i>PIK3CA</i>	<i>SETD2</i>	<i>XRCC2</i>
<i>CALR</i>	<i>DDR1</i>	<i>FGFR2</i>	<i>KDM6A</i>	<i>MUTYH</i>	<i>PIK3CB</i>	<i>SF3B1</i>	<i>ZNF217</i>
<i>CARD11</i>	<i>DDR2</i>	<i>FGFR3</i>	<i>KDR</i>	<i>MYB</i>	<i>PIK3R1</i>	<i>SGK1</i>	<i>ZNF703</i>

22 **SUPPLEMENTARY FIGURES**

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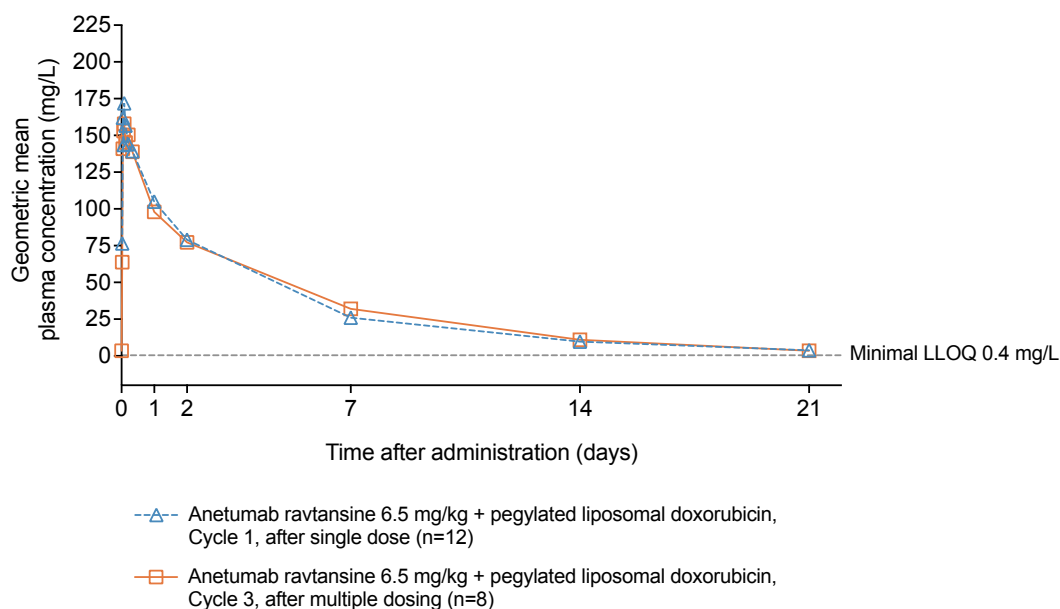
24 **Supplementary Figure S1. Kaplan-Meier estimates of progression-free survival**  
25 **in patients with high ( $\geq$  median) or low ( $<$ median) mesothelin expression (n=62).**26 The median value of mesothelin expression is 70% of tumor cells staining positive for  
27 mesothelin at the intensity level of 2+/3+.

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30 **Supplementary Figure S2. Geometric mean plasma concentration-time profiles**  
31 **of anetumab ravtansine antibody-drug conjugate after administration of**  
32 **6.5 mg/kg anetumab ravtansine plus 30 mg/m<sup>2</sup> pegylated liposomal**  
33 **doxorubicin every three weeks.** Minimal lower limit of quantification (LLOQ) was  
34 0.4 mg/L. Samples in parts 1, 2 and 3 of study were collected at 0.5, 1, 1.5, 2, 3, 5,  
35 8, 24, 48, 168 and 336 hours after the start of infusion on cycle 1; in less frequency  
36 on cycles 2 and 3; and every third cycle after cycle 4.

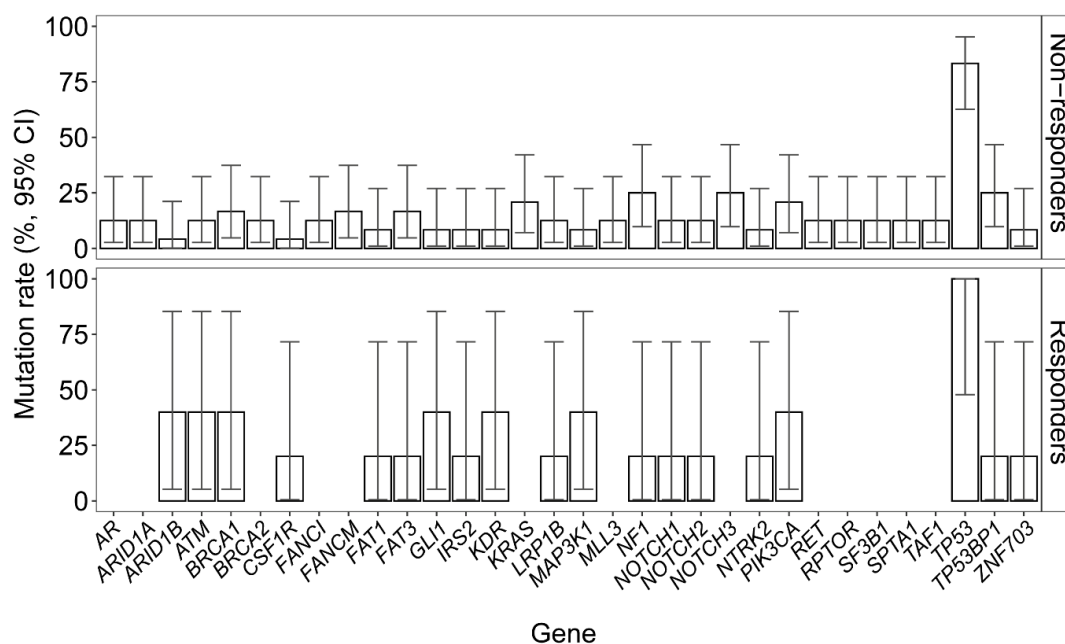


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39 **Supplementary Figure S3. The mutation rate of genes in ovarian cancer patients**  
 40 **with response or non-response to anetumab ravtansine plus pegylated**  
 41 **liposomal doxorubicin.** Responders are patients with partial response or complete  
 42 response and non-responders are patients with stable disease, or progressive  
 43 disease. Error bars represent 95% Clopper-Pearson confidence intervals.

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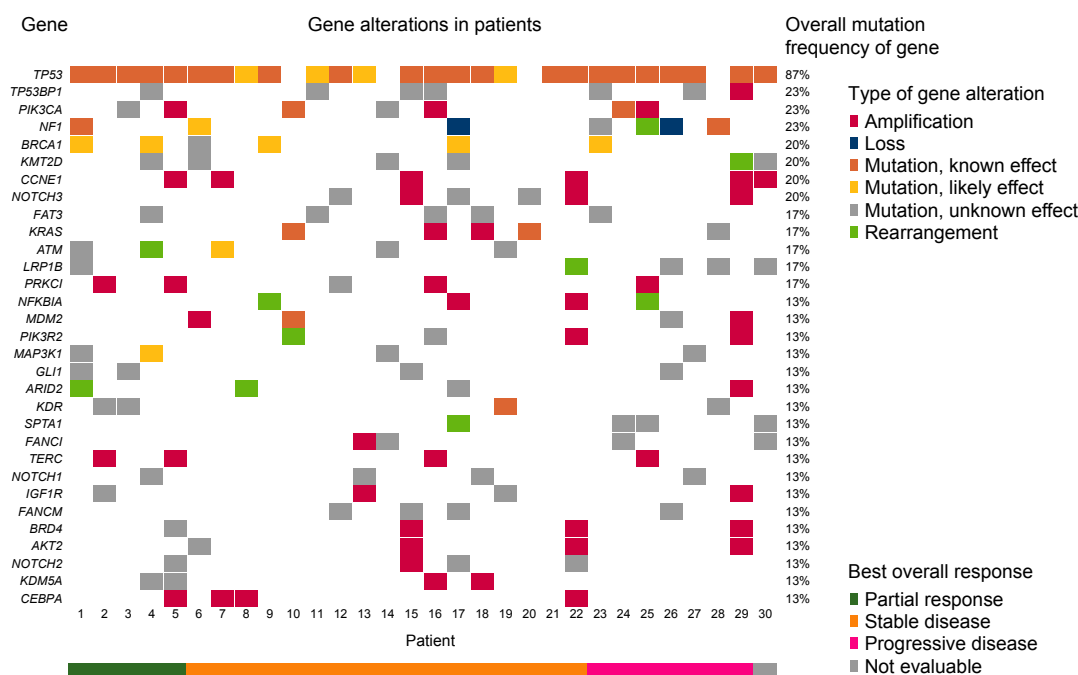


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48 **Supplementary Figure S4. Somatic mutations detected in the tumor tissue**  
 49 **samples of ovarian cancer patients with best overall response.** Patient samples  
 50 are shown in columns. Genes and their overall mutation frequencies are represented  
 51 in rows (only the genes with mutation frequencies greater than 11% are shown). Matrix  
 52 cells are colored according to genomic functional consequence. Best overall response  
 53 status is shown as a heatmap bar at the bottom of the figure.



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