

Hematologic complications in patients exposed to poly-ADP ribose polymerase inhibitors

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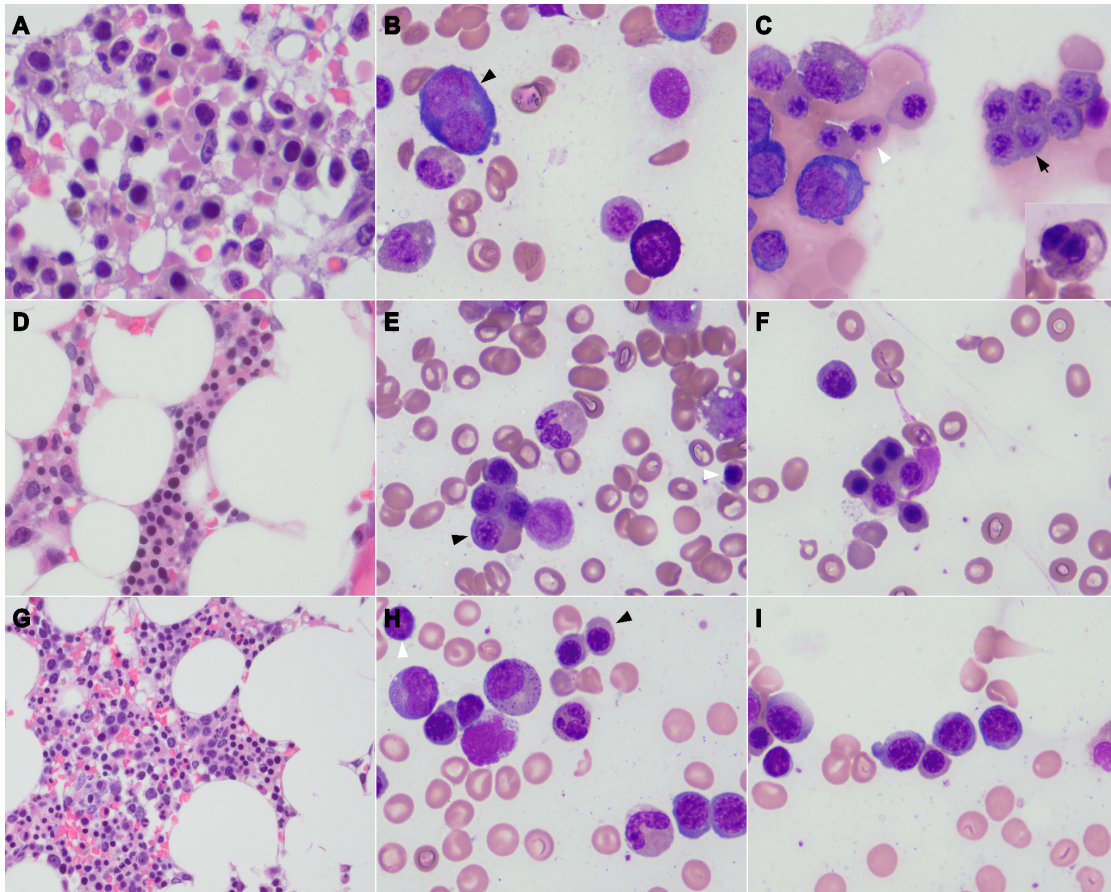
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Supplemental Table 1. Patient diagnosis, myeloid molecular features, cytogenetics, and family history.

Patient ID	Hematologic Diagnosis	Karyotype Findings	Gene with Germline Mutation	Variant on Bone Marrow NGS	VAF, %	Genes with Somatic Mutation	Somatic Mutations	VAF, %	History of other cancers	Lines of Prior Chemotherapy	First-degree family history of cancer
1	t-MDS	Not available	BRCA1	p.Q1777Pfs*74	48	TP53	p.H193Y	29	Breast	9	Breast, non-melanoma skin cancer
2	t-AML	Not available	BRCA1	p.Q1777Pfs*74	48	TP53 CHEK2	p.M237I c.1260-1G>A, p.?	18 8	Breast (two primaries), ovarian	4	None
3	t-AML	Complex	BRCA1	p.V1734*	43	TP53 TP53	p.P177R p.H179P	41 20	Pancreatic	2	None
4	t-MDS, progressed to t-AML	Complex	BRCA1	p.S1217fs*2	45 (blood)	TP53	p.H193L	84	Ovarian	3	None
5	t-CCUS	del(7q) on FISH	BRCA2	p.K1381Lfs*8	50	None			Pancreatic, prostate	4	Gastric, ovarian
6	t-AML	Complex	BRCA2	p.R3128*	47	TP53	c.672+2T>G, p.?	22	Breast, ovarian	3	None
7	t-CCUS	46XX	ATR	p.D1324Vfs*4	46	DNMT3A	p. Q816*	8	Ovarian	5	Bladder, prostate
8	t-MDS/AML	Complex	RAD51D	p.L164P	Not on NGS panel. Heterozygous on germline report	TP53	p.H193R	69	Ovarian	2	None
9	t-AML	Not available	None			TP53	p.V157G	13	Prostate	2	Breast, prostate
10	t-MDS, progressed to t-MDS/AML	Monosomy 7 and 18, then complex on later marrow	BRCA1	Not documented, separate BRCA assay and only myeloid panel sent at OSH		TP53 RUNX1 TET2	p.R175H p.T148fs p.S271fs	55 20 27	Breast, ovarian	4	Breast, lung, pancreatic, ovarian
11	t-MDS, progressed to t-AML	Complex	None			TP53	p.V218dup	42	Ovarian	2	Bladder, lymphoma
12	t-MDS	46XX,der(1:7)(q10;p10) 46XX,del(20)(q11.2q13.3)	None			Not done			Ovarian	7	Melanoma, prostate, skin cancer
13	t-MDS	46XX, del(5)(q13q21)	None			None			Ovarian	4	None

Supplemental Table 2 – Genes Assayed on Next-Generation Sequencing Oncoplus Panel					
<i>ABL1</i>	NM_005157.6	<i>ERCC3</i>	NM_000122.2	<i>NFE2L2</i>	NM_006164.5
<i>AKT1</i>	NM_001382430.1	<i>ESR1</i>	NM_018010.4	<i>NOTCH1</i>	NM_017617.5
<i>ALK</i>	NM_004304.5	<i>ETV6</i>	NM_001987.5	<i>NOTCH2</i>	NM_024408.4
<i>APC</i>	NM_000038.5	<i>EZH2</i>	NM_004456.5	<i>NPM1</i>	NM_002520.7
<i>ARID1A</i>	NM_006015.6	<i>FANCA</i>	NM_000135.3	<i>NRAS</i>	NM_002524.5
<i>ARID2</i>	NM_152641.4	<i>FAT3</i>	NM_001367949.2	<i>PALB2</i>	NM_024675.3
<i>ASXL1</i>	NM_015338.6	<i>FBXW7</i>	NM_001349798.2	<i>PBRM1</i>	-
<i>ATM</i>	NM_000051.3	<i>FGFR1</i>	NM_023110.3	<i>PDGFRA</i>	NM_006206.6
<i>ATR</i>	NM_001184.4	<i>FGFR2</i>	NM_000141.5	<i>PDGFRB</i>	NM_002609.4
<i>AXL</i>	NM_021913.5	<i>FGFR3</i>	NM_000142.5	<i>PIK3CA</i>	NM_006218.4
<i>B2M</i>	NM_004048.4	<i>FH</i>	NM_000143.3	<i>PIK3CB</i>	NM_006219.3
<i>BAP1</i>	NM_004656.3	<i>FLT3</i>	NM_004119.3	<i>PIK3R1</i>	NM_181523.3
<i>BARD1</i>	NM_004656.3	<i>FOXL2</i>	NM_023067.4	<i>PLCG2</i>	NM_002661.5
<i>BIRC3</i>	NM_001165.5	<i>GATA2</i>	NM_032638.4	<i>POLE</i>	NM_006231.3
<i>BRAF</i>	NM_001374258.1	<i>GNA11</i>	NM_002067.5	<i>POT1</i>	NM_006231.3
<i>BRCA1</i>	NM_007294.4	<i>GNAQ</i>	NM_002072.5	<i>PPP2R1A</i>	NM_014225.6
<i>BRCA2</i>	NM_000059.3	<i>GNAS</i>	NM_000516.7	<i>PTCH1</i>	NM_000264.5
<i>CALR</i>	NM_004343.4	<i>GRIN2A</i>	NM_001134407.3	<i>PTEN</i>	NM_000314.7
<i>CBL</i>	NM_005188.3	<i>IKZF1</i>	NM_006060.6	<i>PTPN11</i>	NM_002834.4
<i>CBLB</i>	NM_170662.5	<i>H3F3A</i>	NM_002107.7	<i>RAD21</i>	NM_006265.3
<i>CCND1</i>	NM_053056.3	<i>HIST1H3B</i>	NM_003537.4	<i>RAD51</i>	NM_002875.4
<i>CCND2</i>	NM_001759.4	<i>HIST1H3C</i>	NM_003531.3	<i>RAD51C</i>	NM_058216.3
<i>CCND3</i>	NM_001760.5	<i>HNF1A</i>	NM_000545.8	<i>RAD51D</i>	NM_002878.3
<i>CDH1</i>	NM_004360.4	<i>HRAS</i>	NM_005343.4	<i>RB1</i>	NM_000321.3
<i>CDK4</i>	NM_000075.3	<i>IDH1</i>	NM_005896.4	<i>RET</i>	NM_020975.5
<i>CDK6</i>	NM_001145306.2	<i>IDH2</i>	NM_002168.4	<i>RUNX1</i>	NM_001754.4
<i>CDKN2A</i>	NM_000077.4	<i>ITPKB</i>	NM_002221.4	<i>SAMD9</i>	NM_017654.3
<i>CEBPA</i>	NM_004364.4	<i>JAK2</i>	NM_004972.4	<i>SDHA</i>	NM_004168.4
<i>CHEK1</i>	NM_00111412.2	<i>KDR</i>	NM_002253.4	<i>SDHAF2</i>	NM_017841.2
<i>CHEK2</i>	NM_007194.4	<i>KIT</i>	NM_000222.3	<i>SDHB</i>	NM_003000.2
<i>CSF1R</i>	NM_001288705.3	<i>KMNT2A</i>	NM_001197104.2	<i>SDHC</i>	NM_003001.3
<i>CSF3R</i>	NM_000760.4	<i>KRAS</i>	NM_004985.5	<i>SDHD</i>	NM_003002.4
<i>CTCF</i>	NM_006565.4	<i>MAP2K1</i>	NM_002755.4	<i>SETBP1</i>	NM_015559.3
<i>CTNNA1</i>	NM_001903.5	<i>MAPK1</i>	NM_002745.5	<i>SF3B1</i>	NM_006842.3
<i>CTNNB1</i>	NM_001904.4	<i>MDM2</i>	NM_002392.6	<i>SMAD4</i>	NM_005359.5
<i>CUX1</i>	NM_181552.4	<i>MET</i>	NM_000245.4	<i>SMARCB1</i>	NM_003073.5
<i>CXCR4</i>	NM_003467.3	<i>MLH1</i>	NM_000249.3	<i>SMC3</i>	NM_005445.4
<i>DAXX</i>	NM_001141969.2	<i>MLH3</i>	NM_001040108.2	<i>SMO</i>	NM_005631.5
<i>DDR2</i>	NM_006182.4	<i>MPL</i>	NM_005373.3	<i>SRSF2</i>	NM_001195427.2
<i>DDX41</i>	NM_016222.3	<i>MRE11A</i>	NM_005591.3	<i>STAT3</i>	NM_139276.3
<i>DICER</i>	NM_177438.2	<i>MSH2</i>	NM_000251.3	<i>STAT5B</i>	NM_012448.4
<i>DNMT3A</i>	NM_022552.5	<i>MSH6</i>	NM_000179.3	<i>STK11</i>	NM_000455.4
<i>EGFR</i>	NM_005228.5	<i>MTOR</i>	NM_004958.4	<i>TERT</i>	NM_198253.2
<i>EP300</i>	NM_001429.4	<i>MYC</i>	NM_002467.6	<i>TET2</i>	NM_001146069.2
<i>EPHA3</i>	NM_005233.6	<i>MYCN</i>	NM_005378.6	<i>TP53</i>	NM_000546.6
<i>EPHA5</i>	NM_001281766.3	<i>MYD88</i>	NM_002468.5	<i>TSC1</i>	NM_000368.5
<i>ERBB2</i>	NM_004448.4	<i>NBN</i>	NM_002485.4	<i>TSC2</i>	NM_000548.5
<i>ERBB3</i>	NM_001982.4	<i>NF1</i>	NM_000267.3	<i>U2AF1</i>	NM_006758.3
<i>ERBB4</i>	NM_005235.3	<i>NF2</i>	NM_000268.3	<i>VHL</i>	NM_000551.3
				<i>WT1</i>	NM_024426.5

Supplemental Table 2: Next-Generation Sequencing Oncoplus Panel: Listed above are the 151 genes included on the Oncoplus panel. In addition to the listed genes, sequencing data for *PPM1D* was collected but not clinically published. For each patient with t-MN and available Oncoplus data no *PPM1D* mutations were detected.



Supplemental Figure 1: Bone marrow biopsy and aspirate findings for patient with spontaneous remission of t-MDS after olaparib discontinuation. A. Bone marrow biopsy immediately after olaparib therapy showing erythroid hyperplasia on core biopsy with prominent cell drop out and apoptosis with irregular nuclear contours (Hematoxylin & Eosin stain, 400x) B. In the same marrow, aspirate smears showing left shifted binucleate (black arrow head) early pronormoblasts (Wright-Giemsa, 400x) C. Other areas showing megaloblastoid intermediate erythroid precursors (black arrow) with binucleate late erythroid precursors (white arrowhead & inset) D. Bone marrow biopsy after early cessation of olaparib showing striking reduction in erythroid atypia after cessation. (H&E, 200x) E. Aspirate smears after early cessation showing normoblastic intermediate erythroid precursors (black arrowhead, Wright-Giemsa, 400x) F. Same aspirate smears as panel E showing normoblastic late erythroid precursors G. Bone marrow biopsy after late cessation of olaparib showing normalized cellularity with more intermingled myeloid precursors (H&E, 200x) H. Aspirate smears at the late time point showing normoblastic erythroid precursors (black arrowhead) without any atypia of nuclear contours (Wright-Giemsa, 400x) I. Other areas in the same aspirate smears with normoblastic intermediate and late erythroid precursors (Wright-Giemsa, 400x)