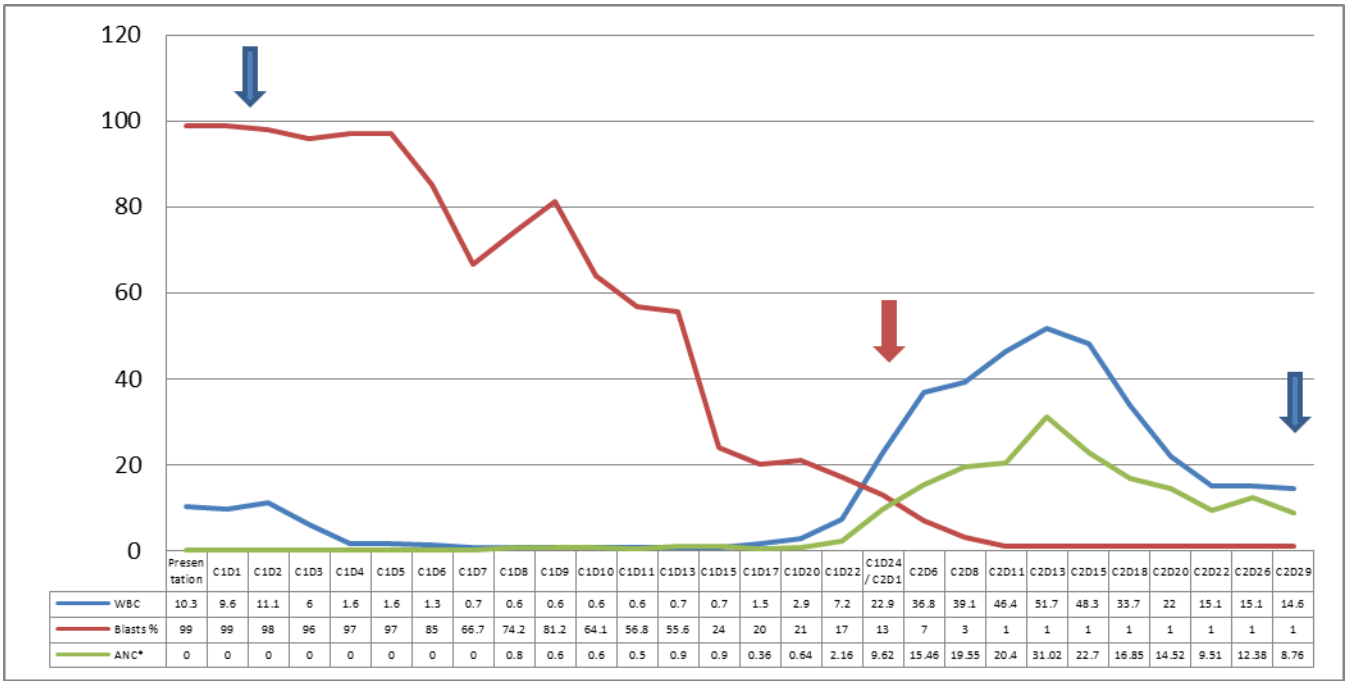
SUPPLEMENTAL DATA

A 39-year old female was diagnosed with AML associated with normal karyotype (NK), mutated *NPM1* and *FLT3*-ITD at an outside facility in May 2011. She received induction chemotherapy with the 7+3 (cytarabine and idarubicin) regimen with bortezomib and achieved complete remission (CR). She then completed 4 cycles of consolidation chemotherapy with high dose cytarabine but relapsed after 8 months. She was then treated with clofarabine with no response. She then received a combination of Cytoxan, Idarubicin, and Vorinostat, again with no response. Subsequently, she was referred to our institution and bone marrow exam was consistent with AML with 96% blasts and normal karyotype, mutated *NPM1*, *FLT3*-ITD, mutated *NRAS* and *DNMT3a*. She was enrolled in the protocol and was started on 5-azacitidine 75 mg/m^2 x 7 days and sorafenib 400 mg orally twice daily. Her WBC declined to 0.7 X 10^9/L by day 14 but rose to 22.9 X 10^9/L by day 23 with rising neutrophil %, when she was started on the second cycle. The peripheral blood WBC, neutrophils and blasts are shown in figure 1. Testing of peripheral blood at the peak of the WBC was positive for mutated *FLT3, NPM1, NRAS,* and *DNMT3a* and a repeat bone marrow examination on day 29 of the second cycles showed reduction in the blasts (7%) with persistent mutations (arrows on figure 1) suggestive of persistence of the original clone with differentiation to mature myeloid cells.

Supplemental Figure 1 Legend

Figure 1. Bone marrow and peripheral blood samples before and after treatment with sorafinib and 5-azacytidine. (A) Peripheral blood white blood cell count, blast percentage, and absolute neutrophil count, (B) Peripheral blood and bone marrow smears samples, (C) Representative electropherogram showing *FLT3*-ITD wild to mutated type allelic ratio.

A

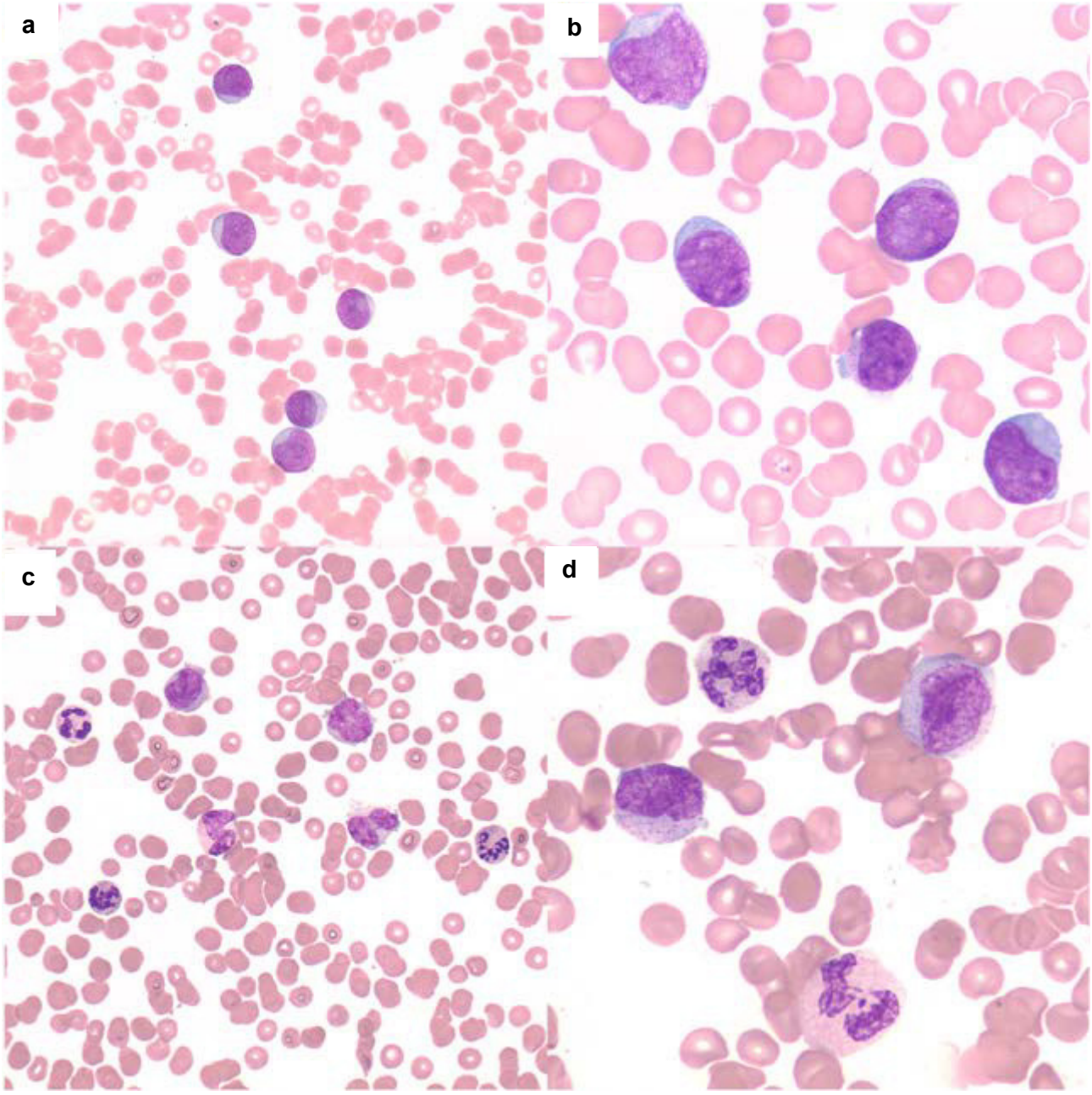


	Presentation	C1D1	C1D2	C1D3	C1D4	C1D5	C1D6	C1D7	C1D8	C1D9	C1D10	C1D11	C1D13	C1D15	C1D17	C1D20	C1D22	C1D24 / C2D1	C2D6	C2D8	C2D11	C2D13	C2D15	C2D18	C2D20	C2D22	C2D26	C2D29
WBC	10.3	9.6	11.1	6	1.6	1.6	1.3	0.7	0.6	0.6	0.6	0.6	0.7	0.7	1.5	2.9	7.2	22.9	36.8	39.1	46.4	51.7	48.3	33.7	22	15.1	15.1	14.6
Blasts %	99	99	98	96	97	97	85	66.7	74.2	81.2	64.1	56.8	55.6	24	20	21	17	13	7	3	1	1	1	1	1	1	1	1
ANC*	0	0	0	0	0	0	0	0	0.8	0.6	0.6	0.5	0.9	0.9	0.36	0.64	2.16	9.62	15.46	19.55	20.4	31.02	22.7	16.85	14.52	9.51	12.38	8.76

ANC = absolute neutrophil count

Peripheral blood white blood cell count, blast percentage, and absolute neutrophil count before and after initiation of treatment with sorafenib and 5-azacytidine. Arrows indicate mutational analysis (Bone marrow specimen and Peripheral Blood)

B

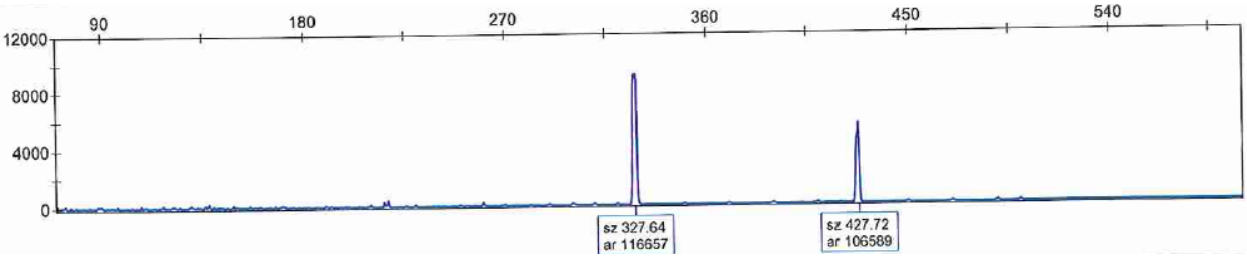


Peripheral blood and bone marrow smears before (a, b) and after (c, d) sorafenib and 5-azacytidine therapy. (a) Peripheral blood smear shows numerous blasts. (b) Wright-Giemsa stain of the marrow aspirate smear shows myeloblasts with high nuclear to cytoplasmic ratio, fine chromatin and small nucleoli. (c) Peripheral blood smear shows myeloid differentiation and

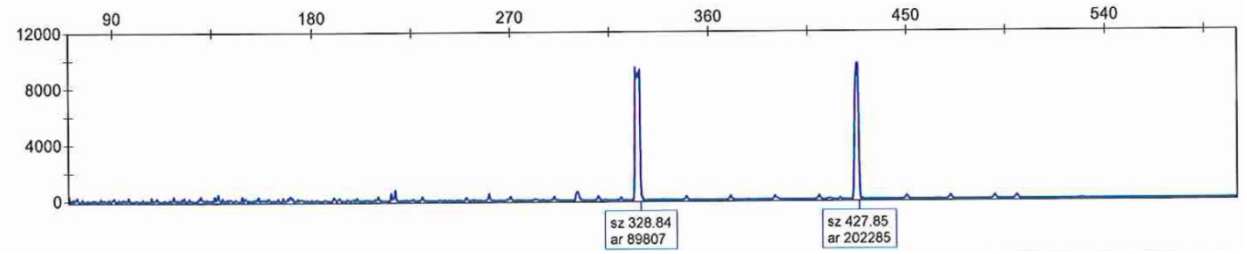
rare blast. (d) The mature neutrophils in this field show pronounced nuclear segmentation. Monocytic differentiation is also present in this bone marrow aspirate smear.

C

C1



C2



Electropherogram of *FLT3*-ITD showing the allelic ratio before (C1) and after treatment (C2). Wild type is on the left and mutated is on the right.