

Figure S1. AXL antigen expression in drug-resistant K562/ADM and U937/Ara-c AML cell lines was significantly upregulated compared with that in drug-sensitive K562 and U937 cell lines ($P < 0.001$). AXL antigen expression (R5) in AML cell lines was detected by flow cytometry. AXL, AXL receptor tyrosine kinase; AML, acute myeloid leukemia.

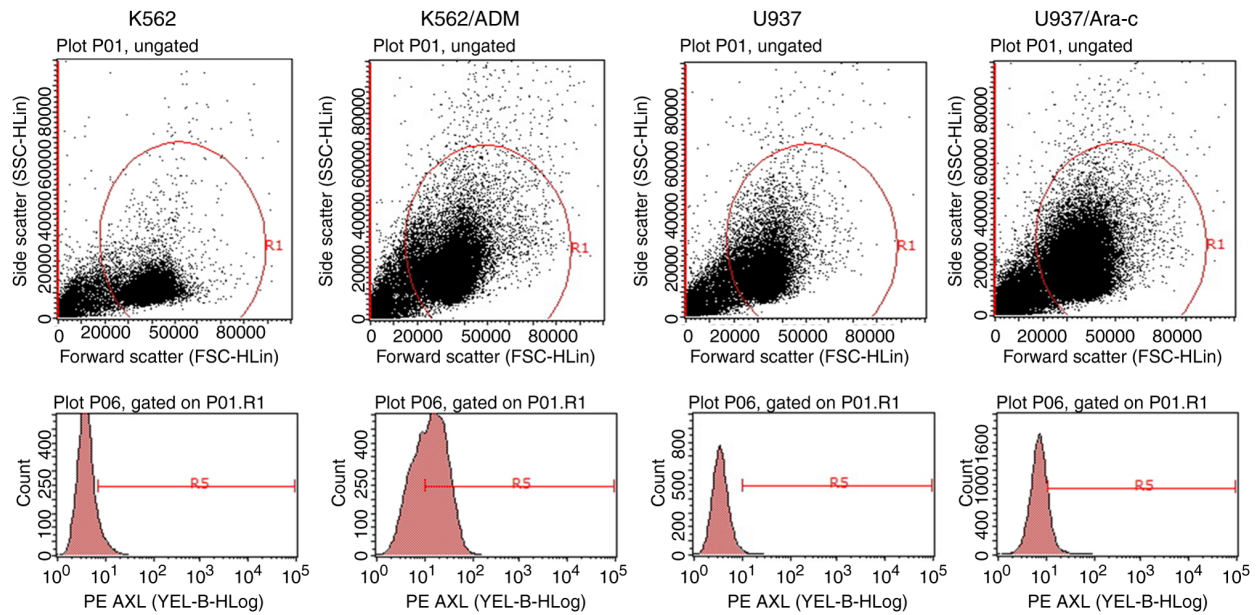


Figure S2. A 19-year-old male patient with FLT3-ITD⁺ AML experienced three relapses and four complete remissions during clinical treatment between June 2018 and November 2019. AML blast cells were dynamically collected five times (samples 029, 039, 063, 071 and 077), and AXL antigen expression was detected by flow cytometry, revealing that the dynamic changes in AXL antigen expression were consistent with clinical resistance to the FLT3 inhibitors sorafenib and midostaurin (PKC412). BM, bone marrow; FCM, flow cytometry; CR, complete remission; Allo-HSCT, allogeneic hematopoietic stem cell transplantation; DLI, donor lymphocyte infusion. AXL, AXL receptor tyrosine kinase; AML, acute myeloid leukemia; FLT3, FMS-like tyrosine kinase 3; ITD, internal tandem duplication.

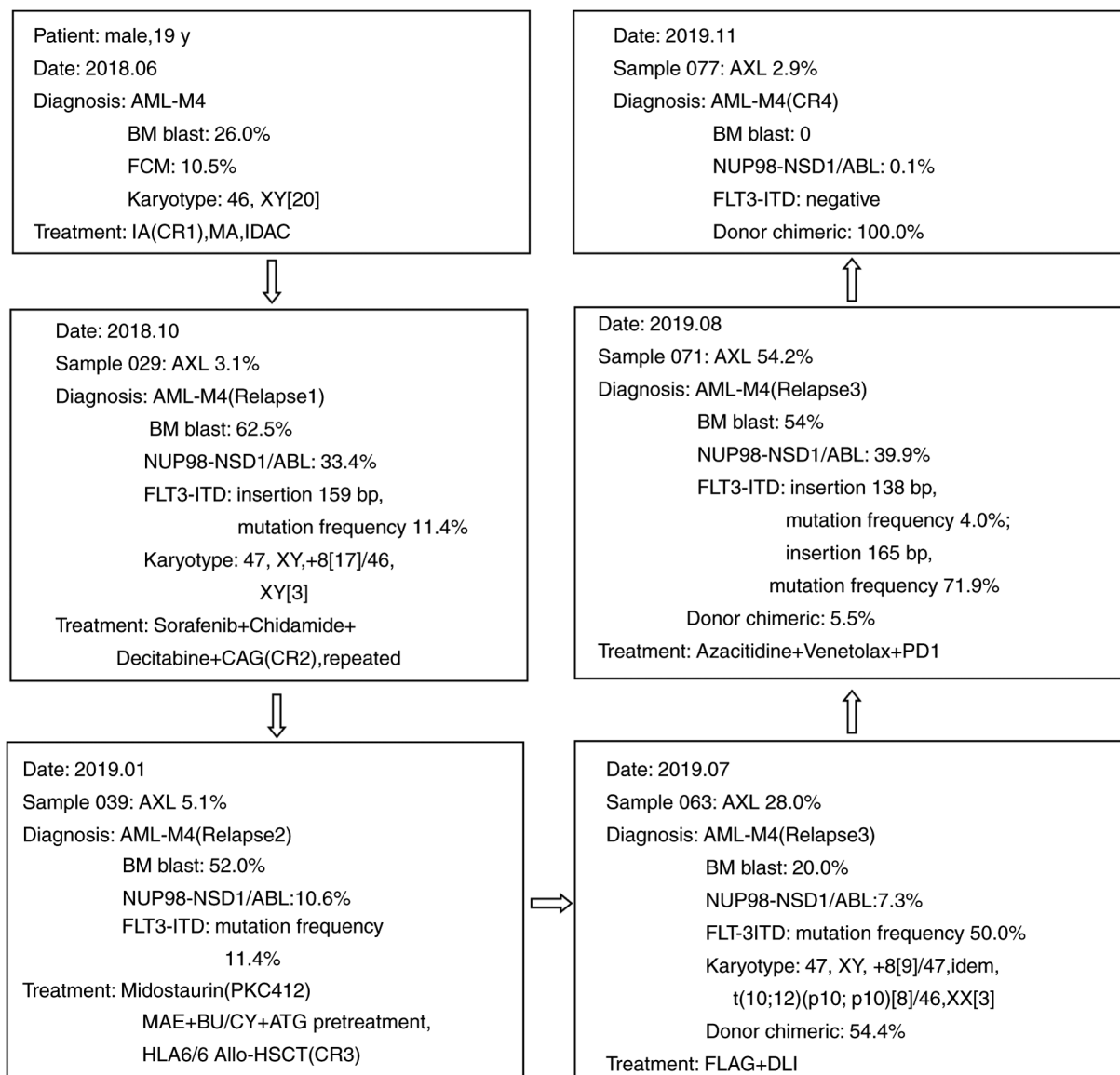


Table SI. Cytotoxic effects of DAXL-88, DAXL-88-MMAE, R428 and MMAE on AML cell lines.

AML cell lines	AXL antigen expression (%)	48-h IC ₅₀			
		DAXL-88 (µg/ml)	DAXL-88-MMAE (µg/ml)	R428 (µM/l)	MMAE (nM/l)
U937 (FLT3-ITD ⁻)	1.12±0.06	No effect	0.03±0.01	1.83±0.02	0.22±0.07
THP-1 (FLT3-WT ⁺)	1.54±0.05	23991±1.83	24.69±1.16	2.65±0.05	0.59±0.12
MV4-11 (FLT3-ITD ⁺)	5.03±0.04	402.8±1.32	37.98±1.09	0.43±0.11	189.6±2.38
MV4-11/AC220 (FLT3-ITD ⁺)	30.53±1.14	809.5±1.78	488.8±1.42	2.94±0.02	109.0±1.19

Values presented as median ± SD. AXL, AXL receptor tyrosine kinase; AML, acute myeloid leukemia; FLT3, FMS-like tyrosine kinase 3; WT, wild-type; ITD, internal tandem duplication; MMAE, monomethyl auristatin E; IC₅₀, half maximal inhibitory concentration.

Table SII. Cytotoxic effects of DAXL-88, DAXL-88-MMAE, R428 and MMAE on AML blast cells.

AML blast cells	AXL antigen expression (%)	48-h inhibitory rate (%)		48-h IC ₅₀	
		DAXL-88 (128 µg/ml)	DAXL-88-MMAE (128 µg/ml)	R428 (µM/l)	MMAE (nM/l)
Sample 069 (FLT3-ITD ⁻)	1.98±0.05	4.47±0.57	14.05±0.72	4.98±1.09	35.03±1.98
Sample 047 (FLT3-ITD ⁺)	5.3±0.25	21.41±2.11	22.83±2.28	2.15±0.12	32.47±2.05
Sample 065 (FLT3-ITD ⁺)	2.38±0.16	11.01±1.28	13.79±1.94	3.17±0.12	77.20±1.22
Sample 071 (FLT3-ITD ⁺)	54.16±2.56	31.29±1.08	33.26±0.84	6.54±1.12	659.0±11.56
Sample 076 (FLT3-ITD ⁺)	1.03±0.06	17.50±2.72	21.48±1.47	5.24±1.16	73.99±1.22
Sample 079 (FLT3-ITD ⁺)	1.93±0.10	10.68±1.63	17.99±2.13	3.21±0.16	279.0±9.56

Values presented as median ± SD. AXL, AXL receptor tyrosine kinase; AML, acute myeloid leukemia; FLT3, FMS-like tyrosine kinase 3; WT, wild-type; ITD, internal tandem duplication; MMAE, monomethyl auristatin E; IC₅₀, half maximal inhibitory concentration.