Supplementary Data

Lane, et al. Phase 1b trial of tagraxofusp in combination with azacitidine with or without venetoclax in acute myeloid leukemia.

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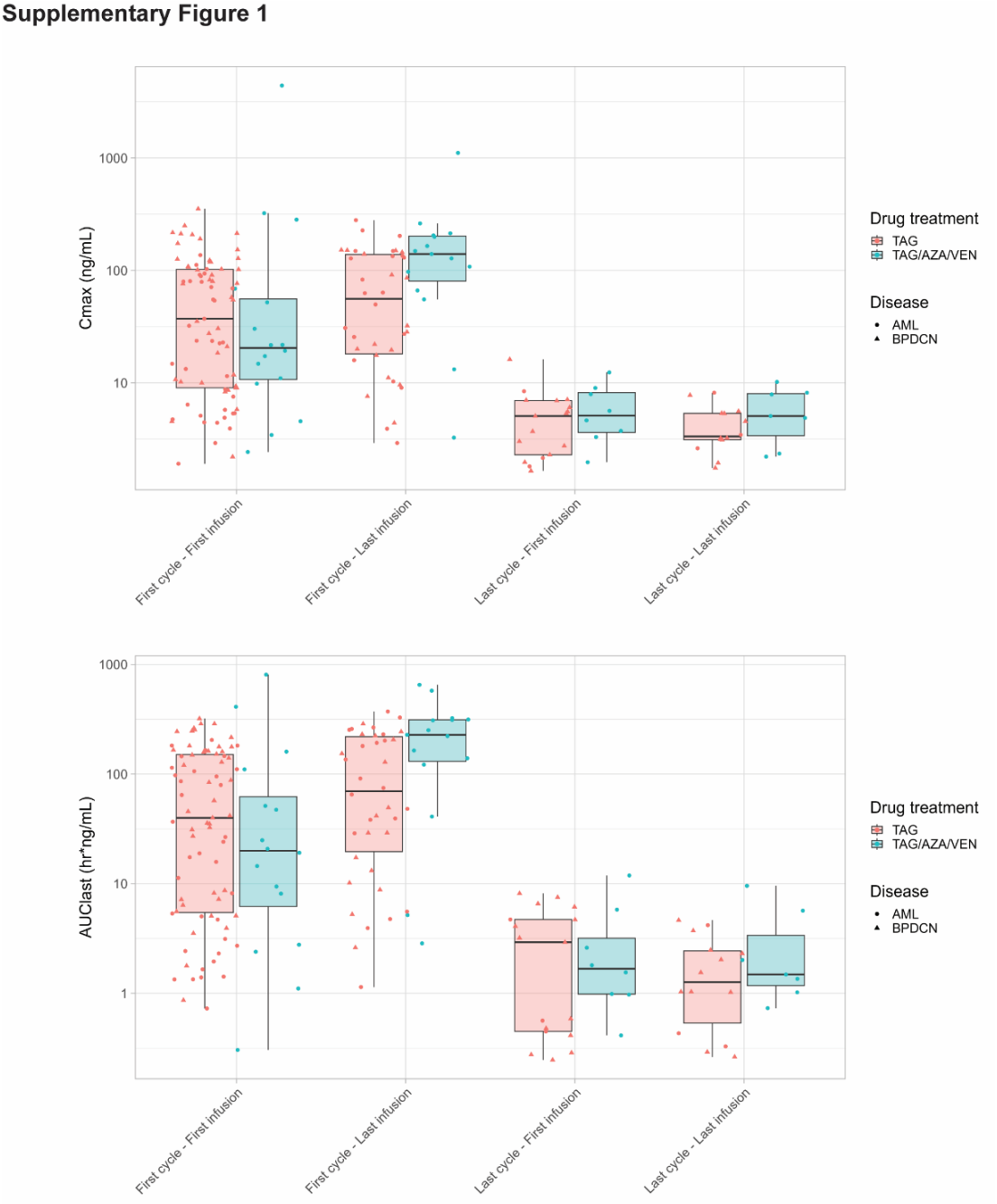
Supplementary Table 1. Demographic and genetic data at time of diagnosis for the 1L AML TAG-AZA-VEN cohort.

Patient	Age	Gender	Karyotype	Gene mutations	TP53 VAF	Baseline marrow blast %
17	74	M	normal	ASXL1, BCOR, RUNX1	NA	34
19	59	M	-3,-5q,-7,-7q,-9q,-12,-16,-18,+22	BRCC3, TP53, U2AF1	0.76	83
24	81	M	normal	FLT3-ITD, SF3B1	NA	57
26	71	F	+8,+8	BCOR, DNMT3A, IDH2, WT1	NA	64
27	67	M	dup(1)(q12q44)	ASXL1, CBL, GATA2, PHF6, NRAS, SF3B1, SMC1A, SMC3	NA	47
28	81	M	del(12)(p12.2p13.3),+21	ASXL1, KRAS, NRAS, SRSF2, TET2, RUNX1	NA	24
31	78	F	normal	DDX41 x2, SETBP1, SRSF2	NA	41
33	79	M	+8	ASXL1, NPM1, SRSF2, TET2	NA	71
34	71	M	-5q,-13,-17p,-18	GATA2, SF3B1, TP53	0.18	43
41	73	M	del(2p21),-17p	ASXL1, CEBPA, EZH2, JAK2, NFE2 x2, STAG2, TP53 x2	0.48, 0.14	56
42	60	F	-5q,+11,-17	NF1, TP53, U2AF1	0.73	58
43	68	M	-5q,-7,+8,del(12p),-17p	DNMT3A, RUNX1, TP53	0.21	25
44	70	M	-5q,del(12p),-17p	TP53	0.13	27
47	69	F	normal	BCOR, CSF3R, DNMT3A, SF3B1, TET2, RUNX1	NA	81
48	62	F	-5q,-11q	RUNX1 x2	NA	12
49	73	M	+2,-7,-7,+11,-17	DNMT3A, IDH1, TP53	0.58	83
51	70	M	normal	FLT3-TKD, PTPN11, RUNX1, U2AF1	NA	20
52	71	F	-5q,+8	EZH2, TP53	0.68	50
56	65	F	-9q	TP53	0.62	38
59	63	M	normal	ASXL1, CBL, JAK2, RUNX1, SRSF2	NA	21
60	71	M	complex, including -17	TP53	unk	58
62	66	F	+8	DNMT3A, TP53	unk	29
63	69	M	normal	FLT3-ITD, RUNX1	NA	91
64	62	M	-5,-7	TP53 x2	0.27, 0.21	26
65	67	F	-5q,+8,+15,+18	TP53 x2	0.35, 0.34	80
66	70	M	normal	BCOR, BCORL1, CSF3R, RUNX1	NA	27

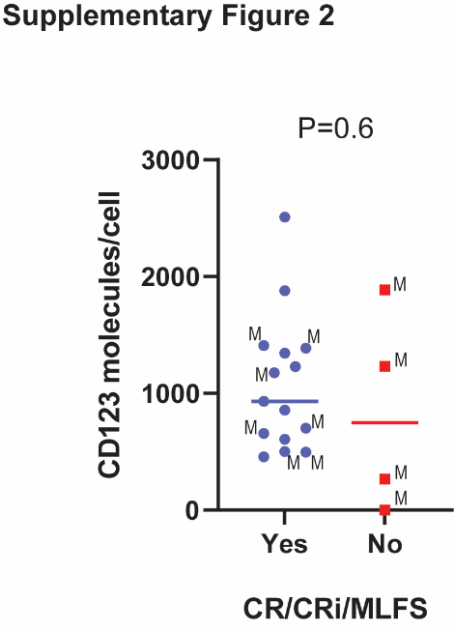
VAF, variant allele fraction

Supplementary Figure 1



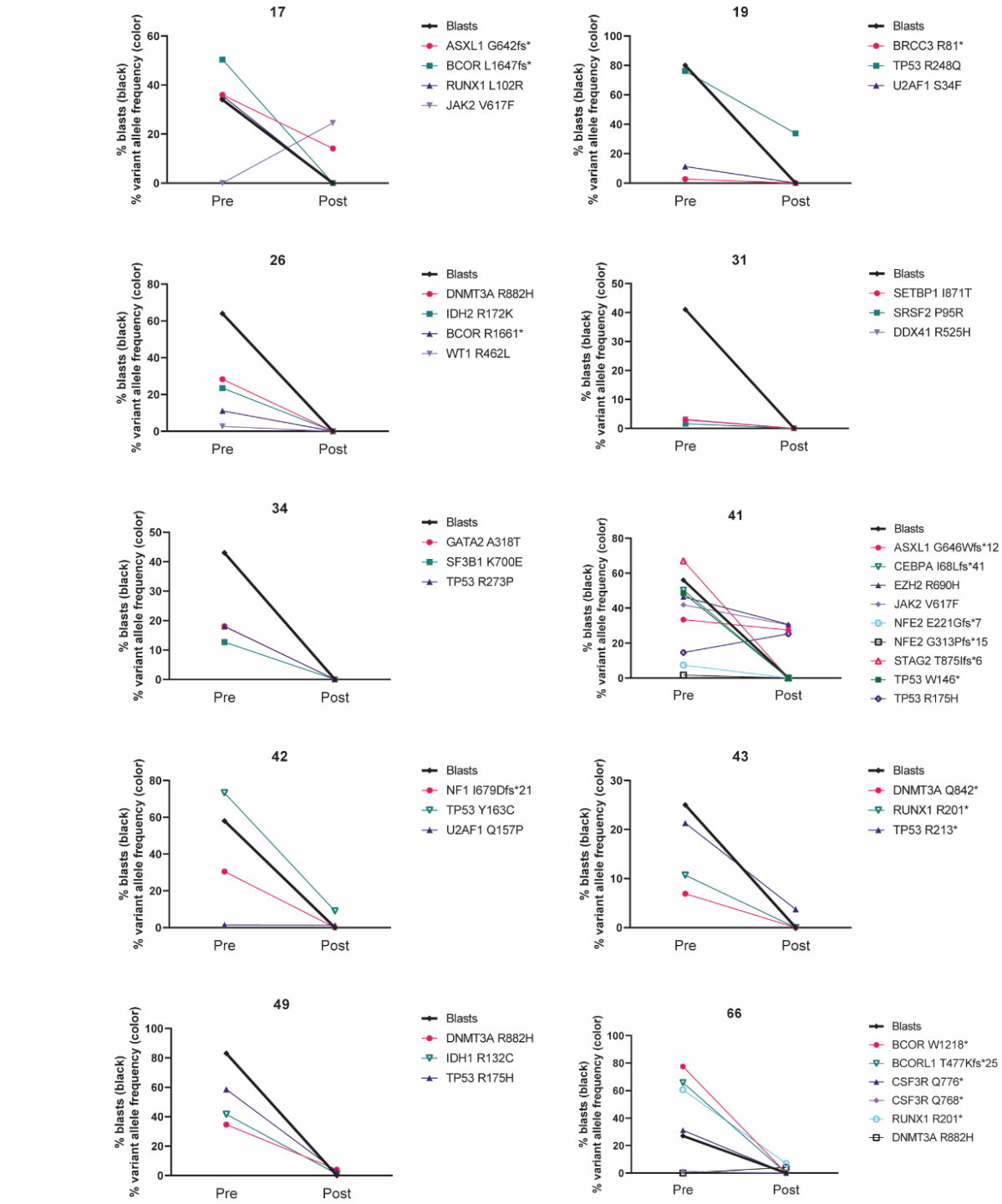
Supplementary Figure 1. Pharmacokinetic analyses.
(Top) Cmax and (Bottom) AUClast pharmacokinetic analyses of TAG with 12 µg/kg dosing from the previously reported STML-401-0114 single agent study (TAG, red) and in the triplet combination in this trial (TAG/AZA/VEN, blue). In STML-401-0114 study, TAG was given daily for five days and PKs were collected on the first day and the last day of TAG in cycle 1 and 3. In this trial, TAG as part of TAG-AZA-VEN was given daily for three days and PKs were collected on the first and the last day of TAG in cycle 1 and 2. Lower free drug levels after cycle 1 were as have been reported for TAG in STML-401-0114, associated with antidrug antibodies (Jen et al., Clinical Cancer Research 2020).

Supplementary Figure 2



Supplementary Figure 2. Quantitation of cell surface CD123 among patients in the previously untreated AML cohort receiving TAG-AZA-VEN.
Central laboratory quantitation of CD123 on blasts in available pre-treatment samples from patients with AML in the 1L cohort who received with TAG-AZA-VEN. Each dot represents a patient sample separated by those who did and did not achieve CR/CRi/MLFS as best response. Groups compared by two-tailed Student's t-test. Samples from patients with TP53 mutation are annotated as 'M'.

Supplementary Figure 3

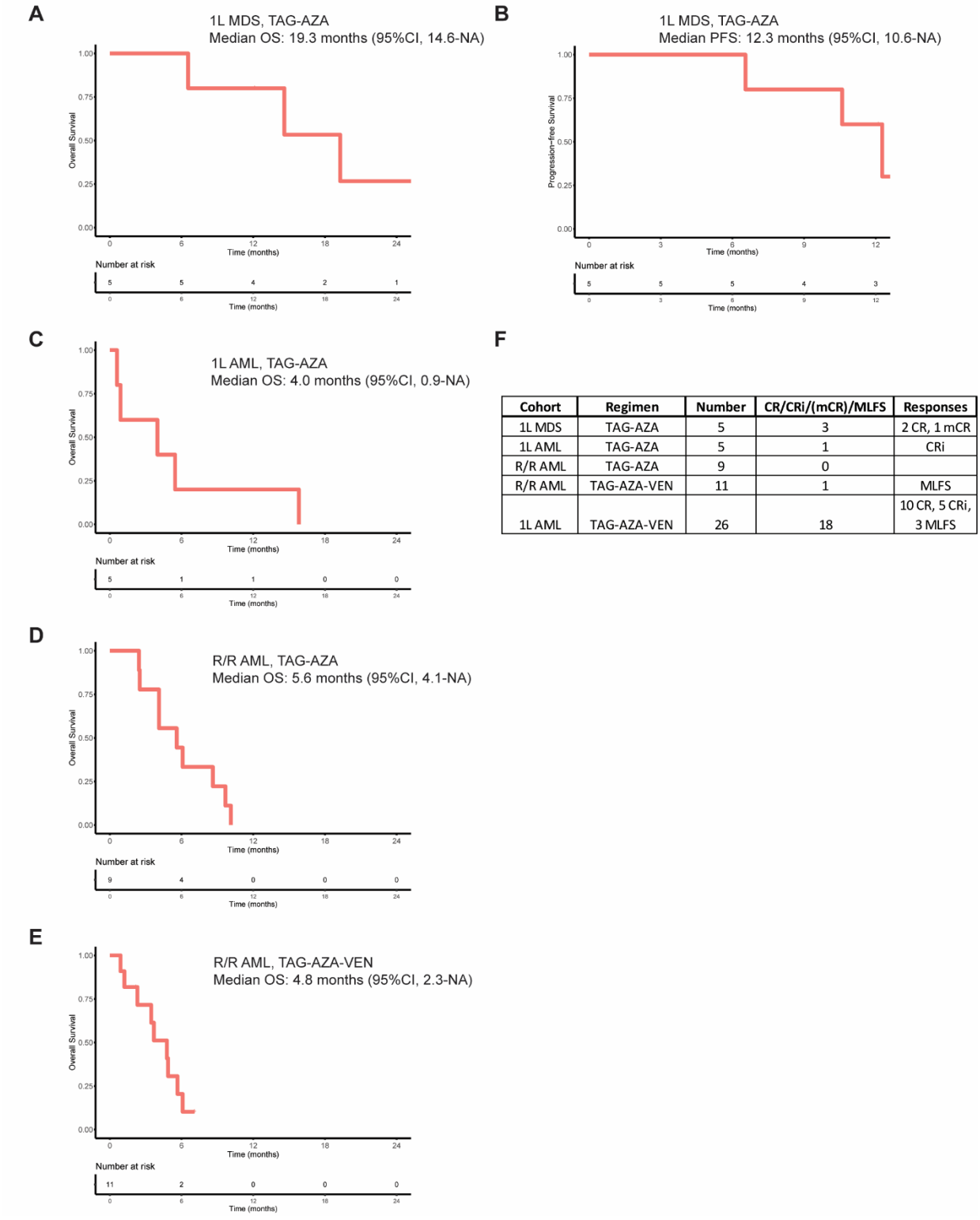


Supplementary Figure 3. Changes in bone marrow DNA mutations before and after TAG-AZA-VEN among patients in the frontline AML cohort.

DNA sequencing was not mandatory in the trial protocol but was performed at the treating physician's preference per standard clinical care. In ten patients, DNA sequencing results using

a myeloid malignancy gene panel were available prior to treatment and at a timepoint of best response (ranging from cycles 2-6) and are shown. All patients were in CR/CRi/MLFS at the time of the post-treatment sampling. The heavy black line shows the bone marrow blast percentage at each timepoint, and the colored lines represent the percentage of the DNA variant allele encoding the amino acid change as annotated for each protein at each timepoint.

Supplementary Figure 4



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Cohort	Regimen	Number	CR/CRi/(mCR)/MLFS	Responses
1L MDS	TAG-AZA	5	3	2 CR, 1 mCR
1L AML	TAG-AZA	5	1	CRi
R/R AML	TAG-AZA	9	0	
R/R AML	TAG-AZA-VEN	11	1	MLFS
1L AML	TAG-AZA-VEN	26	18	10 CR, 5 CRi, 3 MLFS

Supplementary Figure 4. Survival and response data across additional cohorts.
A. Overall survival (OS) probability in the previously untreated (1L) MDS TAG-AZA cohort.
B. Progression-free survival (PFS) probability in the previously untreated MDS TAG-AZA cohort.

C. OS probability in the previously untreated AML TAG-AZA cohort.
D. OS probability in the relapsed/refractory (R/R) AML TAG-AZA cohort.
E. OS probability in the R/R AML TAG-AZA-VEN cohort.
F. Summary of responses by cohort.