LETTER TO THE EDITOR

Venetoclax and gilteritinib combination for *FLT3*-mutated relapsed/refractory acute myeloid leukemia: a real-world single-center experience

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Supplemental data

Figure S1.

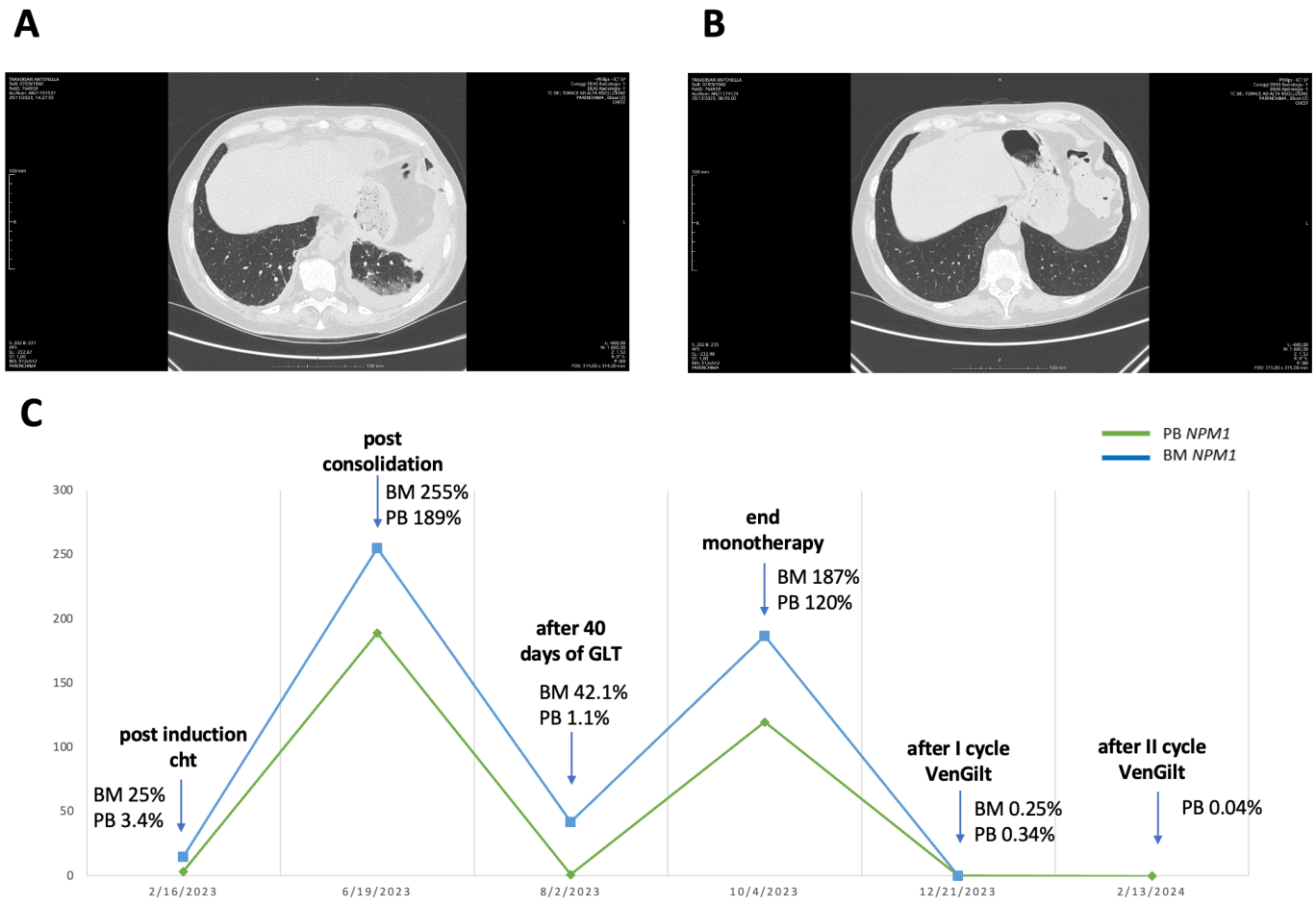


Figure S1. Visual summary of relevant clinical issues in patient # 3. (A) CT chest scans along with gilteritinib monotherapy (A), showing differentiation syndrome-related features (pulmonary infiltrates, pleural effusion), and (B) after the introduction of venetoclax, with resolution of imaging findings. (C) Trends of NPM1 transcript during treatment course. Cht, chemotherapy; Glt, gilteritinib monotherapy; VenGilt, venetoclax and gilteritinib combination; PB, peripheral blood; BM, bone marrow.

Table S1. Characteristics and outcome of patients.

Case n°	Gender	Age	Disease characteristics	Previous treatments	Response	Status
1	M	65 y	sAML Normal karyotype NGS: *ASXL1, PTPN11, SRSF2, STAG2* and *FLT3*-TKD (VAF 34%) mutations	1st line: CPX-351 2nd line: gilteritinib (1 cycle) 3rd line: gilteritinib + venetoclax (1 cycle) Bridged to HSCT with active disease	1st line: NR 2nd line: NR 3rd line: NR CR MFC-MRD negative after HSCT	Alive, still in CR
2	M	18 y	AML with *CEBPA* mutation Normal karyotype, NGS: *CEBPA*, *FLT3-ITD* (ratio 0.5) and *WT1* mutations	1st line: Induction (3+7), I consolidation (unknown), II consolidation (Ida-HDAraC) 2nd line: azacitidine + venetoclax (1 cycle) 3rd line: gilteritinib (1 cycle) 4th line: gilteritinib + venetoclax (2 cycles) Bridged to HSCT with active disease	1st line: CR, MFC-MRD positive Relapse during II consolidation 2nd line: NR 3rd line: NR 4th line: NR CR MFC-MRD negative after HSCT	Alive, still in CR
3	F	61 y	AML with *NPM1* mutation Normal karyotype NGS: *FLT3*-ITD (ratio 0.63), *TET2* and *DNMT3A* mutations	1st line: According to GIMEMA AML1919 protocol: Induction chemotherapy: 3+7+midostaurin Two consolidation cycles: HDAC + midostaurin 2nd line: gilteritinib (7 cycles) 3rd line: gilteritinib + venetoclax (3 cycles) Bridged to HSCT with MRD pos	1st line: CR, Mol-MRD positive Relapse during II consolidation 2nd line: NR 3rd line: CRi, MRD positive (*NPM1* 0.04% in BM)	Death due to septic shock and MOF after HSCT
4	F	49 y	AML with *NPM1* mutation Normal karyotype NGS: *FLT3*-ITD ITD (ratio 1), *DNMT3A, TET2* mutations	1st line: Induction (Ida-HDAraC), consolidation cycle (HDAC + midostaurin) 2nd line: gilteritinib (4 cycles) 3rd line: salvage chemotherapy (HAM) 4th line: gilteritinib + venetoclax (1 cycle)	1st line: CR, Mol-MRD positive Relapse during I consolidation 2nd line: NR 3rd line: NR 4th line: NR	Death due to septic shock

5	M	58 y	AML with *NPM1* mutation Normal karyotype NGS: *FLT3*-ITD ITD (ratio 0.19), *PTPN11, IKZ11* and *CBL* mutations	1st line: Induction (3+7+midostaurin) 2nd line: gilteritinib (3 cycles) 3rd line: gilteritinib + venetoclax (1 cycle) 4th line: salvage chemotherapy (HDAC)	1st line: NR 2nd line: NR 3rd line: NR 4th line: NR	Death due to septic shock
6	M	72 y	AML with *NPM1* mutation Normal karyotype NGS: *FLT3*-ITD (ratio 7) and *DNMT3A* mutations	1st line: azacitidine + venetoclax (1 cycle) 2nd line: gilteritinib (22 cycles) 3rd line: gilteritinib + venetoclax (8 cycles)	1st line: NR 2nd line: CR, Mol-MRD negative Molecular Relapse during Gilt 3rd line: CR, Mol-MRD negative	Alive, still in CR
7	F	78 y	AML Normal karyotype NGS: *FLT3*-ITD ITD (ratio 0.03), *ASXL1, STAG2* and *EZH2* mutations	1st line: azacitidine + venetoclax (17 cycles) 2nd line: gilteritinib (5 cycles) 3rd line: gilteritinib + venetoclax (6 cycles)	1st line: CR, MFC-MRD positive Relapse during AzaVen 2nd line: NR 3rd line: CR, MFC-MRD positive	Alive, still in CR
8	F	33 y	AML del7q; t (3;11) (MECOM-r) NGS: *FLT3*-ITD (ratio 0.88) and *SF3B1* mutations	1st line: According to GIMEMA AML1919 protocol: Induction chemotherapy: 3+7+midostaurin 2nd line: gilteritinib (1 cycle) 3rd line: gilteritinib + venetoclax (1 cycle) Bridged to HSCT in CR, Mol-MRD neg	1st line: PR 2nd line: PR 3rd line: CR, Mol-MRD negative	Alive, still in CR
9	F	40 y	AML Normal karyotype NGS: *FLT3*-ITD (ratio 0.88) mutation	1st line: According to GIMEMA AML1919 protocol: Induction chemotherapy: 3+7+midostaurin 2nd line: gilteritinib (1 cycle) 3rd line: gilteritinib + venetoclax (2 cycles) Bridged to HSCT in CR, Mol-MRD neg	1st line: NR 2nd line: NR 3rd line: CR, Mol-MRD negative	Alive, still in CR
10	M	53 y	AML with *NPM1* mutation Normal karyotype NGS: *CEBPA, DNMT3A* and *FLT3*-ITD (ratio 0.92) mutations.	1st line: According to GIMEMA AML1919 protocol: Induction chemotherapy: 3+7+midostaurin Two consolidation cycles: HDAC + midostaurin 2nd line: gilteritinib (1 cycle) 3rd line: gilteritinib + venetoclax (1 cycle) Bridged to HSCT in CR, Mol-MRD pos	1st line: CR, Mol-MRD positive Molecular Relapse during II consolidation 2nd line: CR, Mol-MRD positive	Alive, still in CR

					3rd line: CR, Mol-MRD positive	
11	F	63 y	AML with *NPM1* mutation Normal karyotype NGS: *DNMT3A, NF1* and *PHF6* mutations. positive *FLT3*-ITD (ratio 0.75) retesting at relapse	1st line: Induction (3+7) and 3 consolidations cycles (HDAC) 2nd line: gilteritinib (2 cycles) 3rd line: gilteritinib + venetoclax (2 cycles)	1st line: CR, Mol-MRD negative Relapse 5 months after III consolidation 2nd line: NR 3rd line: CRi, Mol-MRD positive	Alive, ongoing
12	F	60y	AML with *NPM1* mutation Normal karyotype NGS: *TET2, DNMT3A, GATA2* and *FLT3*-ITD (ratio 11.9) mutations.	1st line: According to GIMEMA AML1919 protocol: Induction chemotherapy: 3+7+midostaurin 2nd line: gilteritinib (1 cycle) 3rd line: gilteritinib + venetoclax (1 cycle) Bridged to HSCT in CRi, Mol-MRD positive	1st line: NR 2nd line: NR 3rd line: CRi, Mol-MRD positive	Alive, ongoing

Abbreviations: sAML, secondary to MDS; NGS, next generation sequencing; HSCT, allogeneic hematopoietic stem cell transplantation; CR, complete remission; CRi, complete remission with incomplete hematopoietic recovery; NR, no response; IdaHDAraC, Idarubicin, high dose cytarabine; HDAC, high dose cytarabine; Gilt, gilteritinib; AzaVen, azacitidine + venetoclax; MRD, measurable residual disease; Mol, by molecular assessment (PCR for *NPM1*, amplicon-based NGS assay for *FLT3*-ITD); MFC, multi-parameter flow cytometry; HAM, high dose cytarabine, mitoxantrone.