

Supplemental Table 1. Details in regard to timing, blood counts and status of AML in 34 patients who experienced a cardiac event

Type of event	Context	Timing	Upfront vs. R/R	Blood counts at time of event	Status of AML at time of event	Ven dose (if reduced which concomitant med)	HMA or schedule adjustment?	Infection at time of event?	If troponin elevation or RV dysfunction: clinical scenario?	CTCAE grade	EF
Patient (PT) 1 69 F: Atrial fibrillation with rapid ventricular response	Neutropenic fever	Cycle 2	R/R	WBC: 0.1 Hb: 8.4 Pit: 27	Not assessed	200mg (fluconazole)	No	Pneumonia (based on imaging, not culture-proven)		3	66
PT 2 92 M: LVEF decrease [†] , Atrial fibrillation with rapid ventricular response, other symptomatic arrhythmia	Acute hypoxic respiratory failure	Cycle 22	Upfront	WBC: 0.7 Hb: 6.4 Pit: 10	PR	400mg (no concurrent meds)	C4 delayed for neutropenic fever	COVID with superimposed bacterial pneumonia		Atrial fibrillation: 5 LVEF: 3 Other arrhythmia: 2	36
PT 3 81 F: Troponin elevation, Worsening HFpEF, Atrial fibrillation with rapid ventricular response	Tumor lysis syndrome	Cycle 1	Upfront	WBC: 2.8 Hb: 7.8 Pit: 33		200mg (fluconazole)	None	No	Chest pain	Troponin elevation: 3 Worsening HFpEF: 1 Atrial fibrillation: 2	57
PT 4 85 M: Troponin elevation, LVEF decrease*	Combined (septic, cardiogenic) shock	Cycle 12	Upfront	WBC: 0.3 Hb: 10 Pit: 8	PR	200mg (fluconazole)	Yes – q6wk cycle starting C7 due to cytopenia	No	Hypotension, tachycardia	Troponin elevation: 4 LVEF: 5	15-20
PT 5 56 M: Pericardial effusion	Chronic, asymptomatic pericardial effusion	Cycle 1	Upfront	WBC: 0.5 Hb: 6.6 Pit: 5		200mg (fluconazole)	No	No		2	74
PT 6 47 F: LVEF decrease	Dyspnea, symptomatic HFrEF	Cycle 1	R/R	WBC: <0.1 Hb: 6.7 Pit: 29		100mg (posaconazole)	No	Aspergillus pneumonia, Rothia/ Stenotrophomonas bacteremia		3	35
PT 7 71 M: LVEF decrease	Cardiogenic shock	Cycle 1	R/R	WBC: 0.8 Hb: 7.1 Pit: 24		200mg (fluconazole)	No	Mucorales		5	55

PT 8 68 F: Cardiogenic pulmonary edema	Neutropenic fever	Cycle 1	R/R	WBC: 0.4 Hb: 6.9 Plt: 8		200mg (fluconazole)	No	Culture negative neutropenic fever		3	68
PT 9 40 M: Myopericarditis	Chest pain, dyspnea	Cycle 5	R/R	WBC: 0.8 Hb: 8.4 Plt: 21	Primary refractory disease	100mg (posaconazole)	No	No		2	61
PT 10 61 M: Atrial fibrillation with rapid ventricular response, Pericarditis*	Septic shock	Cycle 3	R/R	WBC: 3 Hb: 8 Plt: 11	Primary refractory disease	100mg (posaconazole)	No	Pneumonia with septic shock		Atrial fibrillation: 3 Pericarditis: 2	61
PT 11 74 F: Cardiogenic pulmonary edema	Admission for Pain control	Cycle 1	R/R	WBC: 6.9 Hb: 4.6 Plt: 43		200mg (fluconazole)	No	No		1	68
PT 12 79 F: Worsening HFpEF	Not admitted	Cycle 2	R/R	WBC: 3.5 Hb: 7.5 Plt: 51	CR	200mg (fluconazole), 14- day cycle	No	No		1	62
PT 13 72 M: Worsening CAD*	Failure to thrive	Cycle 3	Upfront	WBC: 0.8 Hb: 7 Plt: 11	CR	100mg (posaconazole)	Yes- C3 delayed by 2 wks (infection)	ESBL E. Coli		2	71
PT 14 75 F: LVEF decrease	Heart failure	Cycle 2	Upfront	WBC: 6.2 Hb: 10.5 Plt: 247	CR	100mg (posaconazole)	No	No		3	55
PT 15 58 M: Atrial fibrillation with rapid ventricular response *	Respiratory and cardiac failure	Cycle 1	R/R	WBC: 5.9 Hb: 8.2 Plt: 7		100mg (posaconazole)	2 days decitabine	Culture negative neutropenic fever		5	55
PT 16 72 M: Cardiogenic pulmonary edema*	Anemia	Cycle 1	Upfront	WBC: 3.1 Hb: 6.3 Plt: 67		200mg (fluconazole)	3 doses Dacogen (held for rising Cr)	Culture negative (Aspergillus Ag +) febrile neutropenia		5	74
PT 17 77 M: Other symptomatic	Renal failure	Cycle 1	Upfront	WBC: 0.3 Hb: 7.5		200mg (due to fluconazole, diltiazem)		No		2	63

arrhythmia (SVT)				Pt: 10							
PT 18 70 M: NSTEMI type 1*	Chest pain	Cycle 1	Upfront	WBC: 1.9 Hb: 8 Pt: 24		200mg (fluconazole)	No	Culture negative neutropenic fever		3	63
PT 19 68 M: Troponin elevation, LVEF decrease *	Heart failure	Cycle 3	R/R	WBC: 12.2 Hb: 8.2 Pt: 230	CR	100mg (posaconazole)	No	No	Dyspnea	Troponin elevation: 2 LVEF: 5	35
PT 20 84F: Other symptomatic arrhythmia (recurrent narrow complex tachycardia)	Azacitidine + venetoclax ramp-up	Cycle 1	Upfront	WBC: 1.8 Hb: 7.6 Pt: 35		200mg (fluconazole)	No	No		2	65
PT 21 80 M: Atrial fibrillation with rapid ventricular response ¹ , cardiopulmonary arrest	Out of hospital arrest	Cycle 7	Upfront	WBC: 0.6 Hb: 6.1 Pt: 13	CRi MRD+	200mg (fluconazole)	25% decitabine dose reduction for pancytopenia	No		Cardiopulmonary arrest: 5 Afib with RVR: 2	60
PT 22 73 F: Worsening HFpEF	Not admitted; pleural effusion	Cycle 2	Upfront	WBC: 3.3 Hb: 7.8 Pt: 22	Not assessed	200mg (fluconazole)	No	No		1	68
PT 23 86 F: RV dysfunction	Not admitted; incidental finding	Cycle 5	Upfront	WBC: 3.6 Hb: 13 Pt: 212	CR	200mg (fluconazole)	Yes- start C5, 3 days aza and spaced to 6 weeks	No	Echo obtained for dyspnea, pleural effusion	1	>60
PT 24 67 F: Cardiopulmonary arrest	Femur fracture	Cycle 2	Upfront	WBC: 0.2 Hb: 8.1 Pt: 10	Not assessed	200mg (fluconazole)	No	No		5	68
PT 25 70 M: Other symptomatic arrhythmia	Subdural hematoma	Cycle 5	Upfront	WBC: 3.3 Hb: 8.3 Pt: 114	CR	200mg (fluconazole)	Decitabine only days 1-5 15mg/m2. Ven 14D cycle	No		2	45-50
PT 26	Sepsis	Cycle 2	Upfront	WBC: 0.5	Not assessed	200mg (fluconazole)	C2 delayed x 4 wks (Fatigue,	Staph Aureus	Echo obtained for hypotension	Worsening HFpEF: 3	72

78 F: Worsening HFpEF, RV dysfunction				WBC: 6.8 Plt: 26						RV dysfunction: 3	
PT 27 88 M: LVEF decrease, Atrial fibrillation with rapid ventricular response, RV dysfunction	Tumor lysis syndrome	Cycle 1	Upfront	WBC: 17.6 Hb: 9.1 Plt: 25		100mg, then held day 13 for severe thrombocytopenia (fluconazole)	No	No	Echo obtained for hypotension, new atrial fibrillation	LVEF: 3 RV dysfunction: 3 Atrial fibrillation: 3	45-50
PT 28 62 F: LVEF decrease *	Pleural effusion	Cycle 1	R/R	WBC: 0.7 Hb: 6.9 Plt: 34		200mg (fluconazole)	No	Culture negative febrile neutropenia		5	40
PT 29 82 M: Atrial fibrillation with rapid ventricular response, troponin elevation*	COVID	Cycle 2, Cycle 3	Upfront	WBC: 27.6 Hb: 8.5 Plt: 261	PR	200mg (fluconazole)	C3 delayed for COVID	No	Chest pain	Atrial fibrillation: 4 Troponin elevation: 3	57
PT 30 80 M: Troponin elevation	GI Bleed	Cycle 2	Upfront	WBC: 0.4 Hb: 6.8 Plt: 8	CRi	200mg (fluconazole), 14-day cycle	No	No	Chest pain	3	45-50
PT 31 69 M: Troponin elevation, LVEF decrease	Subdural hematoma	Cycle 1	Upfront	WBC: 2.7 Hb: 6.8 Plt: 8		200mg (fluconazole)	No	Culture negative febrile neutropenia	Chest pain, dyspnea	LVEF: 3 Troponin elevation: 2	33
PT 32 61 M: Troponin elevation	Unstable angina	Cycle 3	Upfront	WBC: 1.1 Hb: 13.2 Plt: 359	CR	200mg (fluconazole)	No	No	Chest pain, palpitations	2	55
PT 33 71 M: NSTEMI type 1	NSTEMI type 1	Cycle 2	Upfront	WBC: 6.9 Hb: 7.6 Plt: 312	PR	100mg (posaconazole)	No	No		4	62
PT 34 71 M: LVEF decrease, NSTEMI type 1	NSTEMI type 1	Cycle 1	Upfront	WBC: 0.9 Hb: 8.7 Plt: 28		200mg (fluconazole)	No	No		NSTEMI: 4 LVEF decrease: 3	40

*=admission to Intensive Care Unit or Cardiac Intensive Care Unit. R/R: HMA + venetoclax used for relapsed or refractory AML. Status of AML assessed for all patients beyond cycle 1 per 2017 ELN response criteria. CR: complete response. CRi: complete response with incomplete hematologic recovery. PR: partial response. MRD: minimal residual disease. EF=ejection fraction. All cardiac events graded per Common Terminology Criteria for Adverse Events (CTCAE), version 5.0. Troponin elevation graded in category ‘myocardial infarction.’

† = non-concurrent cardiac events; event demarcated by † preceded other cardiac events

Supplemental Table 2. Details of nine fatal cardiac events

Type of event:	Cause of death:
PT 2 92 M: LVEF decrease, Atrial fibrillation w/ RVR, other symptomatic arrhythmia	Non-perfusing arrhythmia
PT 4 85 M: Troponin elevation, LVEF decrease	Heart failure with reduced ejection fraction
PT 7 71 M: LVEF decrease	Cardiogenic shock
PT 15 58 M: Atrial fibrillation w/ RVR	Non-perfusing arrhythmia
PT 16 72 M: Cardiogenic pulmonary edema	Respiratory failure due to pulmonary edema
PT 19 68 M: Troponin elevation, LVEF decrease	Respiratory failure
PT 21 80 M: Atrial fibrillation w/ rapid ventricular response (prior), cardiopulmonary arrest	Out-of-hospital arrest
PT 24 67 F: Cardiopulmonary arrest	In-hospital arrest
PT 28 62 F: LVEF decrease	Respiratory failure due to pulmonary edema

Supplemental Figure 1. Cumulative incidence of cardiac events in AML patients treated with HMA + venetoclax vs. AML patients treated with HMA alone.

