Outcomes based on sequential use of venetoclax based therapy and targeted therapy in acute myeloid leukemia (AML)

Maximilian Stahl, MD[1]*, Rory M. Shallis, MD[2], Andriy Derkach, PhD[3], Aaron D. Goldberg, MD, PhD[4], Anthony Stein, MD[5], Eytan M. Stein, MD[4], Guido Marcucci, MD[5], Amer M. Zeidan, MBBS, MHS[2], Shai Shimony, MD[1], Daniel J. DeAngelo, MD PhD[1], Richard M. Stone, MD[1], Ibrahim Aldoss, MD[5], Brian J. Ball, MD[5], Jan Philipp Bewersdorf, MD

[1]Dana-Farber Cancer Institute [2]Yale Cancer Center, [3]Department of Biostatistics, Memorial Sloan-Kettering Cancer Center, [4]Memorial Sloan Kettering Cancer Center [5]City of Hope Medical Center

Background

- Treatment options for patients with AML have expanded with the approval of targeted therapies including FLT3 and IDH1/IDH2 inhibitors and venetoclax-based therapies.
- However, therapeutic efficacy based on alternate sequencing of these agents is not well described

Objective

- To describe the efficacy of targeted therapies following venetoclax-based therapy and contrast it with the efficacy of venetoclax post targeted therapy in AML.

Materials & Methods

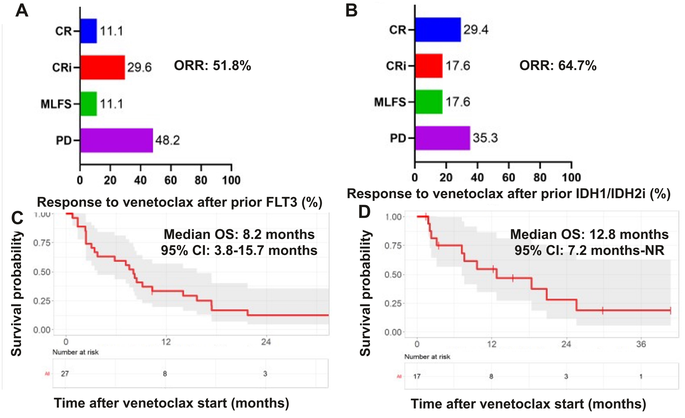
- Multicenter, retrospective cohort study
- Venetoclax after prior targeted therapy: 44 pts
- Targeted agent therapy after prior venetoclax: 53 pts
- ORR = CR + CRi + MLFS

Conclusion

- Venetoclax can be an effective salvage therapy in patients previously treated with targeted therapy.
- The FLT3 inhibitor gilteritinib retains clinical efficacy post venetoclax failure
- IDH1 and 2 inhibitors have very limited efficacy post venetoclax failure
- Future clinical trials will test triplet combination therapy

Venetoclax therapy after prior targeted agents

	Total (N=44)	FLT3 (N=27)	IDH1/2 (N=17)
Patient age (years) Median (R)	63 (29-90)	63 (29-90)	63 (29-90)
ELN risk			
Favorable	8 (18%)	5 (19%)	3 (18%)
Intermediate	16 (36%)	10 (37%)	6 (35%)
Adverse	20 (45%)	12 (44%)	8 (47%)
Disease status before targeted therapy			
Newly diagnosed AML	10 (23%)	8 (30%)	2 (12%)
R/R AML	34 (77%)	19 (70%)	15 (88%)
Targeted agent			
Ivosidenib	5 (11%)	0	5 (29%)
Enasidenib	12 (27%)	0	12 (71%)
Gilteritinib	14 (30%)	14 (52%)	0
Midostaurin	8 (20%)	8 (30%)	0
Sorafenib	2 (5%)	2 (7%)	0
Quizartinib	1 (2%)	1 (4%)	0
Crenolanib	2 (5%)	2 (7%)	0
Targeted agent combination therapy			
Targeted agent monotherapy	28 (64%)	13 (48%)	15 (88%)
Targeted agent + intensive chemotherapy	12 (27%)	12 (44%)	0
Targeted agent + non-intensive therapy	4 (9%)	2 (7%)	2 (12%)
Venetoclax based therapy			
azacitidine + venetoclax	16 (36%)	11 (41%)	5 (29%)
decitabine + venetoclax	22 (50%)	13 (48%)	9 (53%)
ASTX727 + venetoclax	1 (2%)	1 (4%)	0
low dose Ara-C + venetoclax	5 (11%)	2 (7%)	3 (18%)



Targeted agent therapy after prior venetoclax therapy

	Total (N=53)	FLT3 (N=31)	IDH1/2 (N=22)
Patient age (years) Median (R)	74 (37-89)	73 (37-89)	74 (37-88)
ELN risk			
Favorable	9 (17%)	7 (23%)	2 (9%)
Intermediate	15 (28%)	6 (19%)	9 (41%)
Adverse	27 (51%)	16 (52%)	11 (50%)
Disease status at time of venetoclax			
Newly diagnosed AML	31 (58%)	21 (68%)	10 (45%)
Relapsed or refractory AML	22 (42%)	10 (32%)	12 (55%)
Prior treatment before venetoclax			
Intensive chemotherapy	16 (30%)	9 (29%)	7 (32%)
HMA	7 (13%)	2 (6%)	5 (23%)
Targeted agent monotherapy	3 (6%)	0	3 (14%)
Allo-HCT	2 (4%)	2 (6%)	0
None	30 (57%)	20 (65%)	10 (45%)
Disease status at time of targeted therapy			
Newly diagnosed AML	0	0	0
R/R AML	53 (100%)	31 (100%)	22 (100%)
Targeted agent			
Ivosidenib	5 (9%)	0	5 (23%)
Enasidenib	17 (32%)	0	17 (77%)
Gilteritinib	27 (51%)	27 (87%)	0
Midostaurin	2 (4%)	2 (6%)	0
Sorafenib	2 (4%)	2 (6%)	0
Quizartinib	0	0	0
Crenolanib	0	0	0

