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615.ACUTE MYELOID LEUKEMIAS: COMMERCIALLY AVAILABLE THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Gilteritinib and Venetoclax for Relapsed/Refractory FLT3-Mutated Acute Myeloid Leukemia - a Real-World Multicenter Retrospective Study

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Introduction: Relapsed/Refractory (R/R) FLT3-mutated AML is a challenging clinical scenario with a dismal outcome. Gilteritinib, a selective and potent oral FLT3 tyrosine kinase inhibitor (TKI), is approved for treatment of FLT3 mutated R/R AML, and was shown to improve response rates and overall survival (OS) as compared to standard chemotherapy (Perl et al, NEJM 2019). However, remission rates and long-term survival with gilteritinib monotherapy are still unsatisfactory, highlighting the need for new therapies to improve patient outcomes.
Recently, the combination of gilteritinib and venetoclax (Gilt-Ven) was shown to achieve a response rate of 75% in R/R FLT3 AML patients (Daver et al, JCO 2022). Data regarding Gilt-Ven based combinations in patients outside of clinical trials is lacking. We therefore aimed to investigate the characteristics and outcomes of real-world patients with R/R FLT-3 mutated AML treated with Gilt-Ven based combinations.
Methods: A multicenter retrospective cohort study in seven academic centers in Israel. Demographic, clinical and treatment related data were collected. The decision to treat a patient with Gilt-Ven (with or without azacitidine) as well as dosing were at discretion of the treating physician.
Results: Eighteen patients were treated with Gilt-Ven based therapies for FLT-3 mutated R/R AML between January 2018 and June 2023. Median follow-up time was 5 months (range 0-24). Median age at treatment initiation was 48 years (range 24-79). Twelve patients (66.7%) had relapsed disease, while 6 (33.3%) had refractory disease. Thirteen patients (72.2%) had a normal karyotype; two had complex karyotype and one had monosomal karyotype. Sixty-one percent had prior therapy with a FLT3 inhibitor, and 33% had prior venetoclax exposure. Eighty-eight percent received a prior intensive induction regimen and 61% had prior Allogeneic Hematopoietic Stem Cell Transplantation (AlloHSCT) (Figure 1A).
Most patients received Gilt-Ven doublet, while 27% received Gilt-Ven in combination with other agents (three patients with azacitidine, one with low-dose cytarabine and one with FLAG-IDA). The median dose for gilteritinib was 120 (range, 80-120) mg and all patients received 400 mg venetoclax (or equivalent dose adjustment to azoles).
Overall Response Rate (CR+CRi+MLFS) was 83%; Complete remission rate was 50% (Figure 1B). The median number of cycles was 1.5 (range 1-34) for the whole cohort. Five patients (27%) proceeded to alloHSCT. Of these, four patients required one

course of Gilt-Ven, and one patient received 6 courses and proceeded to AlloHSCT after a subsequent relapse and another line of therapy. Median OS was not reached for all patients (range 6-NR), but was only 6 months (range 0-10) for patients who did not proceed to AlloHSCT. Hematologic adverse events were most common with 89% of patients experiencing grade 3/4 neutropenia; however, infections were relatively uncommon with only 17% of patients experiencing grade 3/4 Infection. Transaminitis grade 1/2 was observed in 38.9% of patients while no patient developed grade 3/4. No cases of differentiation syndrome were recorded.

Conclusion: In a real-world setting, Gilt-Ven based therapy is effective for heavily pre-treated patients with FLT-3 mutated R/R AML, especially as a bridge to AlloHSCT.

Disclosures Ram: *MSD:* Honoraria; *BMS, Takeda, Sanofi, Pfizer:* Honoraria; *Novartis:* Honoraria, Research Funding; *Gilead:* Honoraria. **Nachmias:** *Medison:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria; *Astellas:* Consultancy, Honoraria. **Raanani:** *Janssen:* Consultancy, Research Funding; *BMS:* Consultancy, Research Funding; *Pfizer:* Consultancy, Research Funding; *Novartis:* Consultancy, Research Funding. **Wolach:** *Abbvie:* Consultancy, Honoraria, Research Funding; *Astellas:* Consultancy, Honoraria; *Medison:* Honoraria.

OffLabel Disclosure: Gilteritinb is a selective and potent oral FLT3 tyrosine kinase inhibitor (TKI) approved for treatment of FLT3 mutated R/R AML. Venetoclax is an oral BCL-2 inhibitor currently approved as part of different treatment regimens for AML, most commonly given in combination with azacytidine as induction therapy in patients who are ineligible for intensive chemotherapy-based induction. Their combination was recently shown to achieve a response rate of 75% in R/R FLT3 AML patients (Daver et al, JCO 2022). In our study we aimed to investigate the characteristics and outcomes of real-world patients with R/R FLT-3 mutated AML treated with Gilt-Ven based combinations.

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Figure 1 – Patient Characteristics and Response

A Patient Demographics and Baseline Characteristics

	Total (n=18)				
Gender		**FLT3 Mutation Type**		**Prior Lines of Therapy**	
Male	9 (50%)	ITD	15 (83.3%)	1	6 (33.3%)
Female	9 (50%)	TKD	1 (5.6%)	2	7 (38.9%)
Age (years)		Both	1 (5.6%)	3	4 (22.2%)
Mean (SD)	50.2 (20.0)	Unknown	1 (5.6%)	4	1 (5.6%)
Median (range)	48 (24-79)	**FLT3 Mutation Status**		**Prior FLT3 TKI**	
Disease Status		De Novo	12 (66.7%)	None	7 (38.9%)
Relapse	12 (66.7%)	At relapse	6 (33.3%)	Sorafenib	2 (11.1%)
Refractory	6 (33.3%)	**Risk Category**		Midostaurin	9 (50%)
Secondary AML	3 (16.7%)	Favorable	1 (5.6%)	**Prior Venetoclax**	6 (33.3%)
		Intermediate	11 (61.1%)	**Prior AlloHSCT**	
		Adverse	6 (33.3%)	HSCT in CR1	10 (55.6%)
				HSCT in R/R	1 (5.6%)

B Treatment Response

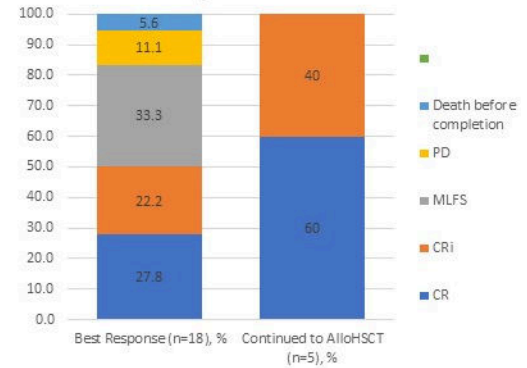

Figure 1