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615.ACUTE MYELOID LEUKEMIAS: COMMERCIALY 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

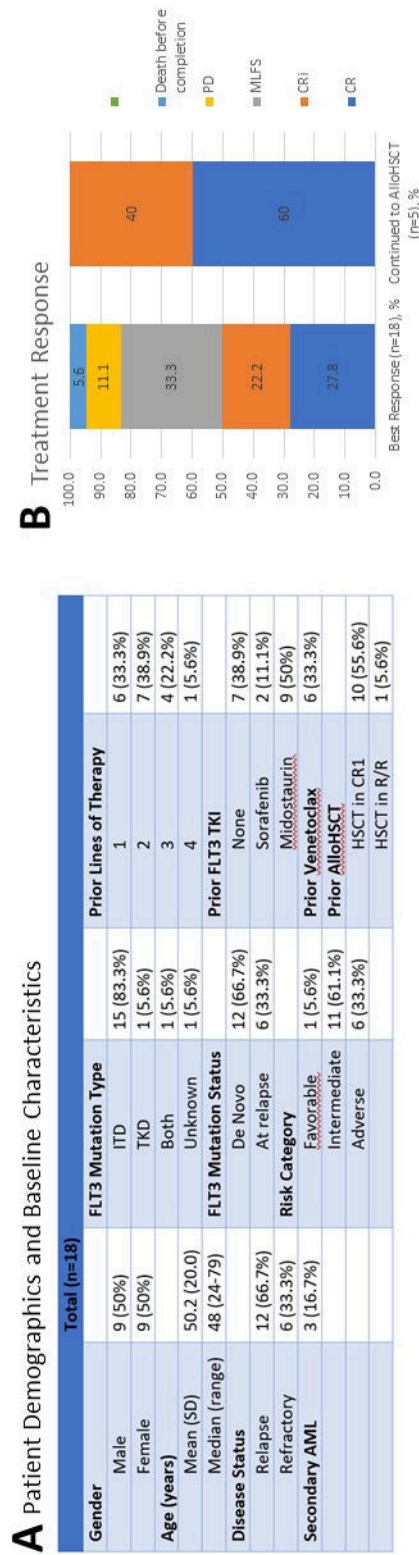


Figure 1