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POSTER ABSTRACTS

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

Real World Outcome of Unfit Patients with Acute Myeloid Leukemia Treated with the Combination Venetoclax Plus Hypomethylating Agents in the Gimema AML2320 Observational Trial

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Introduction:
Based on the results of the phase 1b (NCT02203773) and phase 3 (VIALE-A; NCT02993523) studies, venetoclax (VEN) in combination with hypomethylating agents (HMAs) was approved by FDA and EMA for the treatment of patients (pts) with newly diagnosed (ND) acute myeloid leukemia (AML) who are ineligible for intensive chemotherapy (IC) or whose age is 75 years or more. In particular, in the VIALE-A trial the association Ven+Azacitidine (AZA) has proven to induce rapid and durable remissions, with a median overall survival (OS) of 14.7 vs 9.6 months of pts enrolled in the placebo+Aza arm. The GIMEMA 2320 Trial (NCT04589728) is a prospective, observational study intended to investigate the outcome of pts treated with the combination Ven+HMA, in a real-world setting.

Methods:
Pts not candidate to IC because of age (≥75 years), performance status (PS) or comorbidities according to the SIE/SIES/GITMO (Ferrara) criteria, were eligible to the AML2320 trial and to receive the combination HMA plus venetoclax. VEN (400 mg a day, orally, day 1-28), AZA (75 mg/m ^{2} a day, day 1-7) and Decitabine (DEC) (20 mg/m ^{2} a day, day 1-5) were given at conventional doses during a 28-day cycle. Evaluation of OS was the primary end-point of the trial; response rate, time to response, event free survival (EFS), disease free survival (DFS), cumulative incidence of relapse (CIR), and safety profile were secondary end-points.

Results:
From November 2020 to December 2021, 188 pts were enrolled to the observational trial with 178 being evaluable at the time of this analysis. Ninety-six (54%) males and 82 (46%) females; median age 74 years (49-85) with 74 (42%) pts being 75 years old or more. One-hundred and 20 (68%) pts had " *de novo*" AML and 58 (32%) secondary AML. In pts below the age of 75 years, reasons that contraindicated exposure to IC were: pulmonary diseases (6%), active infections poorly controlled with antibiotic therapy (5%); cardiac ejection fraction < 50% (4.5%), ECOG PS ≥ 3 not related to the underlying AML (4%); psychiatric illnesses requiring specific therapy (3%). In 54% of the pts below the age of 75, there was also a miscellanea of other conditions which physicians recognized as incompatible with IC. ELN2017 risk-category assignment was feasible in 151 pts with 34 (23%), 69 (46%) and 48 (32%) belonging to the favorable, intermediate and adverse category, respectively. One-hundred and 34 (75%) pts received VEN+AZA and 44 (25%) VEN+DEC. The median no. of delivered courses was 5 (1-27). Eleven (6%) pts were submitted to an allogeneic stem cell transplant after having received 4 courses of VEN+HMA and being in CR/CRi. After the first course, response assessment was evaluated in 123/178 (69%) pts with 70 (57%) being in CR/CRi. One-hundred and 53 pts were given a second course, and response assessment was available in 73; at this stage, 47/73 (64%) were in CR/CRi. With a median follow-up of 19.9 months, the median OS for the whole population is 14.2 months (12.4-18.4) (Figure 1A) and the median DFS 13.7 months (10-NR) (Figure 1B). One- and 2-year OS is 58% (51%-67%) and 33% (26%-43%), respectively; 1- and 2-year DFS is 53% (42%-67%) and 44% (33%-59%), respectively. No significant differences were found in OS and DFS when the survival analysis was split by age (< or ≥ 75 years). Median OS for favorable-, intermediate- and adverse-risk category was 24.5 months (14.2-NR), 15.4 months (11.9-NR) and 8.9 months (6.8-13.4), respectively. Median DFS for favorable-, intermediate- and adverse-risk category was NR (10.8-NR), 14.1 months (8-NR) and 9.9 months (3.2-NR), respectively.

Conclusions:
To our knowledge this is one of the largest series of pts with AML treated with VEN+HMA in a real-world setting. With all the limitations of a data collection still to implement, we reported for this Italian cohort of pts a median OS that is similar to that observed in the VIALE-A study (14.2 vs 14.7 months); also, our median follow-up is similar to the one of the VIALE-A study, at the time of its publication (19.9 vs 20.5 months). This real-life experience confirms that the combination VEN+HMA is an effective treatment for a very difficult to treat population of pts. This analysis also denotes the need for educational activities intended to sensitize physicians towards a more appropriate and timely evaluation of response; indeed, a sizeable proportion of Italian hematologists still approach assessment of response to VEN+HMA the same way they did when using HMA alone.

Disclosures Venditti: *Medac:* Consultancy; *Novartis:* Consultancy, Honoraria, Other: travel support ; *Janssen:* Consultancy, Honoraria, Other: travel support ; *AbbVie:* Consultancy, Honoraria, Other: travel support ; *Jazz:* Consultancy, Honoraria, Other: travel support ; *Amgen:* Consultancy, Honoraria, Other: travel support ; *Pfizer:* Consultancy, Honoraria, Other: travel support , Speakers Bureau. **Frigeni:** *AbbVie:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Jazz Pharmaceutical:* Honoraria. **Palmieri:** *Pfizer:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria; *Jazz:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria. **Borlenghi:** *Amgen, Incyte:* Other: travel grants; *AbbVie, BMS:* Consultancy. **Fracchiolla:** *AbbVie, Jazz, Pfizer, Amgen:* Other: Travel grants, Speakers Bureau. **Martelli:** *Jazz Pharmaceuticals:* Consultancy, Honoraria; *Pfizer:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria; *BMS:* Consultancy, Honoraria; *Laboratoires Delbert:* Consultancy, Honoraria. **Vetro:** *BMS:* Honoraria; *Jazz Pharmaceuticals:* Honoraria; *ABBVIE:* Honoraria. **Curti:** *Novartis:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Membership on an entity's Board of Directors or advisory committees. **Mulè:** *Astellas:* Honoraria; *Pfizer:* Honoraria; *Incyte:* Honoraria; *ABBVIE:* Honoraria. **Breccia:** *Pfizer:* Honoraria; *Incyte:* Honoraria; *BMS:* Honoraria; *AbbVie:* Honoraria; *AOP:* Honoraria; *Novartis:* Honoraria. **Fozza:** *BMS:* Research Funding; *Amgen:*

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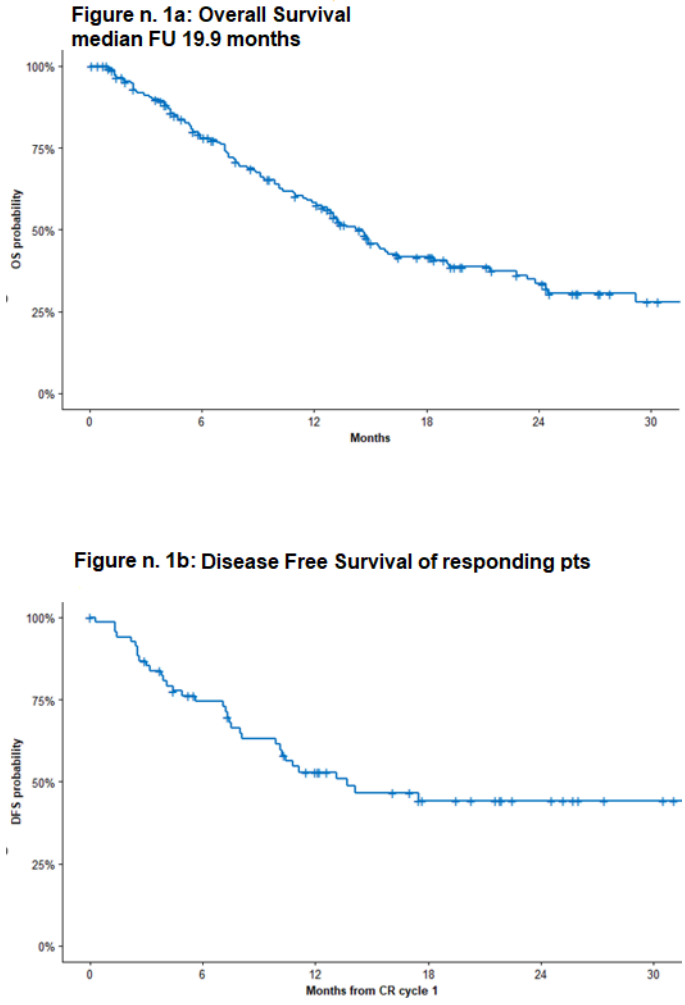

Figure 1

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