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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

LONG-TERM Outcomes after Venetoclax-Hypomethylating Agent Combination Therapy Discontinuation, in Patients with ACUTE Myeloid Leukemia. Experience of a Single Center

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BACKGROUND The combination of azacitidine and venetoclax has become the standard of care in patients with acute myeloid leukemia (AML) who are not eligible for intensive chemotherapy (*Di Nardo et al. N Engl J Med 2020; 383:617-629*). Despite being considered a low-intensity treatment, long-term administration of venetoclax based combinations treatment can be challenging due to a multitude of factors, ranging from drug-related toxicity to logistical and quality of life obstacles often bringing to dose adjustments or discontinuation.

AIM We analyzed long-term outcomes of patients with AML treated with venetoclax in combination with hypomethylanting agents who required discontinuation of treatment, after reaching complete remission (CR), due to toxicity or patient decision treated at the Institut Català d'Oncologia-Hospital Duran i Reynals.

METHODS Observational and retrospective study that includes patients diagnosed with AML who received treatment with venetoclax in combination with hypomethylating agents as first line or as salvage therapy, between May 2019 and April 2023. Bone marrow was analyzed pre-treatment for somatic mutations via targeted next-generation sequencing (NGS).

RESULTS 68 patients were included in the study. The median age at diagnosis was 75 years (range 33-85 years), with a predominance of males (69%). Twenty-eight (41.2%) patients were classified according to the 2022 ELN classification as an adverse risk, 33 (48.5%) as intermediate risk and 7 (10.3%) as a favourable risk subgroup. Forty-eight (70.6%) patients received the combination as first line treatment and 20 (29.4%) as salvage therapy. No significant differences were found between the two groups regarding sex, age or ELN2022 risk. The median number of cycles received was 7 (range 1-23 cycles). The overall response rate (ORR) was 76.5% (52 of 68 patients), of which 46 (68%) patients achieved a composite CR (CRc) (CR, CR with partial hematologic recovery, and CR with incomplete hematologic recovery). Among the 52 responding patients, 88.5% of

the patients obtained the best response in the first 2 treatment cycles. Median overall survival (OS) and event-free survival (EFS) of the series were 12.7 and 10.9 months, respectively. 30 days mortality was 7.7% (3 patients due to infectious event and 1 patient due to progression). Seven of the 52 responding patients (13.5%) discontinued treatment after achieving CRc. The median number of cycles received prior to discontinuation was 2 (range 1-11 cycles). The reasons for treatment discontinuation were: patient decision (4), grade 4 myelotoxicity (2) and recurrent infections (1). Pre-treatment NGS data (n=7) from the patients who discontinued the treatment showed a median of 4 (range 2-9) mutations with a predominance of mutations in genes that encode epigenetic modifiers (*DNMT3A* n=4 and *TET2* n=3). *RUNX1* mutation was also frequently seen at diagnosis in 3 patients. The median follow-up from the end of treatment until last visit or dead was 8.1 (3.5-10.0) months. Two of the 7 patients have died during the treatment-free period, one of them due to non-haematological cause and the other one due to disease relapse. This last patient had a *TP53* mutation (VAF 78%), and the observation period without treatment for this patient was 8.5 months. No other patients had a *TP53* mutation. Median EFS and OS of patients who discontinued treatment were 7.3 and 8.5 months, respectively. No statistically significant difference was observed in OS of the responding patients according to treatment discontinuation or not (Figure 1).

CONCLUSION Our findings confirm the high efficacy of venetoclax and azacitidine combination in AML. Discontinuation of treatment in responding patients was associated with similar durable responses and OS compared to patients who continue under treatment. Identifying the subgroup of patients who may benefit from de-escalation strategies is mandatory. Further studies are needed to determine which patients might be appropriate for treatment suspension or discontinuation while in remission.

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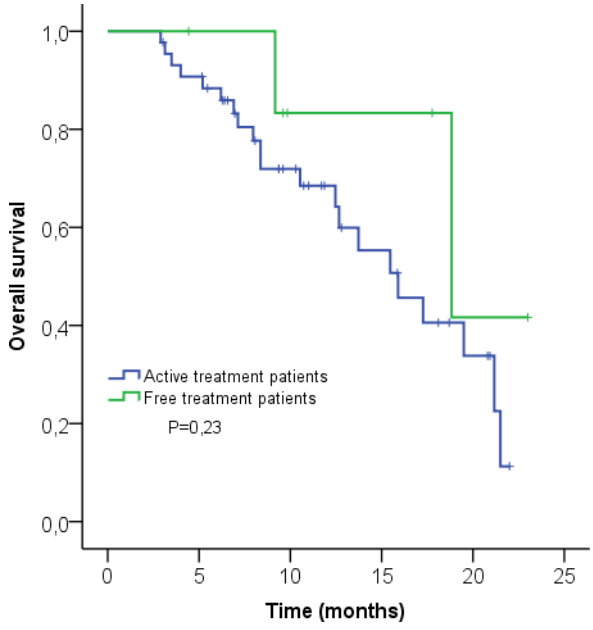

Figure 1

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