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FLAVIDA CHEMOTHERAPY INDUCES MRD-NEGATIVE REMISSION IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA

Topic: 04. Acute myeloid leukemia - Clinical

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Background:

Treatment options for relapsed and refractory (R/R) AML patients are limited. Here, we report safety and efficacy data of a novel combination therapy consisting of the BCL-2 inhibitor venetoclax (VEN) with fludarabine, cytarabine, and idarubicin in patients with R/R acute myeloid leukemia (AML).

Aims:

To assess MRD response, event-free (EFS) and overall survival (OS) of a seven-day course of venetoclax in combination with standard intensive FLA-IDA chemotherapy (FLAVIDA) in patients with R/R AML reported to the venetoclax registry (NCT03662724; venreg.org).

Methods:

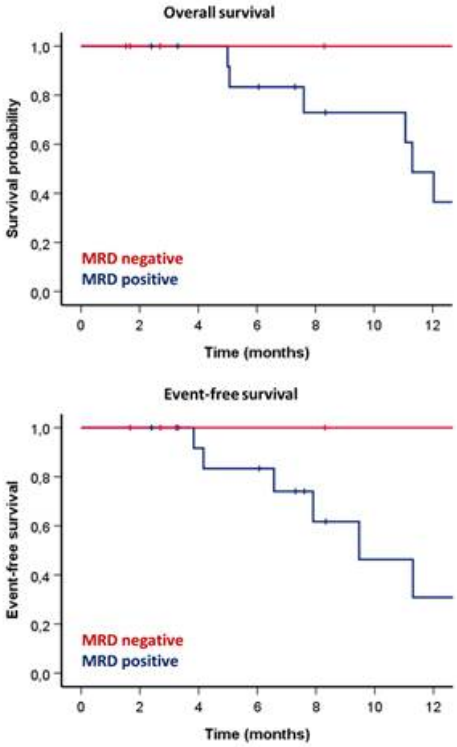
In this retrospective controlled study, we included 30 patients aged 18 years or older with R/R AML previously treated with FLAVIDA. VEN dosing was 100 mg/day orally (days 1–7) due to comedication with posaconazole. Safety and efficacy analyses included all patients who received one cycle of FLAVIDA. The overall response rate (ORR) was defined by complete remission (CR) + CR with incomplete blood count recovery (CRi) + morphologic leukemia-free state (MLFS, defined as less than 5% blasts in an aspirate sample without hematologic recovery). MRD was determined by NGS-MRD with a sensitivity of 0.02% (Thol et al. Blood 2018). This study was approved by the local Ethics Review Committee in accordance with the Declaration of Helsinki. The data cut-off for this analysis was February 9th, 2021.

Results:

Thirty patients with a median age of 54 years (range 19-70 years) received a maximum of 1 course FLAVIDA. 33% of patients had secondary or therapy-related AML. ELN risk was favorable, intermediate, and adverse in 13%, 57%, and 30% of patients. Patients received a median of 1 (range 1-5) prior lines of therapy and 27% of patients had prior allogeneic hematopoietic cell transplantation (alloHCT). ORR was 73% (22 of 30 patients), with 60% of patients (n=18) achieving a CR/CRi, while the 4 MLFS patients underwent alloHCT before blood count recovery and achieved CR only after alloHCT. Molecular MRD negativity was achieved in 8 of 17 (47%) responding patients with known molecular MRD markers. 75%, 71%, and 78% of patients with ELN favorable, intermediate and adverse risk disease achieved an overall response, respectively. One patient died before response assessment. Nineteen patients (63%) were consolidated with alloHCT, four received chemotherapy, three received donor lymphocyte infusions, and four patients received no additional treatment. After a median follow up of 13.3 months, median OS and EFS of the 30 patients was 12 months and 9.5 months, respectively. Median relapse-free survival in CR/CRi patients was not reached. In the 17 patients with available MRD data, the median OS and EFS were longer in patients who achieved a MRD negative response (OS: MRD- vs. MRD+: NR vs. 11.3 months, P= 0.048; EFS: MRD- vs. MRD+: NR vs. 9.5 months, P=0.038, Figure 1). In patients who responded to FLAVIDA, the median time from the first day of chemotherapy to recovery of neutrophils (≥0.5x10^9/L) and platelets (≥50x10^9/L) was 33 (95% CI, 30-36) and 35 days (95% CI, 31-39), respectively. The most common grade 3/4 all-causality events were neutropenic fever (71%) and bacteremia (32%), while thrombocytopenia, anemia, and neutropenia were reported in all patients at nadir

(100%).

Image:



Summary/Conclusion:

Short-term VEN can be safely administered in combination with intensive chemotherapy in younger fit adults with AML with tolerable safety-profile, a high ORR rate of 73%, MRD negativity in 47% of responding patients, and promising survival in MRD negative patients.

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