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POSTER ABSTRACTS

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

Cladribine, High-Dose AraC, Plus Gemtuzumab Ozogamicin (CLAG-GO) As Frontline Intensive Therapy for Fit Patients with Core-Binding Factor Acute Myeloid Leukemia: Preliminary Results

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Background: Core-binding factor (CBF) acute myeloid leukemias (AML) are associated with favorable outcomes when treated with intensive therapy regimens, particularly based on high-dose cytarabine. In addition, gemtuzumab-ozogamicin (GO) added to frontline chemotherapy showed improved survival in patients with CBF-AML in a meta-analysis of five randomized trials (Hills RK, et all. 2014). Since then, GO has been incorporated to the intensive regimen [traditional '3+7' or fludarabine-cytarabine and GCSF (FLAG)] and has become the standard approach for CBF-AML.
Methods: Fit patients with newly diagnosed AML with inv(16) or t(16;16), *CBFB::MYH11* [AML -inv(16)] and AML with t(8;21), *RUNX1::RUNX1T1* [AML -t(8;21)] were eligible to receive cladribine, cytarabine, GCSF and GO (CLAG-GO) regimen as frontline intensive chemotherapy. We evaluated baseline patient's characteristics, disease features, and early molecular-response dynamics, including qPCR for each CBF-AML, along with count recovery after cycle 1 (C1) and 2 (C2). Response criteria were standard as defined by the European Leukemia Net (ELN) 2022.
Results: Fifteen patients (pts) diagnose with CBF-AML were included, with a median age 47 years (range, 20 - 66 years), 53% were males. Median WBC were 15.5x10^9/L (range, 2.4 - 103). Eleven pts (73%) had AML -inv(16) and 4 pts (27%) had AML -t(8;21). Nine of 11 AML -inv(16) had a *CBFB::MYH11* fusion transcript variant A and 2 of 11 pts had a *CBFB::MYH11* fusion transcript variant non-A. Median CBF transcript level by qPCR at diagnose was 54.5% (range, 29.5 - 63.6) for AML -inv(16) and median qPCR of 100% (range, 100 - 100) for AML -t(8;21). Median number of co-mutations was 2 (range, 0 - 5), commonly kinase signaling mutations in components of the RAS/MAPK pathway (Figure 1). All pts received induction therapy with cladribine 5mg/m2 (D1-D5), cytarabine 2g/m2 (D1-D5), GCSF (D1 and D5) and GO 3mg/m2 (D1 or D2). If responses were achieved, subsequent consolidation cycles (up to 6 cycles) could be given with CLAG-GO (CLAG on D1-D3 and GO on D1 of C3 and C5). Thirteen pts (87%) were evaluable after induction therapy. Of the 2 non-evaluable pts, one died during induction, and 1 patient is still receiving induction therapy at the last cut off. All pts (13/13) achieved a complete remission (CR) with full count recovery (complete remission -CR- 100%). Twelve of them had minimal residual disease (MRD) assessed by flow cytometry (FC), and 11/12 (91%) pts achieved MRD negative (MRD-ve). One patient had MRD positive (0.7%) after C1. In one patient, MRD is unavailable. Twelve of 15 pts were monitored using qPCR for variant A *CBFB::MYH11* or *RUNX1::RUNX1T1* in different times points throughout C1. One patient died and 2 pts carried non-A variant *CBFB::MYH11* fusion transcript hence qPCR was not available. Molecular MRD at D14 of C1 showed that 6/7 (86%) pts achieved qPCR <1, and by the end-of-induction 8/12 (67%) achieved qPCR <0.1 (Figure 2). There was 1 death (4-week mortality = 6%) during induction in a patient with intracranial bleeding secondary to thrombocytopenia and platelet-refractoriness. Thirteen of the 13 recovered their counts following C1, with median time to absolute neutrophil count (ANC) ≥1.0x10^9/L of 20 days (range, 13 - 23) and platelets ≥100x10^9/L of 21 days (range, 17 - 28). Ten pts received C2 of therapy in our institution. One patient was transferred to another hospital, one patient just finished induction therapy and 1 patient started consolidation regimen with FLAG-GO per physician discretion. Nine of 10 pts were evaluable after C2, and all them (100%) sustained a CR, all were MRD-ve by FC (including a patient that previously was positive) and 7 of 8 pts achieved qPCR <0.05. After C2, median days to ANC ≥1.0x10^9/L of 16 days (range, 0 - 27) and platelets ≥100x10^9/L of 21 days (0 - 37). In general, CLAG-GO was well tolerated in induction with only 1 patient

had grade 3 increased alanine transferase and 1 patient had grade 3 increased aspartate transferase (both related to GO), which resolved spontaneously; and 9 pts of 15 have had an episode of neutropenic fever (3 of them infection was proved). After a median follow-up of 5 months, overall survival is 92%.

Conclusions:CLAG-GO is highly effective and safe when treating CBF-AML as frontline therapy and seems encouraging treatment. More patients need to be treated and longer follow up is needed to confirm these preliminary results.

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Figure 1. Mutational landscape of patients with CBF-AML (n=15)

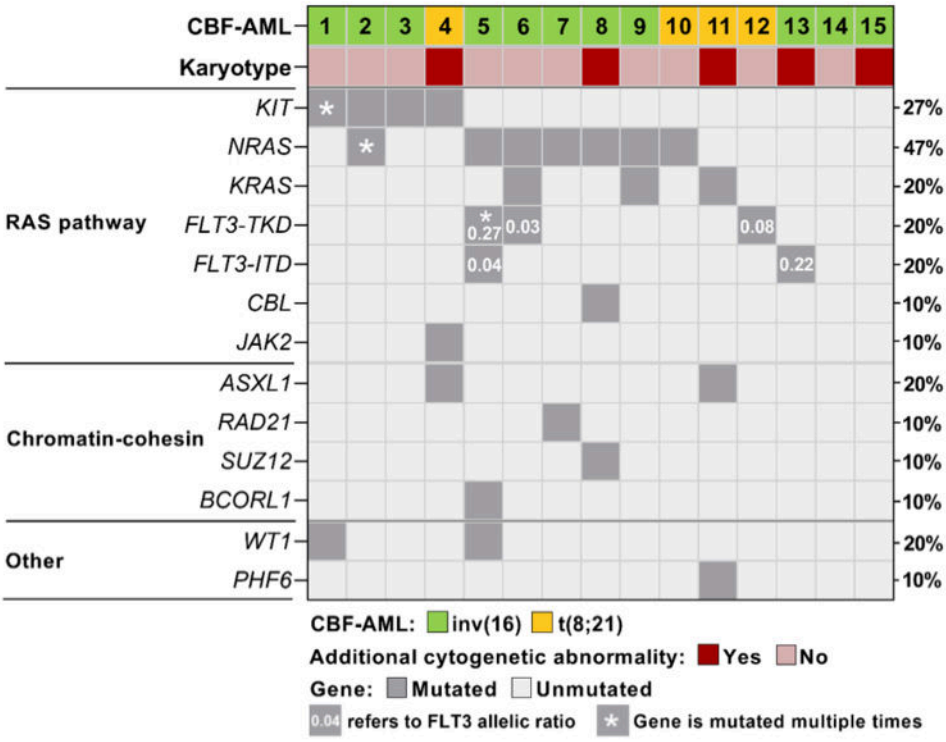

Figure 2. Early molecular-response dynamics using qPCR fusion transcript for CBF-AML (n=12)

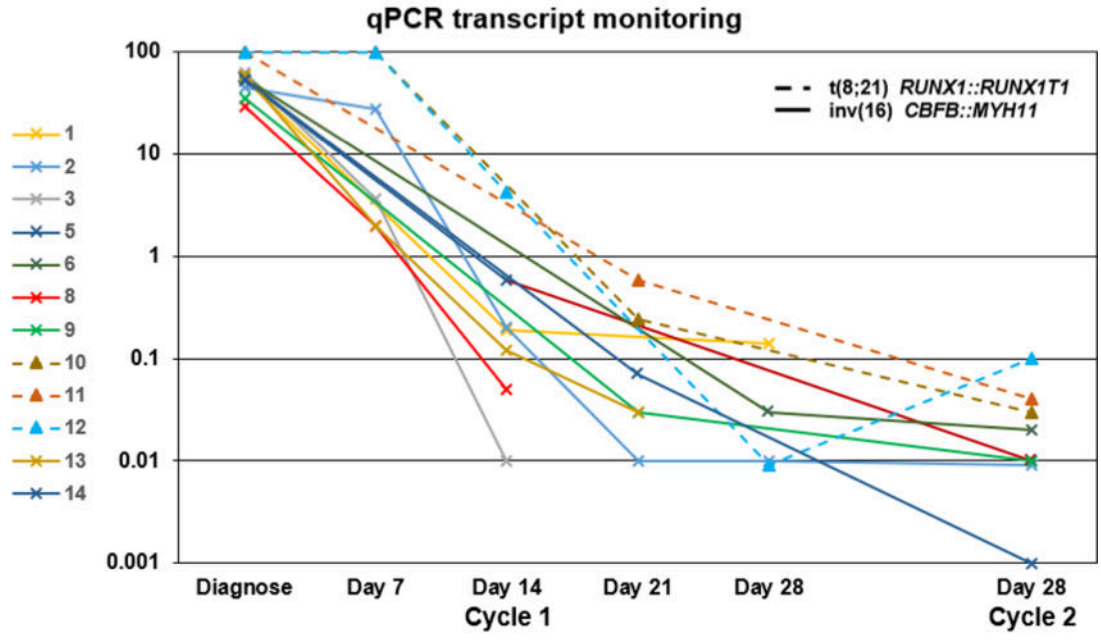

Figure 1

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