Abstract: P603

Title: PHASE II STUDY OF CLADRIBINE, IDARUBICIN, AND HIGHER DOSE CYTARABINE (CLIA) IN PATIENTS WITH RELAPSED AND/OR REFRACTORY (R/R) ACUTE MYELOID LEUKEMIA (AML)

Abstract Type: Poster Presentation

Topic: Acute myeloid leukemia - Clinical

Background:

Long term outcomes for patients with relapsed and/or refractory (R/R) AML are dismal, with a 5-year OS probability of 15% or less. Newer, more effective approaches are needed to achieve response and offer opportunity for allogeneic SCT. The addition of cladribine to cytarabine in AML is synergistic and has demonstrated improved OS in newly diagnosed AML.

Aims:

We studied a higher-dose araC-based regimen of Cladribine, Idarubicin, Cytarabine (CLIA) in patients with R/R* AML.

Methods:

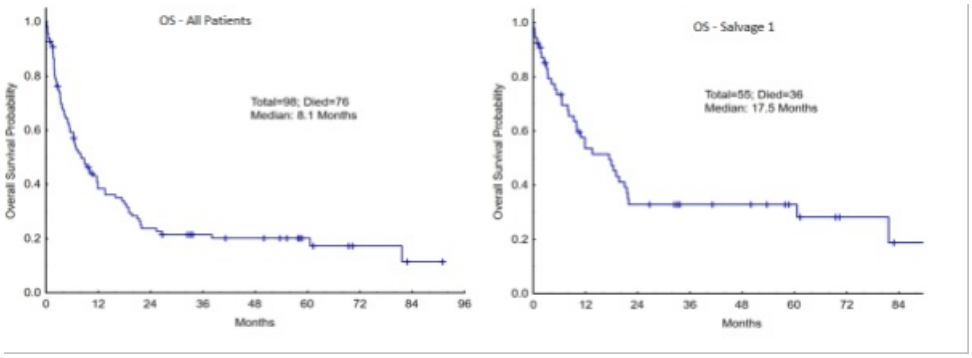
Patients aged 18-65 years, fit for intensive chemotherapy, with relapsed and/or refractory AML were enrolled. Induction was: Cladribine 5 mg/m2 IV on days 1-5, Cytarabine 1 (CLIA1)or 2 (CLIA2) g/m2 IV on days 1-5, Idarubicin 10 mg/m2 IV on days 1-3. Patients with FLT3-ITD mutated AML could receive sorafenib, midostaurin, or gilteritinib on days 1-14. Consolidation consisted of up to 5 more cycles of CLIA: cladribine 5 mg/m2 IV on days 1-3, Cytarabine 1000 - 750 mg/m2 IV on days 1-3, and idarubicin 8 mg/m2 IV on days 1-2. In FLT3-mutated pts, FLT3 inhibitor was given continuously during cycle 2 onward.

Results:

A total of 98 pts were enrolled, with a median age of 51 years (range, 19-65), including 66 (67%) and 32 (33%) receiving CLIA1 and CLIA2, respectively . 24 (24%), 38 (39%), 3 (3%), and 24 (24%) patients had adverse, diploid, favorable, and non-diploid intermediate karyotype, respectively. 31 (32%) pts received sorafenib, 6 (6%) pts gilteritnib, and 1 (1%) pt midostaurin in combination with CLIA for FLT3-mutated AML.** 55 (56%) pts received CLIA as their 1st salvage therapy and 43 (44%) were in salvage 2 (S2) and beyond (S2: 19, S3:13, S4+: 11). After a median of 1 (1-2) course to best response, the overall response rate was 42% (41/98), including 25 (26%) with complete remission (CR) and 16 (16%) CRi. Of the 41 pts who had CR/CRi, 25 (61%) were negative for MRD. Pts received a median of 1 (1-6) cycle of therapy and 21 of the 41 (51%) responders proceeded to SCT. The CR/CRi rates for CLIA1 and CLIA2 were 41% and 44%, respectively. The CR/CRi rates for pts in S1 and S2 and beyond were 53% and 28%, respectively. The median OS overall was 8.1 months, with 1 and 2-year OS rates of 38% and 23%, respectively. For pts in 1st salvage, the median OS was 17.5 months, with 1 and 2-year OS rates of 53% and 33%, respectively. For pts in salvage 2 or beyond, the median OS was 4.5 months, with 1 and 2-year OS rates of 25% and 13%, respectively. The median RFS for pts overall, S1, and S2 and beyond was 5.6, 92., and 3.1 months, respectively. The 4- and 8-week mortality rate was 8% and 10%, respectively.

Summary/Conclusion:

CLIA is an effective therapy for patients with relapsed and/or refractory AML who were receiving their first salvage therapy and may represent a valuable backbone regimen for combination strategies with novel agents. There was no difference in response rates between 1 or 2 grams of cytarabine as part of the CLIA regimen in pts with R/R AML.



Keywords: AML, Salvage chemotherapy, Cladribine, FLT3