OVERALL SURVIVAL (OS) AND CLINICAL OUTCOMES IN OLDER PATIENTS WITH ACUTE MYELOID LEUKEMIA (AML) TREATED WITH AZACITIDINE (AZA) OR INTENSIVE CHEMOTHERAPY (IC) IN THE AZA-AML-001 STUDY

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Abstract | Rate & Comment

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Background
There is no universally accepted approach to AML treatment (Tx) for older pts. IC is recommended for pts aged ≥60 years with favorable prognostic features (NCCN guidelines, 2014). However, many older pts can not tolerate IC. Such pts often receive low-dose cytarabine (LDAC), which is associated with a median OS of only ~5 months (Burnett, *Cancer*, 2007; Kantarjian, *JCO*, 2012). There is an unmet need for tolerable Tx options that prolong OS to a similar or greater extent than IC. The phase 3, randomized AZA-AML-001 study compared AZA with conventional care regimens (CCR) in older pts with AML. Before randomization, pts were preselected to receive 1 of 3 CCR per investigator choice of preferred Tx option: IC, LDAC, or best supportive care only. Pts were then randomized to receive AZA or CCR and received their preselected Tx.

Aims
To compare OS and clinical outcomes with AZA vs IC in the subgroup of pts in AZA-AML-001 preselected to receive IC before randomization.

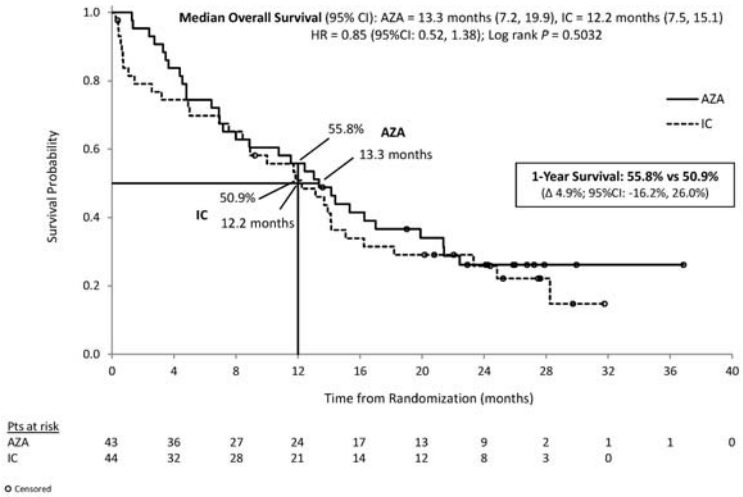
Methods
Pts aged ≥65 years with newly diagnosed *de novo* or secondary AML (>30% bone marrow [BM] blasts) and ECOG PS 0-2, WBC ≤15x10^9/L, and intermediate- or poor-risk cytogenetics were enrolled. Pts received IC (cytarabine IV x7days (d) + an anthracycline IV x3d, with ≤2 subsequent cycles) or AZA (75 mg/m^2/d SC x7d/28d cycle). OS and 1-year survival were estimated using Kaplan-Meier methods. OS was compared between Tx groups by log-rank test. Hazard ratios (HRs) and 95% CI are from an unstratified Cox proportional hazards model. Rates and durations of complete remission (CR) and CR with incomplete blood count recovery (CRi) (IWG 2003), and RBC transfusion independence (TI) in pts transfusion-dependent at baseline, were assessed. Rates of grade 3-4 treatment-emergent adverse events (TEAEs), defined as new or worsening AEs during Tx, were assessed. To account for differences in Tx exposure, TEAE incidence rates (IR) per 100 pt-years of Tx exposure are reported.

Results
Of all pts in AZA-AML-001 (N=488), 87 (18%) were preselected to receive IC (AZA n=43, IC n=44). Median number of Tx cycles of AZA was 8 (range 1–24) and of IC was 2 (1–3). At baseline in the AZA and IC groups, median ages were 71 yrs (AZA range 65–79, CCR 65–81); 16% and 18% of pts, respectively, had ECOG PS of 2; median BM blasts were 72% (7-100%) and 70% (6–100%); median WBC count was 3.8x10^9/L (1-15) and 2.2 x10^9/L (1-90); and 35% and 34% of pts had poor-risk cytogenetics. Median OS was comparable in the AZA and IC groups: 13.3 vs 12.2 months, respectively (HR=0.85 [95% CI 0.52, 1.38], p=0.5032) (**Figure**). One-year survival with AZA was 55.8% (95% CI 39.8%, 69.1%) vs 50.9% (35.2%, 64.6%) with IC (Δ4.9%; 95% CI -16.2%, 26.0%). In the AZA and IC groups, respectively, 30% and 36% of pts attained CR, and 12% and 11% achieved CRi. Median durations of CR+CRi in the AZA and IC groups were 17.3 (95% CI 3.7, not reached) and 19.8 (8.2, 26.3) months, respectively. RBC TI rates with AZA vs IC were 57% vs 35%, respectively. Proportions of pts with grade 3-4 TEAEs and [IRs] in the AZA and IC groups, respectively, were: anemia 12% vs 14% [14 vs 45]; neutropenia 30% vs 33% [37 vs 99]; febrile neutropenia 33% vs 31% [40 vs 92]; thrombocytopenia 23% vs 21% [29 vs 64]; and (any) infections 49% vs 50% [60 vs 149].

Summary
AZA and IC were associated with comparable OS, 1-year survival, and rate and duration of remission in these older pts with AML. AZA was better tolerated than IC, with lower incidence rates of hematologic TEAEs and infections. AZA may be a good option for older pts with AML who are fit for IC but choose not to undergo high-intensity Tx.

Keyword(s): Acute myeloid leukemia, Induction chemotherapy, Survival

Figure. Overall survival in patients preselected to intensive chemotherapy



Pts at risk											
AZA	43	36	27	24	17	13	9	2	1	1	0
IC	44	32	28	21	14	12	8	3	0		

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