56th ASH® Annual Meeting and Exposition
San Francisco, CA • December 6-9, 2014
ABSTRACTS & PROGRAM

-Author name in bold denotes the presenting author
-Asterisk * with author name denotes a Non-ASH member

denotes an abstract that is clinically relevant.

denotes that this is a recommended PHD Trainee Session.

denotes that this is a ticketed session.

Last updated November 6, 2014. Please note that this site represents the latest program changes and differs from the print version in some details.

621 Overall Survival in Older Patients with Newly Diagnosed Acute Myeloid Leukemia (AML) with >30% Bone Marrow Blasts Treated with Azacitidine By Cytogenetic Risk Status: Results of the AZA-AML-001 Study

Program: Oral and Poster Abstracts
Type: Oral
Session: 616. Acute Myeloid Leukemia: Novel Therapy, excluding Transplantation I

Monday, December 8, 2014: 5:00 PM

South Building, Gateway Ballroom 103 (Moscone Center)

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Background: Overall survival (OS) in older patients (pts) with AML and poor-risk cytogenetics is only ~2-3 months (mos) (Burnett, *Cancer*, 2007). Often these pts receive only palliative treatment (Tx) with best supportive care (BSC). Low-dose Ara-C (LDAC) provides no OS benefit in pts with poor cytogenetics (Döhner, *Blood*, 2010). Typically, intensive chemotherapy (IC) is either not suitable for older AML pts with poor cytogenetics or, when it is used, provides no OS benefit (Kantarjian, *Blood*, 2010). The phase 3, multicenter, randomized, open-label AZA-AML-001 trial showed azacitidine (AZA) Tx in older pts with newly diagnosed AML (>30% bone marrow [BM] blasts) prolonged median OS by ~4 mos vs conventional care regimens (CCR) (10.4 vs 6.5 mos; p=0.1009) and improved 1-year survival (46.5% vs 34.2%) (Dombret, *EHA*, 2014). Cytogenetic risk is a prognostic indicator in elderly AML and a frequent determinant of Tx approach and outcomes.

Objective: To determine the effect of Tx with AZA vs CCR on OS and 1-year survival in AZA-AML-001 pt subgroups based on cytogenetic risk classification.

Methods: Pts aged =65 years with newly diagnosed *de novo* or secondary AML who were ineligible for transplant, with intermediate- or poor-risk cytogenetics (pts with favorable cytogenetics were excluded from study), ECOG performance status 0-2, and WBC count =15x10^9/L, were eligible. Before randomization, each pt was preselected to receive 1 of 3 commonly used CCR for older pts with AML, per investigator choice: IC (standard 7+3 regimen), LDAC (20 mg SC BID x 10 days/28-day cycle), or BSC only. Pts were then randomized to AZA (75 mg/m^2/day SC x 7 days/28-day cycle) or to CCR, in which case they received their preselected Tx. The primary endpoint was OS. Cytogenetic risk groups were assessed per NCCN criteria by central review: intermediate (INT; all cases), intermediate with normal karyotype (cytogenetic normal [CN]), and poor. Survival at 1 year was compared between Tx. Median OS for AZA vs CCR was calculated using Kaplan-Meier methods, hazard ratios (HR) and 95% confidence intervals (CI) were determined by unstratified Cox proportional

hazards model, and p values by log-rank test.

Results: In all, 488 pts were randomized, 241 to AZA and 247 to CCR. Cytogenetic risk was balanced between Tx groups: 315 pts had INT-risk cytogenetics (AZA n=155 [64%], CCR n=160 [65%]), including 218 who were CN (AZA n=113 [73%], CCR n=105 [66%]), and 170 pts had poor-risk cytogenetics (AZA n=85 [35%], CCR n=85 [34%]). Within each of the 3 cytogenetic risk subgroups, the distribution of pts receiving individual CCR was very consistent: ~18% of each cytogenetic risk subgroup received BSC, ~64% received LDAC, and ~18% received IC. Baseline characteristics were generally balanced among the AZA and CCR Tx arms and the 3 cytogenetic risk groups (**Table**). At baseline, proportionately more pts with poor-risk cytogenetics in the AZA group were aged =75 years (57.6% vs 47.1% with CCR) and more pts in the CCR group had AML with myelodysplastic changes (45.9% vs 37.6% with AZA). Median OS (95%CI) in poor-risk pts was significantly prolonged with AZA vs CCR: 6.4 mos (4.2, 8.1) vs 3.2 mos (2.2, 4.7), respectively; HR=0.68 (0.50, 0.94), p=0.019 (**Figure**). Median OS in INT-risk pts was 13.0 mos (11.2, 16.3) vs 10.1 mos (7.1, 13.3) with AZA vs CCR; HR=0.90 (0.70, 1.16), p=0.41. Median OS in the CN subgroup was 14.1 mos (12.6, 19.5) vs 10.0 mos (6.4, 13.3); HR=0.81 (0.59, 1.10), p=0.18. Estimated 1-year survival was higher with AZA vs CCR in all cytogenetic risk subgroups. Twice the proportion of AZA-treated pts in the poor-risk subgroup were alive at 1 year vs. CCR pts (30.9% vs 14.0%, respectively), a clinically meaningful difference of 16.9% (95%CI 4.4, 29.5). Similarly, in the CN subgroup, 60.7% vs 44.1% of pts were alive at 1 year in the AZA and CCR groups, a difference of 16.5% (3.2, 29.8). AZA effect on 1-year survival in the INT-risk subgroup was also favorable (55.2% vs 45.5% with CCR) (difference 9.7% [-1.4, 20.8]). Grade 3-4 hematologic adverse event rates with AZA were consistent with previous reports (Santini, *Eur J Haematol,* 2010), with no meaningful differences among all cytogenetic risk groups.

Conclusions: Median OS in older pts with AML and poor-risk cytogenetics was meaningfully improved with AZA compared with the CCR currently used for AML, with those pts receiving AZA twice as likely to be alive at 1 year as those treated with CCR.

Table. Demographic and Disease Characteristics at Baseline and Study Drug Exposure

Baseline Characteristics	AZA*			CCR*		
	Intermediate (n=155)	CN (n=113)	Poor† (n=85)	Intermediate (n=160)	CN (n=105)	Poor† (n=85)
Age (years), median (range)	75 (65, 91)	75 (67, 89)	76 (64, 90)	76 (65, 89)	76 (65, 89)	74 (65, 87)
Age ≥75 years	56.8%	53.1%	57.6%	53.8%	53.3%	47.1%
Gender male, n (%)	84 (54.2)	59 (52.2)	55 (64.7)	105 (65.6)	66 (62.9)	43 (50.6)
AML classification, n (%)						
AML not otherwise specified	107 (69.0)	75 (66.4)	45 (52.9)	108 (67.5)	74 (70.5)	34 (40.0)
AML with myelodysplasia-related changes	43 (27.7)	34 (30.1)	32 (37.6)	44 (27.5)	28 (26.7)	39 (45.9)
Therapy-related myeloid neoplasms	5 (3.2)	4 (3.5)	3 (3.5)	7 (4.4)	3 (2.9)	5 (5.9)
AML with recurrent genetic abnormalities	0	0	5 (5.9)	1 (0.6)	0	7 (8.2)
Prior MDS, n (%)	31 (20.0)	25 (22.1)	18 (21.2)	22 (13.8)	12 (11.4)	16 (18.8)
% BM blasts,† % median (range)	72.5 (3, 100)	75.5 (5, 99)	68 (2, 100)	75 (4, 100)	76 (6, 100)	70.5 (8, 100)
ECOG PS, n (%)						
Grade 0-1	125 (80.6)	96 (85.0)	61 (71.8)	125 (78.1)	81 (77.1)	63 (74.1)
Grade 2	30 (19.4)	17 (15.0)	24 (28.2)	35 (21.9)	24 (22.9)	22 (25.9)

Duration of Treatment Exposure

Cytogenetics	Median (Range) Treatment Cycles§			
	AZA (n=236)	LDAC (n=153)	IC (n=42)	BSC (n=40)
CN	9 (1-28)	5 (1-25)	2 (1-3)	47 (8-245)
Intermediate	8 (1-28)	4 (1-25)	3 (1-3)	72 (8-535)
Poor	5 (1-26)	2 (1-21)	2 (1-3)	60 (6-127)

AZA = azacitidine; CCR = conventional care regimens; CN=cytogenetic normal; AML = acute myeloid leukemia; MDS = myelodysplastic syndrome; BM = bone marrow; ECOG PS = Eastern Cooperative Oncology Group performance status; Hgb = hemoglobin; WBC = white blood cell

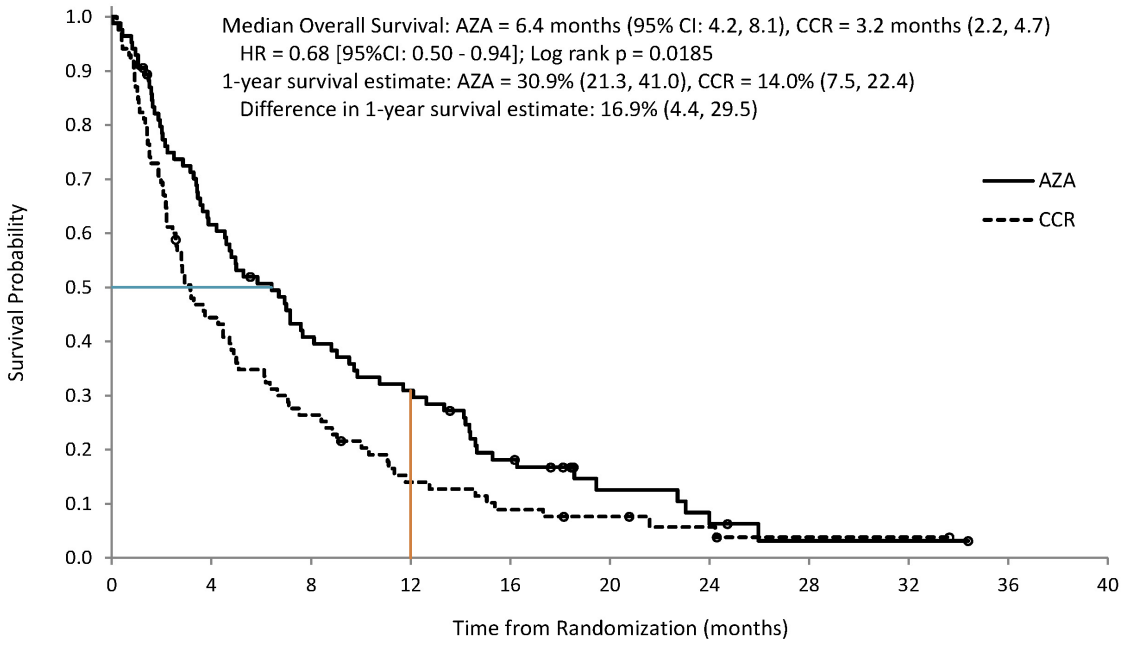
*Cytogenetic data missing for 1 AZA pt and 2 CCR pts.

†Centrally adjudicated

‡Poor-risk abnormalities included: Complex (≥3 abnormalities); -5; 5q-; -7; 7q-; 11q23 – non t(9;11); inv(3); t(3;3); t(6;9)

§AZA, LDAC, IC duration in cycles; BSC duration in days

Figure. OS in Patients with Poor-risk Cytogenetics



Pts at risk										
AZA	85	51	33	25	14	6	3	1	1	0
CCR	85	37	22	11	7	5	3	1	1	0

Censored

Disclosures: Döhner: *Celgene:* Consultancy. **Off Label Use:** Use of azacitidine in AML with blast count >30%. **Seymour:** *Celgene:* Consultancy, Honoraria, Speakers Bureau. **Wierzbowska:** *Celgene:* Honoraria, Speakers Bureau. **Selleslag:** *Celgene:* Consultancy, Research Funding, Speakers Bureau. **Cavenagh:** *Celgene:* Honoraria. **Kumar:** *Celgene:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Schuh:** *Celgene:* Membership on an entity's Board of Directors or advisory committees. **Candoni:** *Celgene:* Consultancy, Speakers Bureau. **Récher:** *Celgene:* Membership on an entity's Board of Directors or advisory committees, Research Funding. **Sandhu:** *Celgene:* Honoraria. **Bernal del Castillo:** *Celgene:* Consultancy. **Al-Ali:** *Celgene:* Honoraria, Research Funding. **Martinelli:** *Novartis:* Consultancy, Speakers Bureau; *BMS:* Consultancy, Speakers Bureau; *Pfizer:* Consultancy; *ARIAD:* Consultancy. **Falantes:** *Celgene:* Consultancy. **Stone:** *Celgene:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Minden:** *Celgene:* Honoraria. **McIntyre:** *Celgene:* Employment. **Songer:** *Celgene:* Employment, Equity Ownership. **Lucy:** *Celgene:* Employment, Equity Ownership. **Beach:** *Celgene:* Employment, Equity Ownership. **Dombret:** *Celgene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees.

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