LETTER TO THE EDITOR

# Survival outcomes with oral azacitidine maintenance in patients with acute myeloid leukemia in remission by receipt of initial chemotherapy: subgroup analyses from the phase III QUAZAR AML-001 trial

Andrew H. Wei,[1,2°] Gail J. Roboz,[3,4] Hervé Dombret,[5,6] Hartmut Döhner,[7] Andre C. Schuh,[8] Pau Montesinos,[9] Dominik Selleslag,[10] Sergey N. Bondarenko,[11] Thomas Prebet,[12] Yinzhi Lai,[12] Barry Skikne,[12,13] C.L. Beach[12] and Farhad Ravandi[14]

[1]Department of Clinical Hematology, The Alfred Hospital, Melbourne, Victoria, Australia; [2]Australian Center for Blood Diseases, Monash University, Melbourne, Victoria, Australia; [3]Weill Cornell Medicine, New York, NY, USA; [4]New York Presbyterian Hospital, New York, NY, USA; [5]Hematology, Hôpital Saint-Louis, Assistance Publique – Hôpitaux de Paris (AP-HP), Paris, France; [6]Institut de Recherche Saint-Louis, Université Paris Cité, Paris, France; [7]Department of Internal Medicine III, Ulm University Hospital, Ulm, Germany; [8]Princess Margaret Cancer Center, Toronto, Ontario, Canada; [9]Hospital Universitario y Politécnico La Fe, Valencia, Spain; [10]AZ Sint-Jan Brugge-Oostende AV, Bruges, Belgium; [11]RM Gorbacheva Research Institute, Pavlov University, St. Petersburg, Russia; [12]Bristol Myers Squibb, Summit, NJ, USA; [13]University of Kansas Cancer Center, Kansas City, KS, USA and [14]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

°*Current address*
*Department of Clinical Hematology, Peter MacCallum Cancer Center and Royal Melbourne Hospital, Melbourne, Vicoria, Australia.*

Correspondence:
A.H. WEI - andrew.wei@petermac.org

https://doi.org/10.3324/haematol.2022.282296

**Supplementary data for the manuscript titled:** Survival outcomes with oral azacitidine maintenance in patients with acute myeloid leukemia in remission by receipt of initial chemotherapy: subgroup analyses from the phase 3 QUAZAR AML-001 trial

**Supplementary Table S1.** Demographic and disease characteristics by randomized treatment arm and number of consolidation cycles received

| | Oral-AZA (N = 238) | | | | Placebo (N = 234) | | | |
|---|---|---|---|---|---|---|---|---|
| | No Consolidation n = 52 | Any Consolidation n = 186* | 1 Consolidation n = 110 | ≥ 2 Consolidations n = 76 | No Consolidation n = 42 | Any Consolidation n = 192* | 1 Consolidation n = 102 | ≥ 2 Consolidations n = 90 |
| **Age, median (range), years** | 71 (59–84) | 67 (55–86) | 68 (55–86) | 66 (55–75) | 70 (58–81) | 68 (55–82) | 68 (55–78) | 68 (55–82) |
| **WHO AML classification, n (%)** | | | | | | | | |
| Recurrent genetic abnormalities† | 10 (19) | 29 (16) | 15 (14) | 14 (18) | 7 (17) | 39 (20) | 18 (18) | 21 (23) |
| Myelodysplasia-related changes | 16 (31) | 33 (18) | 24 (22) | 9 (12) | 10 (24) | 32 (17) | 17 (17) | 15 (17) |
| Not otherwise specified | 26 (50) | 122 (66) | 71 (65) | 51 (67) | 25 (60) | 120 (63) | 66 (65) | 54 (60) |
| **De novo AML, n (%)** | 46 (88) | 167 (90) | 95 (86) | 72 (95) | 40 (95) | 176 (92) | 93 (91) | 83 (92) |
| **ECOG PS score, n (%)** | | | | | | | | |
| 0 | 21 (40) | 95 (51) | 58 (53) | 37 (49) | 20 (48) | 91 (47) | 56 (55) | 35 (39) |
| 1 | 24 (46) | 77 (41) | 44 (40) | 33 (43) | 19 (45) | 87 (45) | 36 (35) | 51 (57) |
| 2–3 | 7 (13) | 14 (8) | 8 (7) | 6 (8) | 3 (7) | 14 (7) | 10 (10) | 4 (4) |
| **Cytogenetic risk at diagnosis, n (%)** | | | | | | | | |
| Intermediate | 44 (85) | 159 (85) | 93 (85) | 66 (87) | 36 (86) | 167 (87) | 85 (83) | 82 (91) |
| Poor | 8 (15) | 27 (15) | 17 (15) | 10 (13) | 6 (14) | 25 (13) | 17 (17) | 8 (9) |
| **CR/CRi status at randomization, n (%)** | | | | | | | | |
| CR | 38 (73) | 145 (78) | 84 (76) | 61 (80) | 36 (86) | 141 (73) | 70 (69) | 71 (79) |
| CRi | 14 (27) | 37 (20) | 25 (23) | 12 (16) | 4 (10) | 40 (21) | 23 (23) | 17 (19) |
| Not in CR/CRi *or* Missing‡ | 1 (2) | 4 (2) | 1 (1) | 3 (4) | 2 (5) | 11 (6) | 9 (9) | 2 (2) |
| **Days from CR/CRi to randomization,§ median (range)** | 35.0 (7–128) | 88.0 (8–154) | 80.5 (8–154) | 92.5 (64–130) | 35.5 (7–125) | 88.5 (37–263) | 82.0 (37–263) | 92.0 (68–134) |
| **MRD status at screening, n (%)** | | | | | | | | |
| Negative | 30 (58) | 103 (55) | 58 (53) | 45 (59) | 15 (36) | 96 (50) | 49 (48) | 47 (52) |
| Positive | 21 (40) | 82 (44) | 51 (46) | 31 (41) | 26 (62) | 90 (47) | 52 (51) | 38 (42) |
| Missing | 1 (2) | 1 (1) | 1 (1) | 0 | 1 (2) | 6 (3) | 1 (1) | 5 (6) |
| **Reason(s) ineligible for HSCT,‖ n (%)** | | | | | | | | |
| Age | 41 (79) | 113 (61) | 77 (70) | 36 (47) | 33 (79) | 119 (62) | 66 (65) | 53 (59) |
| Comorbidities | 8 (15) | 44 (24) | 33 (30) | 11 (14) | 10 (24) | 40 (21) | 22 (22) | 18 (20) |
| No available donor | 9 (17) | 28 (15) | 8 (7) | 20 (26) | 7 (17) | 28 (15) | 14 (14) | 14 (16) |
| Patient decision | 1 (2) | 18 (10) | 9 (8) | 9 (12) | 5 (12) | 27 (14) | 16 (16) | 11 (12) |
| Performance status | 7 (13) | 7 (4) | 5 (5) | 2(3) | 3 (7) | 6 (3) | 3 (3) | 3 (3) |
| Unfavorable cytogenetics | 0 | 6 (3) | 1 (1) | 5 (7) | 1 (2) | 9 (5) | 4 (4) | 5 (6) |
| Other | 5 (10) | 23 (12) | 11 (10) | 12 (16) | 2 (5) | 19 (10) | 7 (7) | 12 (13) |

*Includes patients in the 1 Consolidation and ≥ 2 Consolidations cohorts. †Central assessment by flow cytometry, using a ≥ 0.1% MRD-positive threshold ("different-from-normal" method). ‡All patients must have been in CR/CRi at study screening; CR/CRi status was missing at randomization for two patients in the placebo arm. §Four patients were enrolled beyond the 4-month (± 7 days) inclusion window (protocol violations). ‖Individual patients may be accounted for across multiple categories.

AML, acute myeloid leukemia; CR, complete remission; CRi, CR with incomplete blood count recovery; ECOG PS, Eastern Cooperative Oncology Group performance status; HSCT, hematopoietic stem cell transplant; MRD, measurable residual disease; Oral-AZA, oral azacitidine; WHO, World Health Organization.

**Supplementary Table S2.** Median relapse-free and overall survival with Oral-AZA vs placebo by total number of induction and consolidation cycles received before study entry

| | Oral-AZA | Placebo | Oral-AZA vs Placebo | |
|---|---|---|---|---|
| | N = 238 | N = 234 | Difference [95% CI], months | HR [95% CI] |
| **1 induction, no consolidation, n (%)** | **38 (16)** | **35 (15)** | | |
| RFS, median [95% CI], months | 10.4 [7.7–25.1] | 3.9 [1.9–4.9] | +6.5 [0.6–12.5] | 0.47 [0.27–0.82] |
| OS, median [95% CI], months | 29.3 [13.4–45.3] | 10.8 [6.2–15.7] | +18.5 [3.5–33.5] | 0.48 [0.28–0.82] |
| **1 induction + 1 consolidation, n (%)** | **84 (35)** | **81 (35)** | | |
| RFS, median [95% CI], months | 9.8 [7.0–11.1] | 5.0 [4.0–7.6] | +4.9 [0.5–7.6] | 0.82 [0.58–1.17] |
| OS, median [95% CI], months | 19.4 [14.3–24.8] | 15.0 [12.2–24.3] | +4.3 [−2.6 to +11.3] | 0.91 [0.64–1.29] |
| **1 induction + ≥ 2 consolidations, n (%)** | **59 (25)** | **78 (33)** | | |
| RFS, median [95% CI], months | 13.0 [7.7–21.1] | 6.1 [4.6–7.7] | +6.9 [1.0–12.7] | 0.56 [0.37–0.85] |
| OS, median [95% CI], months | 28.6 [17.7–36.6] | 16.6 [11.6–27.0] | +12.0 [0.9–23.1] | 0.76 [0.49–1.17] |
| **≥ 2 inductions, no consolidation, n (%)** | **14 (6)** | **7 (3)** | | |
| RFS, median [95% CI], months | 4.2 [1.9–8.4] | 2.7 [0.4–9.2] | +1.5 [−3.5 to +5.6] | 0.66 [0.24–1.81] |
| OS, median [95% CI], months | 16.2 [8.9–37.2] | 11.6 [3.1–NE] | +4.7 [NE–NE] | 0.90 [0.31–2.61] |
| **≥ 2 inductions + ≥ 1 consolidation, n (%)** | **43 (18)** | **33 (14)** | | |
| RFS, median [95% CI], months | 12.9 [6.1–46.1] | 4.4 [2.0–7.5] | +8.5 [0.4–16.1] | 0.58 [0.33–1.01] |
| OS, median [95% CI], months | 36.0 [17.9–47.2] | 14.2 [8.5–22.3] | +21.8 [6.0–37.6] | 0.49 [0.28–0.86] |

CI, confidence interval; HR, hazard ratio; NE, not estimable; Oral-AZA, oral azacitidine; OS, overall survival; RFS, relapse-free survival.