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## Review Article

### Trends in Five-Year Overall Survival Among Elderly Patients with Acute Myeloid Leukemia (AML) Between 2000-2009 and 2010-2019

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## Summary

Acute myeloid leukaemia is a disease of older people, with a median age at diagnosis around 70, yet almost every therapeutic advance of the past two decades has been measured in populations younger than that. Population-level survival data show what reached the patients who actually have the disease.

**Objectives:** To review the published evidence on how five-year and shorter-term survival in elderly acute myeloid leukaemia has changed across the 2000s and 2010s: what registry data show, which age bands gained, what the treatment changes were, and why the gains are smaller than the trial literature would suggest.

**Material and Methods:** Narrative review of population-based registry analyses, randomised trials in older or unfit patients, and consensus recommendations indexed in PubMed and the major haematology journals. Studies were eligible if they reported survival by age band and calendar period in a defined acute myeloid leukaemia population, or the efficacy of a therapy studied specifically in older adults. No new patient data were generated and no patients were recruited; every estimate quoted is one published by the original investigators.

**Results:** Across registry analyses spanning 2000 to 2022, five-year survival rose from 9.3 to 19.6 per cent in patients aged 65 to 74 and from 1.9 to 4.7 per cent in those aged 75 and over, against a rise from 27.9 to 44.4 per cent in patients aged 40 to 64. Earlier analysis of roughly 19,000 patients aged 65 and above across three decades showed 12-month survival in the 65 to 74 group rising from 20 to 25 to 30 per cent, with no improvement at all above 75. In randomised comparison restricted to high-risk or secondary disease in 309 patients aged 60 to 75, a liposomal anthracycline-cytarabine formulation extended median overall survival from 5.95 to 9.56 months (HR 0.69, 95% CI 0.52-0.90). Registry work consistently shows that a large minority of older patients receive no antileukaemic therapy at all.

**Conclusion:** Survival in elderly acute myeloid leukaemia improved materially between the two decades, but the absolute gain is 10 percentage points at 65 to 74 and under 3 above 75. Proportional doubling reads impressively and describes a five-year survival that remains below one in five. The largest single determinant at population level is whether the patient is treated at all.

**Abbreviations:** AML – Acute Myeloid Leukaemia, HMA – Hypomethylating Agent, CR – Complete Remission, OS – Overall Survival, RS – Relative Survival, SEER – Surveillance, Epidemiology and End Results, ELN – European LeukemiaNet, alloHCT – Allogeneic Haematopoietic Cell Transplantation, MRD – Measurable Residual Disease, HR – Hazard Ratio, CI – Confidence Interval.

**Keywords:** Acute Myeloid Leukaemia; Elderly; Overall Survival; Hypomethylating Agents; Population-Based Registry

## Introduction

Acute myeloid leukaemia is predominantly a disease of later life. Incidence rises steeply with age and the median age at diagnosis sits around 70 years [1,2]. Age itself carries prognostic weight beyond what comorbidity explains, because adverse cytogenetics, antecedent myelodysplasia and therapy-related disease all cluster in older patients [3].

For most of the period covered here, that population was poorly served by the evidence base. Trials enrolled fitter and younger patients, and registry work repeatedly found that a substantial share of older patients received no antileukaemic treatment at all [4,5,6]. The question of

whether to treat was answered differently in different regions, and those differences translated into measurable survival differences [5].

The 2000s and 2010s then brought two waves of change. Hypomethylating agents offered a lower-intensity option for patients unfit for induction [9,10], and from the late 2010s targeted and combination approaches followed, most consequentially venetoclax added to azacitidine [11]. Guidance was revised to match [17,18,23].

This review sets out what population-level survival data show across these two decades, which age bands benefited, and why the improvement is more modest than the trial literature alone would suggest.

## Material and Methods

**Search strategy:** PubMed and the archives of the major haematology and oncology journals were searched for studies of survival trends in older patients with acute myeloid leukaemia. Search terms combined acute myeloid leukaemia and elderly or older with overall survival, relative survival, population-based, registry, temporal trends, hypomethylating agents and treatment rates. Reference lists of retrieved registry analyses and guidelines were screened by hand.

**Eligibility:** Studies were included if they reported survival stratified by age band and calendar period in a defined acute myeloid leukaemia population, the proportion of older patients receiving antileukaemic therapy, or the efficacy of a treatment evaluated specifically in older or unfit patients. Randomised trials are cited for efficacy and registry analyses for population effect, and the two are distinguished throughout.

**Data extraction and handling:** Design, cohort size, calendar period, age banding and reported survival estimates were extracted as published. Age band is reported alongside every survival figure, and relative and observed survival are distinguished where the source does so, because competing mortality is substantial in this population. No pooling or re-analysis was performed and no patient-level data were obtained. Figures 1 to 4 and Tables 1 to 3 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

## Results

**Survival did improve, and by more than a little:** A registry analysis covering diagnoses from 2000 to 2022, stratified into four therapeutic eras, reported five-year survival in patients aged 65 to 74 rising from 9.3 to 19.6 per cent between the earliest and latest periods. In those aged 75 and over it rose from 1.9 to 4.7 per cent. For comparison, the 40 to 64 group rose from 27.9 to 44.4 per cent and the 15 to 39 group from 50.6 to 66.1 per cent (Figure 1) [7].

Expressed proportionally these are striking numbers: survival slightly more than doubled at 65 to 74 and rather more than doubled

above 75. Expressed in absolute terms the same data describe a gain of 10.3 percentage points and 2.8 percentage points respectively (Figure 2) [7]. Both descriptions are accurate and they leave very different impressions, which is the first thing to notice about this literature.

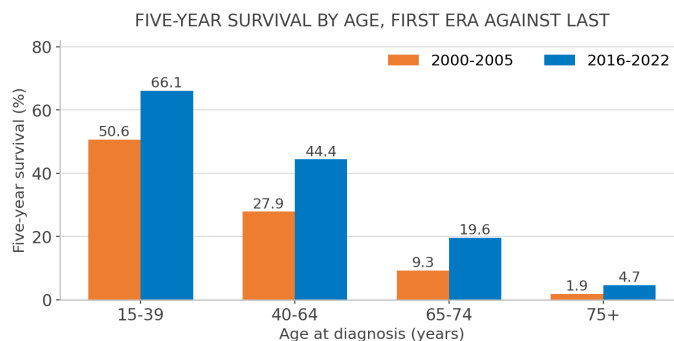


**Figure 1:** Five-year survival by age band in the earliest and latest therapeutic eras of a registry analysis spanning 2000 to 2022 [7]

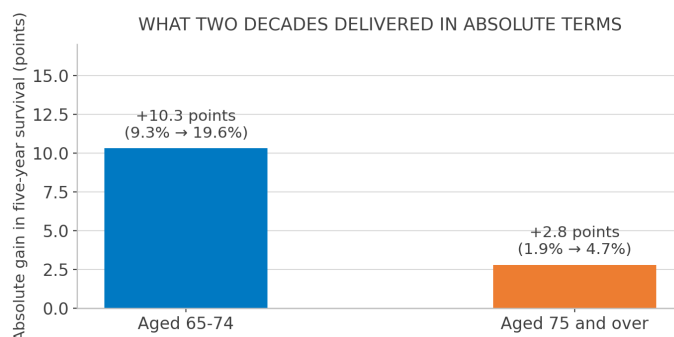


**Figure 2:** The same improvement expressed as an absolute gain in percentage points [7]

**The improvement started earlier in the younger old:** Analysis of roughly 19,000 patients aged 65 and above across three successive decades found 12-month survival in the 65 to 74 band rising from 20 per cent in 1977-1986 to 25 per cent in 1987-1996 and 30 per cent in 1997-2006 (Figure 3). Over the same period, survival did not improve significantly in patients aged 75 or above, and the group aged 85 and over showed no improvement whatever [2].

Population-based work elsewhere describes the same divergence. Patients aged 60 or under showed continuous improvement across the whole registry period, while those aged 61 and above began improving only in the early 2000s, and the benefit was confined to those receiving chemotherapy [6,7]. A Dutch population-based analysis of patients aged 60 and over across two decades tracked how first-line therapy choices, remission rates and survival changed together as guidelines were revised [8].

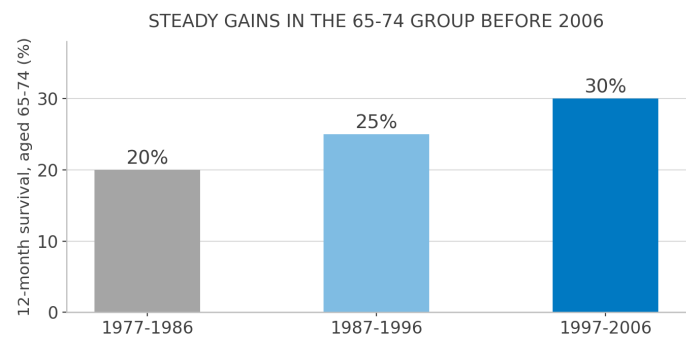


**Figure 3:** Twelve-month survival in patients aged 65 to 74 across three successive decades [2]

| Study                     | n          | Period      | Principal reported finding                               |
|---------------------------|------------|-------------|----------------------------------------------------------|
| Appelbaum et al. 2006 [3] | —          | —           | Age carries prognostic weight beyond comorbidity         |
| Juliusson et al. 2009 [4] | Registry   | Swedish     | Decision to treat varies by region and drives outcome    |
| Thein et al. 2013 [2]     | ~19,000    | 1977-2006   | 12-month survival 20% to 30% at 65-74; no gain above 75  |
| Lancet et al. 2018 [12]   | 309        | Randomised  | Median survival 9.56 against 5.95 months                 |
| DiNardo et al. 2020 [11]  | Randomised | VIALE-A     | Venetoclax with azacitidine improves survival            |
| Diekmann et al. 2024 [8]  | Registry   | Two decades | Therapy choices, remission and survival tracked together |

**Table 1:** Principal studies reviewed, with period and the finding as reported by the original investigators

**What changed in treatment:** The lower-intensity option arrived first. Azacitidine prolonged overall survival against conventional care in elderly patients with low marrow blast counts [9], and a subsequent international phase 3 study examined the same comparison in older patients with more than 30 per cent blasts [10]. Neither produced the step change that trial-era language sometimes implies, but both established that patients ineligible for induction had something to be offered.

Two later developments matter more for the 2010s. Venetoclax added to azacitidine in previously untreated patients unfit for intensive therapy improved response rates and median overall survival in randomised comparison [11], and this is the intervention most plausibly responsible for the gains visible in the latest registry era [7]. Separately, for patients aged 60 to 75 with high-risk or secondary disease who remained candidates for intensive treatment,

a liposomal fixed-ratio formulation of daunorubicin and cytarabine extended median overall survival from 5.95 to 9.56 months against conventional induction (HR 0.69, 95% CI 0.52-0.90, p = .003) in 309 randomised patients (Figure 4) [12,13].

That agent also raised the proportion of patients reaching allogeneic transplantation and improved survival landmarked from the transplant date [14], and its benefit has been examined across European risk subgroups [15] and in real-world cohorts outside trial conditions [16]. Maintenance with oral azacitidine after chemotherapy-induced remission adds a further option for patients in this age range [19,20,21,22].

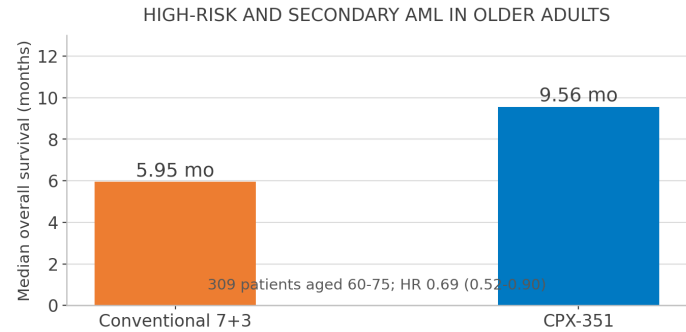


**Figure 4:** Median overall survival with a liposomal formulation against conventional induction in older adults with high-risk or secondary disease [12]

**The largest determinant is whether the patient is treated:** Registry analyses consistently find that a large minority of older patients receive no antileukaemic therapy. Where treatment rates and outcomes have been examined together, the survival difference between treated and untreated patients dwarfs the difference between treatment regimens [4,5,6]. The Swedish registry work made this point most directly by comparing regions with differing attitudes to remission induction and finding that survival in patients aged 70 to 79 tracked how readily those regions judged patients eligible [4,5].

This is a confound as much as a finding. Untreated patients are on average older, frailer and more comorbid, so part of the survival gap reflects selection rather than treatment effect. But the regional comparison controls for that to a degree, because it compares populations rather than individuals, and it found real differences [5].

| Age band          | Earliest era | Latest era | Absolute gain |
|-------------------|--------------|------------|---------------|
| 15-39 years       | 50.6%        | 66.1%      | +15.5 points  |
| 40-64 years       | 27.9%        | 44.4%      | +16.5 points  |
| 65-74 years       | 9.3%         | 19.6%      | +10.3 points  |
| 75 years and over | 1.9%         | 4.7%       | +2.8 points   |

**Table 2:** Five-year survival by age band between the earliest and latest therapeutic eras [7]

**Molecular stratification arrived alongside the new drugs:** The period covered here is also when risk assessment moved from morphology and cytogenetics towards molecular characterisation. Successive expert recommendations reclassified patients on the basis of mutations in NPM1, FLT3, TP53 and others, and the categories that resulted do not map cleanly onto the ones used at the start of the period [17,18,23]. Reviews of targeted agents describe an increasingly subdivided disease in which FLT3, IDH1 and IDH2 inhibitors address defined molecular subsets rather than acute myeloid leukaemia as a whole [24,25].

This matters for interpreting registry trends in a way that is easy to overlook. If molecular testing identifies patients who would previously have been classified differently, and if access to that testing improved over the period, then part of any apparent survival gain reflects better characterisation rather than better treatment. Older patients were also the last to receive routine molecular testing in most health systems, which would delay any such artefact in exactly the age bands under discussion [8,17].

**Measurable residual disease and what it adds in older patients:** Response assessment also changed. Measurable residual disease testing moved from research technique to clinical variable across the period [27], and flow-based measurement of leukaemic stem cell frequency has been shown to predict outcome independently [26]. In the maintenance setting, oral azacitidine prolonged survival in patients in first remission irrespective of residual disease status, which is an unusual result and suggests the benefit is not confined to those with detectable disease [21].

Applied to older patients specifically, residual disease measurement sits awkwardly. Its established value is in guiding whether to proceed to allogeneic transplantation, an option available to a minority of patients over 70, and its prognostic weight has been characterised mainly in younger trial cohorts [22,26,27]. For a patient in whom transplantation is not contemplated, a residual disease result changes the prognosis without changing the plan.

| Development                       | Period            | Effect on older patients                                                                      |
|-----------------------------------|-------------------|-----------------------------------------------------------------------------------------------|
| Hypomethylating agents            | Mid-2000s         | First option for patients unfit for induction; modest survival gain [9,10]                    |
| Liposomal daunorubicin-cytarabine | Late 2010s        | Median survival 5.95 to 9.56 months in high-risk disease [12,13]                              |
| Venetoclax combinations           | Late 2010s        | Improved response and survival in unfit patients; likely driver of the latest era gain [7,11] |
| Oral azacitidine maintenance      | 2020s             | Prolongs survival in first remission after chemotherapy [19,20,21]                            |
| Molecular risk stratification     | Across the period | Reclassifies patients; complicates trend interpretation [17,18,24]                            |

**Table 3:** Therapeutic developments across the two decades and their reported effect in older patients

**Where the remaining need sits:** The oldest band is where almost nothing has changed. Five-year survival of 4.7 per cent above 75, against 1.9 per cent two decades earlier, describes a group for whom the therapeutic revolution has been largely notional [7]. The earlier three-decade analysis found no significant improvement at all above 75 and none whatever above 85 [2].

Two explanations compete and both are probably partly right. Biologically, disease arising above 75 is enriched for adverse cytogenetics, antecedent myelodysplasia and therapy-related origin, so it is intrinsically less curable [1,3]. Practically, these patients are least likely to be offered treatment, least likely to be enrolled in trials, and most likely to die of competing causes before any therapy can take effect [4,5,6]. Distinguishing the two requires data stratified by both fitness and treatment received, which registries do not currently collect [8].

Discussion

Two readings of the same data are both defensible and they conflict. Five-year survival at 65 to 74 more than doubled across two decades, which is a larger proportional improvement than most solid tumours achieved over the same period [7]. It also ended at 19.6 per cent, meaning four patients in five still die within five years, and above 75 the figure is 4.7 per cent [7]. Which framing is chosen usually reveals what the author is arguing for.

The honest synthesis is that the improvement is real, concentrated in the younger old, and driven by two things that arrived a decade apart: hypomethylating agents giving unfit patients an option at all [9,10], and venetoclax combinations substantially improving on that option in the latest era [11]. The oldest patients gained least because they were least often treated and least able to tolerate what was available [2,4].

Why the trial gains do not fully appear at population level

A randomised trial reporting a median survival of 9.56 against 5.95 months describes patients selected for eligibility, treated in specialist centres and monitored intensively [12]. The registry figure covers everyone diagnosed, including those who never reach a haematologist, decline treatment or die before therapy can start [6,7]. The gap between the two is not evidence that the trial was wrong; it is a measure of how much of the population the trial result actually reaches.

Real-world cohorts sit between the two and are informative for that reason. Where a modern regimen has been examined outside trial conditions, the effect persists but is attenuated [16], which is the expected pattern and a reminder that population survival responds to access and referral as much as to efficacy.

Measurement problems specific to this population

Competing mortality complicates every figure quoted here. A patient aged 80 has a substantial annual probability of death from causes unrelated to leukaemia, so observed five-year survival understates disease-specific outcome while relative survival attempts to correct for it [6,7]. Studies reporting one without specifying which are difficult to compare.

Diagnostic classification also shifted over the period. Successive revisions moved the boundary between myelodysplastic syndrome and acute myeloid leukaemia and reclassified risk groups on molecular rather than morphological grounds [17,18,23]. A patient counted as having myelodysplasia in 2002 might be counted as having leukaemia in 2018, and such patients tend to have better outcomes than those with de novo disease, which inflates apparent improvement independently of any treatment effect.

### Study limitations

The limitations belong to the underlying literature. Registry analyses capture diagnosis and vital status reliably but treatment detail poorly, so attributing survival gains to specific agents is inference rather than demonstration [6,7,8]. Era boundaries are chosen by investigators and different choices produce different apparent step changes [7]. Trials in older patients enrol the fitter end of the age band, so their results overstate what is achievable across the population [11,12]. Classification changes over two decades affect who enters the denominator [17,18]. Registry data from different countries reflect different health system access and referral patterns and are not directly comparable [4,5,8]. And the most recent era in any registry analysis has the shortest follow-up, so five-year estimates for it rest on fewer completed observations [7].

Two gaps deserve naming. No analysis reviewed here separates the contribution of improved supportive care from that of new antileukaemic agents, although the paediatric literature suggests supportive care alone can move mortality substantially. And no registry study reports survival stratified simultaneously by age band, fitness measure and treatment received, which is what would allow the treated-untreated confound to be resolved [4,6].

### Conclusion

Five-year survival in elderly acute myeloid leukaemia improved across the 2000s and 2010s, roughly doubling from 9.3 to 19.6 per cent in patients aged 65 to 74 and from 1.9 to 4.7 per cent above 75. Those proportional gains correspond to absolute improvements of 10.3 and 2.8 percentage points, and four patients in five aged 65 to 74 still die within five years. The improvement began later in older patients than younger ones and is concentrated in those who received treatment, which at population level remains a minority in the oldest bands. Hypomethylating agents gave unfit patients an option and venetoclax combinations improved substantially on it, while a

liposomal formulation extended median survival from 5.95 to 9.56 months in fitter older patients with high-risk disease. Reporting these changes proportionally rather than in absolute terms consistently overstates what has been achieved for the patients who actually have this disease.

Two priorities follow for the next decade. The first is closing the gap between trial efficacy and population effect, which is a question of referral, access and willingness to treat rather than of drug development [4,5,6]. The second is generating evidence in patients above 75, who constitute a large share of the disease burden, gained least across two decades, and remain systematically under-represented in the trials that define standard of care [2,7,11].

Registries could contribute more than they currently do. Recording fitness alongside age, and treatment actually received alongside diagnosis, would allow the treated-untreated confound to be separated from biology and would show whether the oldest patients fail to benefit because their disease is different or because they are not offered therapy [4,8]. Until that distinction is made, the survival curves reviewed here describe an outcome without explaining it.

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### Conflict of Interest

No financial or personal relationship has shaped this review.

### Ethics Statement

The article is a synthesis of results already in the public domain. Nobody was enrolled for it and no clinical record was opened afresh, which places the work outside the scope of research ethics review.

### References

1. Deschler, B., Lübbert, M. (2006) Acute myeloid leukemia: epidemiology and etiology. *Cancer*, 107(9): 2099-2107.
2. Thein, MS., Ershler, WB., Jemal, A., Yates, JW., Baer, MR. (2013) Outcome of older patients with acute myeloid leukemia: an analysis of SEER data over 3 decades. *Cancer*, 119(15): 2720-2727.
3. Appelbaum, FR., Gundacker, H., Head, DR., Slovak, ML., Willman, CL., et al. (2006) Age and acute myeloid leukemia. *Blood*, 107(9): 3481-3485.
4. Juliusson, G., Antunovic, P., Derolf, A., Lehmann, S., Möllgård, L., et al. (2009) Age and acute myeloid leukemia: real world data on decision to treat and outcomes from the Swedish Acute Leukemia Registry. *Blood*,

- 113(18): 4179-4187.
5. Juliusson, G. (2011) Older patients with acute myeloid leukemia benefit from intensive chemotherapy: an update from the Swedish Acute Leukemia Registry. *Clin Lymphoma Myeloma Leuk*, 11(Suppl 1): S54-S59.
6. Bacher, U., Haferlach, T. (2012) The benefit of population-based studies for older patients with acute myeloid leukemia. *Haematologica*, 97(12): 1781-1782.
7. Acharya, UH., Halpern, AB., Wu, Q., Voutsinas, JM., Walter, RB., et al. (2018) Impact of region of diagnosis, ethnicity, age, and gender on survival in acute myeloid leukemia. *J Drug Assess*, 7(1): 51-53.
8. Diekmann, B., Veeger, N., Rozema, J., Kibbelaar, R., Franken, B., Güler, Y., Adema, B., van Roon, E., Hoogendoorn, M. (2024) The evolution of treatment policies and outcomes for patients aged 60 and older with acute myeloid leukemia: a population-based analysis over two decades. *Cancers*, 16(23): 3907.
9. Fenaux, P., Mufti, GJ., Hellström-Lindberg, E., Santini, V., Gattermann, N., et al. (2010) Azacitidine prolongs overall survival compared with conventional care regimens in elderly patients with low bone marrow blast count acute myeloid leukemia. *J Clin Oncol*, 28(4): 562-569.
10. Dombret, H., Seymour, JF., Butrym, A., Wierzbowska, A., Selleslag, D., Jang, JH., et al. (2015) International phase 3 study of azacitidine vs conventional care regimens in older patients with newly diagnosed AML with >30% blasts. *Blood*, 126(3): 291-299.
11. DiNardo, CD., Jonas, BA., Pullarkat, V., Thirman, MJ., Garcia, JS., Wei, AH., et al. (2020) Azacitidine and venetoclax in previously untreated acute myeloid leukemia. *N Engl J Med*, 383(7): 617-629.
12. Lancet, JE., Uy, GL., Cortes, JE., Newell, LF., Lin, TL., Ritchie, EK., et al. (2018) CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed secondary acute myeloid leukemia. *J Clin Oncol*, 36(26): 2684-2692.
13. Lancet, JE., Cortes, JE., Hogge, DE., Tallman, MS., Kovacsovics, TJ., et al. (2014) Phase 2 trial of CPX-351, a fixed 5:1 molar ratio of cytarabine/daunorubicin, vs cytarabine/daunorubicin in older adults with untreated AML. *Blood*, 123(21): 3239-3246.
14. Uy, GL., Newell, LF., Lin, TL., Goldberg, SL., Wieduwilt, MJ., Ryan, RJ., Faderl, S., Lancet, JE. (2022) Transplant outcomes after CPX-351 vs 7+3 in older adults with newly diagnosed high-risk and/or secondary AML. *Blood Adv*, 6(17): 4989-4993.
15. Cortes, JE., Lin, TL., Asubonteng, K., Faderl, S., Lancet, JE., Prebet, T. (2022) Efficacy and safety of CPX-351 versus 7+3 chemotherapy by European LeukemiaNet 2017 risk subgroups in older adults with newly diagnosed, high-risk/secondary AML: post hoc analysis of a randomized, phase 3 trial. *J Hematol Oncol*, 15(1): 155.
16. Chiche, E., Rahmé, R., Bertoli, S., Dumas, PY., Micol, JB., et al. (2021) Real-life experience with CPX-351 and impact on the outcome of high-risk AML patients: a multicentric French cohort. *Blood Adv*, 5(1): 176-184.
17. Döhner, H., Wei, AH., Appelbaum, FR., Craddock, C., DiNardo, CD., Dombret, H., et al. (2022) Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. *Blood*, 140(12): 1345-1377.
18. Döhner, H., Estey, E., Grimwade, D., Amadori, S., Appelbaum, FR., Büchner, T., et al. (2017) Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. *Blood*, 129(4): 424-447.
19. Wei, AH., Döhner, H., Pocock, C., Montesinos, P., Afanasyev, B., Dombret, H., et al. (2020) Oral azacitidine maintenance therapy for acute myeloid leukemia in first remission. *N Engl J Med*, 383(26): 2526-2537.
20. Wei, AH., Döhner, H., Sayar, H., Ravandi, F., Montesinos, P., Dombret, H., et al. (2023) Long-term survival with oral azacitidine for patients with acute myeloid leukemia in first remission after chemotherapy: updated results from the randomized, placebo-controlled, phase 3 QUAZAR AML-001 trial. *Am J Hematol*, 98(2): E64-E67.
21. Roboz, GJ., Ravandi, F., Wei, AH., Dombret, H., Döhner, H., et al. (2022) Oral azacitidine prolongs survival of patients with AML in remission independent of measurable residual disease status. *Blood*, 139(14): 2145-2155.
22. Döhner, H., Wei, AH., Roboz, GJ., Montesinos, P., Thol, FR., et al. (2022) Prognostic impact of NPM1 and FLT3 mutations in patients with AML in first remission treated with oral azacitidine. *Blood*, 140(15): 1674-1685.
23. Heuser, M., Ofran, Y., Boissel, N., Brunet Mauri, S., Craddock, C., et al. (2020) Acute myeloid leukaemia in adult patients: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*, 31(6): 697-712.
24. Kantarjian, H., Kadia, T., DiNardo, C., Daver, N., Borthakur, G., Jabbour, E., et al. (2021) Acute myeloid leukemia: current progress and future directions. *Blood Cancer J*, 11: 41.
25. Kayser, S., Levis, MJ. (2021) Updates on targeted therapies for acute myeloid leukaemia. *Br J Haematol*, 196(2): 316-328.
26. Zeijlemaker, W., Grob, T., Meijer, R., Hanekamp, D., Kelder, A., et al. (2019) CD34+CD38- leukemic stem cell frequency to predict outcome in acute myeloid leukemia. *Leukemia*, 33(5): 1102-1112.
27. Ravandi, F., Walter, RB., Freeman, SD. (2018) Evaluating measurable residual disease in acute myeloid leukemia. *Blood Adv*, 2(11): 1356-1366.