

# Azacitidine or Decitabine Monotherapy for the Treatment of AML: A Comparative Systematic Review and Meta-Analysis

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## Background

Both azacitidine and decitabine are well-tolerated and they have shown an improved overall survival compared with best supportive care or low dose Ara-C <sup>1,2</sup>. However, azacitidine and decitabine have not been compared directly in a randomized clinical trial. In spite of the widespread use of these of hypomethylating agents (HMA), there is no consensus regarding their comparative efficacy and clinical benefit, with notable between-study variability, and the choice of HMA depends mostly on the experience and preferences of the physician responsible.

## Materials & Methods

A systematic review and meta-analysis was conducted, including randomized controlled trials and retrospective studies enrolling adults with newly diagnosed AML and treated with azacitidine or decitabine monotherapy. The results were summarized using a point estimate and 95% confidence interval (CI) for the means of thedifferent outcomes between studies.

## Results

A total of 3,000 patients from 23 cohorts were analyzed (12 cohorts of azacitidine and 11 of decitabine). A trend toward lower response rates was observed for azacitidine (31%, 95%CI: 24%–37%) compared to decitabine (40%, 95%CI: 31%–49%, p=0.081). However, there was no significant difference in overall survival (OS) between azacitidine and decitabine (Figure 1).

When comparing azacitidine and decitabine approved regimens, a significantly lower ORR was observed for azacitidine. (Table 1).

Table 1. Summary of response outcomes, overall survival and mortality during azacitidine (75 mg/m2, 7d) and decitabine treatment (20mg/m2, 5d) in monotherapy.

| Drug                          | ORR<br>%, 95% CI                      | 1-year<br>mortality<br>%, 95% CI      | OS (months),<br>95% CI |
|-------------------------------|---------------------------------------|---------------------------------------|------------------------|
| Azacitidine<br>(75 mg/m2, 7d) | 30%, (23-37)<br>I <sup>2</sup> =87.7% | 51%, (46-57)<br>I <sup>2</sup> =77.4% | 10.90 (8.92-12.89)     |
| Decitabine<br>(20mg/m2, 5d)   | 46%, (42-50)<br>I <sup>2</sup> =0%    | 72%, (67-76)<br>I <sup>2</sup> =..%   | 8.57 (7.02-10.13)      |
| p-value                       | <0.001                                | <0.001                                | 0.221                  |

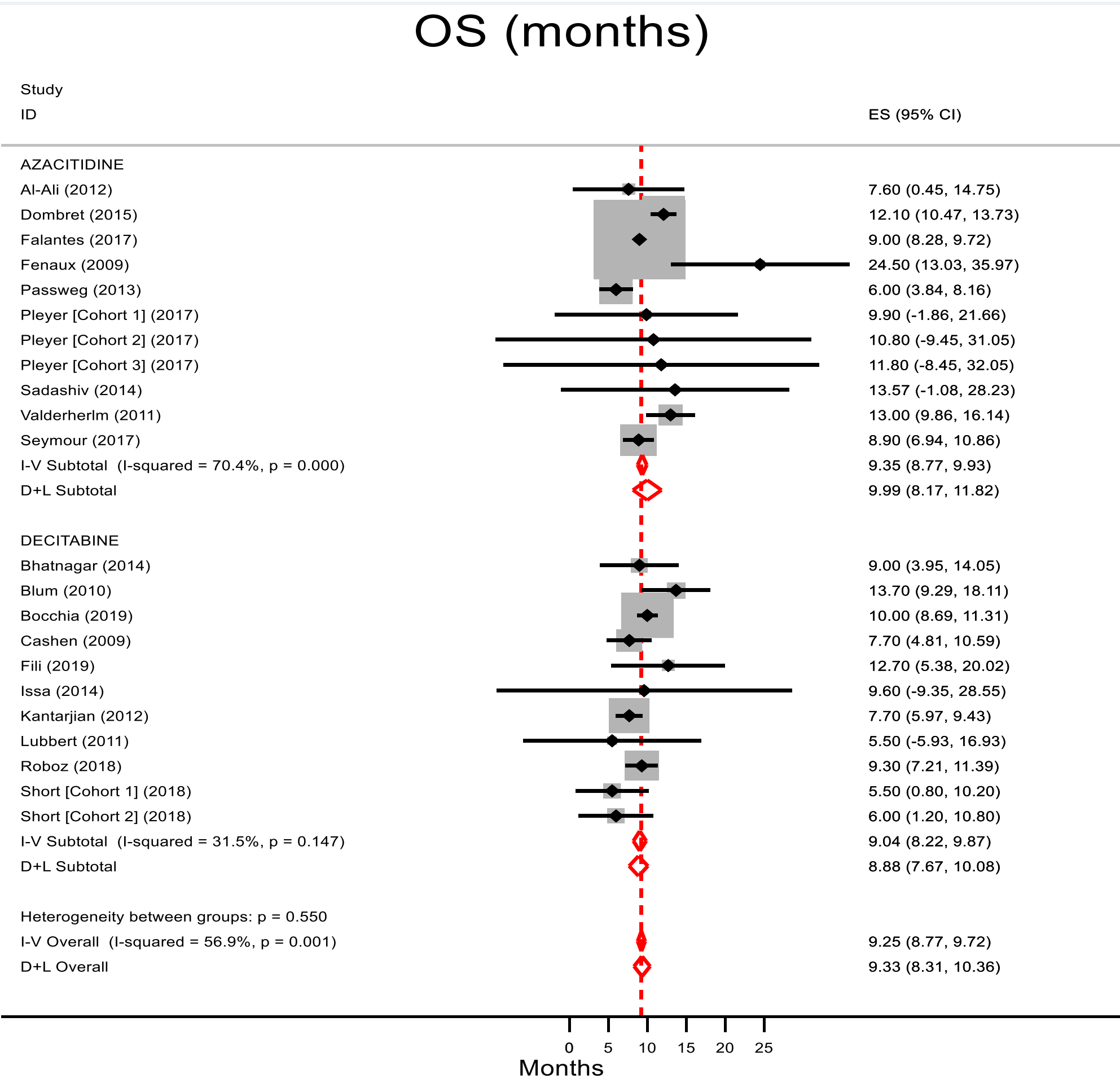


Figure 1. Pooled analysis of overall survival (OS).

Lower 1-year mortality with standard 7-day 75 mg/m<sup>2</sup> azacitidine treatment was observed compared to other azacitidine schedules. Moreover, OS was lower when administered for 5 days versus 7 days. There was no significant difference in response rates, mortality, and OS when comparing the 5-day vs. 10-day decitabine regimens.

## Summary

There were no significant differences in 1-year mortality or OS for azacitidine and decitabine (roughly 9 months). These results exploring single-HMA regimens could be useful for the design and use of new HMA-based combination schedules.

## Discussion

Although no differences in survival were observed, our results provide accurate data supporting the efficacy of the standard dose-schedules over other dosages of these drugs.

In favor of applicability of HMAs in the real world setting, this study shows that single center and retrospective studies have reported median OS, which encompass the estimates in the phase 3 trials.

Since HMA are being used as the backbone for novel combinations regimens, the HMA-dose schedule that could be more appropriate to combine could be selected.

## References

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- Dombret et al. Blood. 2015 Jul 16;126(3):291–9.