

General AML

## HAG Regimen for the Treatment of AML and MDS: A Meta-Analysis with 2,314 Participants

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The combination of homoharringtonine, cytarabine and G-CSF (HAG) is commonly implemented in China and Japan in Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome (MDS) patients. In order to provide the global AML treating community with data on this practice, [Xie M](#) and [Jiang Q](#) from [Zhejiang University](#), China conducted a meta-analysis of 2314 patients.

For this analysis the Complete Response Rates (CRR) of HAG in various patient types: elderly patients, newly diagnosed and Relapsed/Refractory (R/R) AML and MDS patients were observed. This is the first meta-analysis of studies examining the effectiveness of AML and MDS treatment with the HAG regimen. Results of the meta-analysis indicated that the HAG regimen was more efficacious in improving CRR and was better tolerated than intensive chemotherapy in [MDS](#) and [AML](#). This study was published in [PLoS One](#) in October 2016.

### The key published results

- The CRR of HAG-treated patients versus patients treated with standard induction regimens was significantly higher (Odds ratio 2.41; 95% CI, 1.77–3.28; P = 0.000).
- In patients with AML treated with the HAG regimen, the overall CRR was 53% (95% CI, 49%–58%).

### Newly diagnosed AML

- In newly diagnosed patients with AML treated with HAG the CRR was 62%, similar to the CRR observed in patients treated with the standard “3+7” regimen (daunorubicin 45 mg/m<sup>2</sup> and cytarabine 100 mg-200 mg/m<sup>2</sup>; 57%–65%).
- The CRR observed in newly diagnosed AML patients (62%, 95% CI, 56%–67%) was significantly higher than that seen in R/R AML patients (50%, 95% CI, 43%–58%; P = 0.001).

### Elderly AML

- The CRR was 54% (95% CI, 47%–60%) in elderly patients with AML (n = 536) and 38% (95% CI, 18%–54%) in patients with advanced MDS (n = 207).

### Toxicity

- Early death and myelosuppression event rates of patients treated with the HAG regimen (95% CI, 0.09–0.37; P = 0.000) were lower than those seen in patients treated with intensive chemotherapy (95% CI, 0.25–0.67; P = 0.000), with odds ratios of 0.18 and 0.41, respectively.

### Conclusion

Despite the heterogeneity of the data, the results suggest that the HAG regimen may provide an alternative approach to intensive chemotherapy to improve outcomes in high risk patients with MDS, R/R AML and for elderly patients. However, multinational randomized clinical trials are required in homogenized patient cohorts to further demonstrate the effectiveness of this approach internationally.

Please find the published results and abstract below

## Abstract

### Background

In China, the combination of homoharringtonine, cytarabine, and G-CSF (HAG) has been extensively applied for treatment of acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS).

### Methods

We performed a meta-analysis of 2,314 patients (AML, n = 1754; MDS, n = 560) to determine the overall safety and efficacy of this regimen.

### Results

The complete response (CR) rate of AML patients (53%) was significantly higher than that of MDS/transformed-AML patients (45%;  $P = 0.007$ ). The CR rate of patients with newly diagnosed AML (62%) was significantly higher than in patients with relapsed/refractory AML (50%;  $P = 0.001$ ). There were no significant difference in CR rates between elderly AML patients (54%) and all AML patients ( $P = 0.721$ ). When compared with non-HAG regimens for AML/MDS induction therapy, the CR rate of patients treated with HAG was significantly higher than in treated with intensive chemotherapy ( $P = 0.000$ ). No significant differences in CR rates were observed between patients treated with HAG and those treated with CAG (cytarabine, aclarubicin, G-CSF) regimens ( $P = 0.073$ ). HAG regimen was well tolerated, with early death (ED) in 2%, grade IV myelosuppression in 52% and infection in 50%. Reports of ED and rates of myelosuppression were reduced as compared with intensive chemotherapy ( $P = 0.000$  and  $P = 0.000$ , respectively).

### Conclusion

The HAG regimen is an effective and safe regimen for the treatment of AML and MDS, and appears to be more effective and better tolerated than intensive chemotherapy. Future randomized controlled trials and further meta-analyses are strongly needed to confirm its efficacy and safety, especially in comparison with intensive chemotherapy.

### References

1. Xie M., *et al.* HAG (Homoharringtonine, Cytarabine, G-CSF) Regimen for the Treatment of Acute Myeloid Leukemia and Myelodysplastic Syndrome: A Meta-Analysis with 2,314 Participants. *PLoS One*. 2016 Oct 5; 11(10):e0164238. DOI: 10.1371/journal.pone.0164238. eCollection 2016.