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The role of granulocyte colony stimulating factor in AML patients treated with anthracycline-based chemotherapy: a Korean study

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Granulocyte Colony-Stimulating Factor (G-CSF) is a cytokine that stimulates the production and maturation of neutrophils.[1] The standard treatment regimen for newly diagnosed Acute Myeloid Leukemia (AML) patients consist of an induction chemotherapy consisting of anthracycline and cytarabine, called the 7 + 3 regimen. However, this strategy is associated with Treatment Related Mortality (TRM) mostly due to neutropenia. Currently, G-CSF is approved for use to alleviate neutropenia in adult AML patients following induction or consolidation chemotherapy. However, the benefit of administering G-CSF during induction in AML patients is unclear.[2]

Ka-Won Kang and colleagues from the Korea University School of Medicine, Seoul, Korea, published an article in Leukemia Research on 7th February 2017. In this study, the authors retrospectively studied the role of G-CSF in induction treatment in 315 newly diagnosed AML patients enrolled in the Korea University AML registry between 2001 and 2016. They also investigated the impact of G-CSF exposure on the anti-leukemic efficacies of induction chemotherapy.[2]

Patients were split into groups based on the G-CSF administration strategy used during induction therapy and the presence of neutropenia. Patients were either included in the no G-CSF group (no G-CSF administration during induction, n = 112, median age = 56.5 years), preemptive group (G-CSF initiated upon onset of neutropenia [ANC < 1000/μL] but before the development of febrile neutropenia, n = 74, median age = 46.0 years) or the therapeutic G-CSF group (G-CSF initiated after the development of febrile neutropenia, n = 129, median age = 49.0).

The key results of the study were:

- Time to ANC recovery in patients in no G-CSF, preemptive G-CSF and therapeutic G-CSF, 27.5 *vs* 23 *vs* 24 days respectively, $P < 0.001$
- Duration of CIFN in patients in no G-CSF, preemptive G-CSF and therapeutic G-CSF, 10.5 *vs* 6 *vs* 14 days respectively, $P < 0.001$
- Incidence of CIFN in patients in preemptive G-CSF (n = 61) and no G-CSF (n = 95); 82.4% *vs* 84.8%, $P = 0.666$
- Compared with the no G-CSF group, pre-emptive G-CSF administration had a lower risk of TRM; Odds Ratio (OR) = 0.08, $P = 0.076$
- Complete Remission (CR) in no G-CSF (n = 62), preemptive G-CSF (n = 57) and therapeutic G-CSF (n = 84); 55.4% *vs* 77.0% *vs* 65.1% respectively, $P = 0.011$
- RFS and OS were not significantly different between no G-CSF, pre-emptive G-CSF and therapeutic G-CSF administration

- 3-year Cumulative Incidence of Relapse (CIR) in no G-CSF, preemptive G-CSF and therapeutic G-CSF; 55.8% *vs* 40.0% *vs* 46.5%, *P* = 0.471

Preemptive G-CSF administration during induction chemotherapy lead to a faster ANC recovery, improved TRM and reduced CIFN duration without affecting survival outcomes and the anti-leukemic efficacy of induction chemotherapy. However, the authors noted that their study had some limitations and their findings should be validated in prospective clinical studies.

The authors concluded by stating initiation of G-CSF administered during induction chemotherapy can accelerate neutrophil recovery in AML patients without affecting treatment outcomes. They further suggested that during induction therapy, G-CSF should preferably be administered upon neutropenia onset and latest before the development of febrile neutropenia.

Abstract

We analyzed the effects of granulocyte colony-stimulating factor (G-CSF) on outcomes in 315 anthracycline-based induction chemotherapy-treated patients with non-M3 acute myelogenous leukemia (AML). Patients were classified as follows: no G-CSF administration during induction (no G-CSF group; 112 patients); administration immediately upon neutropenia onset (absolute neutrophil counts (ANC) < 1000/μL), but before febrile neutropenia (preemptive group; 74 patients); and administration following febrile neutropenia development (therapeutic group; 129 patients). G-CSF users had a shorter time to ANC recovery than the no G-CSF group (p < 0.001). The chemotherapy-induced febrile neutropenia (CIFN) duration was significantly shorter in the preemptive group than in other groups (p < 0.001). The incidence of CIFN was not significantly different between preemptive and non-G-CSF users (84.8% versus 82.4%). Preemptive G-CSF administration modestly improved treatment-related mortality (TRM), compared with no G-CSF administration (p = 0.076 in multivariate analysis). G-CSF administration did not affect relapse-free or overall survivals or the cumulative relapse incidence among the groups. In conclusion, preemptive G-CSF administration reduced CIFN duration and modestly improved TRM without affecting chemotherapy outcomes. These effects were not observed in the therapeutic group; therefore, initiation of G-CSF during induction therapy before the development of febrile neutropenia may be desirable.

References

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2. Kang K. *et al*. Effect of granulocyte colony-stimulating factor on outcomes in patients with non-M3 acute myelogenous leukemia treated with anthracycline-based induction (7+3 regimen) chemotherapies. Leuk Res. 2017 Feb 7. DOI: 1016/j.leukres.2017.02.003. [Epub ahead of print].