

## Fractionated vs single-dose gemtuzumab for AML

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Freeman SD, Thomas A, Thomas I, Hills RK, Vyas P, Gilkes A, Metzner M, Jakobsen NA, Kennedy A, Moore R, Marquez Almuina N, Burns S, King S, Andrew G, Gallagher KME, Sellar RS, Cahalin P, Weber D, Dennis M, Mehta P, Knapper S, Russell NH. Fractionated vs single-dose gemtuzumab ozogamicin with determinants of benefit in older patients with AML: the UK NCRI AML18 trial. *Blood*. 2023;142(20):1697-1707.

- Your patient is a 64-year-old man with acute myeloid leukemia (AML) who is not known to have any adverse genetic mutations. According to the randomized NCRI AML18 trial of older adults with AML by Freeman and colleagues, which of the following statements about survival, response, and toxicity outcomes of single (gemtuzumab ozogamicin [GO] on day 1; GO1) vs fractionated (GO on days 1 and 4; GO2) GO dosing in the first induction course is correct?**

  - Complete remission (CR) rates after course 1 were significantly better with GO2 than GO1
  - The percentage of patients who achieved CR with measurable residual disease (MRD) <0.1% did not differ significantly for GO2 vs GO1
  - Compared with single-dose GO, fractionated GO increased response depth across most AML molecular groups without increasing toxicity
  - Units of blood needed and days receiving antibiotics or hospitalization were significantly greater with GO2 than with GO1
- According to the randomized NCRI AML18 trial of older adults with AML by Freeman and colleagues, which of the following statements about differential efficacy between the GO schedules across molecular subgroups and other factors affecting outcomes among older adults with AML is correct?**

  - Differential MRD reduction with GO2 varied across molecular subtypes and was greatest for isocitrate dehydrogenase (IDH) mutations
  - Five-year OS did not differ significantly in GO2 or GO1 with or without adverse cytogenetics/TP53 mutations
  - Allogeneic stem cell transplantation (ASCT) was not associated with OS
  - Survival advantage from GO2 vs GO1 was least apparent for the subgroup of patients with DNA methylation type (DNMT) mutations
- Based on the randomized NCRI AML18 trial of older adults with AML by Freeman and colleagues, which of the following statements about clinical implications of outcomes of single vs fractionated GO dosing and of factors affecting outcomes is correct?**

  - GO2 was linked to greater reduction in MRD and improved survival in older adults with nonadverse risk genetics, independent of ASCT
  - A fractionated schedule of GO can be administered safely as 2 doses with the first course, with slower platelet recovery the only increased toxicity seen in the GO2 group
  - Unimproved leukemia clearance explained lack of benefit from GO2 in patients aged >70 years
  - This study proved that optimizing induction therapy for older patients is no longer important