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Capelli, D. et al. Feasibility and Outcome of a Phase II Study of Intensive Induction Chemotherapy in 91 Elderly Patients with AML Evaluated Using a Simplified Multidimensional Geriatric Assessment

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This slide deck represents the opinions of the authors. For a full list of declarations, including funding and author disclosure statements, please see the full text online.

Abbreviations

- Acute myeloid leukaemia (AML)
- Complete response (CR)
- Disease-free survival (DFS)
- Event-free survival (EFS)
- Haematopoietic cell transplantation co-morbidity index (HCT-CI)
- Multidimensional geriatric assessment (MGA)
- Overall survival (OS)
- Treatment-related death (TRD)

Why carry out this study?

Background:

- This prospective phase II study evaluates the feasibility and efficacy of an intensive induction schedule, including high-dose aracytin plus idarubicin, preceded by amifostine, in a cohort of elderly patients with Acute myeloid leukaemia (AML), whose fitness was evaluated by simplified Balducci's multidimensional geriatric assessment (MGA). This subset of patients still represents an unmet medical need with 30-50% complete response (CR) rates and 5% 10-year overall survival (OS) probability.

The hypothesis of the study was to:

- This study aimed to demonstrate a survival advantage of 15% compared to the historical long-term data of 5%. Secondary end points were disease-free survival (DFS), event-free survival (EFS), induction treatment-related death (TRD), haematological and non-haematological toxicities.

What were the study outcomes/conclusions?

- 91 out of 149 elderly patients with AML (61%), were considered fit and eligible to receive this intensive treatment. Patients receiving the intensive treatment showed very high CR rate (73,6%), low induction/consolidation death rates, accounting for 5.5% and 9.2% respectively.

- The 8-year OS was 20.4% (11.1-34.8%): our primary endpoint was achieved. Multivariate analysis identified three risk groups assuming that the presence of unfavourable karyotype and hyperleukocytosis accounts for a score of 1 and 2 respectively: one with no risk factor (score=0) and 30% 8-year OS, RR of dying of 1; one with unfavourable karyotype alone (score=1), 1.8 RR of dying (95% CI: 1.1-3,p= 0.02) and 12% 8-year OS; one with hyperleukocytosis alone or with unfavourable karyotype (score>1) with 3 RR of dying (95% CI: 1.5-5.9, p=0.002) and 0% 3-year OS.

What was learned from the study?

- This approach with intensified dose aracytin plus idarubicin in elderly patients with AML, selected using a simplified MGA, is feasible in > 60% of patients.
- The survival rate was more than double and CR rate was 20% higher than those reported in the literature, with low induction death rate (5% vs 10–20% reported).
- MGA identified frail patients ineligible for intensive therapy while fit and partially fit patients with AML had similar tolerance and outcome apart from delay of PMN recovery > 1500/ml after induction (15 days in fit patients vs 21 days in partially fit patients, $p = 0.03$)
- MGA represents an accurate tool to define eligibility for chemotherapy since FDI and Sorror haematopoietic cell transplantation co-morbidity index (HCT-CI) did not influence outcome and tolerance. Considering the very poor outcome of elderly patients, even in the new drugs era, this regimen represents an excellent backbone for future protocols, exploring new post-remission treatments in this unfavourable setting.