

Outcome of FLAG with or without Idarubicin Regimen in Children with Refractory or Relapsed Acute Leukemia:

A single center retrospective study

Achiraya Neatpracha¹, Chayamon Takpradit¹, Kleebsabai Sanpakit¹, Bunchoo Pongtanakul¹, Kamon Phuakpet¹, Nassawee Vathana¹, Nattee Narkbunnam¹, Jassada Buaboonnam¹

¹ Division of Hematology/Oncology, Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background

- The treatment of relapsed or refractory (R/R) acute leukemia in children remains challenging.
- Several studies have shown that the FLAG±IDA salvage regimen (fludarabine, high-dose cytarabine, and G-CSF, with or without idarubicin) can effectively induce complete remission in pediatric and adult patients before undergoing HSCT.
- Evidence suggests that this regimen has the potential to improve survival rates and long-term disease-free outcomes.

Objective

- To evaluate the efficacy and regimen-related toxicity of the FLAG±IDA regimen in children with R/R acute leukemia.

Methods

- A retrospective study was conducted on pediatric patients aged ≤18 years with R/R acute leukemia who were treated with FLAG±IDA between January 2012 and December 2022.
- Identified through chart review.
- The outcomes evaluated included complete remission (CR), Minimal residual disease (MRD) status, overall remission (OR), and regimen related toxicity.

Results

After the first course of FLAG±IDA

- 52.2% of ALL patients achieved MRD negativity, while 8.7% remained MRD positive. The OR rate was 60.9%.
- 54.5% of AML patients achieved MRD negativity, while 9.1% remained MRD positive. The OR rate was 63.6%.
- Grade III-IV myelosuppression occurred in all cases, with a neutrophil recovery time of 21 days.
- Non-hematologic toxicities: febrile neutropenia, septicemia, oral mucositis, and non-infectious diarrhea
- No patients died from this regimen.

Table 1. Patient characteristics and Response after FLAG±IDA.

Variables	ALL (N=23.0)	AML (N=11.0)	Total (N=34.0)	P-value
Male	17.0 (73.9%)	8.0 (72.7%)	25.0 (73.5%)	1.000
Age at first diagnosis (years)	4.7 (1.6,16.7)	1.9 (0.4,13.8)	4.5 (0.4,16.7)	0.114
Age at salvage treatment (years)	9.4 (2.5,18.0)	4.9 (0.6,17.2)	7.0 (0.6,18.0)	0.065
Disease status				0.672
❖ 1 st relapsed disease	16.0 (69.6%)	10.0 (90.9%)	26.0 (76.5%)	
❖ 2 nd relapsed disease	2.0 (8.7%)	0.0 (0.0%)	2.0 (5.9%)	
❖ ≥3 rd relapsed disease	1.0 (4.3%)	0.0 (0.0%)	1.0 (2.9%)	
❖ Refractory disease	4.0 (17.4%)	1.0 (9.1%)	5.0 (14.7%)	
Relapsed site				0.090
❖ BM	12.0 (63.2%)	10.0 (100.0%)	22.0 (75.9%)	
❖ BM + CNS	4.0 (21.1%)	0.0 (0.0%)	4.0 (13.8%)	
❖ BM + testicular	3.0 (15.8%)	0.0 (0.0%)	3.0 (10.3%)	
Previous treatment				0.002
❖ Standard chemotherapy	6.0 (26.1%)	10.0 (90.9%)	16.0 (47.1%)	
❖ 1 st salvage regimen	13.0 (56.5%)	1.0 (9.1%)	14.0 (41.2%)	
❖ 2 nd salvage regimen	4.0 (17.4%)	0.0 (0.0%)	4.0 (11.8%)	
Regimen				0.000
❖ FLAG alone	2.0 (8.7%)	10.0 (90.9%)	12.0 (35.3%)	
❖ FLAG+IDA	21.0 (91.3%)	1.0 (9.1%)	22.0 (64.7%)	
Response after FLAG±IDA				1.000
❖ Overall remission	14.0 (60.9%)	7.0 (63.6%)	21.0 (61.8)	
• CR with MRD negative	12.0 (85.7%)	6.0 (85.7%)	18.0 (85.7%)	
• CR with MRD positive	2.0 (14.3%)	1.0 (14.3%)	3.0 (14.3%)	
❖ Non-response	9.0 (39.1)	4.0 (36.4%)	13.0 (38.2%)	
2 nd FLAG	8.0 (34.8%)	3.0 (27.3%)	11.0 (32.4%)	0.489
Outcome				0.388
• Alive	4.0 (17.4%)	4.0 (36.4%)	8.0 (23.5%)	
• Death	19.0 (82.6%)	7.0 (63.6%)	26.0 (76.5%)	

References

- Fleischhack G, Hasan C, Graf N, Mann G, Bode U. Br J Haematol. 1998;102(3):647-55.
- Yılmaz Bengoç Ş, E. Ataseven, D. Kızmaçoğlu, F. Demir Yenigülbüz, M. Erdem and Ören H. Turk J Haematol 2017 Vol. 34 Issue 1 Pages 46-51.

Conclusion

- FLAG±IDA for R/R acute leukemia is a favorable option due to its high efficacy, low toxicity profile, and affordability.