

The role of Clofarabine in the treatment of adults with acute myeloid leukemia

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Abstract

The therapeutic scenario available for adult patients with acute myeloid leukemia (AML) has shown only partial progresses over the last few years. This is especially true for refractory and relapsed AML whose outcome is still extremely disappointing. In this context Clofarabine has offered new promising perspectives within first and second line protocols. This review will firstly describe the initial development in monotherapy, considering then the different potential combination strategies which include both polichemotherapeutic regimens and less conventional approaches with new generation drugs. The potential use of Clofarabine as induction treatment for patients candidate to stem cell transplantation and within conditioning regimens will be finally evaluated.

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1. Introduction

With the exception of small subgroups of patients characterized by favorable prognostic factors, the general outcome

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Table 1
Studies evaluating the impact of Clofarabine monotherapy and in combination in patients with acute myeloid leukemia.

Reference	Study phase	Disease phase	Number of patients	Median age	Overall response rate	Complete remission rate	Median overall survival	Induction mortality
Monotherapy								
Kantarjian et al. [4]	Phase 2	Relapsed/refractory	31	54	55%	42%	Not reported	5%
Kantarjian et al. [5]	Phase 2	Untreated	112	71	46%	38%	41 weeks	10%
Burnett et al. [6]	Phase 2	Untreated	106	71	48%	32%	19 weeks	18%
Burnett et al. [9]	Phase 3	Untreated AML and MDS	203	74	38%	22%	13% at 2 years	32%
Combination with Cytarabine								
Faderl et al. [12]	Phase 1–2	Relapsed/refractory	25	63	40%	28%	23 weeks	4%
Faderl et al. [13]	Phase 2	Untreated	60	61	60%	52%	41 weeks	7%
Faderl et al. [14]	Phase 3	Untreated	70	71	67%	63%	45 weeks	19%
Agura et al. [16]	Phase 2	Untreated and relapsed/refractory	30	67	53%	47%	24 weeks	20%
Becker et al. [18]	Phase 1–2	Relapsed/refractory	46	53	61%	46%	36 weeks	12%
Faderl et al. [20]	Phase 3	Relapsed/refractory	163	67	47%	35%	26 weeks	16%
Scappini et al. [21]	Phase 2	Relapsed/refractory	47	50	61%	51%	28 weeks	13%
Other combinations (in brackets)								
Zeidan et al. (Cyclophosphamide) [25]	Phase 1	Relapsed/refractory	28	48	25%	11%	15 weeks	2%
Nazha et al. (Cytarabine + Idarubicin) [27]	Phase 2	Untreated	57	48	79%	74%	Not reached with a median follow up of 11 months	4%
Willemze et al. (Cytarabine + Idarubicin) [28]	Phase 1	Untreated AML and MDS	25	56	84%	76%	Not reported	16%
Amadori et al. (Temsilolimus) [28]	Phase 2	Relapsed/refractory	53	69	21%	8%	16 weeks	13%
Foster et al. (Gemtuzumab) [29]	Phase 1	Relapsed/refractory	20	43	42%	11%	19 weeks	20%
Vigil et al. (Daunorubicin) [31]	Phase 2	Untreated	21	69	38%	29%	45 weeks	14%

List of abbreviations: AML, acute myeloid leukemia; MDS, myelodysplastic syndromes.

of patients with acute myeloid leukemia (AML) has shown only partial progresses over the last 20 years. Within the first line approach the conventional back bone represented by the so-called 3 + 7 regimen has not been substantially modified, if not for the possible advantage offered by higher doses of Anthracyclines [1]. For refractory and relapsed patients the perspectives are even worse as, among the large number of strategies explored in this context, none has consistently offered encouraging response rates. If possible the scenario is even dimmer for elderly patients only a small fraction of which is candidate to potentially curative therapeutic regimens. Over the last 10 years Clofarabine has progressively gained some attention as a possible new weapon available

for patients with AML. If data regarding its potential use for refractory and relapsed patients are nowadays quite consolidated, more recently new findings concerning its application in first line have been made available. The present review will firstly describe the initial development in monotherapy, considering then the different potential combination strategies which include both polichemotherapeutic regimens and less conventional approaches with new generation drugs. All the most relevant studies reported in this context are summarized in Table 1. The potential use of Clofarabine as induction treatment for patients candidate to stem cell transplantation (SCT) and within conditioning regimens will be finally evaluated.

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