

INTRODUCTION

Assessment of early response to induction therapy in acute myeloid leukemia (AML) is typically performed on day 14 after the start of treatment. While the decision to wait until bone marrow (BM) recovery (in the absence of residual disease, usually defined as < 5% of blasts in BM aspiration) or to start the re-treatment (in presence of significant residual disease, usually defined as ≥ 20% blasts) is generally accepted, most of the dilemma occurs in patients with low residual blast count (5-20% blast on day 14). BM re-analysis at day 21 is recommended in this subgroup to make the decision to begin a second induction..

OBJECTIVES

We aimed to analyse whether:

1. BM assessment on day 21 can modulate day 14 findings in the group of patients with < 5% of blasts
2. BM analysis on day 21 in patients with 5-20% of blasts on day 14 could identify the subgroup with high probability to achieve complete remission (CR) without second induction
3. BM minimal residual disease (MRD) assessed by flowcytometry (FCM) on day 14 can already identify this subgroup.

METHODS

Early response assessment (BM cytology, BM MRD – LAIP/DfN) in patients with AML treated with 3+7 induction was performed on day 14.

In the group of patients with < 5% of blasts, as well as in patients with 5-20% of residual blast BM re-analysis was performed on day 21.

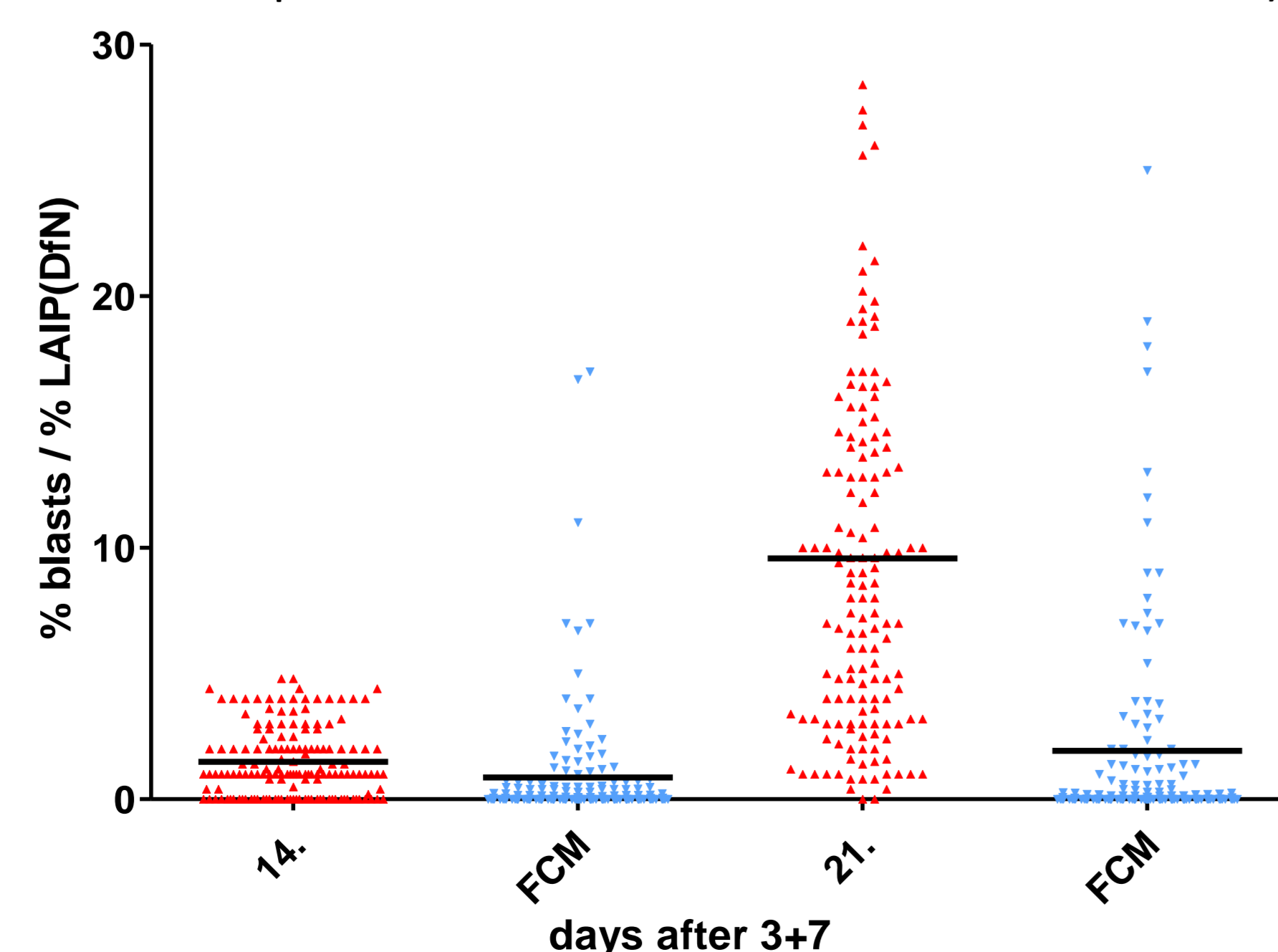
Majority of patients with ≥ 20% blasts on day 14 routinely received second induction, already based on this first BM assessment.

281 patients treated between 2011-2019 were available for this retrospective study.

RESULT I. – <5% BLASTS ON DAY 14

- 152 (54,1%) patients had < 5% of blasts on day 14 BM assessment and 87,5% of them achieved CR without second induction.
- BM re-analysis in this favourable subgroup on day 21 identify “paradoxical” increase of blast percentage to ≥ 5% in 63,3% of patients. However, while reflecting BM recovery, this finding did not influence the CR rate (91,5% of these patients achieved CR without re-treatment).

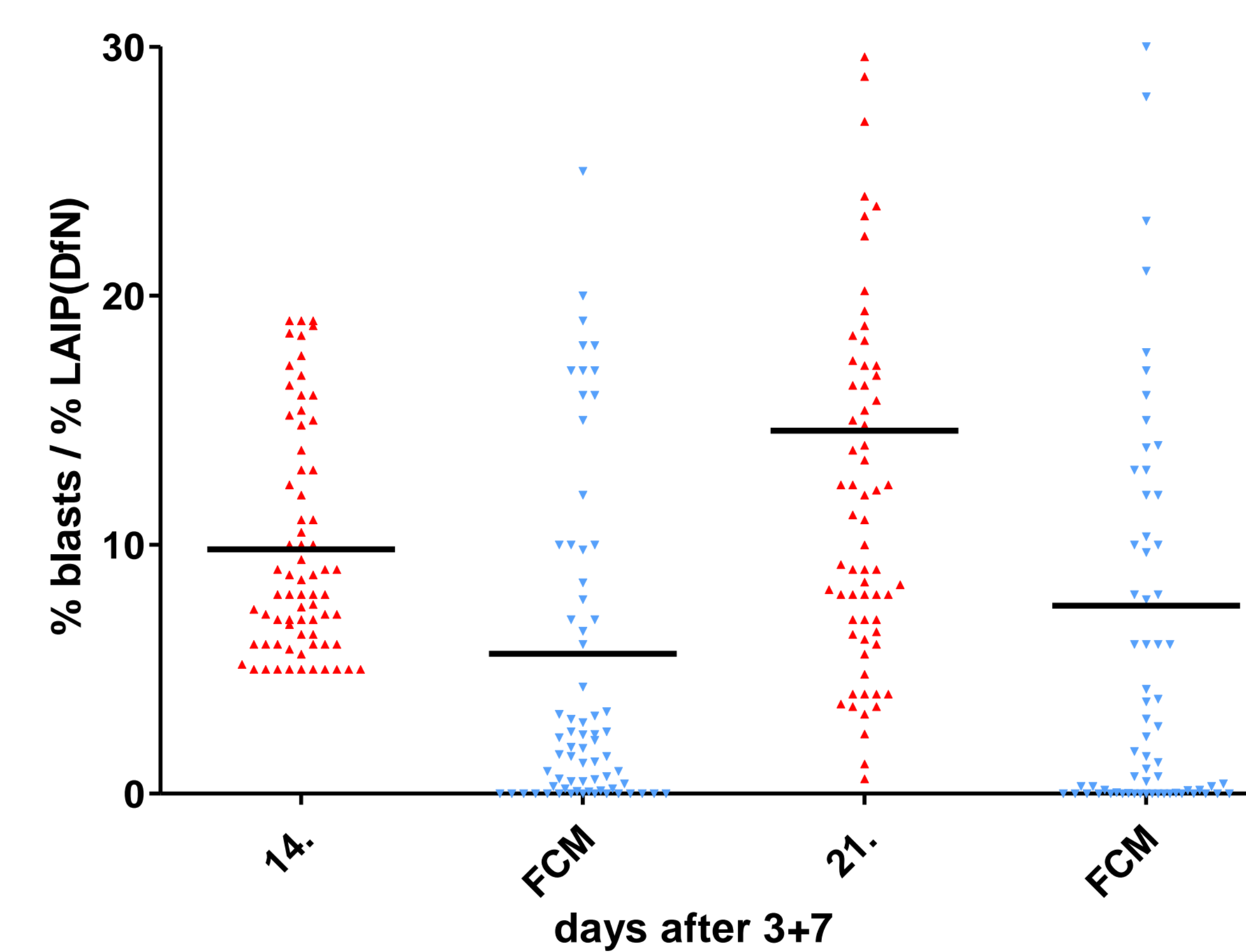
Fig. 1: % of BM blasts and BM LAIP/DfN on day 14 and 21 in patients with < 5% blasts on day 14 from the start of 3+7



RESULT II. – 5 - <20% BLASTS ON DAY 14

- 71 (25,2%) patients had 5 - < 20% blasts on day 14 and 47,8% did not require re-treatment and achieved CR.
- In recommended BM re-assessment on day 21 - 63,4% of patients had again inconclusive BM blast percentage (5 - < 20%), however, still with 51,1% chance to achieve CR without re-treatment.
- However, when cut-off of blast percentage at day 21 was increased to 10%, two subgroups with significantly different chance to achieve CR without the second induction could be identified - BM blasts on day 21 < 10% - n = 32, CR rate 65,6% vs. BM blasts on day 21 > 10% - n = 39, CR rate 33,3%; p = 0,009.

Fig. 2: % of BM blasts and LAIP/DfN on day 14 and 21 in patients with 5 - <20% blasts on day 14 from the start of 3+7



- Moreover, day 14 BM MRD assessment in this group of 71 patients with 5 - < 20% blasts on day 14 using LAIP/DfN cutoff 2% found already on day 14 two separate groups – patients with BM MRD on day 14 < 2% - n = 36, CR rate 69,4% vs. ≥ 2% - n = 35, CR rate 25,7%; p = 0,003.

RESULT III. – PREDICTIVE VALUE OF BM BLASTS ON DAY 14

Probability to achieve remission (not requiring second induction) - D14 assessment

D14 BM blasts (N = 281)	N (%)	N of CR/non CR/NA	% of CR
< 5%	152 (54,1%)	133/19/2	87,5%
5% - < 20%	71 (25,2%)	34/37/5	47,8%
5% - < 10%	44 (15,6%)	25/19	56,8%
10% - < 20%	27 (9,6%)	9/18	33,3%
≥ 20%	58 (20,6%)	2/56/0	3,5%

RESULT III. – PREDICTIVE VALUE OF COMBINATION OF BM BLASTS ON DAY 14 & 21

Probability to achieve remission (not requiring second induction) - D14 & 21 assessment

D14 < 5% BM blasts

D21 BM blasts (N = 150)	N (%)	N of CR/non CR/NA	% of CR
< 5%	55 (36,6%)	46/9	83,6%
5% - < 20%	83 (55,3%)	79/4	95,1%
5% - < 10%	35 (23,3%)	34/1	97,1%
10% - < 20%	48 (32,0%)	45/3	93,8%
≥ 20%	12 (8,0%)	8/4	66,0%

D14 5% - < 20% BM blasts

D21 BM blasts (N = 71)	N (%)	N of CR/non CR/NA	% of CR
< 5%	12 (16,9%)	10/2	83,3%
5% - < 20%	45 (63,4%)	23/22	51,1%
5% - < 10%	20 (28,1%)	11/9	55,5%
10% - < 20%	25 (35,2%)	12/13	48,0%
≥ 20%	14 (19,7%)	1/13	7,1%

CONCLUSION(S)

- Finding of < 5% during early BM assessment on day 14 in AML patients treated with 3+7 is highly predictive for achieving CR without second induction.
- BM re-assessment on day 21 identifies “paradoxical” increase of BM blasts in majority of these patients with BM blasts < 5% on day 14, which is not associated with the lack of treatment response.
- In the most questionable group of patients with 5 - < 20% blasts on day 14, BM MRD with LAIP/DfN < 2% on day 14 or BM blast percentage < 10% during re-assessment on day 21 is significantly predictive for achievement of CR without second induction.