TREATMENTS AND OUTCOMES OF ADULT PATIENTS WITH AML IN THE REAL-LIFE – THE FRENCH OBSERVATIONAL ALFA-PPP STUDY

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INTRODUCTION

AML treatment options have been recently enriched. New agents like gemtuzumab ozogamicin (GO), FLT3 or IDH inhibitors, or CPX-351 have been approved for some patient subsets. Less-intensive options, like the AZA-VEN combination, are used in older/unfit patients.

However, while treatments and indications are standardized, their choice is not, depending on often-subjective factors.

This makes observational studies so important to describe real-life management and outcomes of AML patients.

AIM

The French ALFA group initiated a prospective 2-cohort (newly-diagnosed, relapsed/refractory) observational study in 2022.

This ALFA-PPP study (NCT04777916) aims to prospectively collect clinical data and bio-samples in all AML patients aged 18 years old or more referred to 27 ALFA centers.

Here is the first study report, focusing on newly diagnosed patients with a special interest for less intensive therapies

METHODS

All patients were screened at baseline for disease/patient characteristics including centralized genomics (50-gene panel) and biobanking (French AML Intergroup Lab. Lille, France).

Data/sample collection was then structured by currently approved therapies selected in each individual patient. Patients included frontline into a clinical trial were tagged and followed.

Treatment decision-making criteria were prospectively collected.

Were report here on the first 648 eligible patients who entered the study between April 2022 and September 2023

RESULTS

First 648 patients included in the study

1) DEMOGRAPHY

Clinical characteristics

Median age, years (range)	65y (18-100)
Gender M/F, N (%)	340/308 (52/48%)
ECOG-PS 0-1/2/3+/NA, N	490/97/41/20
HCT-CI 0/1-2/3+/NA, N	54/375/216/3
Median WBC, G/L (IQR)	6.9 (2.4-26)
Median BM blast percentage (IQR)	53% (29-79)
AML type, N (%)	
• *de novo*	467 (72%)
• Post-MDS	54 (8%)
• Post-MPN	58 (9%)
• Therapy-related	69 (11%)

HCT-CI, hematopoietic cell transplantation comorbidity index
(ML. Sorror et al. JAMA Oncol 2017;3:1675-1682)

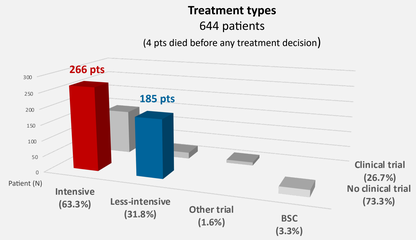
Biological characteristics

ELN-2022 risk group, N (%)	
• Favorable	136 (21%)
• Intermediate	129 (20%)
• Adverse	340 (52.5%)
• Non classified	43 (6.5%)
Selected gene mutation, N/N tested (%)	
• *NPM1*	162/594 (27%)
• *FLT3*-ITD	115/595 (19%)
• *IDH1/2*	131/595 (22%)
• *TP53*	73/595 (12%)
• Secondary AML-like genes*	284/595 (48%)

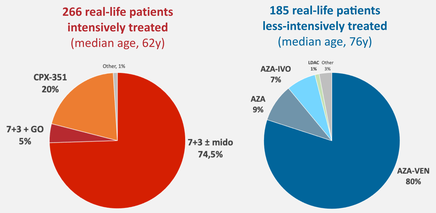
*: including ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1, and/or ZRSR2, as defined in the ELN-2022 classification *(H. Döhner et al. Blood 2022;140:1345-1377)*

– **With a median age of 65 years, more than half of real-life patients have ELN adverse-risk AML. The incidence of secondary-AML like gene mutations is 48%**

2) TREATMENTS



A total of 172 patients (26.5%) were included into a clinical trial frontline (81% IST, 19% company-sponsored)



Therapeutic options offered to the other 476 patients were relatively well balanced between intensive and less-intensive ones

– **Overall, 89/476 (18.5%) patients received an allogeneic SCT during the first 6 months of follow-up, including 81 intensively and 8 less-intensively treated patients.**

3) LESS-INTENSIVE THERAPIES

Real-life selection criteria

Criteria leading the physician to select a less-intensive therapy (185 patients)

– Advanced age	138 (75%)
– Comorbidities	50 (27%)
– AML characteristics	36 (19%)
– Other reason	11 (6%)
– Patient's choice	1 (1%)

The choice was based on AML characteristics only in 18 patients (10%)

Multivariate analysis of criteria objectively associated with the choice of less-intensive therapy

Criteria	OR (95% CI)	P value
Age ≥65y	21.2 (9.6-46.7)	<0.001
Higher ECOG-PS	3.2 (1.8-5.8)	<0.001
Higher HCT-CI	2.7 (1.5-4.9)	0.001
Lower WBC	0.99 (0.98-0.99)	0.022
Post-MDS AML	6.3 (2.1-18.9)	0.001
Post-MPN AML	6.6 (2.4-18.1)	<0.001
Poor ELN-2017 cytogenetics	2.1 (1.01-4.4)	0.046
TP53 mutation	5.4 (1.8-16.6)	0.003
IDH1/2 mutation	3.1 (1.4-6.5)	0.003

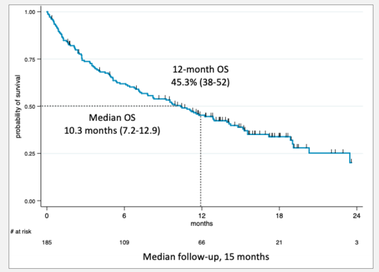
The covariates entering the model were age (65y), sex, ECOG-PS (3 classes), HCT-CI (3 classes), WBC and BM blast % as continuous covariates, post-MDS, post-MPN and t-AML, poor cytogenetics (*according to the ELN-2017 classification; Blood 2017;129:424-447*), *NMP1*, *FLT3*-ITD, *IDH1/2*, and *TP53* gene mutations.

– **A myriad of independent factors governs real-life choice of a less-intensive *vs.* intensive treatment**

– **A good correlation between the reasons given by the physician and the objective factors was observed (not shown)**

4) LESS-INTENSIVE THERAPIES

Real-life outcome



Stepwise Cox model for a shorter overall survival in less-intensively treated patients

Factor	HR (95% CI)	P value
Higher ECOG-PS	1.3 (1.01-1.6)	0.038
Presence of comorbidity	1.9 (1.2-3.0)	0.003
Marrow blast percentage	1.01 (1.0-1.02)	0.024
Therapy-related AML	1.8 (1.01-3.3)	0.046
sAML-like mutations	1.6 (1.01-2.5)	0.048
TP53 mutation	3.6 (2.1-6.4)	<0.001
No *IDH1/2* mutation	2.7 (1.5-4.8)	0.001

The covariates entering the model were age (65y), sex, ECOG-PS, HCT-CI (3 classes), presence of comorbidity by investigator's judgement, WBC and BM blast % as continuous covariates, post-MDS, post-MPN and t-AML, poor cytogenetics (*according to the ELN-2017 classification; Blood 2017;129:424-447*), ELN-2022 risk, *NMP1*, *FLT3*-ITD, *IDH1/2*, *N/K-RAS*, *TP53* and sAML-like gene mutations.

– **Rather than age by itself, survival after less-intensive treatment is governed by multiple independent clinical and genomic factors.**

CONCLUSIONS

- **This first ALFA-PPP study report illustrates the current real-life management of French adult patients with AML, confirming the rising place of less-intensive treatment options in a European context (annual reports are planned in the next future)**
- **The outcome of less-intensively treated patients appears to be somewhat inferior to that reported for instance in the pivotal VIALE-A AZA-VEN trial** *(CD DiNardo et al. NEJM 2020;383:617-629)*
- **The risk classification of less-intensively treated patients likely depends on a composite set of clinical and biological factors which remains to be standardized despite recent proposals** *(H. Döhner et al. Blood 2024 Aug 12; FW. Hoff et al. Blood Adv. 2024 Oct 22)*

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