EPH190

# REAL-WORLD TREATMENT OF NEWLY DIAGNOSED PATIENTS WITH ACUTE MYELOID LEUKEMIA AND AGED BETWEEN 60 AND 75 YEARS: ANALYSIS OF KEY DRIVERS FOR CHEMOTHERAPY SELECTION IN FRANCE AND GERMANY

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## BACKGROUND

Major goals of treatment in acute myeloid leukemia (AML) are obtaining remission, minimizing toxicity and potential disease eradication. Typically, it includes optimal induction chemotherapy to obtain CR, followed by consolidation and/or maintenance often including allogeneic stem cell transplantation.
Among prognostic criteria, age at diagnosis greater than 60 years is one of the major markers due to higher proportion of high risk cytogenetic/molecular features and decrease tolerance of higher dose chemotherapy.
In previously untreated patients who are unfit for intensive treatment, VIALE-A phase III trial compared azacitidine + venetoclax vs azacitidine + placebo and showed improved OS with longer duration of CR and CR/CRi compared to azacitidine monotherapy (1,2).
In this setting, eligibility for intensive chemotherapy is a key point for patients' management, especially with an age between 60 and 75. There is however a wide heterogeneity in this subset of patients and key drivers to choose between intensive or non intensive chemotherapy is still a matter of debate with few randomized clinical trials being conducted to address this specific question (3).

## OBJECTIVES

This study explores patients' characteristics, eligibility criteria and key drivers for the choice between intensive and non-intensive chemotherapy (IC) in real-world AML patients with an age between 60 and 75 years treated in France and Germany.

## METHODS

Anonymous patient charts were analyzed based on data reported by onco-haematologists making treatment decisions for patients with AML in France (FR) and Germany (DE) over the period between October 2023 and December 2023 (i.e Q4 2023).

## RESULTS

A total of 293 unique patient charts were included in the analysis with 152 treated in France and 141 in Germany over the study period. Overall, the breakdown between different ages are: 95 unique patients between 60 and 64 years, 84 between 65 and 69 and 114 between 70 and 74. Out of the total population, 166 patients were fit for intensive chemotherapy (IC), 17 borderline fit and 110 unfit for IC. (Fig 1.)
Analysis of patients fit for IC showed favorable ELN risk category in 39%, intermediate in 58% and adverse in 3%. As expected, most patients were ECOG 0 (43%) and 1 (48%) with no difference between France and Germany. NPM1 molecular status was mutated in 8% of case, unmutated in 51% and not tested in 29% with a higher proportion in France (42%) as compared to Germany (11%). The same finding was made regarding lack of testing for both Flt3 ITD and TKD patients which was greater in France (33% for ITD and 28% for TKD) than in Germany (6% for ITD and 6% for TKD, respectively). (Fig 2.)

| | France | | | Germany | | |
|---|---|---|---|---|---|---|
| | **Total tested or not** (n= 152) | **Fit** (n= 96) | **Unfit** (n= 49) | **Total tested or not** (n= 141) | **Fit** (n= 70) | **Unfit** (n= 61) |
| **60 - 64 yrs** | 33% | 46% | 10% | 32% | 41% | 15% |
| **65 - 69 yrs** | 27% | 27% | 20% | 30% | 37% | 23% |
| **70 - 75 yrs** | 40% | 27% | 69% | 38% | 21% | 62% |

***Fig 1. Patient age currently in 1L induction (Source: APLUSA AMLsyndiTrack™ - Q4.23)***

| | **NPM1** | | | | **FLT-3 ITD** | | | | **FLT-3 TKD** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | France | | Germany | | France | | Germany | | France | | Germany | |
| | **Fit** | **Unfit** | **Fit** | **Unfit** | **Fit** | **Unfit** | **Fit** | **Unfit** | **Fit** | **Unfit** | **Fit** | **Unfit** |
| **Tested** | 40% (n= 38) | 76% (n= 37) | 86% (n= 60) | 49% (n= 30) | 46% (n= 44) | 73% (n= 36) | 91% (n= 64) | 69% (n= 42) | 57% (n= 55) | 73% (n= 36) | 91% (n= 64) | 67% (n= 41) |
| Positive | 13% | 22% | 13% | 17% | 2% | 8% | 17% | 7% | 4% | 8% | 9% | 20% |
| Negative | 87% | 78% | 87% | 83% | 98% | 92% | 83% | 93% | 96% | 92% | 91% | 80% |
| **Not tested** | 42% | 20% | 11% | 46% | 33% | 16% | 6% | 28% | 28% | 22% | 6% | 28% |
| **Inconclusive / DK** | 19% | 4% | 3% | 5% | 21% | 10% | 3% | 3% | 15% | 4% | 3% | 5% |

***Fig 2. Conducted tests and results when test performed currently in 1L induction and tested for each mutation (Source: APLUSA AMLsyndiTrack™ - Q4.23)***

In this fit population, 30% of patients received 1st line IC with « 3+7 » regimen and 25% received « 3+7 » regimen combined with midostaurin with some discrepancies between France (21% received 3+7 regimen and 16% the 3+7+ midostaurin) and Germany (37% received 3+7 and 41% received 3+7+midostaurin). There is aslo a significant different regarding the use of venetoclax-based treatment in this fit population (3% for France and 23% for Germany). (Fig 3.)
Analysis of unfit population revealed favorable ELN risk category in 25%, intermediate in 33% and adverse in 31%. Compared to the fit population, a higher proportion of patients was ECOG 1 (54%), 2 (27%) and 3 (11%). Molecular assessment for NPM1 status revealed higher proportion of unknown status in Germany (46%) vs. France (20%).

The same findings were also made for Flt3 ITD and TKD mutation status between the 2 countries (28% and 28% not tested in Germany vs. 16% and 22% in France).

When considering treatments received by unfit population of patients, 0% received the 3+7 regimen, only 2% the 3+7+midostaurin and 49% venetoclax-based chemotherapy, mainly azacytidine + venetoclax (41%). This proportion is similar between France (45%) and Germany (52%). (Fig 3.)

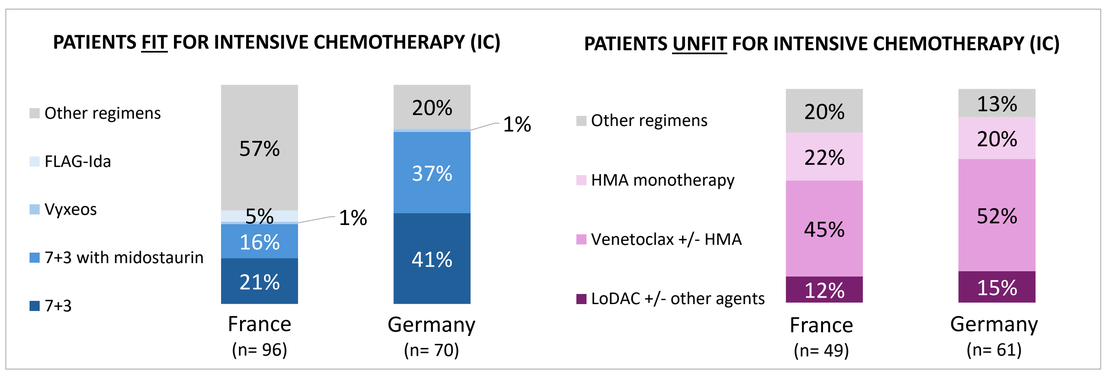


***Fig 3. Treatments received in 1L induction (Source: APLUSA AMLsyndiTrack™ - Q4.23)***

When examining the primary comorbidities among patients deemed unfit for intensive chemotherapy, the most prevalent conditions were hypertension, diabetes mellitus, dyslipidemia, chronic obstructive pulmonary disease (COPD), and moderate to severe heart disease, including previous myocardial infarction and arrhythmia.
Notably, only a small portion of patients had no significant comorbidities, accounting for 16% of unfit patients in France and 11% in Germany. Differences emerged between the two countries, with hypertension and diabetes more common in France than in Germany (47% vs. 38% for hypertension and 39% vs. 28% for diabetes).
In contrast, higher rates of COPD, vascular disease, and rheumatologic disorders were observed in Germany than in France (28% vs. 10%, 16% vs. 10%, and 10% vs. 2%, respectively) (Fig. 4).
Overall, these comorbidities align with the expected medical profile of patients unfit for chemotherapy, with a high prevalence of cardiovascular and metabolic conditions.

| | France | Germany |
|---|---|---|
| **Comorbidity** | (n= 49) | (n= 61) |
| Hypertension | 47% | 38% |
| Diabetes | 39% | 28% |
| Hypercholesterolemia | 22% | 21% |
| COPD | 10% | 28% |
| Hypo-/Hyperthyroidism | 16% | 18% |
| Heart Disease (history of MI, AF) | 14% | 16% |
| Vascular Disease | 10% | 16% |
| Renal Disease | 10% | 13% |
| Neuropathy | 8% | 7% |
| Thromboembolic event | 8% | 5% |
| Rheumatological Disease | 2% | 10% |
| Dementia | 4% | 2% |
| Liver Disease | 0% | 5% |
| Autoimmune disease | 6% | 0% |
| AIDS/HIV Positive | 2% | 0% |
| None | 16% | 11% |

***Fig 4. Comorbidities at induction treatment onset among patients unfit for IC (Source: APLUSA AMLsyndiTrack™ - Q4.23)***

## CONCLUSION

In this real-world analysis with newly diagnosed AML patients with an age between 60 and 75 years, key drivers to consider eligibility for IC are age, comorbidities and ECOG status. In patients who are borderline fit, molecular markers defining favorable and intermediate ELN risk group are also considered to propose more intensive treatment, including until age 75 for NPM1 mutation. Some discrepancies are shown regarding some molecular testing with a higher proportion of patients not tested in France in the fit population and in Germany for the unfit population.

## REFERENCES

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