

Abstract Submission

4. Acute myeloid leukemia - Clinical

EHA-3542

FLT3 TESTING IN RELAPSED ACUTE MYELOID LEUKEMIA SETTING IS BECOMING INCREASINGLY COMMON, BUT LABORATORY TURNAROUND TIMES (TAT) MAY BE A BARRIER TO TREATMENT WITH SECOND GENERATION FLT3 INHIBITORS.

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Does the study abide by applicable national and international regulations and guidelines, including but not limited to ethical committees, data protection and privacy regulations, informed consent and off-label use of drugs?: Yes

Background: The treatment landscape in AML has developed at an astonishing pace in the last 3 years, with >5 therapies being approved by the FDA. FLT3 inhibitors gilteritinib (Gil) and quizartinib (Quiz) present an unprecedented opportunity for improved survival in relapse and refractory AML. As FLT3 status is known to be dynamic, with acquisition, loss, and swapping of FLT3 mutational status seen in a significant number of patients - especially after first-line midostaurin use - it will be important to confirm FLT3 positivity prior to Gil or Quiz therapy, especially in relapsed patients.

Aims: Establish if FLT3 testing behavior in relapsed AML has evolved, both in physicians and laboratories, in support of therapy selection in relapsed AML in the 12 months between February 2018 and February 2019.

Methods: We conducted online quantitative surveys with physicians (hemato-oncologists with comparable median patient loads) across 5 European countries (UK, De, Sp, Fr, and It) in Feb 2018 (N=243) and 2019 (N=163), to compare FLT3 (re)testing behavior in AML. This study adopted the quantitative method in collecting and analyzing data; the data was analyzed using unpaired t-tests. The Diaceutics database of laboratories conducting FLT3 in the same markets was used to understand the prevailing TAT in those countries.

Results: From 2018 to 2019 we see an increase in prevalence of FLT3 retesting rates among clinicians; 43.0% on average across EU5 (92.0% vs 49.0% in 2019 vs 2018) (Table 1). The population surveyed and recruitment were comparable, so the rise appears to result from increased awareness of the unstable status of FLT3 and an increase in education on targeted therapies in the second line setting. The reported percentage of patients being tested increased in both FLT3 positive and negative patients; a weighted analysis shows that the % of AML patients retested for FLT3 increased by 2.6 (14.9% to 38.3%) and 2.9 (15.9% to 45.4%) fold in FLT3 positive and negative patients respectively. Follow on attitudinal questions revealed that more physicians would only prescribe an FLT3 inhibitor based on a recent test result in 2019 (29.6%) vs. 2018 (22.2%), again attributable to increased awareness of the unstable status of FLT3 during disease progression. Similarly, there is increasing awareness of the importance of fast TAT in the relapsed setting, with 35.7% of physicians citing the critical nature of fast TAT. Diaceutics database analysis suggests that despite the increasing demand for faster results, the TAT provided by laboratories is not changing, with an average TAT remaining suboptimal at 12.6 days (ranging from 6 days in Germany to 16 days in the UK).

Image/Pictures:

Surveyed population			
	2018	2019	Δ and/or p value
N of respondents	243	163	
N (%) of respondents retesting in any situation	119 (49.0%)	150 (92.0%)	+43.0 percentage points / 1.9 fold increase
Median (interquartile range) patient load of respondents retesting in any situation	60 (45-120)	60 (35-135)	NS
Retesting behaviors			
	2018	2019	Δ and/or p value
Calculated % of population retested (weighted average)			
Patients who are FLT3-positive at diagnosis	14.9	38.3	2.6 fold increase
Patients who are FLT3-negative at diagnosis	15.9	45.4	2.9 fold increase
Attitudes section			
	2018	2019	Δ and/or p value
I would only prescribe a FLT3 inhibitor at relapse if I had recent FLT3 status results (i.e. able to redo the test before prescribing decision)			
% of respondents agreeing (Strongly agree, Agree)	22.2%	29.6%	+7.4 percentage points / 1.3 fold increase
Mean (st dev) score (1-7 point scale)	5.0 (+1.4)	4.9 (+1.7)	NS (p=0.4397)
A quick turnaround time of FLT3 testing is very important in relapse/refractory AML patients			
% of respondents agreeing (Strongly agree, Agree)	32.2%	35.7%	+3.5 percentage points / 1.1 fold increase
Mean (st dev) score (1-7 point scale)	5.4 (+1.3)	5.3 (+1.6)	NS (p=0.3806)

Summary/Conclusion: Prescribing FLT3 inhibitors in relapsed patients based on an FLT3 result from diagnosis is suboptimal, as clonal evolution may lead to a change of FLT3 negative to positive status, leading to these patients missing out on the opportunity to

benefit from 2nd generation FLT3 inhibitors if the test is not repeated at relapse. Education about the new clinical utility of FLT3 is still needed to increase testing rates among treating physicians, although evidence suggests that awareness of the need for testing of at least some patients is increasing. Despite this increase in awareness, we have not seen significant changes in the provision of testing in most EU5 countries, especially in TAT, which is critical to enable timely therapeutic decisions. Reimbursement barriers will need to be addressed to ensure that laboratories meet the demand for fast TAT, which is particularly essential at the relapse treatment decision point.

Keywords: AML, Diagnosis, FLT3, flt3 inhibitor