AML: **DEVASTATING**

WITH A FLT3 MUTATION: **DISASTROUS**

THINK FLT3

AML=acute myeloid leukemia; FLT3=FMS-like tyrosine kinase 3.

IN PATIENTS WITH AML,

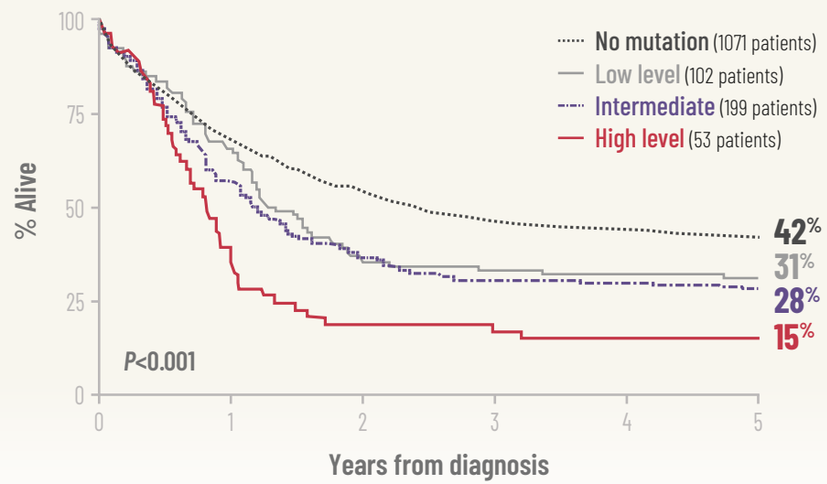
FLT3 is the most common mutation at diagnosis and is associated with lower* patient survival[1,2]

- While there are many mutations in AML, it has been shown that, of patients newly diagnosed with AML and tested for FLT3 mutations, up to **1 in 3 patients may have a FLT3 mutation**[1]

**FLT3-ITD*

AFTER INDUCTION THERAPY[3]

The 5-year survival rate is as low as 15% in patients with a *FLT3-ITD* mutation[3]



Data from DNA samples of 1425 young adult patients with AML (1307 with de novo AML) treated with conventional chemotherapy who entered into two clinical trials between 1988 and 2002. Overall survival stratified according to total FLT3-ITD level. Shown here: The distribution of FLT3/ITD cases according to total mutant level suggested 3 different groups: those with less than 25% mutant (low), 25% to 50% mutant (intermediate), and greater than 50% mutant (high).

ITD=internal tandem duplication.

AT RELAPSE[2]

Overall survival rate is more than 1.5x lower in relapsed/refractory patients with a *FLT3-ITD* mutation[2]

2-YEAR OVERALL SURVIVAL RATE [2]

40%* survival with **no *FLT3-ITD* mutation** (n=96)

vs

P=0.03

23%* survival with ***FLT3-ITD*** (n=37)

**±5 for no mutation and ±7 for FLT3-ITD.*

Data from a retrospective, multicenter study including 138 adult patients with refractory (n=57) or relapsed (n=81) AML treated with a combination of gemtuzumab ozogamicin and intensive salvage chemotherapy (96 patients had no FLT3-ITD mutation, 37 had FLT3-ITD mutation, and 5 had an unknown mutation status).

A FLT3-ITD mutation drives progression and may lead to lower survival rates[2-4]

The prevalence of FLT3-ITD mutations can increase with each relapse[5*]

Mutation status changes throughout treatment[5*]

22% of patients had a change in mutational status at relapse (n=11/50)[5]

- **10% GAINED** a *FLT3-ITD* mutation (5/50)
- **8% LOST** a *FLT3-ITD* mutation (4/50)
- **4% CHANGED** mutational status from *FLT3-TKD* to *FLT3-ITD* (2/50)

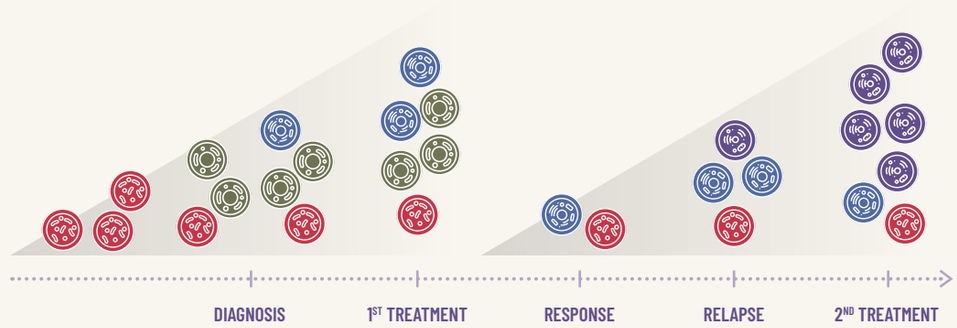
Incidence of a FLT3 mutation can increase with each relapse,* and may lead to **lower overall survival rates**[2,3,5]

DIAGNOSIS	1ST RELAPSE	2ND RELAPSE
22% of patients had a *FLT3-ITD* mutation **AT DIAGNOSIS**[5] (n=11/50)	**32%** of patients had a *FLT3-ITD* mutation **AT 1ST RELAPSE**[5] (n=16/50, *P*=0.37)	**43%** of patients had a *FLT3-ITD* mutation **AT 2ND RELAPSE**[5] (n=6/14, *P*=0.17)

**A retrospective analysis of 50 adult patients with FLT3 mutations at diagnosis and relapse with chemoresistant AML to correlate mutation status with multiple variables.*

TKD=tyrosine kinase domain.

Clonal evolution during therapy can lead to a change in mutational status[6]



- **AML cells often gain or lose mutations,** including FLT3 mutations, and these cells can proliferate[7]
- Some clones may become dominant, while others may emerge, leading to **a change in mutation status**[7]

GENETICALLY DIFFERENT AML CLONES

- **Clone with early founder mutation**
- **Initial driver mutation clone** with disease-defining mutation
- **Late driver mutation** additional subclones

FLT3 mutation status can change, thus it is important to test patients at relapse or progression[5,8]

NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®)

Recommend expediting FLT3 mutation testing at diagnosis.[8]

Retest at relapse or progression to inform treatment decisions[8]

Use a quick and accurate FLT3 (ITD, TKD) test[9,10]

PCR RESULTS:

UP TO 3 BUSINESS DAYS

NGS RESULTS:

UP TO 20 DAYS

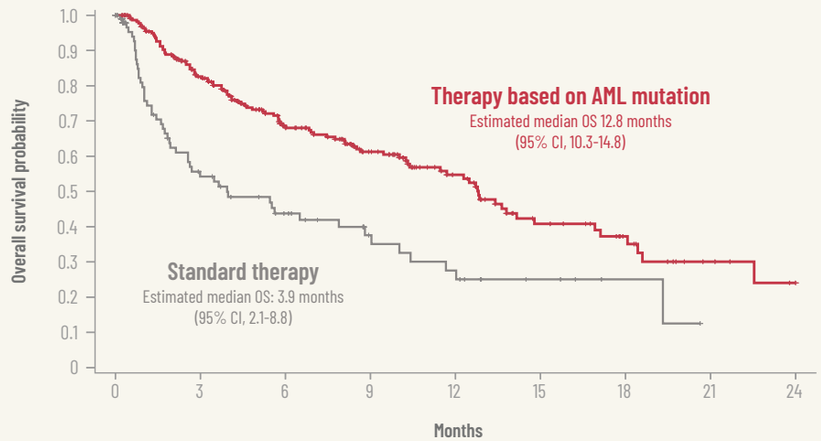
Know what you're up against:[8]

Confirming a FLT3 mutation can **help inform treatment decisions**

NCCN=National Comprehensive Cancer Network® (NCCN®).

Research highlights the importance of testing to tailor treatment

In the BeatAML study, newly diagnosed patients who received mutation-specific treatment had higher OS rates compared to standard therapy[11]



Patients at risk

Therapy based on AML mutation	224	168	114	79	49	27	17	7	3
Standard therapy	103	39	26	15	11	5	2	0	

Data selected from a prospective analysis (November 2016 through January 2019) of 395 eligible patients with suspected AML across 14 clinical sites aimed to provide cytogenetic and mutational data within 7 days. Patients were assigned treatment based on cytogenetic and molecular results. Eligible patients had been untreated and were ≥60 years old and assigned to a sub-study based on the dominant clone determined through testing. Overall survival results data from patients given therapy based on AML mutation (n=224) vs standard therapy (n=103) were included. 30-day mortality data from all 395 eligible patients was reviewed and analyzed. Median follow-up for OS was 7.1 months (range: 0-24.8 months)

This study does not distinguish the benefit of treatment compared to clinical trial enrollment. The treatment arms within this trial are designed with specific considerations of newer agents with therapeutic relevance and will continue to adapt to changes in the AML treatment landscape. For more details regarding study design and limitations, please see the full study article.

Waiting up to 7 days for biomarker results did not adversely impact overall survival[11]

AML: DEVASTATING | WITH A FLT3 MUTATION: DISASTROUS

- *FLT3-ITD* is a common mutation in AML and is **associated with lower survival**[1,2*]
- The incidence of *FLT3-ITD* mutations **can increase with each relapse**[5]
- NCCN Guidelines® recommend **expediting FLT3 mutation testing at diagnosis**[8]
- Confirm FLT3 mutation status at relapse or progression to make **informed treatment decisions**[8,11]

THINK FLT3

**FLT3-ITD.*

Retest at relapse or progression to inform treatment decisions[8]

Visit ThinkFLT3.com to learn more

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