

# Maintenance Therapy after Transplant: Acute Myeloid Leukemia (AML)

## Celebrating a Second Chance at Life Survivorship Symposium

April 29 – May 5, 2023



**Eytan Stein MD**  
Memorial Sloan Kettering Cancer Center



2023 SURVIVORSHIP SYMPOSIUM

# Treatment of Acute Myeloid Leukemia



2023 SURVIVORSHIP SYMPOSIUM

## Fundamental Questions

- What do we mean when we talk about maintenance therapy and how does this differ from “consolidation?”
- What are some maintenance therapies that have been used to treat patients with AML who don't have a transplant?
- Is there data to support the benefit of maintenance therapy after a transplant for patients with AML?
- What is the future of maintenance therapy after a transplant for patients with AML?

## Phases of AML Treatment

- The treatment of AML is generally divided into two phases:
  - Induction, where chemotherapy is given to obtain a complete remission
  - Consolidation, where additional therapy is given to eliminate residual leukemia cells that may not be identified on a bone marrow biopsy.
- Consolidation can take three forms:
  - Repeated rounds of additional chemotherapy without a transplant
  - An autologous stem cell transplant (not typically done in the United States)
  - An allogeneic stem cell transplant

## What is Maintenance Therapy?

- Maintenance therapy is
  - low-intensity treatment (i.e. therapy that is easy to take, and has few side effects)
  - aims to keep a lid on any leukemia cells that might come back.
- Maintenance therapy has proven effective in patients with acute lymphoblastic leukemia and multiple myeloma.

## Potential Pitfalls of Maintenance Therapy

- Overtreatment:
  - It is possible many patients are cured after a transplant and don't need maintenance to prevent a relapse.
- Overtreatment can cause various problems:
  - Side effects with long periods of treatment
  - Committing patients to indefinite treatment without an endpoint
  - Financial toxicity – i.e., treatment can be very expensive.



International Bone Marrow Transplant  
Center Group

## What is the Role of Maintenance Therapy for Patients Who Don't Have a Transplant?

BMT 30 YEARS EMPOWERING PATIENTS  
infontet.org

2023 SURVIVORSHIP SYMPOSIUM

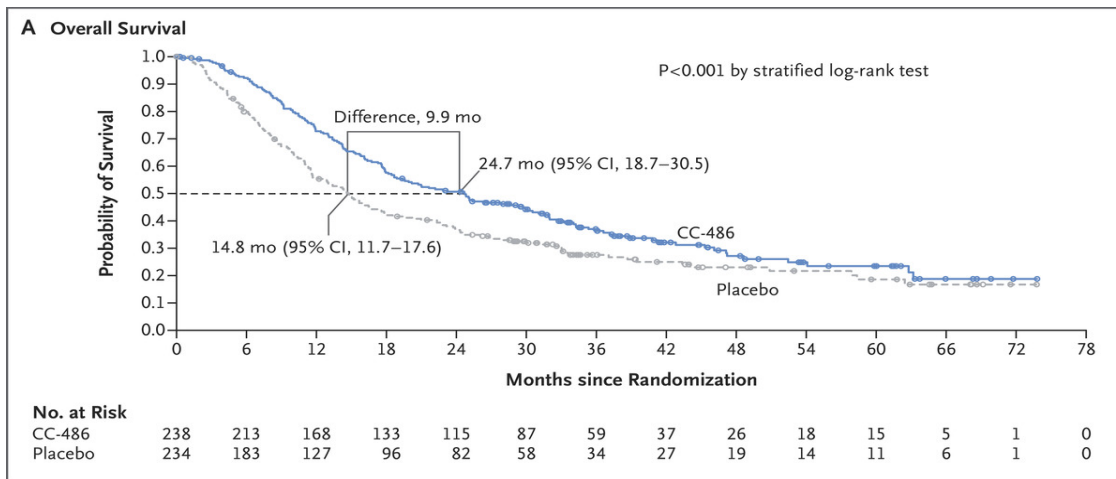
### Oral Azacitidine as Maintenance Therapy For Acute Myeloid Leukemia without a Transplant

- International, multicenter, placebo-controlled, double-blind, randomized, phase III study that enrolled patients from 148 sites in 23 countries (NCT01757535).
- Enrolled patients older than 55 with intermediate or unfavorable risk AML.
- Patients did not have an allogeneic stem cell transplant.
- Randomized to receive oral azacitidine or a matched placebo as maintenance.
- Those who received the oral azacitidine had an increased median overall survival, 9.9 months longer, than those who received placebo.
- For those patients with intermediate or unfavorable risk AML who don't have a transplant, oral azacitidine is a standard of care.

BMT 30 YEARS EMPOWERING PATIENTS  
infontet.org

2023 SURVIVORSHIP SYMPOSIUM

## Oral Azacitidine Improves Overall Survival



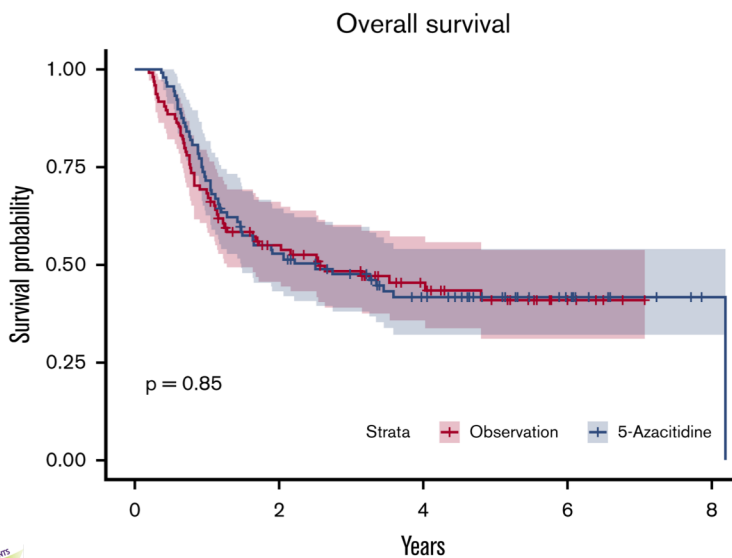
International Bone Marrow Transplant Centre Group

## What about Maintenance Therapy after an Allogeneic Stem Cell Transplant?

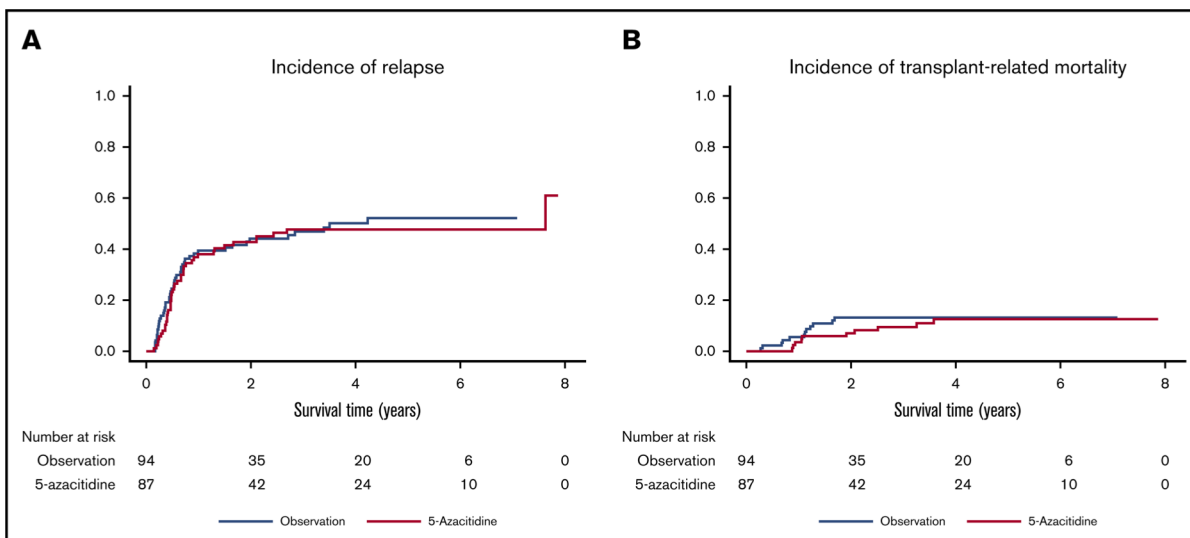
## Azacitidine as Maintenance Therapy after an Allogeneic Transplant

- Randomized trial giving IV azacitidine to patients with AML after they received an allogeneic stem cell transplant.
- 50% of patients allocated to receive IV azacitidine and 50% to observation alone

## Azacitidine as Maintenance after Allogeneic Transplant



## Azacitidine as Maintenance after Allogeneic Transplant



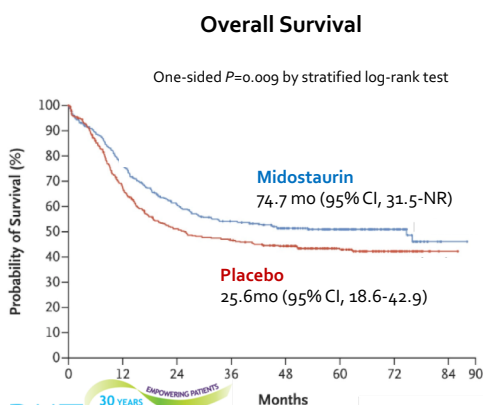
International Bone Marrow Transplant Centre Group

## FLT3 Inhibition

## What is FLT3?

- FLT3 is a gene that is mutated in approximately 30% of patients with AML.
- In the past, the presence of a FLT3 mutation was considered a negative prognostic factor.
- The use of FLT3 inhibitors with chemotherapy has improved the outcomes of patients with FLT3 mutant AML.

## Midostaurin - Newly Diagnosed FLT3 Mutant AML



### Efficacy

- Midostaurin benefit on OS similar across *FLT3* subtypes
- 5-year survival rate: Midostaurin, 50.9% vs placebo, 43.3%

### Safety

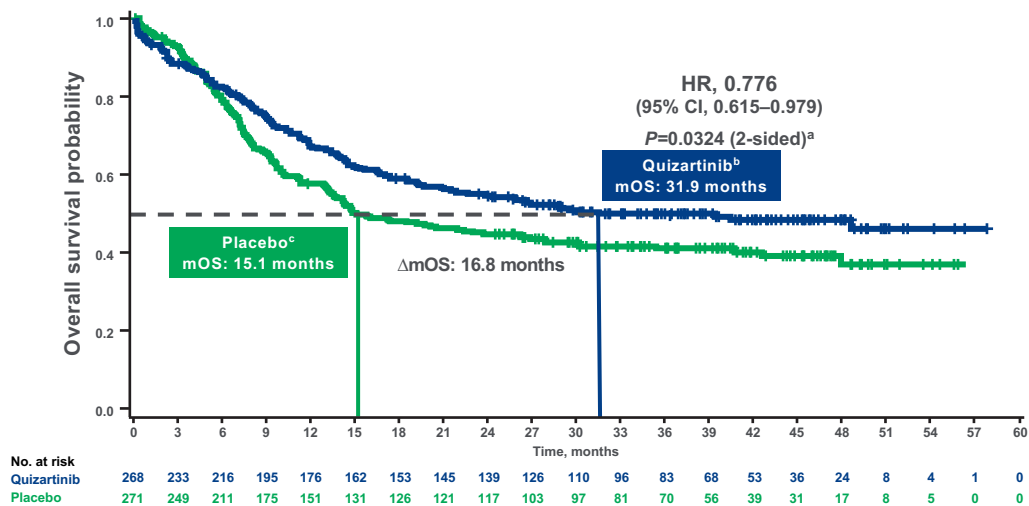
- Rates of  $\geq$  Grade 3 anemia and rash were higher in the midostaurin group
- Rate of  $\geq$  Grade 3 nausea was higher in the placebo group



## New FLT3 Inhibitor - Quizartinib

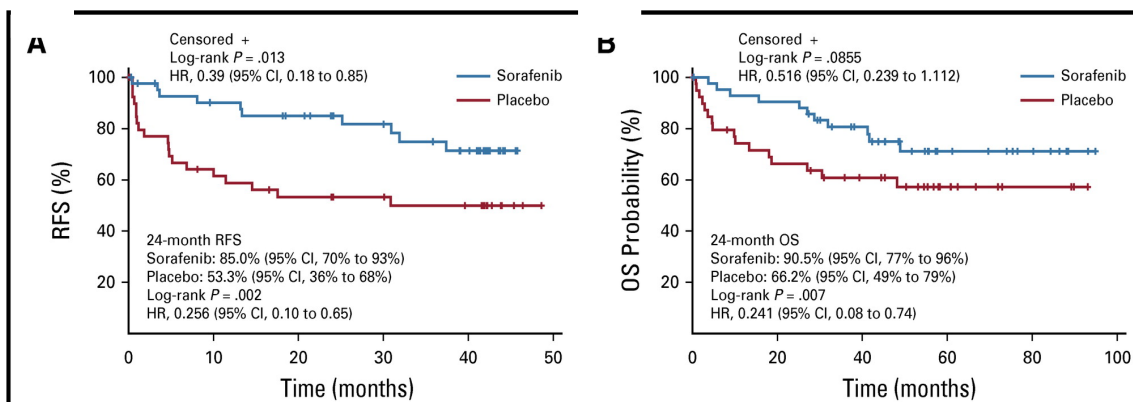
- For newly diagnosed AML patients of any age
- Randomized trial of chemotherapy with quizartinib versus chemotherapy with placebo.
- Primary outcome of trial is overall survival

## Overall Survival for Quizartinib with Chemotherapy



<sup>a</sup>P-value was calculated using a stratified log-rank test. <sup>b</sup>Median follow-up time for quizartinib arm, 39.2 months. <sup>c</sup>Median follow-up time for placebo arm, 39.2 months.  
Erba H, et al. Presented at the European Hematology Association Annual Meeting, Vienna, Austria, June 9–12, 2022. Abstract S100.

## Maintenance Sorafenib after Allogeneic Transplant for Patients with a FLT3 Mutation



2023 SURVIVORSHIP SYMPOSIUM

Rollig C, et. al, JCO 2021

References

19

## FLT3 Inhibitor Gilteritinib Does Not Improve Relapse-Free Survival after Transplant



Breaking news!!

Press Release

### Astellas and BMT CTN Announce Topline Results from Phase 3 MORPHO Trial of Gilteritinib

TOKYO and ROCKVILLE, Md., March 9, 2023 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., “Astellas”) and the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) today announced topline results from the Phase 3 MORPHO clinical trial evaluating gilteritinib as a maintenance therapy following allogeneic hematopoietic stem cell transplantation (HSCT) for patients with FMS-like tyrosine kinase 3 (FLT3)-internal tandem duplication (ITD) mutated acute myeloid leukemia (AML). Based on the data, the study did not meet its pre-defined primary endpoint of relapse-free survival (RFS) for patients treated with gilteritinib compared to placebo. The study was conducted in collaboration with BMT CTN.

The Phase 3 MORPHO trial is a randomized, double-blind, placebo-controlled, multi-center trial that compares gilteritinib to placebo as maintenance therapy over a period of two years following HSCT in 356 patients with FLT3-ITD mutated AML and in remission after induction therapy. The most frequent treatment-emergent adverse events (TEAEs) were decrease in neutrophil count, diarrhea and nausea, which were generally consistent with previous studies of gilteritinib. Detailed results will be submitted for publication and for consideration at upcoming medical meetings. Since RFS was not statistically significant at the primary



2023 SURVIVORSHIP SYMPOSIUM

## Future of Maintenance Therapy after a Transplant

- Benefit of maintenance after a transplant is unclear based on randomized data both in genetically defined and more general subsets of patients with AML
- It may be that the best candidates for maintenance therapy are those patients who have an elevated risk of relapse because they have measurable residual disease (MRD) at the time of their transplant
- For now, best strategy is frequent monitoring for disease recurrence by sensitive molecular methods and early intervention for disease eradication
- Multiple trials are aiming to use newer agents as maintenance therapy. Results are unknown so far.

Thank You!





## QUESTIONS?



**Eytan Stein MD**  
Memorial Sloan Kettering Cancer Center



2023 SURVIVORSHIP SYMPOSIUM

## LET US KNOW HOW WE CAN HELP YOU



Visit our website: [bmtinfonet.org](http://bmtinfonet.org)

Email us: [help@bmtinfonet.org](mailto:help@bmtinfonet.org)

Phone: 888-597-7674 or 847-433-3313

**Find us on:**

Facebook, [facebook.com/bmtinfonet](https://facebook.com/bmtinfonet)

Twitter, [twitter.com/BMTInfoNet](https://twitter.com/BMTInfoNet)



2023 SURVIVORSHIP SYMPOSIUM