For every expert there is an equal and opposite expert

-Arthur C. Clarke
FLT3-ITD positive patient

AML
AML 2017 Prognostic Factors*

• Cytogenetics and Molecular Studies
  - Favorable
    - CBF inv(16); t(16;16), t(8,21)
    - \( NPM1 \) in absence of \( FLT3-ITD \) or \textit{biallelic CEBPA}
  - Intermediate
    - CN, +8 alone, t(9;11)
    - \( CBF \) with \( c-KIT \)
  - Unfavorable
    - Complex, MK, -5 (q), -7(q), 11q23, inv(3), t(3;3), t(6;9), t(9,22)
    - CN with \textit{FLT3-ITD}, \textit{TP53} mutation

*NCCN Guidelines 6.2017
Activating *FLT3* Mutations in AML

**Prevalence:**
- **ITD:** 25-30%
  - High relapse, poor prognosis
- **TKD:** 5-10%

**Effect:**
- Constitutive tyrosine phosphorylation

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MV Risk Classification of Intermediate-Risk AML: FLT 3

Patel JP et al.
OS curves of FLT3-ITD, DNMT3A, and NPM1 mutant AML

Marlise R. Luskin et al.
Blood 2016;127:1551-1558

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Overall Survival

A Median Overall Survival

Midostaurin 74.7 mo (95% CI, 31.5–NR)
Placebo 25.6 mo (95% CI, 18.6–42.9)

One-sided P=0.009 by stratified log-rank test

No. at Risk
Midostaurin 360 269 208 181 151 97 37 1
Placebo 357 221 163 147 129 80 30 1

Stone RM et al.
**FT3-ITD Today: What we know**

- PCR to diagnose - quick TAT
  - Midostaurin ASAP in induction

- Use in consolidation, maintenance

- HCT still important in consolidation
  - Midostaurin is safe post HCT (RADIUS trial results (ASH 2016))

Overall Survival - Post-transplant

Treatment with Mido increases OS after SCT in CR1

- SCT in CR1 (HR 0.61)
- SCT outside CR1 (HR 0.98)

% alive vs time (months)

- Midostaurin
- Placebo
Newly Diagnosed Multiple Myeloma

• Incurable disease

• Impact of
  – Tumor burden       High ISS (β-2-microglobulin)
  – Cytogenetics       Unfavorable cytogenetics
    o t(4;14), t(14;16), t(14;20), -17p

• Induction
  – Triplet therapy
    o Proteosome inhibitor
    o Immunomodulatory Agent

• Consolidation
  – Autologous HCT

• Maintenance
Fig 3. (A) Kaplan-Meier distribution curve (intent-to-treat analysis) for the key efficacy end point of progression-free survival. (B) Forest plot of hazard ratios for progression-free survival, for the individual studies and the integrated analysis, plus for the published study GIMEMA (Gruppo Italiano Malattie Ematologiche Maligne dell’Adulto) MM-BO2005. The I² values indicate limited heterogeneity between studies. GMMG, German-Speaking Myeloma Multicenter Group; HOVON, Dutch Hemato-Oncology Group; IFM, Intergroupe Francophone du Myélome; n, No. of patients; PETHEMA, Spanish Cooperative Group for Hematological Malignancies Treatment.

Published in: Pieter Sonneveld; Hartmut Goldschmidt; Laura Rosiñol; Joan Bladé; Juan José Lahuerta; Michele Cavo; Paola Tacchetti; Elena Zamagni; Michel Attal; Henk M. Lokhorst; Avinash Desai; Andrew Cakana; Kevin Liu; Helgi van de Velde; Dixie-Lee Esseltine; Philippe Moreau; JCO 2013, 31, 3279-3287.
DOI: 10.1200/JCO.2012.48.4626
Copyright © 2013
Kaplan–Meier Curves for PFS and OS.

## Subgroup Analyses of Progression-free Survival.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Transplantation</th>
<th>RVD Alone</th>
<th>Hazard Ratio (95% CI) for Progression or Death</th>
<th>P Value for Interaction</th>
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<td>no. of events/no. of patients</td>
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Kaplan–Meier Estimates of PFS and OS

Palumbo A et al.
Kaplan–Meier Estimates of Progression-free and Overall Survival.