UCSF Helen Diller Family Comprehensive Cancer Center

ANCO Hematological Malignancies Update:

Acute Leukemia

Gabriel Mannis, MD
Assistant Professor, Hematology/Blood and Marrow Transplant Program
Co-Director, UCSF Cancer Immunotherapy Clinic

Sacramento, CA
June 16, 2018

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Overview

- **The year in review**
  - Midostaurin
  - Vyxeos
  - Gemtuzumab ozogamicin
  - Enasidenib
- **The year in preview**
  - Ivosidenib
  - Gilteritinib
  - Venetoclax
  - Immunotherapy
- **MRD in AML/ALL**

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28 November 1970 — 513

Papers and Originals

Combination Chemotherapy using L-Asparaginase, Daunorubicin, and Cytosine Arabinoside in Adults with Acute Myelogenous Leukaemia

D. CROWTHER,* PH.D., M.B., M.R.C.P. ; C. J. T. BATEMAN,† B.M., B.CH. ; C. P. VARTAN,‡ M.B., M.R.C.P. ; J. M. A. WHITEHOUSE,‡ M.B., M.R.C.P. ; J. S. MALPAS,§ M.B., D.PHIL., M.R.C.P. ; G. HAMILTON FAIRLEY,‖ D.M., F.R.C.P. ; Sir RONALD BODLEY SCOTT,¶ K.C.V.O., D.M., F.R.C.P.

British Medical Journal, 1970, 4, 513-517

Summary: Cytosine arabinoside and daunorubicin used in an intensive intermittent regimen have been shown to be an effective combination for the induction of complete remissions in 14 out of 23 adult patients with acute myelogenous leukaemia. This gives an overall complete remission rate of 60%. A further patient had a good partial remission. The addition of L-asparaginase to the regimen has not increased the incidence of remission and there were more side effects in the L-asparaginase-treated group. Of the 10 patients treated with L-asparaginase in addition to cytosine arabinoside and daunorubicin, five achieved a complete remission. Of the 13 patients treated with cytosine arabinoside and daunorubicin without L-asparaginase, nine achieved a complete remission and one a good partial remission.

myelogenous leukaemia have been obtained with daunorubicin, which is an anti... from *Streptomyces caeruleorubidus*. It... complexing with p... the biggest series ... disease was repor... for the Treatment... Seventy-one patie... sions were obtaine... single centres hav... rates are of the s... pean Co-operative... complete remissio... myelogenous leuka... better than other ...

British Journal of Haematology, 1974, **27**, 373.

Treatment of Acute Myeloid Leukaemia with Daunorubicin, Cytosine Arabinoside, Mercaptopurine, L-Asparaginase, Prednisone and Thioguanine: Results of Treatment with Five Multiple-Drug Schedules

REPORT OF THE MEDICAL RESEARCH COUNCIL'S WORKING PARTY ON LEUKAEMIA IN ADULTS

The work was carried out under the auspices of the Medical Research Council's Leukaemia Committee (Chairman: Sir Richard Doll). The members of the Working Party over the period of the trials were Professor L. J. Witts (Chairman until March 1969), Professor J. V. Dacie (Chairman from March 1969), Dr D. A. G. Galton (Secretary), Dr K. D. Bagshawe, Dr P. Barkhan, Professor E. K. Blackburn, Dr S. T. E. Callender, Professor W. M. Davidson, Dr I. W. Delamore, Professor A. S. Douglas, Dr E. C. Easson, Professor G. Hamilton Fairley, Dr J. R. Fountain, Professor F. G. J. Hayhoe, Dr C. A. Holman, Professor J. R. Hobbs, Professor A. Jacobs, Dr H. E. M. Kay, Dr G. A. McDonald, Dr I. C. M. MacLennan, Dr B. Murphy, Professor M. G. Nelson, Dr C. R. Newman, Mr R. Peto, Dr M. C. Pike, Dr O. S. Roath, Dr B. E. Roberts, Dr P. D. Roberts, Dr L. S. Sacker, Sir Ronald Bodley Scott, Professor J. W. Stewart, Dr J. J. Taylor, Dr R. B. Thompson, Professor D. J. Weatherall, Professor G. Wetherley-Mein, Dr J. A. Whittaker and Dr E. Wiltshaw. This report was prepared by Miss Susannah Howard, Dr D. A. G. Galton and Dr M. C. Pike.

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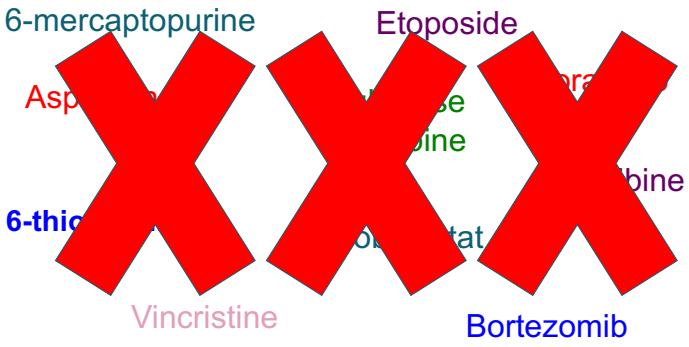
1970s to 2017:
Additions/Modifications to "7+3"



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1970s to 2017:
FDA Approvals in AML

- ***2000: Gemtuzumab ozogamicin***
- ***Removed from market in 2010***
- ***"Boulevard of Broken Dreams"***

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Sekeres and Steensma, *JCO* 2012

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FDA Approvals in 2017

- ***4/28/17:*** **Midostaurin (Rydapt)**
- ***8/1/17:*** **Enasidenib (IDHIFA)**
- ***8/3/17:*** **Liposomal 7+3 (CPX-351/Vyxeos)**
- ***9/1/17:*** **Gemtuzumab ozogamicin (Mylotarg)**
- ***8/17/17: Inotuzumab ozogamicin (Besponsa)***

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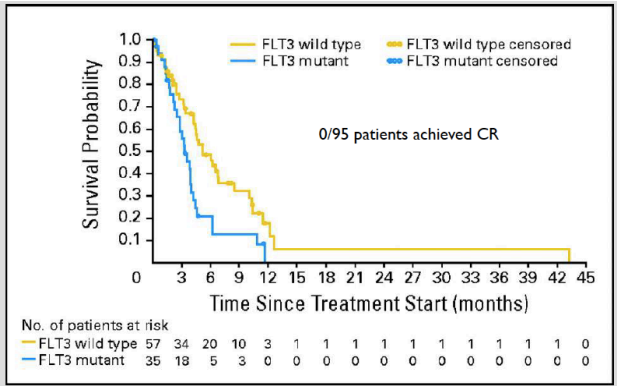
AML Induction Therapy in 2018:
Midostaurin



Ineffective as monotherapy

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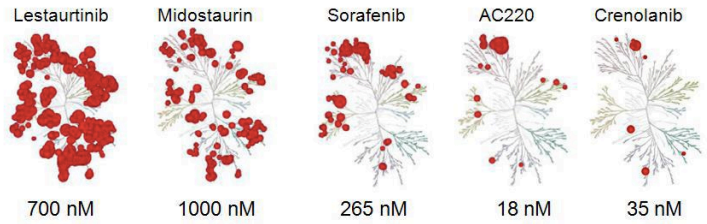
AML Induction Therapy in 2018:
Midostaurin



Relative selectivity and potency (IC_{50}) against FLT3/ITD in human plasma of 5 FLT3 inhibitors. Selectivity determined by KinomeScan (Nat Biotechnol. 2008 26:127-32). Potency determined by immunoblot analysis using Molm14 cells in 100% human plasma.

Relatively non-selective FLT3 inhibitor

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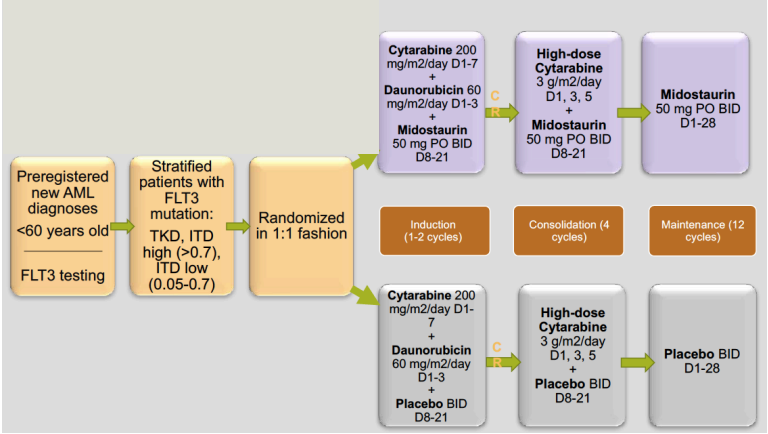
AML Induction Therapy in 2018:
Midostaurin



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Stone et al, *NEJM* 2017 9

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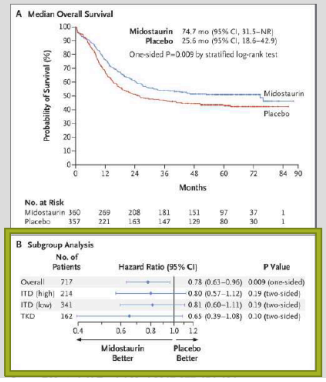
AML Induction Therapy in 2018:
Midostaurin



- Median follow-up was 59 months for 359 patients who survived
- Midostaurin had superior median overall survival (74.7 vs 25.6 months), p=0.009
- Hazard ratio for death was 0.78 (95% CI, 0.63 to 0.96, p=0.009)
- **4-year OS favored Midostaurin (51.4% versus 44.3% placebo)**
- **OS did not significantly differ between the FLT3-mutation subgroups**
- **57% of patients underwent transplantation during the study**

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Stone et al, *NEJM* 2017 10

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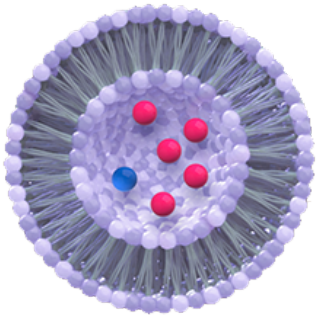
AML Induction Therapy in 2018:
CPX-351/Vyxeos



- 100 nm bilamellar liposomes
- 5:1 molar ratio of cytarabine to daunorubicin
- 1 unit = 1 mg cytarabine plus 0.44 mg daunorubicin

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AML Induction Therapy in 2018:
CPX-351/Vyxeos

Final Results of a Phase III Randomized Trial of VYXEOS™ (CPX-351) Versus 7+3 in Older Patients With Newly Diagnosed High-Risk (Secondary) AML

Jeffrey E. Lancet, Geoffrey L. Uy, Jorge E. Cortes, Laura F. Newell, Tara L. Lin, Ellen K. Ritchie, Robert K. Stuart, Stephen Anthony Strickland, Donna Hogge, Scott R. Solomon, Richard M. Stone, Dale L. Bixby, Jonathan E. Kolitz, Gary J. Schiller, Matthew Joseph Wieduwilt, Daniel H. Ryan, Antje Hoering, Michael Chiarella, Arthur C. Louie, Bruno C. Medeiros

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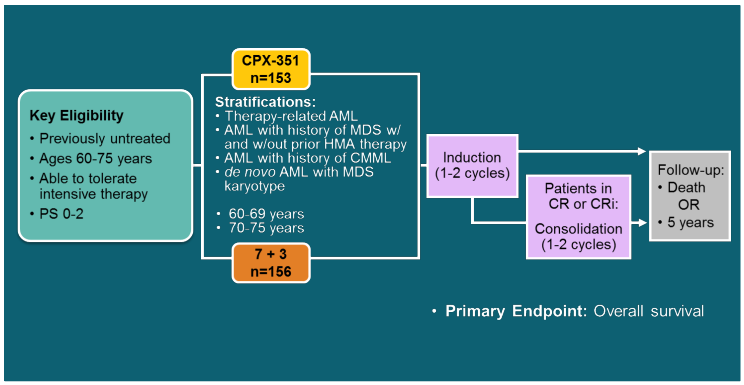
AML Induction Therapy in 2018:
CPX-351/Vyxeos



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AML Induction Therapy in 2018:
CPX-351/Vyxeos

	CPX-351 1 unit = 1 mg cytarabine + 0.44 mg daunorubicin	7 + 3
First Induction	• 100 units/m^2 • Days 1, 3 and 5	• Cytarabine: 100 mg/m^2 x 7 d • Daunorubicin: 60 mg/m^2 x 3 d
Re-induction	• 100 units/m^2 • Days 1 and 3	• Cytarabine: 100 mg/m^2 x 5 d • Daunorubicin: 60 mg/m^2 x 2 d
Consolidation	• 65 units/m^2 • Days 1 and 3	• Cytarabine: 100 mg/m^2 x 5 d • Daunorubicin: 60 mg/m^2 x 2 d

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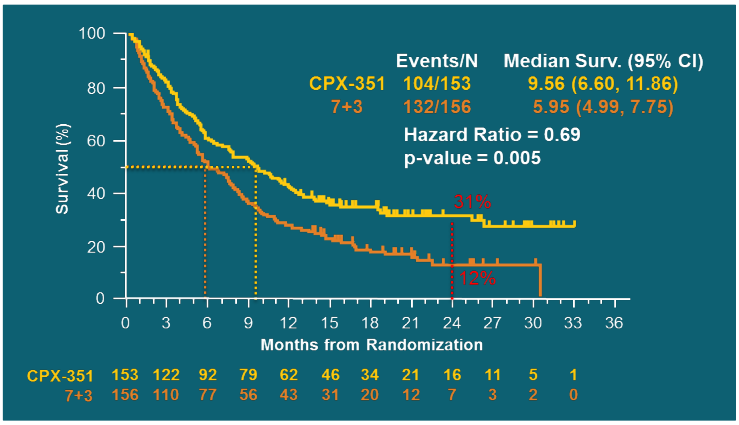
AML Induction Therapy in 2018:
CPX-351/Vyxeos



Median OS 9.56 months vs 5.95 months (HR 0.69, p=0.005)

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AML Induction Therapy in 2018:
CPX-351/Vyxeos

- CR: 37.3% vs 25.6% (p=0.04)
- CR + CRi: 47.7% vs 33.3% (p=0.016)
- Deaths ≤30 days: 5.9% vs 10.6%
- Patients proceeding to HCT: 34% vs 25%
- Median OS after HCT:
  NR vs 10 months (HR 0.46, p=0.0046)

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AML Induction Therapy in 2018:
CPX-351/Vyxeos

- **Ongoing issues/challenges:**
  - Should it be used for patients with t-AML or sAML who are <60 years old?
  - Cost and reimbursement issues may have ramifications for choosing inpatient versus outpatient-based initiation of therapy
  - Significantly longer time to neutrophil and platelet recovery
  - How does this compare to venetoclax + HMA?

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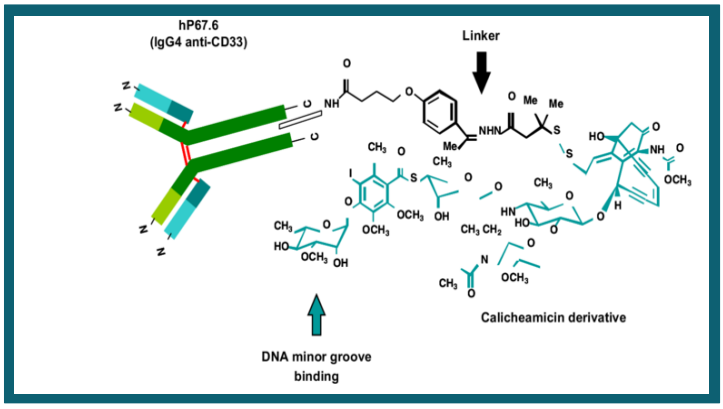
AML Induction Therapy in 2018:
Gemtuzumab ozogamicin



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AML Induction Therapy in 2018:
Gemtuzumab ozogamicin

RANDOMIZATION

Cytarabine 200 mg/m2 x7 days
Daunorubicin 60 mg/m2 x3 days
GO 3 mg/m2 on days 1,4,7
(max dose 5 mg)
→ 2 cycles HiDAC/dauno
GO 3 mg/m2 day 1

Cytarabine 200 mg/m2 x7 days
Daunorubicin 60 mg/m2 x3 days
→ 2 cycles HiDAC/dauno

ALFA 0701

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Lancet 2012; 379: 1508-16 19

ACUTE LEUKEMIA

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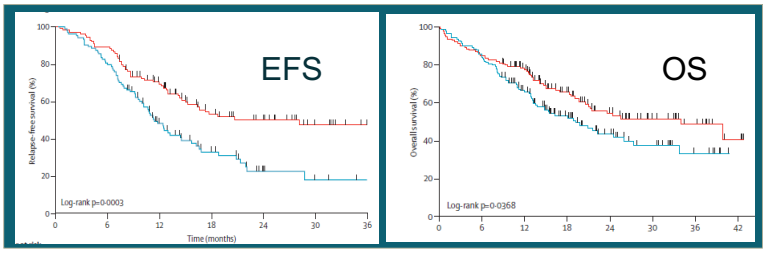
AML Induction Therapy in 2018:
Gemtuzumab ozogamicin



- **278 patients randomized**
- **EFS 40.8% vs 17.1% at 2 years (p=0.0003)**
- **OS 53.2% vs 41.9% at 2 years (p=0.0368)**

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Lancet 2012; 379: 1508-16 20

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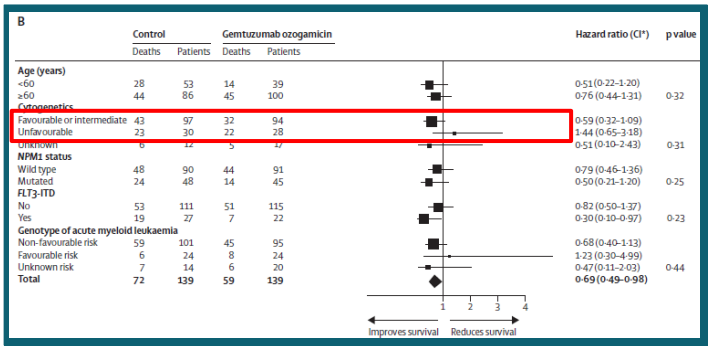
AML Induction Therapy in 2018:
Gemtuzumab ozogamicin



B	Control		Gemtuzumab ozogamicin		Hazard ratio (CI*)	p value
	Deaths	Patients	Deaths	Patients		
Age (years)						
<60	28	53	14	39	0·51 (0·22–1·20)	
≥60	44	86	45	100	0·76 (0·44–1·31)	0·32
Cytogenetics						
Favourable or intermediate	43	97	32	94	0·59 (0·32–1·09)	
Unfavourable	23	30	22	28	1·44 (0·65–3·18)	
Unknown	6	12	5	17	0·51 (0·10–2·43)	0·31
***NPM1* status**						
Wild type	48	90	44	91	0·79 (0·46–1·36)	
Mutated	24	48	14	45	0·50 (0·21–1·20)	0·25
***FLT3*-ITD**						
No	53	111	51	115	0·82 (0·50–1·37)	
Yes	19	27	7	22	0·30 (0·10–0·97)	0·23
Genotype of acute myeloid leukaemia						
Non-favourable risk	59	101	45	95	0·68 (0·40–1·13)	
Favourable risk	6	24	8	24	1·23 (0·30–4·99)	
Unknown risk	7	14	6	20	0·47 (0·11–2·03)	0·44
Total	**72**	**139**	**59**	**139**	**0·69 (0·49–0·98)**	

1 2 3 4

Improves survival Reduces survival

Largest survival benefit in favorable-risk disease

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Lancet 2012; 379: 1508-16 21

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AML Induction Therapy in 2018:
Gemtuzumab ozogamicin

- **Gemtuzumab should be considered for use as part of standard induction chemotherapy for patients with favorable-risk AML**
  - Will require more rapid turnaround times for FISH/molecular testing (and/or more patience)
- **VOD risk with fractionated dosing remains unclear**
  - Currently using sparingly when treating patients with treatment-naïve, intermediate-risk AML who may benefit from HCT in CR1
- **Also approved in the R/R setting, though its role in the salvage setting is less clear**

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R/R AML Therapy in 2018:
IDH inhibitors

Regular Article — blood

CLINICAL TRIALS AND OBSERVATIONS

Enasidenib in mutant *IDH2* relapsed or refractory acute myeloid leukemia

Regular Article — blood

CLINICAL TRIALS AND OBSERVATIONS

Enasidenib induces acute myeloid leukemia cell differentiation to promote clinical response

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Stein et al, *Blood* 2017; Amatangelo et al, *Blood* 2017 23

ACUTE LEUKEMIA

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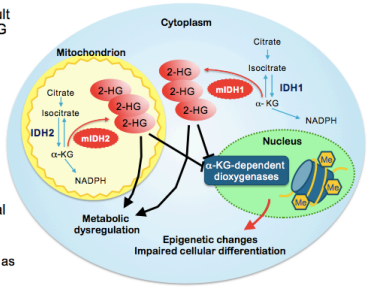
R/R AML Therapy in 2018:
IDH inhibitors

Isocitrate Dehydrogenase (IDH) Mutations as a Target in AML

- Somatic IDH1 and IDH2 mutations result in accumulation of oncometabolite 2-HG
  - → epigenetic changes, impaired cellular differentiation
- mIDH identified in multiple solid and hematologic tumors

	mIDH1	mIDH2
% of AML patients	~6–10%	~9–13%

- **Ivosidenib (AG-120):** an investigational first-in-class, oral, potent, reversible, targeted inhibitor of mIDH1 enzyme
  - under evaluation in multiple clinical trials as a single agent and in combinations



2-HG, 2-hydroxyglutarate; mIDH, mutant IDH

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DiNardo et al, *ASH* 2017 24

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R/R AML Therapy in 2018:
IDH inhibitors

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Durable Remissions with Ivosidenib in *IDH1*-Mutated Relapsed or Refractory AML

C.D. DiNardo, E.M. Stein, S. de Botton, G.J. Roboz, J.K. Altman, A.S. Mims, R. Swords, R.H. Collins, G.N. Mannis, D.A. Pollyea, W. Donnellan, A.T. Fathi, A. Pigneux, H.P. Erba, G.T. Prince, A.S. Stein, G.L. Uy, J.M. Foran, E. Traer, R.K. Stuart, M.L. Arellano, J.L. Slack, M.A. Sekeres, C. Willekens, S. Choe, H. Wang, V. Zhang, K.E. Yen, S.M. Kapsalis, H. Yang, D. Dai, B. Fan, M. Goldwasser, H. Liu, S. Agresta, B. Wu, E.C. Attar, M.S. Tallman, R.M. Stone, and H.M. Kantarjian

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R/R AML Therapy in 2018:
IDH inhibitors

Response in R/R AML (n=125)

	Primary R/R AML Set (n=125)
CR+CRh rate, n (%) [95% CI]	**38 (30.4%) [22.5, 39.3]**
Time to CR/CRh, median (range) months	2.7 (0.9, 5.6)
Duration of CR/CRh, median [95% CI] months	8.2 [5.5, 12.0]
CR rate, n (%) [95% CI]	27 (21.6%) [14.7, 29.8]
Time to CR, median (range) months	2.8 (0.9, 8.3)
Duration of CR, median [95% CI] months	9.3 [5.6, 18.3]
CRh rate, n (%)	11 (8.8%)
Overall Response Rate, n (%) [95% CI]	**52 (41.6%) [32.9, 50.8]**
Time to first response, median (range) months	1.9 (0.8, 4.7)
Duration of response, median [95% CI] months	6.5 [4.6, 9.3]

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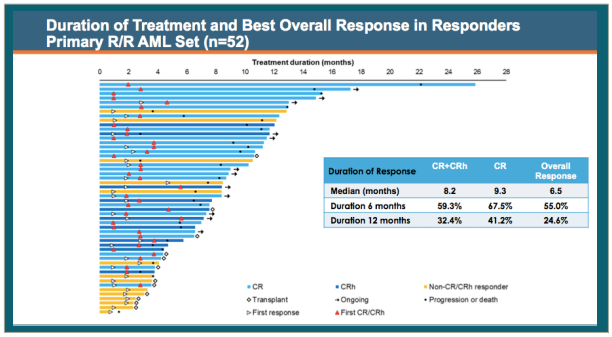
R/R AML Therapy in 2018:
IDH inhibitors



Duration of Response	CR+CRh	CR	Overall Response
Median (months)	8.2	9.3	6.5
Duration 6 months	59.3%	67.5%	55.0%
Duration 12 months	32.4%	41.2%	24.6%

Very well-tolerated

- Leukocytosis (1.7% ≥ Grade 3)
- IDH-Differentiation Syndrome (3.9% ≥ Grade 3)
- QTc prolongation (8% Grade 3)

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DiNardo et al, ASH Meeting 2017 27

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R/R AML Therapy in 2018:
IDH inhibitors

- **Enasidenib (FDA approved) and Ivosidenib (not yet FDA approved) are very well-tolerated oral agents as monotherapy for R/R IDH-mutated AML with CR rates of ~20% and ORR rates of ~40%**
- **Delayed time to response may make use challenging in patients with rapidly proliferative disease**
- **Combination and front-line studies underway**

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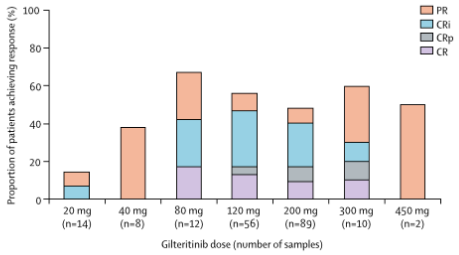
R/R AML Therapy in 2018:
FLT3 inhibitors

- Novel FLT3 inhibitors (eg. quizartinib, crenolanib, and gilteritinib) are more potent, able to overcome common kinase domain resistance mutations



- In the Phase I/II CHRYSALIS trial, >40% composite CR rate with gilteritinib monotherapy in R/R AML with FLT3 mutation treated at doses ≥80mg

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Perl et al, *Lancet Oncology* 2017

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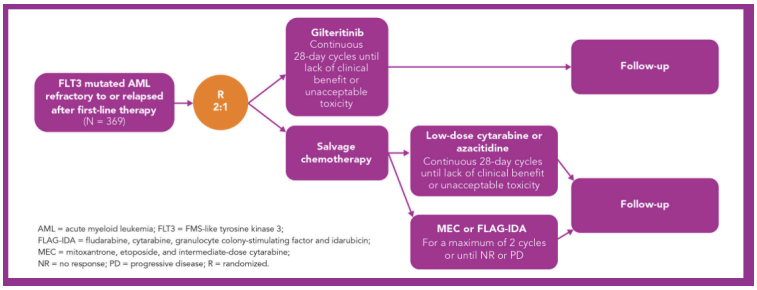
R/R AML Therapy in 2018:
FLT3 inhibitors

- Gilteritinib likely to be approved based on results of the Phase III ADMIRAL Trial



- BMT-CTN Phase III study of post-HCT gilteritinib maintenance underway

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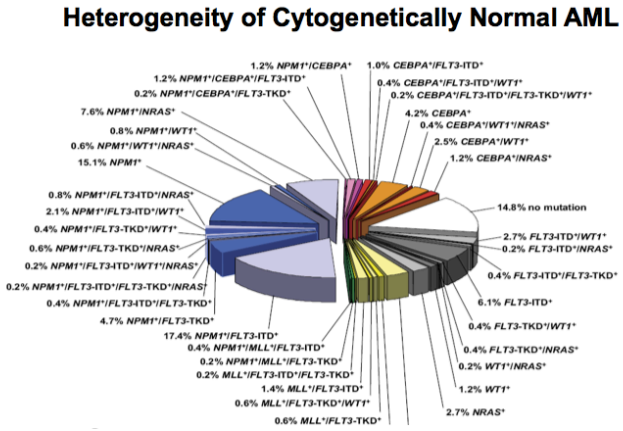
AML Therapy in 2018:
BEAT AML Study



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AML Therapy in 2018:
BEAT AML Study

- **Overall intent to yield measurable efficiencies in terms of**
  - Improving genomic screening of cancer patients for clinical trial entry
  - Improved timelines for drug biomarker testing
  - Precedent with Lung Map and i-SPY trials
- **Multi-arm master protocol**
  - Each arm independent from one another with consistent eligibility
  - Infrastructure facilitates opening new arms faster
  - Window design allows for testing of “large effects”
  - Could lead to or support other trials for accelerated approval
- **Bring safe and effective treatments to patients FASTER**

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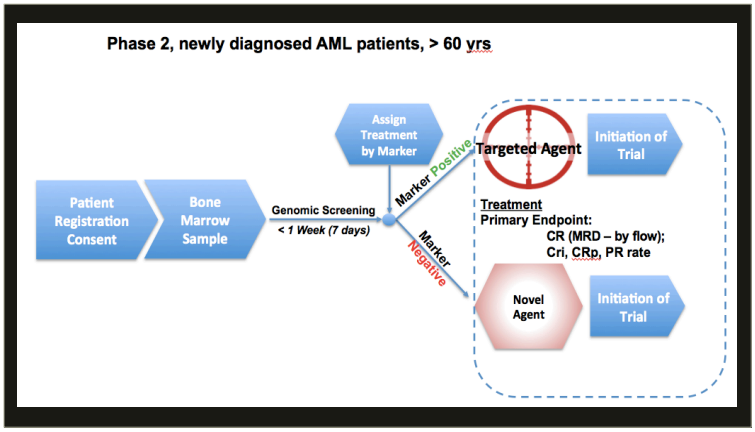
AML Therapy in 2018:
BEAT AML Study



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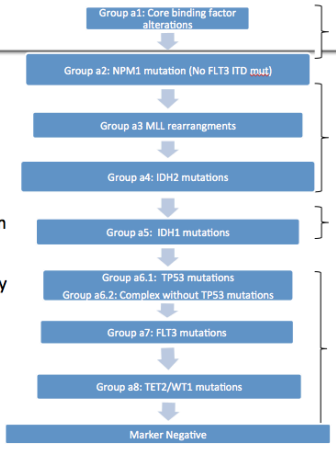
AML Therapy in 2018:
BEAT AML Study

Order chosen based upon

1. Responsive potential (curability)
2. Rationale or strong data in trials around biology
3. Higher risk group that may confound efficacy (Complex and TP53)
4. Less convincing biology
5. Marker Negative



Responsive; will remain high but groups may change

Strong biology and/or therapy; could move up and group may change

High risk group that confound efficacy; could move up or down

Less convincing uniform biology; may move up/down and groups may change

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AML Therapy in 2018:
BEAT AML Study

Site Number	Site Name	PI Name
101	The Ohio State University	Alice Mims
104	Oregon & Health Science University	Uma Borate/Brian Druker
105	Memorial Sloan Kettering	Eytan Stein
106	University of Colorado	Daniel Pollyea
110	University of Maryland	Maria Baer
111	University of Chicago	Wendy Stock
112	University of Texas Southwestern	Robert Collins
Summer 2018	University of California, San Francisco	Gabriel Mannis

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AML Therapy in 2018:
Venetoclax + HMA

		CR/CRi	Duration of CR/CRi	
Patient subgroup	n	n (%)	median months	OS
All VEN doses	145	97 (67)	11.3	17.5
Intermediate cytogenetic risk	74	55 (74)	12.9	NR
Poor cytogenetic risk	71	42 (59)	6.7	9.6
Secondary AML	36	24 (67)	NR	NR
Age ≥75 years	62	40 (65)	9.2	11.0
VEN 400 mg				
+ AZA	29	22 (76)	NR	NR
+ DEC	31	22 (71)	12.5	15.2
VEN 800 mg				
+ AZA	37	21 (57)	11.7	14.2
+ DEC	37	27 (73)	9.2	17.5

- N=145
- 75% poor risk or sAML
- 67% CR/Cri
- Median duration of CR/Cri = 11.3 months
- Median OS = 17.5 months

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DiNardo et al, *ASCO* 2018

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AML Therapy in 2018:
Venetoclax + HMA

- **Venetoclax + HMA will likely become the standard of care for AML patients who are unfit for intensive chemotherapy**
  - Likely to be FDA approved for AML within the next year
- **Unclear role of Vyxeos versus Venetoclax + HMA in patients with sAML**

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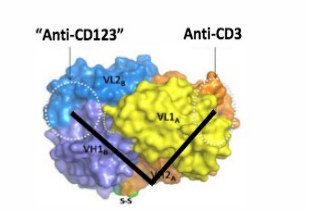
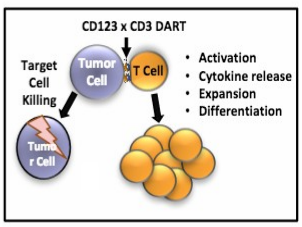
AML Therapy in 2018:
Immunotherapy

- **Flotetuzumab**
  - CD123 x CD3 Dual Affinity Re-Targeting (DART) protein
  - CD123 differentially overexpressed in >90% of AML patients
  - Re-directed killing of CD123+ cells





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Uy et al, *2017 ASH Meeting*

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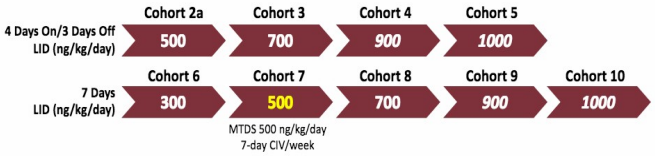
AML Therapy in 2018:
Immunotherapy

Dosing Scheme in Multi-Patient Dose Escalation



Lead-in Dose (LID)	• Week 1: 30 ng/kg/day x 3 days, 100 ng/kg/day x 4 days
Cycle 1 Weeks 2-4	• Arm A: (Cohorts 2-5): 4 days on, 3 days off schedule • Arm B: (Cohorts 6-10): 21 days continuous infusion
Cycle 2 and Beyond	• 4 days on, 3 days off schedule

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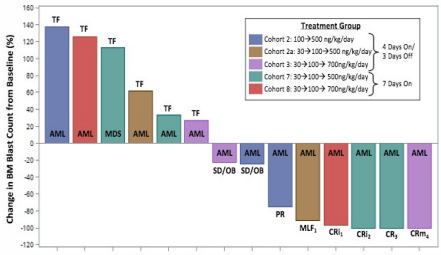
AML Therapy in 2018:
Immunotherapy

Anti-Leukemic Activity at Threshold Dose ≥ 500 ng/kg†

Of 14 patients treated with flotetuzumab in dose escalation phase at threshold dose ≥ 500 ng/kg/day who received ≥ one cycle of treatment and had post-treatment bone marrow biopsy



- Rapid responses after single cycle of therapy in majority of patients that respond (cycles ≤ 2)
- Anti-leukemic activity observed in 8/14 pts (57%)
- Objective resp. rate (CR/CRi/MLF/PR): 6/14 pts (43%)
- CR Rate: 4/14 (28%) (CR/CRi)

CR = Complete Response; CRm = molecular CR; CRi = Complete Response with incomplete hematological improvement; MLF = Morphologic Leukemia-free state; PR = Partial Response; SD/OB = Stable Disease/Other Anti-Leukemic Benefit; PD= Progressive Disease; (Modified ELN 2017 criteria) *† Data cut-off Aug. 1, 2017; presented at ESMO 2017*

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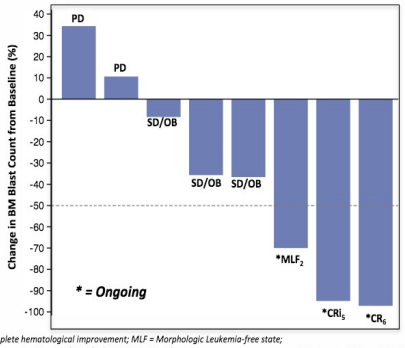
AML Therapy in 2018:
Immunotherapy

Expansion Cohort-Evaluable Population

- Cohort expansion at MTDS (500 ng/kg/day 7-day CIV) will enroll 24 AML and 24 MDS patients
- 11 AML patients dosed to date, with eight evaluable at data cutoff
- Six patients (75%) have evidence of anti-leukemic activity; three patients are still ongoing
- Expansion cohort open in 13 sites worldwide (7 US, 6 EU)



CR = Complete Response; CRm = molecular CR; CRi = Complete Response with incomplete hematological improvement; MLF = Morphologic Leukemia-free state; PR = Partial Response; SD/OB = Stable Disease/Other Anti-Leukemic Benefit; PD= Progressive Disease; (Modified ELN 2017 criteria)

† Data cut-off Dec. 4, 2017

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Uy et al, *2017 ASH Meeting*

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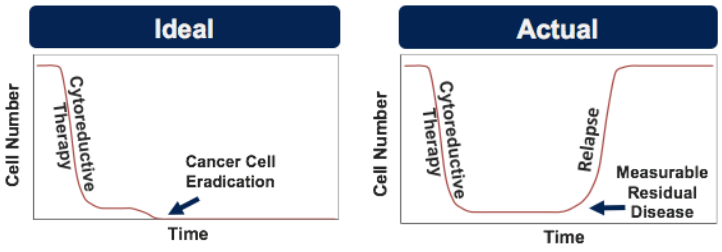
MRD in 2018:
ALL



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MRD in 2018:
ALL

	Flow Cytometry	ASO-PCR	NGS
Sensitivity	10^{-4} (to 10^{-5})	10^{-4} to 10^{-5}	10^{-6}
Samples	Fresh	Fresh or Frozen	Fresh or Frozen
Availability	Widely available*	Not widely available	Universally via centralized reference lab
Customization	Not needed†	Patient specific probes and primers	None
Cost	Expensive	Expensive	Expensive

*Conventional analysis may not be adequate for MRD quantification.
†Phenotype of cancer cells must be different from normal cells.

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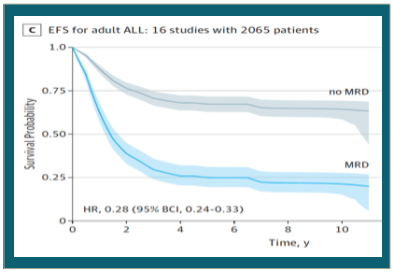
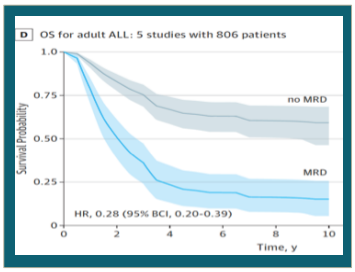
MRD in 2018:
ALL





- **MRD strongly predicts both EFS and OS in adult ALL**
- **Intervention based on MRD can improve outcomes**

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Berry et al, JAMA Oncol *2017*

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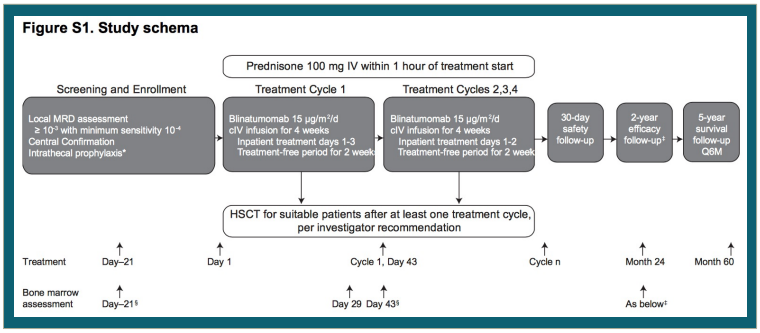
MRD in 2018:
ALL



- **BLAST Trial: Pre-emptive treatment of MRD with blinatumomab to prevent ALL relapse**
- **Patients eligible if MRD >10^{-3} after at least 3 cycles of intensive chemotherapy**

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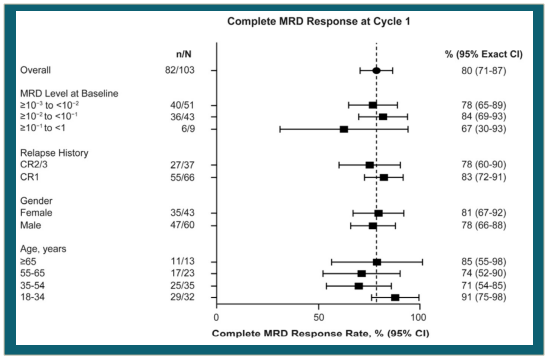
MRD in 2018:
ALL



- **80% achieved MRD negativity**
- **Median RFS, treated in CR1 = 35.2 months**
- **Median RFS, treated in CR2 = 12.3 months**

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MRD in 2018:
ALL

----------INDICATIONS AND USAGE----------

BLINCYTO is a bispecific CD19-directed CD3 T-cell engager indicated for the treatment of adults and children with:

- B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%. This indication is approved under accelerated approval based on MRD response rate and hematological relapse-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. (1.1)
- Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). (1.2)

- **Blinatumomab now approved for B-ALL in CR1 or CR2 with MRD ≥10^{-3}**

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Gokbuget et al, *Blood* 2018 47

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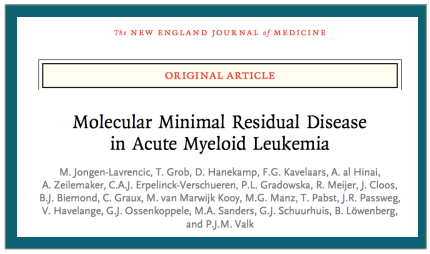
MRD in 2018:
AML

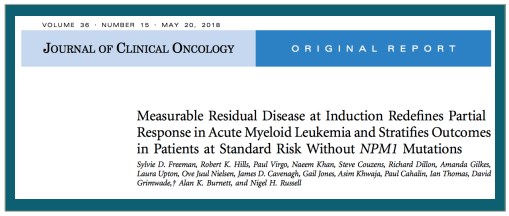


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Molecular Minimal Residual Disease in Acute Myeloid Leukemia

M. Jongen-Lavrencic, T. Grob, D. Hanekamp, F.G. Kavelaars, A. al Hinai, A. Zeilemaker, C.A.J. Erpelinck-Verschueren, P.L. Gradowska, R. Meijer, J. Cloos, B.J. Biemond, C. Graux, M. van Marwijk Kooy, M.G. Manz, T. Pabst, J.R. Passweg, V. Havelange, G.J. Ossenkoppele, M.A. Sanders, G.J. Schuurhuis, B. Löwenberg, and P.J.M. Valk



VOLUME 36 · NUMBER 15 · MAY 20, 2018

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Measurable Residual Disease at Induction Redefines Partial Response in Acute Myeloid Leukemia and Stratifies Outcomes in Patients at Standard Risk Without *NPM1* Mutations

Sylvie D. Freeman, Robert K. Hills, Paul Virgo, Naeem Khan, Steve Couzens, Richard Dillon, Amanda Gilkes, Laura Upton, Ove Juul Nielsen, James D. Cavenagh, Gail Jones, Asim Khwaja, Paul Cahalin, Ian Thomas, David Grimwade,† Alan K. Burnett, and Nigel H. Russell

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Jongen-Lavrencic et al, *NEJM* 2018; Freeman et al, *JCO* 2018 48

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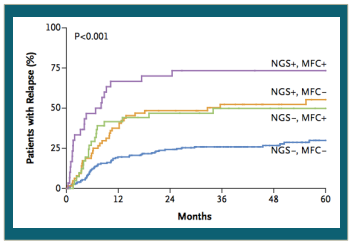
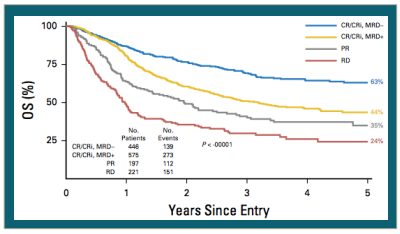
MRD in 2018:
AML





- MRD+ by either NGS or MFC confers a high risk of relapse; higher if MRD+ by both
- An MRD+ CR/CRi has a prognosis approaching that of a PR

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Jongen-Lavrencic et al, *NEJM* 2018; Freeman et al, *JCO* 2018 49

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MRD in 2018:
AML/ALL

- MRD testing should be standard for all adult patients with ALL
- Increasing evidence suggests that MRD testing should be done for all patients with AML

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Jongen-Lavrencic et al, *NEJM* 2018; Freeman et al, *JCO* 2018 50

Questions?

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