

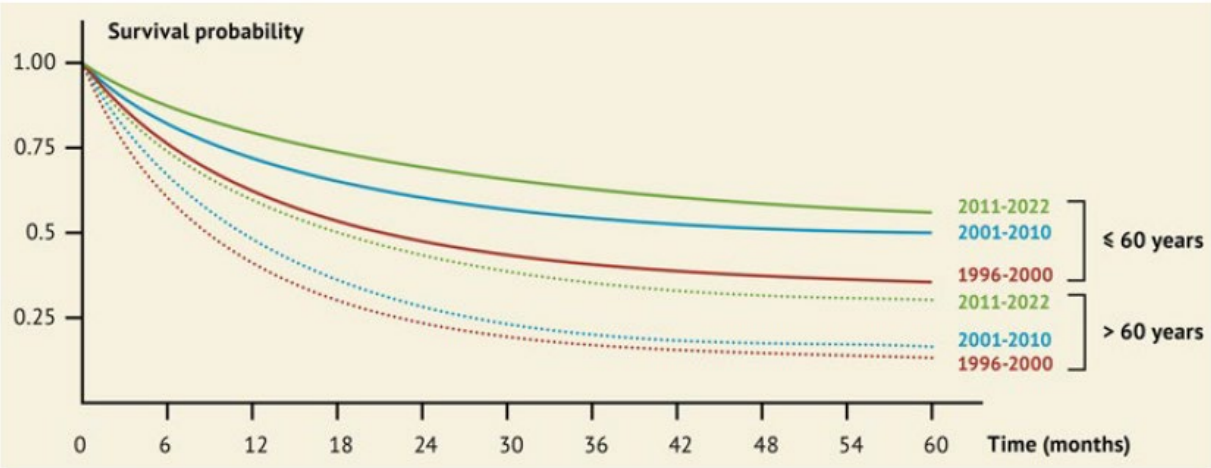
Actualités

Approches intensives

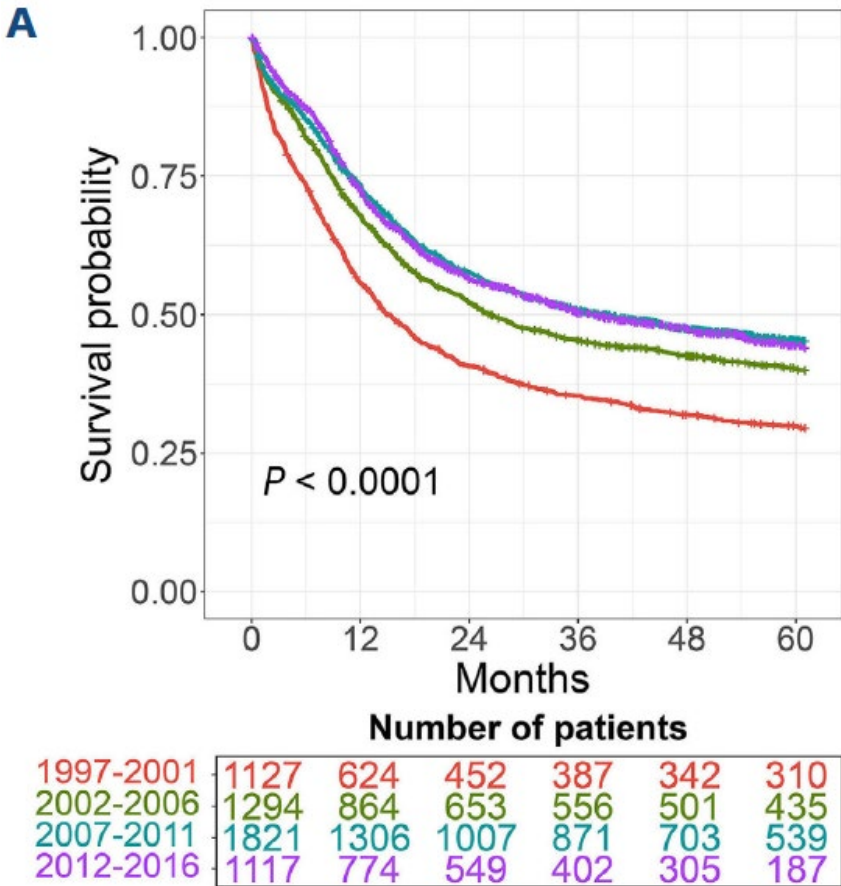
Pr Sarah BERTOLI

1^{eres} Journées scientifiques du CIGAL
Bordeaux, 1^{er} octobre 2026

Improving long-term outcomes with intensive induction chemotherapy for patients with AML



Outcomes with intensive treatment for acute myeloid leukemia: an analysis of two decades of data from the HARMONY Alliance

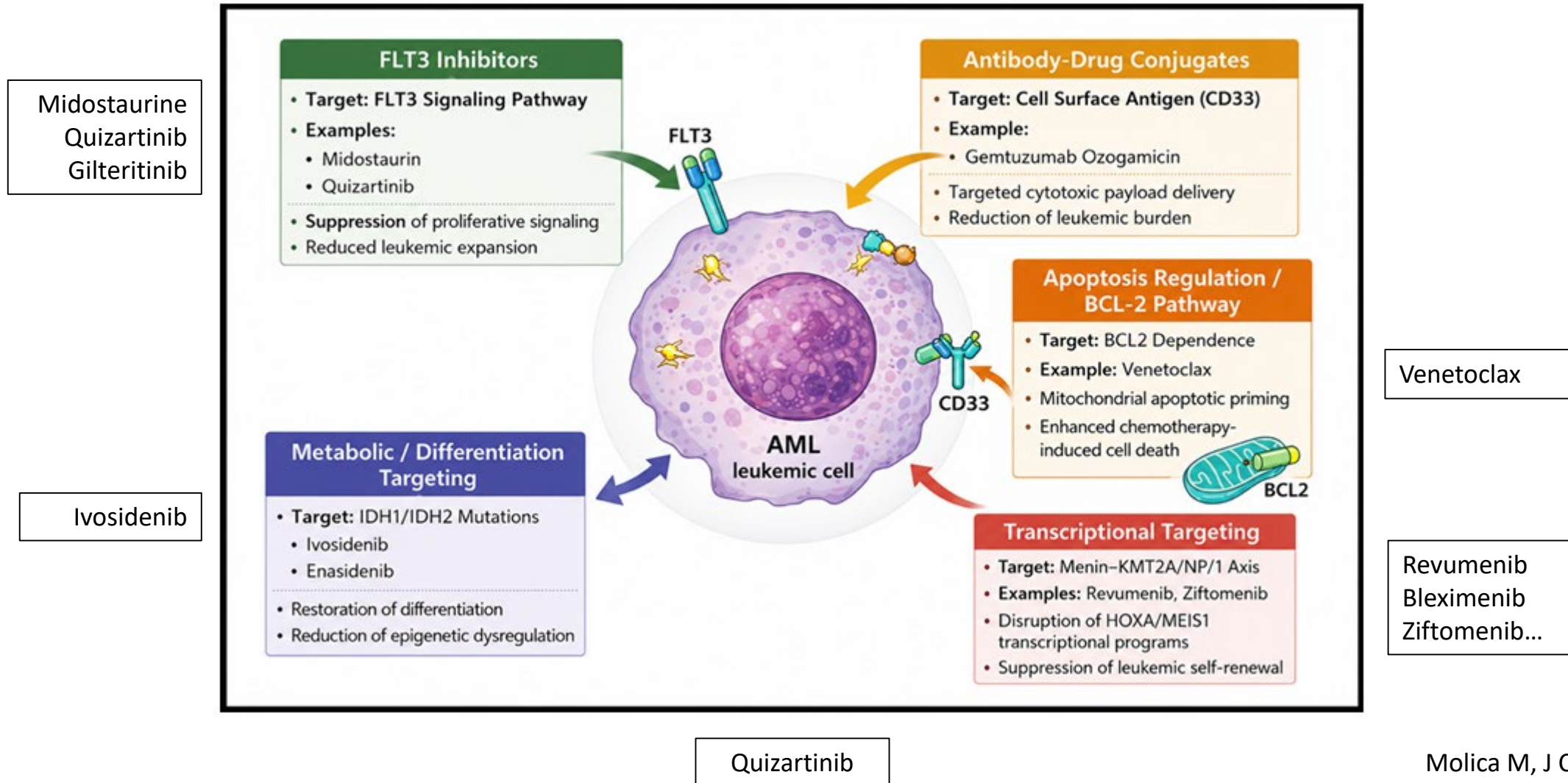


Comment continuer à améliorer les résultats de la chimiothérapie intensive ?

- **Améliorer le 3+7 et les consolidations : ajout de thérapies ciblées**

Comment améliorer les résultats du 3+7 ?

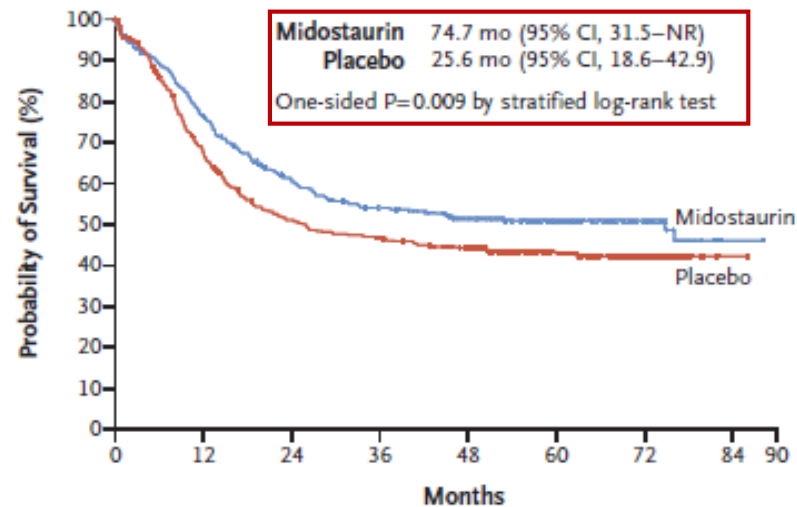
Thérapies ciblées



Ajout de thérapie ciblée *FLT3*-ITD et TKD : midostaurine

RATIFY

Median Overall Survival

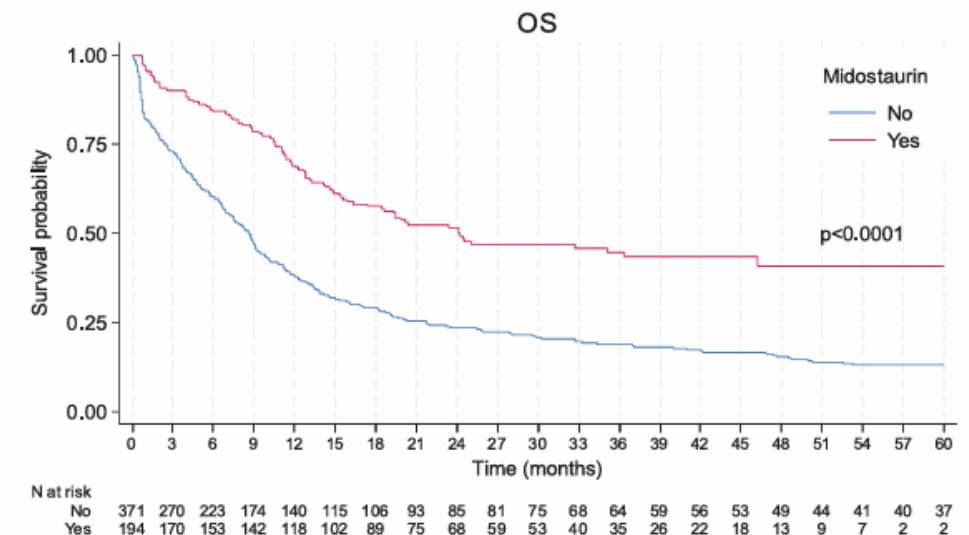


No. at Risk

Midostaurin	360	269	208	181	151	97	37	1
Placebo	357	221	163	147	129	80	30	1

	RC	OS	EFS	RFS
3+7+Mido	58,9%	74,7 mois	8,2 mois	26,7 mois
3+7+Pbo	53,5%	25,6 mois	3,0 mois	15,5 mois
P	0,15	0,009	0,002	0,002

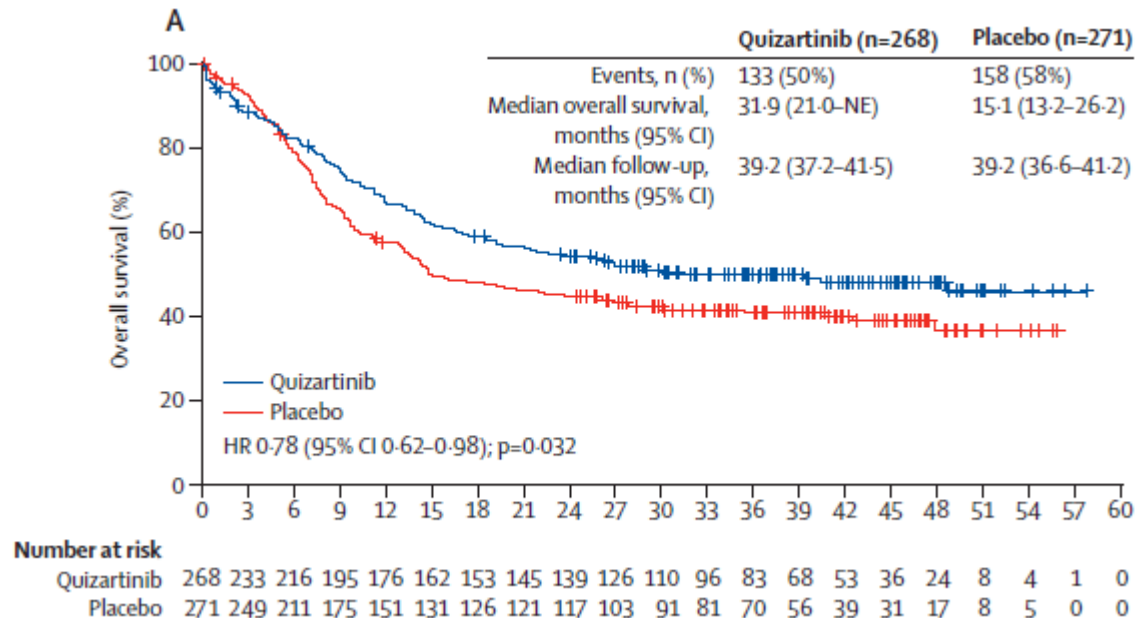
Intensive Chemotherapy With or Without Midostaurin in Adults ≥ 60 Years Old With *FLT3*-Mutated AML: A FILO-DATAML-PETHEMA Real-World Study



	RCc	OS	EFS	RFS
3+7+Mido	71,1%	24,2 mois	13,5 mois	20,2 mois
3+7	55,0%	8,7 mois	4,6 mois	8,0 mois
P	<0,0001	<0,0001	<0,0001	<0,0001

Ajout de thérapie ciblée *FLT3*-ITD : quizartinib

QuANTUM-First



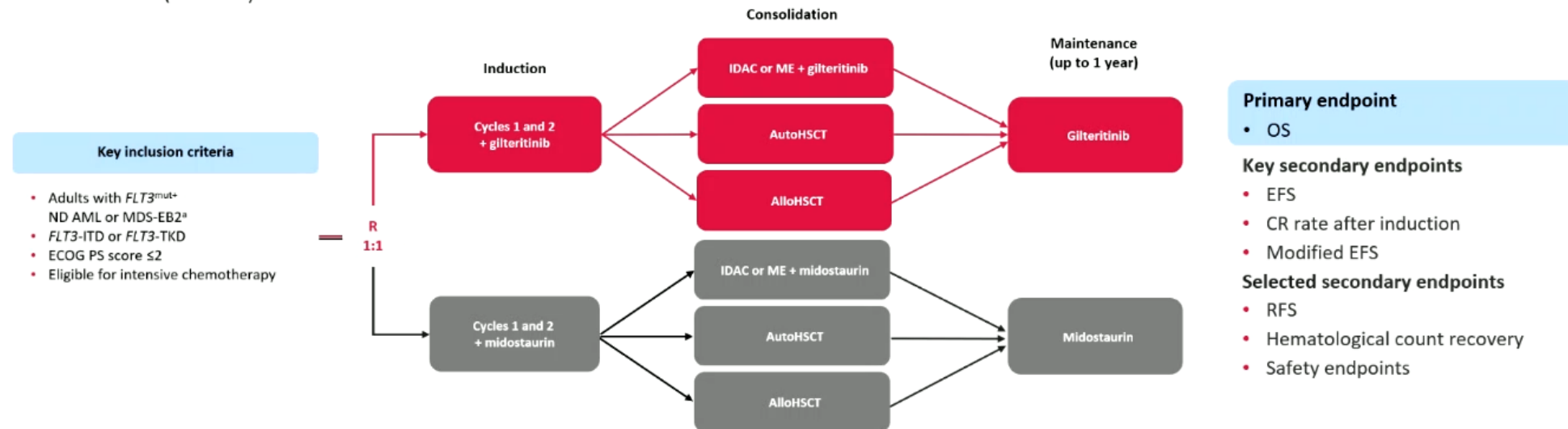
Patients 60-70 ans inclus
Uniquement *FLT3*-ITD

	RC	OS	EFS	RFS
3+7+Quiz	71,6%	31,9 mois	11,9 mois	39,3 mois
3+7+Pbo	64,9%	15,1 mois	5,7 mois	13,6 mois
		P=0,032	HR=0,73	HR=0,61

Ajout de thérapie ciblée *FLT3*-ITD et TKD : gilteritinib

HOVON156/AMLSG28-18/PASHA: A head-to-head comparison between midostaurin and gilteritinib: Trial design

- HOVON156/AMLSG28-18/PASHA (NCT04027309) is a **phase 3, multicenter, open-label trial** conducted at 193 sites in 12 countries across Europe plus Australia (13 total)



7+3: Cytarabine (Cycle 1: 200 mg/m²/day IV Days 1–7; Cycle 2: 2000 mg/m²/day IV Days 1–6); daunorubicin 60 mg/m²/day IV Days 1–3 (Cycle 1 only; Cycle 2 only for patients ≤60 years)

Consolidation chemotherapy: Mitoxantrone 10 mg/m² IV and etoposide 100 mg/m² IV Days 1–5 (Days 1–3 patients ≥61 years); or cytarabine 3000 mg/m² (patients ≤60 years) or 2000 mg/m² (patients ≥61 years) IV Days 1–3

Gilteritinib: 120 mg PO daily on Days 8–21 (induction/consolidation); daily in 28-day cycles (maintenance)

Midostaurin: 50 mg PO twice daily on Days 8–21 (induction/consolidation); daily in 28-day cycles (maintenance)

Stratification factors:

- Patient age (≤60 years vs ≥61 years)
- Mutation status (*FLT3*-TKD, *FLT3*-ITD AR <0.5, *FLT3*-ITD AR ≥0.5)
- Chemotherapeutic consolidation policy (ME vs IDAC)

^aPatients with MDS-EB2 were excluded from this analysis.

alloHSCT, allogeneic hematopoietic stem cell transplantation; AML, acute myeloid leukemia; AR, allelic ratio; autoHSCT, autologous hematopoietic stem cell transplantation; CR, complete remission; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; *FLT3*, *FMS*-like tyrosine kinase 3; IDAC, cytarabine; ITD, internal tandem duplication; IV, intravenously; MDS-EB2, myelodysplastic syndrome with excess of blasts 2; ME, mitoxantrone-etoposide; mut+, mutated; ND, newly diagnosed; OS, overall survival; PO, by mouth; R, randomization; RFS, relapse-free survival; TKD, tyrosine kinase domain.

Ajout de thérapie ciblée *FLT3*-ITD et TKD : gilteritinib

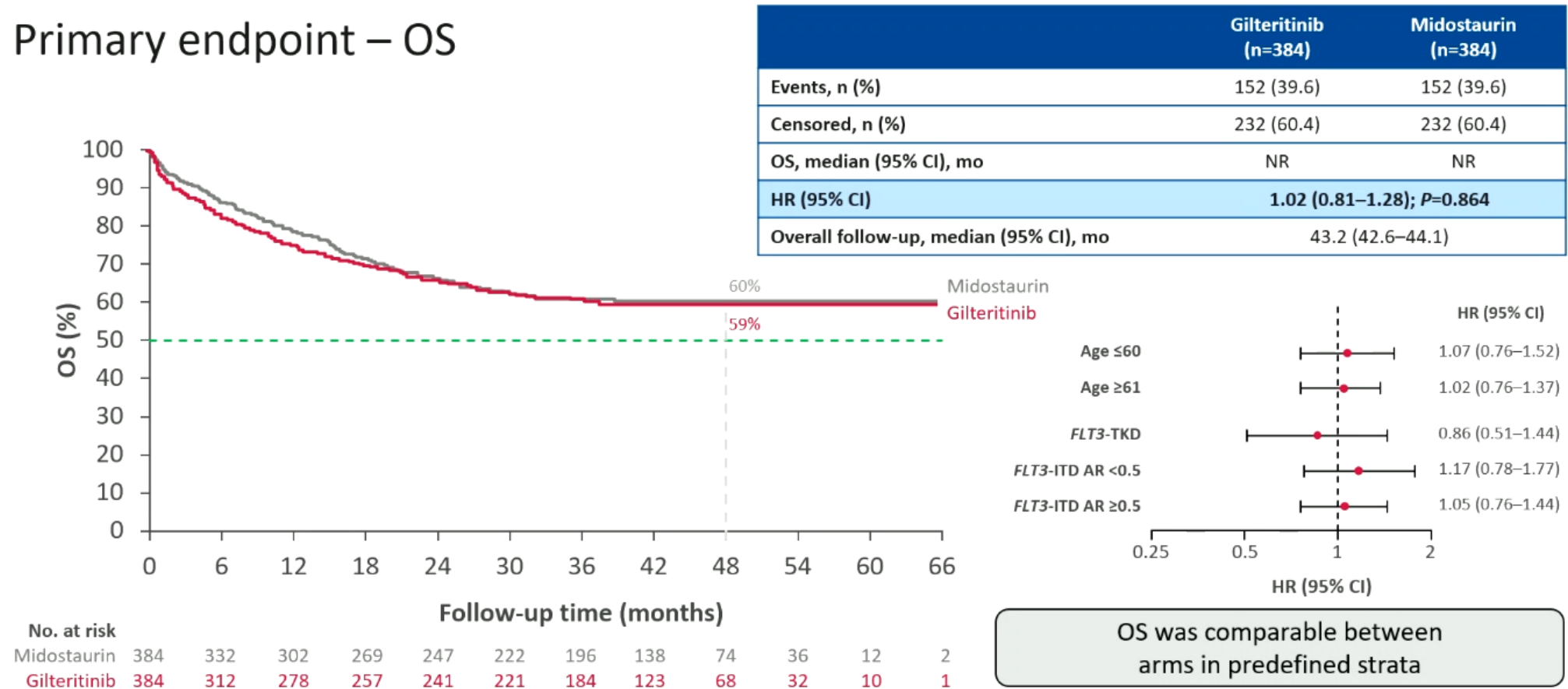
- 5499 patients with AML/MDS-EB2 were screened between December 20, 2019, and June 13, 2023; the data cutoff for analysis was October 15, 2025

	Gilteritinib (n=384)	Midostaurin (n=384)	Total (N=768)
Age, median (range), y	59 (18–78)	58 (18–78)	59 (18–78)
Age ≥61 years, n (%)	175 (45.6)	174 (45.3)	349 (45.4)
Male, n (%)	210 (54.7)	206 (53.6)	416 (54.2)
Region, n (%)			
Europe	371 (96.6)	365 (95.1)	736 (95.8)
Asia Pacific	13 (3.4)	19 (4.9)	32 (4.2)
<i>FLT3</i> mutation status, n (%)			
<i>FLT3</i> -ITD AR <0.5	117 (30.5)	119 (31.0)	236 (30.7)
<i>FLT3</i> -ITD AR ≥0.5	188 (49.0)	180 (46.9)	368 (47.9)
<i>FLT3</i> -TKD	79 (20.6)	85 (22.1)	164 (21.4)
Consolidation chemotherapy policy, n (%)			
HOVON ^a	134 (34.9)	136 (35.4)	270 (35.2)
AMLSG ^a	250 (65.1)	248 (64.6)	498 (64.8)
WHO/ECOG PS score, n (%)			
0–1	351 (91.4)	357 (93.0)	708 (92.2)
≥2	33 (8.6)	27 (7.0)	60 (7.8)

	Gilteritinib (n=384)	Midostaurin (n=384)	Total (N=768)
WBC count×10 ⁹ /L, median (range)	14.7 (0.7–287.8)	14.2 (0.5–490.0)	14.3 (0.5–490.0)
Disease type, n (%)			
De novo	331 (86.2)	352 (91.7)	683 (88.9)
Secondary	27 (7.0)	14 (3.6)	41 (5.3)
Therapy related	16 (4.2)	12 (3.1)	28 (3.6)
Unknown	10 (2.6)	6 (1.6)	16 (2.1)
ELN 2017 cytogenetic risk, n (%)			
Favorable	128 (33.3)	140 (36.5)	268 (34.9)
Intermediate	142 (37.0)	143 (37.2)	285 (37.1)
Adverse	113 (29.4)	100 (26.0)	213 (27.7)
Unknown	1 (0.3)	1 (0.3)	2 (0.3)
<i>NPM1</i> mutation present, n (%)	215 (56.0)	228 (59.4)	443 (57.7)

Ajout de thérapie ciblée *FLT3*-ITD et TKD : gilteritinib

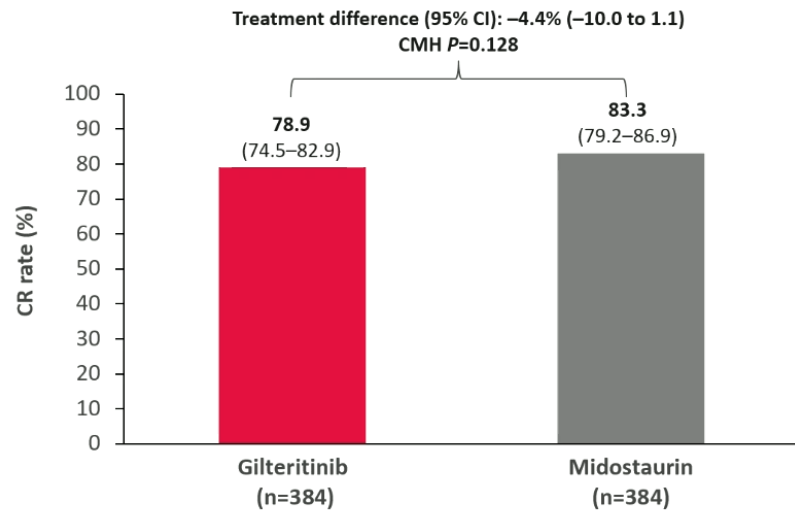
Primary endpoint – OS



Primary endpoint of OS was not met; both arms showed comparable survival

Ajout de thérapie ciblée *FLT3*-ITD et TKD : gilteritinib

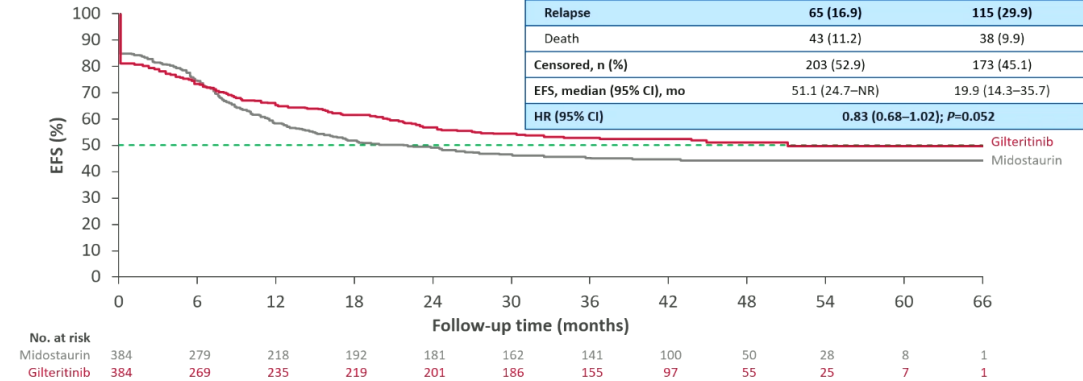
Key secondary endpoint – CR rate after induction



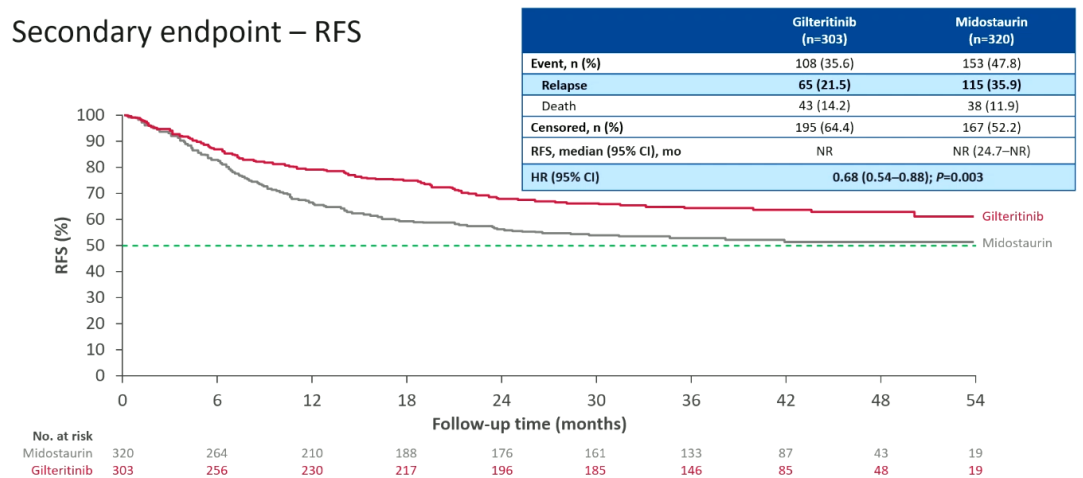
	Midostaurin (n=384)	Gilteritinib (n=384)
CR	320 (83.3)	303 (78.9)
CRi	14 (3.6)	11 (2.9)
MLFS	1 (<0.1)	15 (3.9)
Total	335 (87.2)	329 (85.7)

The CR rates were comparable between arms

Key secondary endpoint – EFS



Secondary endpoint – RFS



Ajout de thérapie ciblée *FLT3*-ITD et TKD : gilteritinib

Posthoc analyses: Survival after first relapse and use of salvage therapies including gilteritinib

Ad hoc analysis ^c Survival after first relapse	Gilteritinib arm (n=65)	Midostaurin arm (n=115)
Deaths, n (%)	48 (74)	71 (62)
OS, median (95% CI), mo	7.2 (5.6–11.2)	10.2 (7.5–18.0)
OS, 24-mo rate (95% CI)	17.8 (8.6–29.6)	37.3 (28.1–46.4)

Salvage therapy, n (%) ^a	Gilteritinib arm (n=65)(%)	Midostaurin arm (n=115)(%)
FLT3 inhibitor ^b	16 (25)	63 (55)
Gilteritinib ^b	11 (17)	57 (50)
Other FLT3 inhibitors ^b	8 (12)	17 (15)
AlloH SCT	14 (22)	39 (34)
Other treatment	49 (75)	81 (70)

Among relapsed patients in the midostaurin treatment arm, gilteritinib is the most frequently used subsequent therapy (50%)

A small minority of patients on the gilteritinib arm received subsequent FLT3 inhibitor salvage therapy or allo-HCT, after relapse.

^aA patient may have received ≥1 of these therapies during follow-up. ^bGiven either as monotherapy or in combination with other therapies. ^cOS post first relapse is an ad hoc analysis limited to patients experiencing first relapse; consequently, groups were not balanced between treatment arms (eg, sample size, age and on-study consolidation regimen).
alloH SCT, allogeneic hematopoietic stem cell transplantation; FLT3, *FLT3*-like tyrosine kinase 3; OS, overall survival.



Ajout de thérapie ciblée

FLT3-ITD : midostaurine ou quizartinib ?

Intensive Chemotherapy in Combination with Quizartinib versus Midostaurin for *FLT3*-ITD Mutated Acute Myeloid Leukemia: A multicenter cohort study

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Ajout de thérapie ciblée *FLT3*-ITD : midostaurine ou quizartinib ?

Baseline Characteristics of *FLT3*-ITD AML Cohort

	Total (n=215)	IC+Midostaurin (n=127)	IC+Quizartinib (n=88)
Age, median in years [IQR]	56.0 (45.0, 65.0)	58.0 (46.0, 66.0)	55.0 (44.0, 62.5)
<60 years, no. (%)	128 (59.5)	72 (56.7)	56 (63.6)
Male sex, no. (%)	96 (44.7)	61 (48.0)	35 (39.8)
Race/ethnicity, no. (%)			
White	157 (73.0)	98 (77.2)	59 (67.0)
Black	16 (7.4)	8 (6.3)	8 (9.1)
Asian	14 (6.5)	7 (5.5)	7 (8.0)
Hispanic	26 (12.1)	12 (9.4)	14 (15.9)
Other or unknown	2 (1.0)	2 (1.6)	0 (0.0)
De novo AML, no. (%)	204 (94.9)	119 (93.7)	85 (96.6)
ELN cytogenetic risk, no. (%)			
Favorable	3 (1.4)	2 (1.6)	1 (1.1)
Intermediate	191 (88.8)	112 (88.2)	74 (84.1)
Adverse	16 (7.4)	8 (6.3)	8 (9.1)
NA/Missing	5 (2.3)	5 (3.6)	5 (5.7)
Concurrent mutations, no. (%)			
IDH1	8 (3.7)	5 (3.9)	3 (3.4)
IDH2	29 (13.5)	18 (14.2)	11 (12.5)
NPM1 without DNMT3A	59 (27.4)	31 (24.4)	28 (31.8)
NPM1 + DNMT3A*	62 (28.8)	45 (35.4)	17 (19.3)
RAS	22 (10.2)	12 (9.4)	10 (11.4)
TP53	3 (1.4)	1 (0.8)	2 (2.3)



IQR, interquartile range, ELN, European LeukemiaNet; * $p < 0.05$

Ajout de thérapie ciblée *FLT3*-ITD : midostaurine ou quizartinib ?

Real-world Induction Treatment Selection

	Total (n=215)	Midostaurin (n=127)	Quizartinib (n=88)
Anthracycline, no. (%)*			
Daunorubicin	162 (75.4)	102 (80.3)	60 (68.2)
Daunorubicin 60 mg/m ² /day	118 (72.8)	60 (58.8)	58 (96.7)
Daunorubicin 90 mg/m ² /day	34 (21.0)	32 (31.4)	2 (3.3)
Daunorubicin 45 mg/m ² /day	1 (0.6)	1 (0.8)	0 (0.0)
Idarubicin 12 mg/m²/day	53 (24.7)	25 (19.7)	28 (31.8)
Cytarabine, no. (%)			
Cytarabine 100 mg/m²/day	139 (64.7)	81 (63.8)	58 (65.9)
Cytarabine 200 mg/m²/day	76 (35.3)	46 (36.2)	30 (34.1)

* $p=0.04$

- 27% in the quizartinib cohort received a modified dose (17.7 mg or 26.5 mg daily) versus the on-label dose of 35.4 mg daily due to concomitant administration of a CYP3A4 inhibitor.
- 5 patients (3.9%) in the midostaurin cohort received 50 mg daily, 1 patient received 200 mg daily, as opposed to the recommended 50 mg BID.



Ajout de thérapie ciblée *FLT3*-ITD : midostaurine ou quizartinib ?

Induction response	Total (n=215)	Midostaurin (n=127)	Quizartinib (n=88)
CR	134 (62.3)	81 (63.8)	53 (60.2)
CRh	7 (3.3)	1 (0.8)	6 (6.8)
CRi	27 (12.6)	11 (8.7)	16 (18.2)
PR	11 (5.1)	8 (6.3)	3 (3.4)
MLFS	7 (3.3)	6 (4.7)	1 (1.1)
Refractory	23 (10.7)	16 (12.6)	7 (8.0)
NA	6 (3.8)	4 (3.1)	2 (2.2)
CRc* (CR+CRh+CRi)	168 (78.1)	93 (73.2)	75 (85.2)

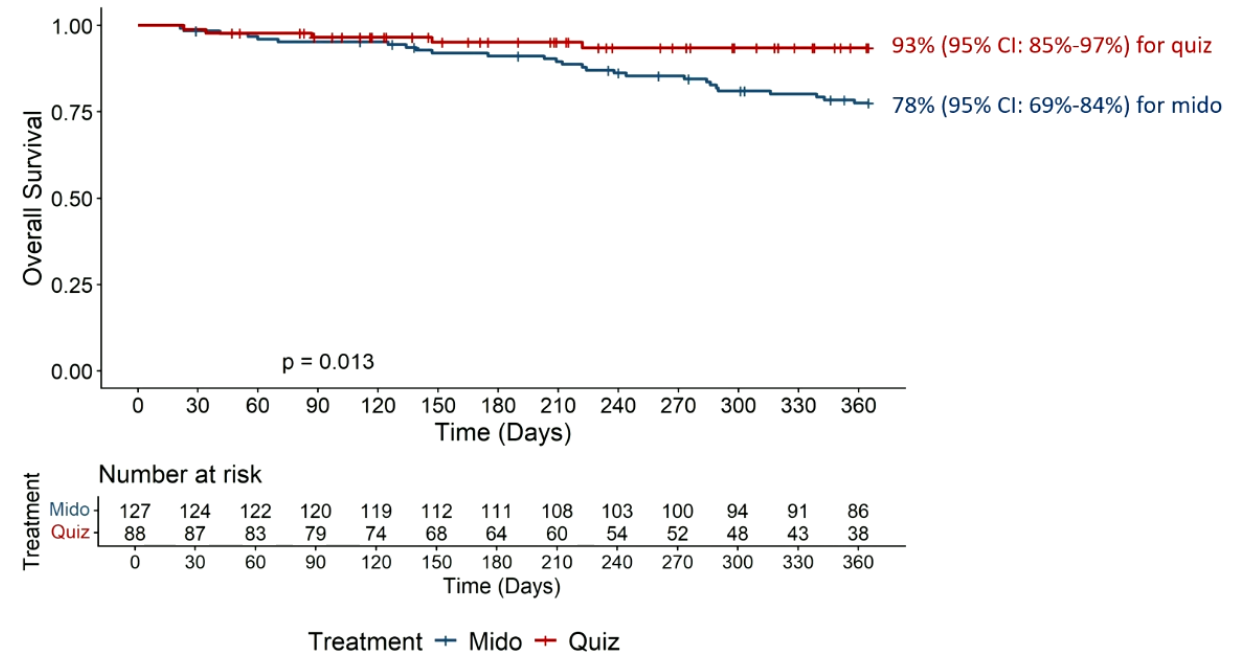
* $p < 0.05$

16.5% of midostaurin and 14.8% of quizartinib cohorts required re-induction ($p=0.73$).

Primary Endpoint: 1-year OS for *FLT3*-ITD AML

Median Follow-up (FU): 464 days (IQR: 230-815)

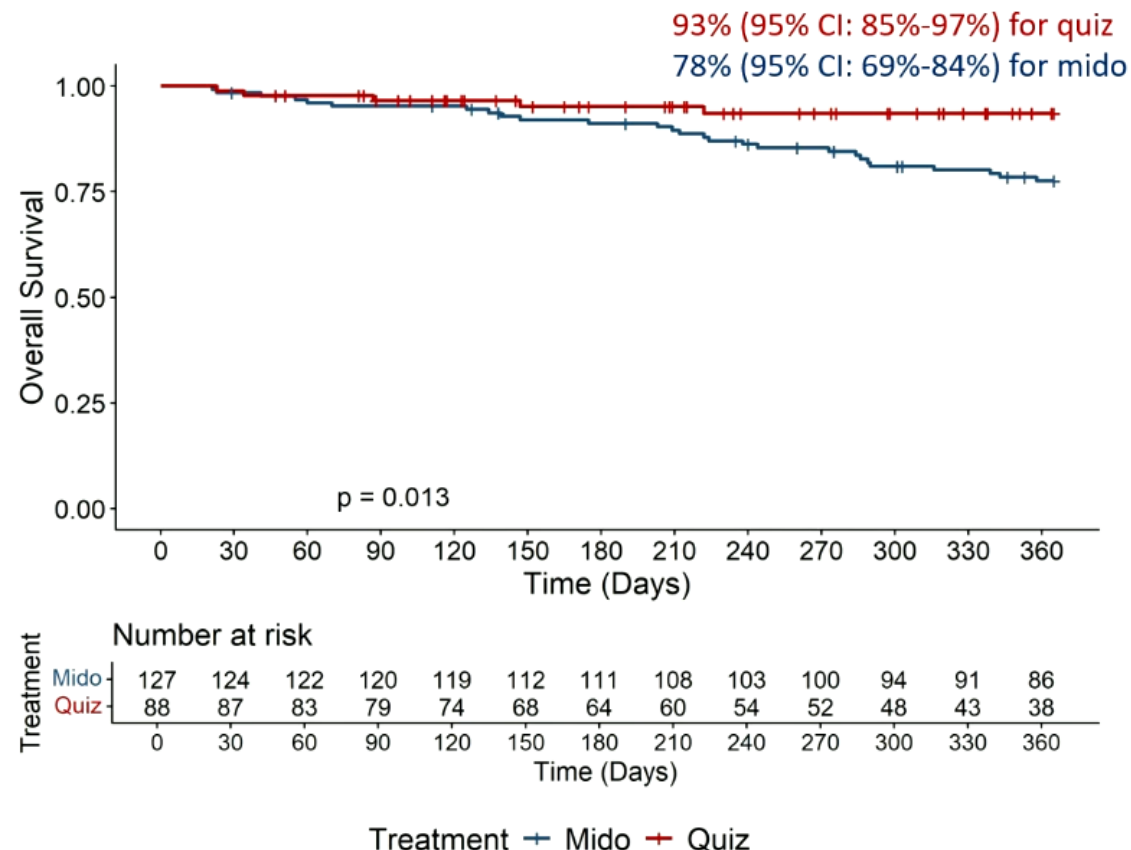
Within 1 year of induction, 27 deaths (21.3%) in the mido arm versus 5 deaths (5.7%) in the quiz arm.



Ajout de thérapie ciblée *FLT3*-ITD : midostaurine ou quizartinib ?

Primary Endpoint: 1-year OS for *FLT3*-ITD AML

Median Follow-up (FU): 464 days (IQR: 230-815)



Characteristic	1-year OS (HR, 95% CI)
Quiz (ref=Mido)	0.19 (0.07-0.52)
Age≥60 (ref≤60)	2.20 (1.02-4.74)
Male (ref=Female)	1.01 (0.51-1.97)
Race/ethnicity (ref=White)	
Asian	1.03 (0.13-8.29)
Black	1.36 (0.39-4.77)
Hispanic	2.49 (0.92-6.77)
De Novo AML Type	0.48 (0.14-1.67)
Adverse ELN Risk	1.79 (0.63-5.04)
IDH (ref=No)	2.23 (1.04-4.76)
NPM1 only (ref=No)	0.54 (0.23-1.27)
NPM1 and DNMT3a (ref=No)	0.33 (0.13-0.82)
Transplant in CR1 (ref=No)	0.3 (0.12-0.72)



HR=0.19 (95% CI: 0.07-0.52) with IC+Quiz versus IC+Mido

Ajout de thérapie ciblée *IDH1* : ivosidenib

Phase 1 ouverte multicentrique (NCT02632708)

Critères d'inclusion :

≥ 18 ans

ECOG PS 0-2

LAM 1ere ligne *de novo* ou secondaire

Mutation d'*IDH1*

Objectif primaire :

Safety de l'IVO combiné à la chimio intensive

Schéma :

Induction

IVOSIDENIB 500 mg/jr dès C1J1 en continu

Associé à un 3+7 avec Dauno/ida + cytarabine

Si ≥ PR :

IVOSIDENIB 500 mg/jr en continu

Consolidations ≤4 cycles de cytarabine

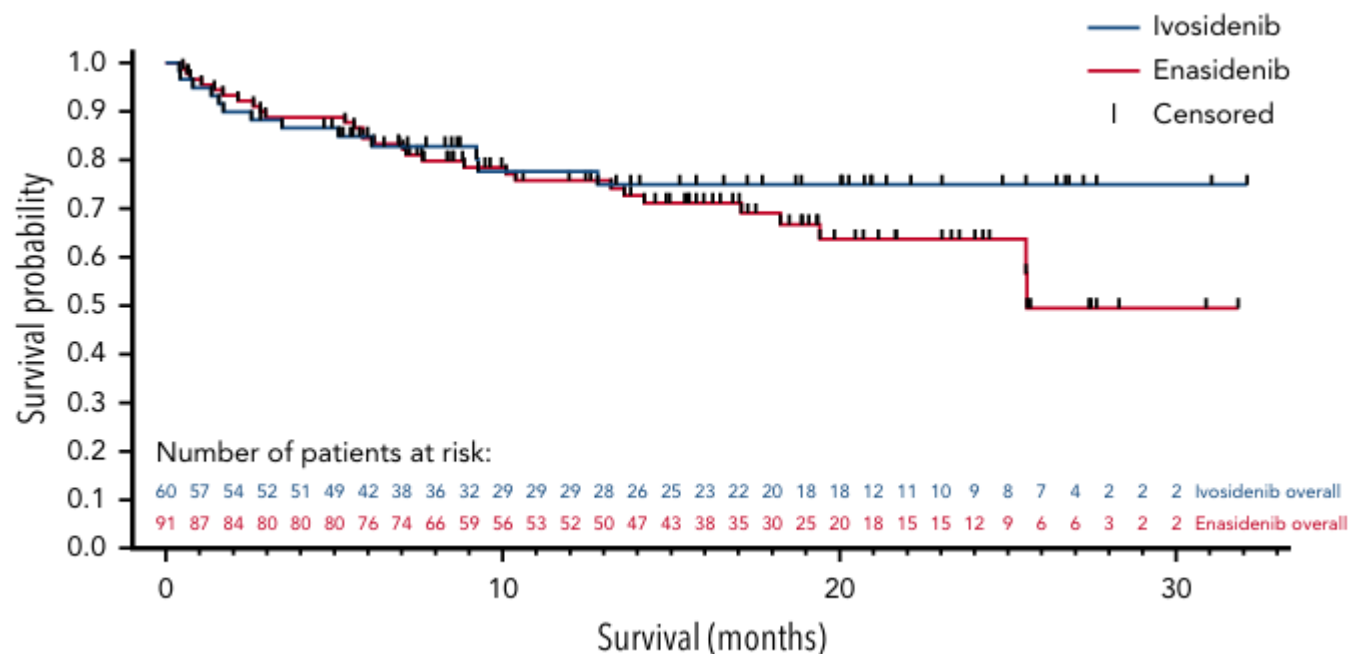
Si RC/RCi/RCp :

Entretien par IVOSIDENIB 500 mg/jr jusqu'à progression

Ajout de thérapie ciblée *IDH1* : ivosidenib

Response category	Ivosidenib 500 mg + chemotherapy, n (%)		
	All, N = 60	De novo AML, n = 42	Secondary AML, n = 18
CR/CRi/CRp	46 (77)	37 (88)	9 (50)
CR	41 (68)	32 (76)	9 (50)
CRi/CRp	5 (8)	5 (12)	—
MLFS	4 (7)	3 (7)	1 (6)
PR	2 (3)	—	2 (11)
Treatment failure†	8 (13)	2 (5)	6 (33)

Treatment	n	IDH mutation clearance, n (%)	n	MRD ⁻ , n (%)
Ivosidenib + chemotherapy	41	16 (39)	20	16 (80)



Ajout de thérapie ciblée *IDH1* : ivosidenib

RC + RCh : 76,7%

Temps médian à la RC : 34 jours

Durée médiane de la RC : 25,1 mois

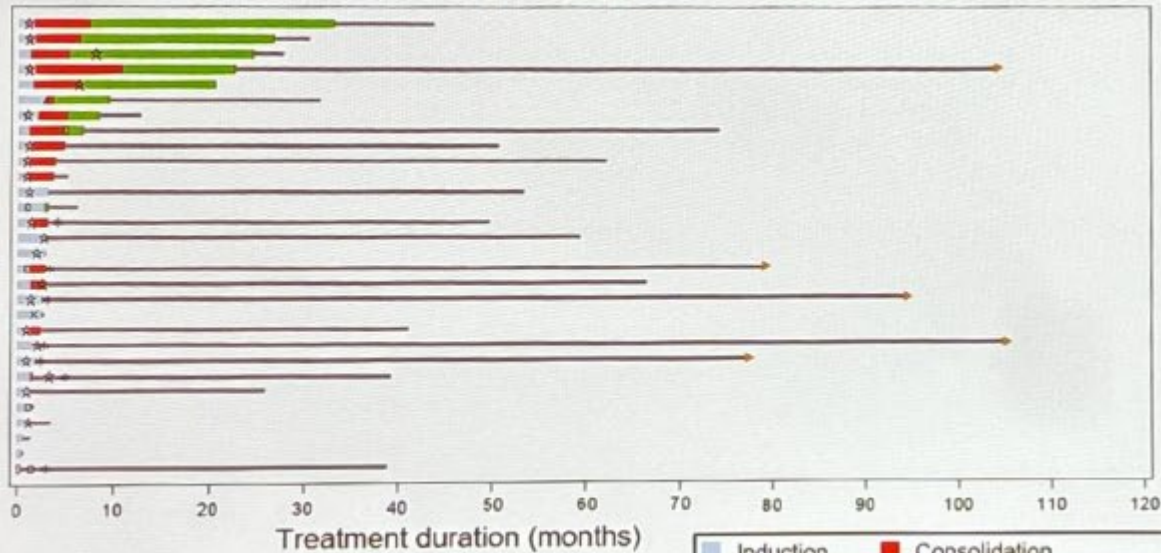
Survie globale à 3 ans : 67%

OS médiane non atteinte

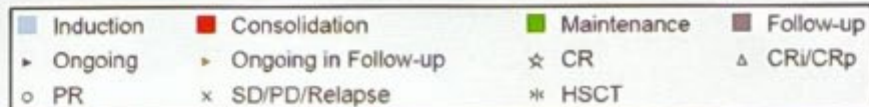
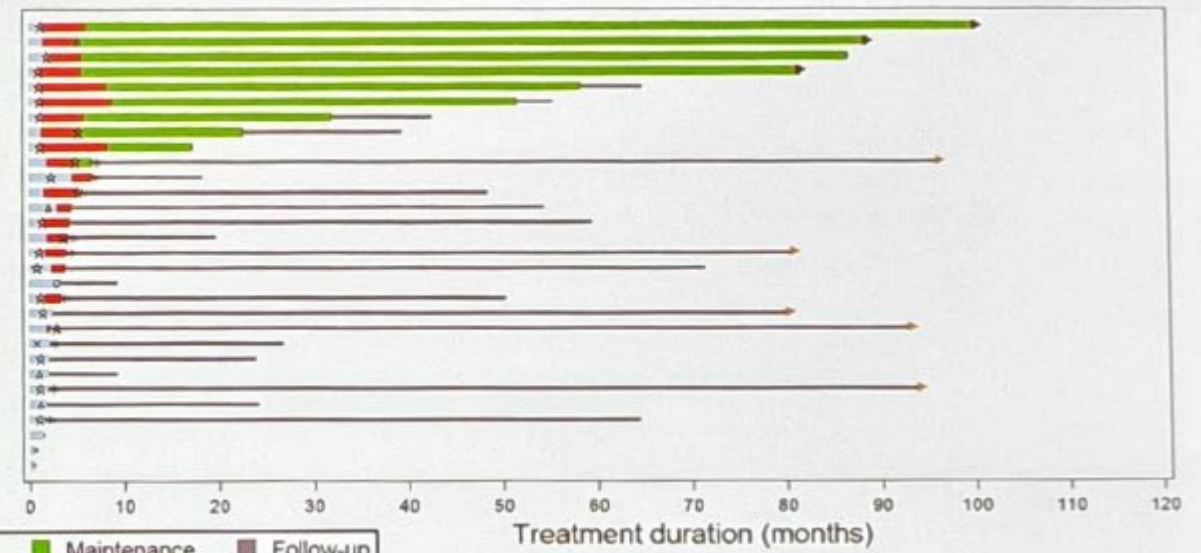
EFS à 1 an : 49%

IVO maintenance treatment showed durable responses

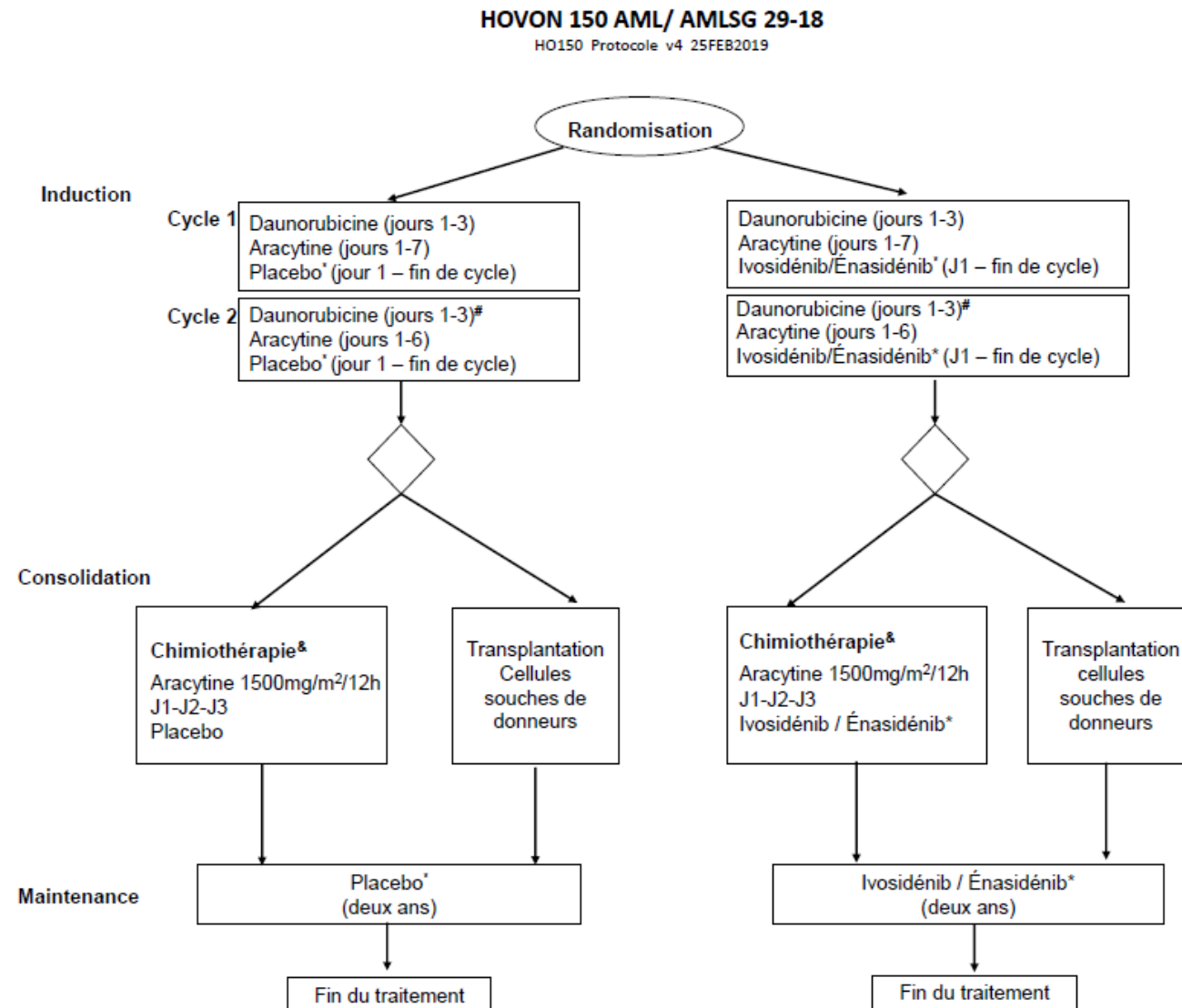
Treatment: IVO 500 mg + cytarabine + daunorubicin



Treatment: IVO 500 mg + cytarabine + idarubicin



Ajout de thérapie ciblée *IDH1* : ivosidenib



La suite à l'ASH 2026 !

**68TH ASH ANNUAL MEETING AND
EXPOSITION**



Plenary Session, Sunday December 13th

Ajout de thérapie ciblée Venetoclax

Regimen	Median age, years (range)	N	CR+CRi	Median OS	Allo-HCST
7+3 + VEN	40 (18-60)	33	91%	Not reached	36%
5+2 + VEN	72 (63-80)	69	73%	15.4 mo	1%
7+3 + VEN	59 (27-71)	34	85%	Not reached	29%
CLIA + VEN	48 (18-64)	50	94%	Not reached	32%
FLAG-Ida-VEN	44 (20-67)	68	96%	Not reached	57%

Dose-Escalation Study of Venetoclax Plus Standard "7+3" Induction Chemotherapy in Fit Patients with Newly Diagnosed AML

Patients and Methods

Dose-escalation (3x3 Design)

"7+3" + Venetoclax x8 days (n = 14)

Ven 100mg D1 → Ven 200mg D2 → Ven 400mg D3-8



"7+3" + Venetoclax x11 days (n = 9)

Ven 100mg D1 → Ven 200mg D2 → Ven 400mg D3-11



"7+3" + Venetoclax x14 days (n = 11)

Ven 100mg D1 → Ven 200mg D2 → Ven 400mg D3-14



Safety

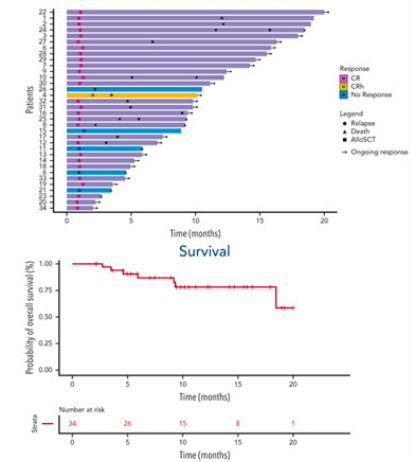
- Manageable side effects
- No dose-limiting toxicities
- No 30- or 60-day induction mortality
- Median time to ANC $\geq 1000/\mu\text{L}$: 27 (22-49) days
- Median time to PLT $\geq 100\text{K}/\mu\text{L}$: 28 (22-72) days

Efficacy

- 29/34 (85.3%) achieved CRc (1 CRh)
- 25/29 (86%) MRD-negative CRc by multiparameter flow cytometry

Durability/Survival

- With a median follow-up time of 9.6 months, median DoR, EFS and OS have not been reached



Conclusion: In patients with newly diagnosed AML who are up to 75 years of age, venetoclax in combination with "7+3" chemotherapy, irrespective of venetoclax duration, was found to be tolerable and led to high rates of MRD-negative complete remissions.

Mantzaris et al. DOI: 10.1182/*blood*.2024026700



Ajout de thérapie ciblée Venetoclax

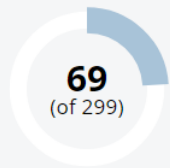
AMLSG HO501 AML

Open 

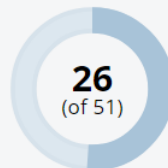
Main info

Identifier: HO501 AML
Sponsor: AMLSG
Working group party: Leukemia
Stage: 1st Line
Echelon: Level C-HIC&C-SCT

Included patients:



Active sites:



25 sites are pending

Title:

A Randomized, Placebo-Controlled Phase III Study of Induction and Consolidation Chemotherapy With Venetoclax in Adult Patients With Newly Diagnosed Acute Myeloid Leukemia or Myelodysplastic Syndrome With Excess Blasts-2

Phase III Study of Induction and Consolidation Chemotherapy With Venetoclax in Patients With Newly Diagnosed AML or MDS-EB-2

ClinicalTrials.gov ID  **NCT04628026**

Sponsor  University of Ulm

Information provided by  Prof. Dr. Hartmut Doehner, University of Ulm (Responsible Party)

Last Update Posted  2026-09-09

Recruiting 

[Find contact information](#)

[Check who can join](#)

Study Start (Actual) 

2022-09-13

Primary Completion (Estimated) 

2029-03

Study Completion (Estimated) 

2032-02

Enrollment (Estimated) 

650

Study Type 

Interventional

Phase 

Phase 3

Ajout de thérapie ciblée Quizartinib

QUIWI Phase 2 Trial design: upfront newly diagnosed fit *FLT3*-ITD negative AML

- Safety run-in phase: open-label cytarabine 200 mg/m² (days 1-7), Idarubicin 12 mg/m² (days 1-3) Quizartinib 60 mg/d x 14 days (30mg with strong CYP3A inhibitor)

Enrollment dates: September 2019 to November 2021

Data cutoff: May 2023, median follow-up 21 months

Pre-planned interim analyses: 12 months after last patient included

- 18-70 years of age
- ECOG <3
- Newly diagnosed *FLT3*-ITD negative AML (ratio <0.03)
- *FLT3*-ITD centrally screened (capillary electrophoresis)
- Patients begin 7+3 chemotherapy during screening

Stratification factors

- Patient age: <60 years, ≥60 years

Selected endpoints

- Primary endpoint: EFS
- Secondary endpoints: OS, CR/CRc, Safety
- Exploratory endpoints: RFS, DoCR

Patients with newly diagnosed AML 18-70 years with *FLT3*-ITD negative (N=272)

Randomization 2:1 (Stratification by age)

Induction (Cycle 1)

Idarubicin + cytarabine 3+7, day 1-7
Quizartinib 60 mg/day or placebo, days 8-21

Response Assessment

CR/CRi

PR/Resistant disease

Induction (Cycle 2)
(as Induction cycle 1)

CR/CRi

PR/Resistant disease

Consolidation (1-4 cycles)

Cytarabine 3 g/m²/12h day 1,3,5*
Quizartinib 60 mg/day or placebo, days 6-19

Allo-HCT
if indicated

Maintenance

(up to 12 cycles, every 28 days)
Quizartinib 60 mg/day or placebo, 28 days

Study treatment
discontinuation

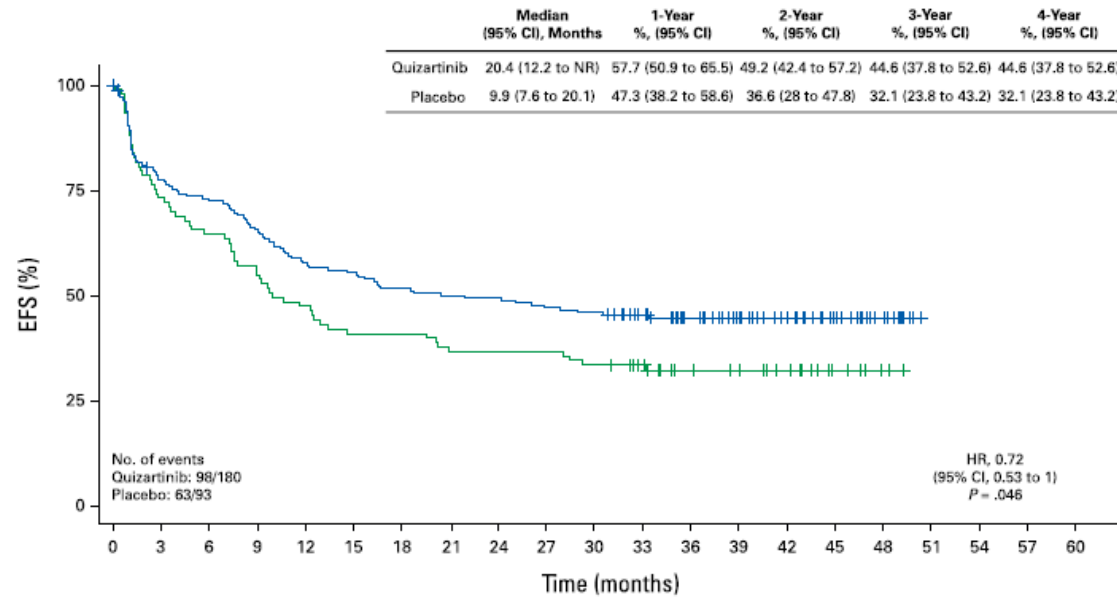
Ajout de thérapie ciblée Quizartinib

Patient Characteristics	Quizartinib (N=180)	Placebo (N=93)	P
Age, years			
Median (range)	57.1 (19-70)	58.5 (21-70)	0.23
≥60 years, n (%)	74 (41.1)	41 (44.1)	0.63
Sex, n (%)			
Male	103 (57)	54 (58)	0.89
Female	77 (43)	39 (42)	
ECOG, n (%)			
0	113 (64)	56 (61)	0.57
1	49 (28)	30 (33)	
2	14 (8)	5 (5)	
ELN2017^a, n (%)			
Favorable	34 (19)	25 (27)	0.01
Intermediate	81 (45)	25 (27)	
Adverse	64 (36)	43 (46)	

6,5% des patients avaient une mutation de type *FLT3*-TKD

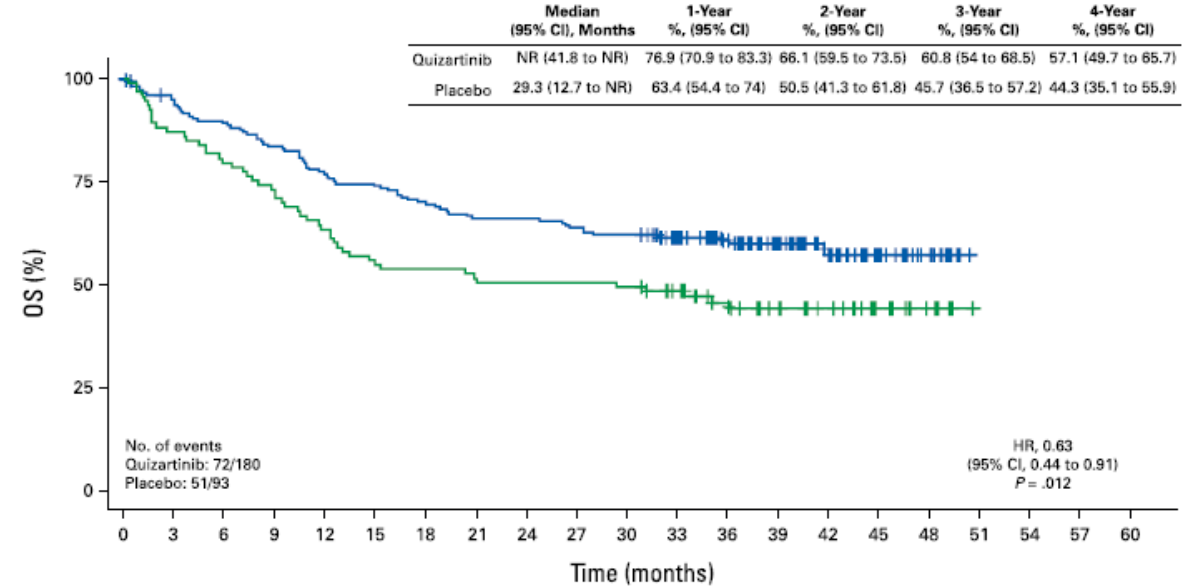
Ajout de thérapie ciblée Quizartinib

A



Number at risk (number censored)																			
		0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51
Quizartinib	180 (0)	137 (3)	128 (3)	116 (3)	102 (3)	98 (3)	91 (3)	88 (3)	87 (3)	83 (3)	81 (3)	70 (13)	55 (27)	44 (38)	33 (49)	21 (61)	11 (71)	0 (82)	0 (82)
Placebo	93 (0)	68 (0)	60 (0)	51 (0)	44 (0)	38 (0)	38 (0)	34 (0)	34 (0)	34 (0)	31 (0)	27 (4)	20 (10)	18 (12)	13 (17)	6 (24)	2 (28)	0 (30)	0 (30)

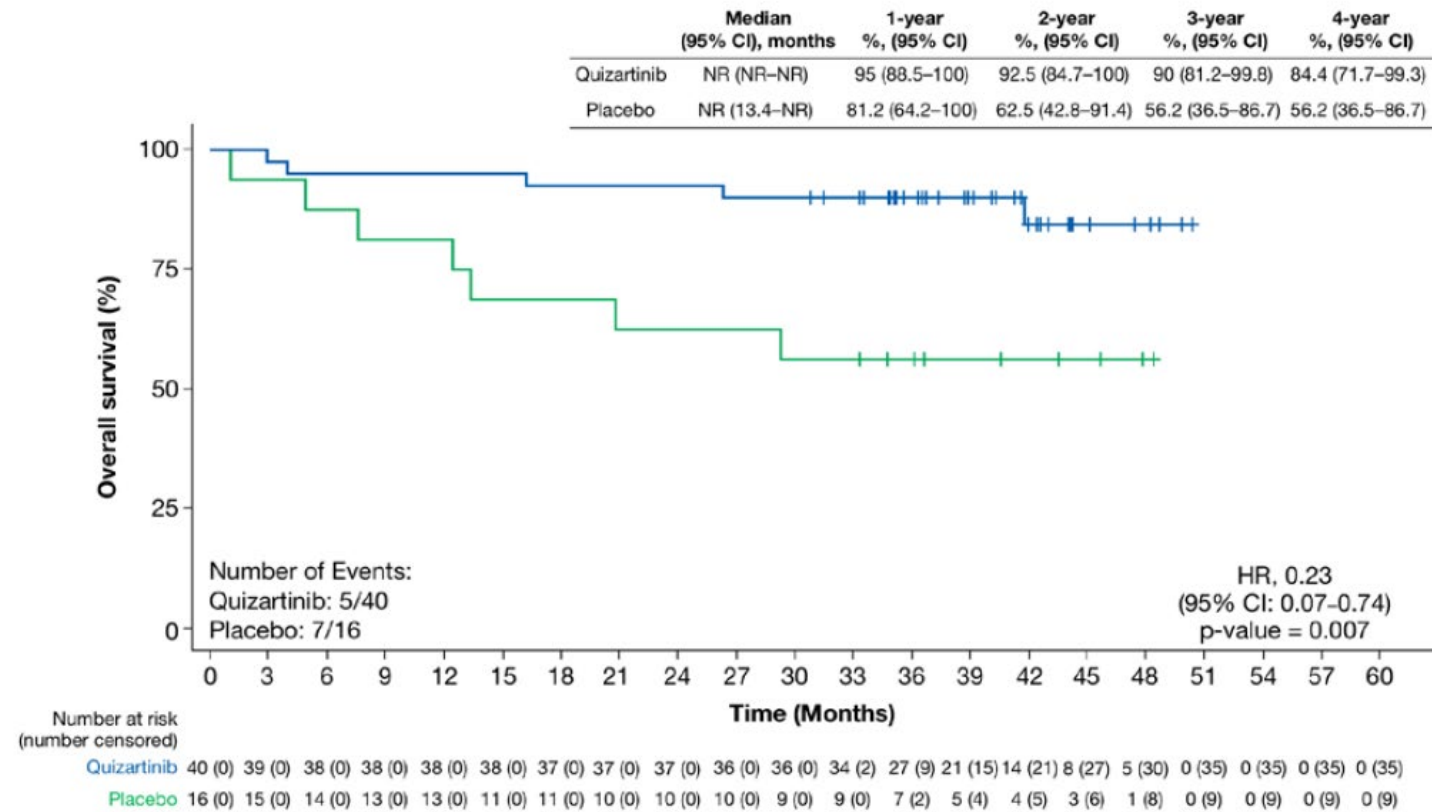
B



Number at risk (number censored)																			
		0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51
Quizartinib	180 (0)	166 (3)	158 (3)	148 (3)	136 (3)	131 (3)	123 (3)	117 (3)	117 (3)	113 (3)	110 (3)	94 (18)	75 (36)	56 (54)	38 (70)	22 (86)	11 (97)	0 (108)	0 (108)
Placebo	93 (0)	81 (0)	74 (0)	66 (0)	59 (0)	51 (0)	50 (0)	47 (0)	47 (0)	47 (0)	46 (0)	40 (5)	32 (11)	25 (17)	17 (25)	10 (32)	5 (37)	0 (42)	0 (42)

Ajout de thérapie ciblée Quizartinib

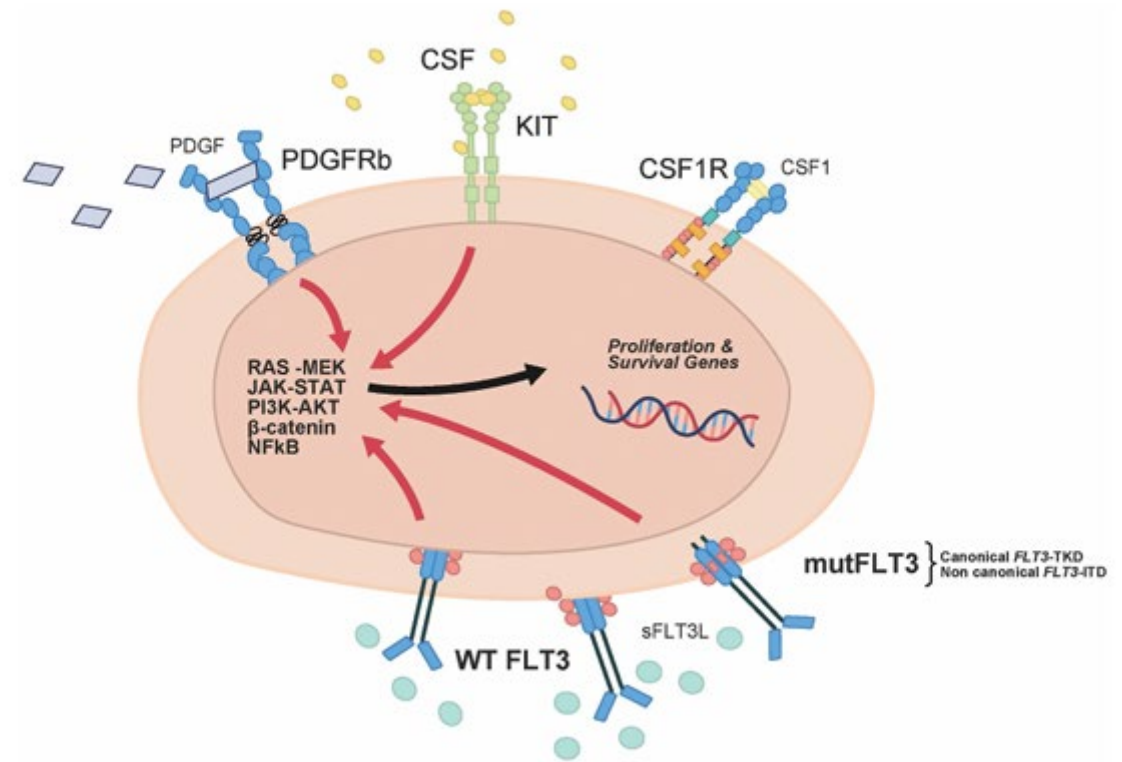
NPM1



Ajout de thérapie ciblée

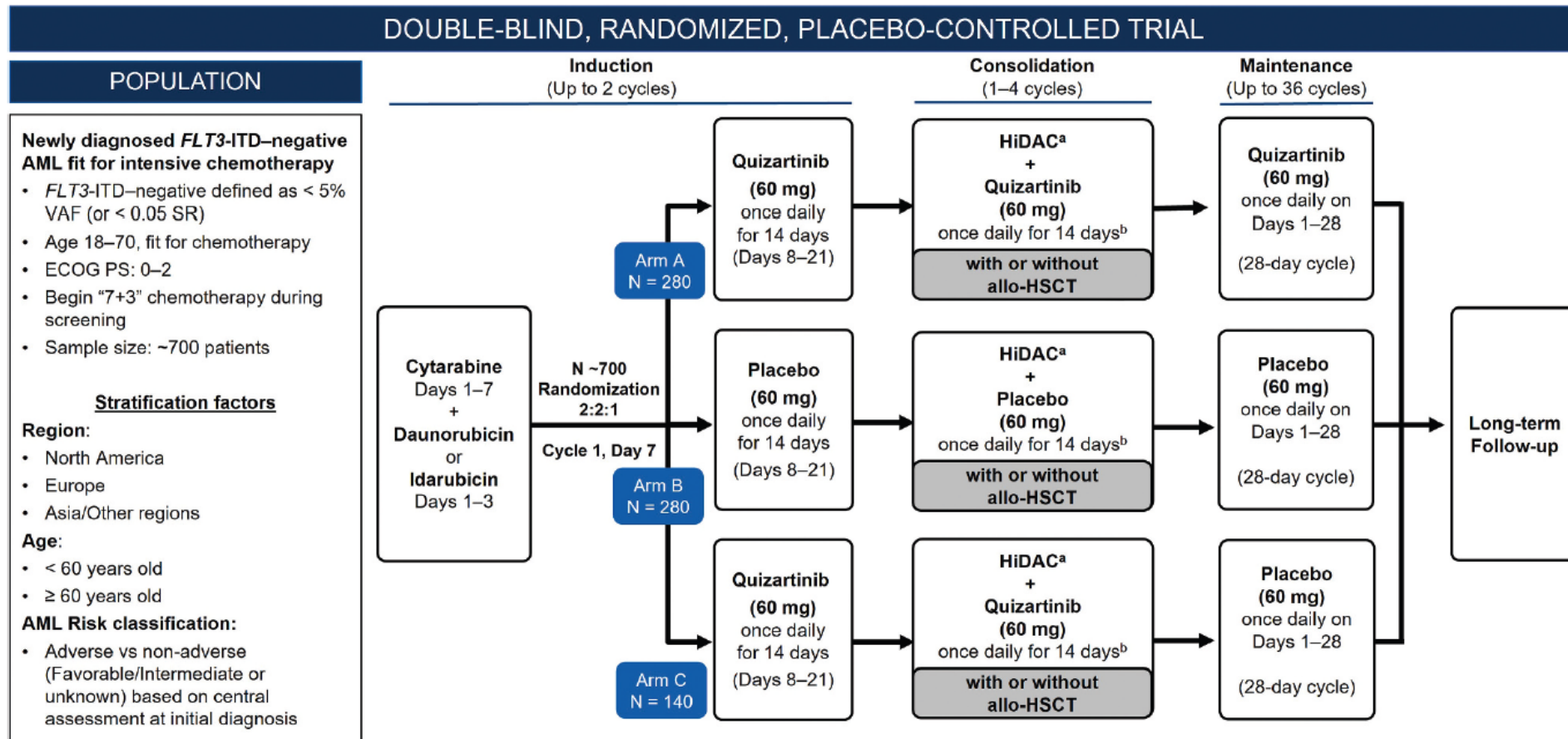
Quizartinib

- Surexpression de FLT3 (70-100%)
- Expression du FLT3L (boucle autocrine ou paracrine)
- Augmentation de l'expression de FLT3 (*WT1m*)
- Quiz inhibe *KIT* et *PDGFRA*
- Affinité pour récepteur FLT3-WT (à une plus forte dose)



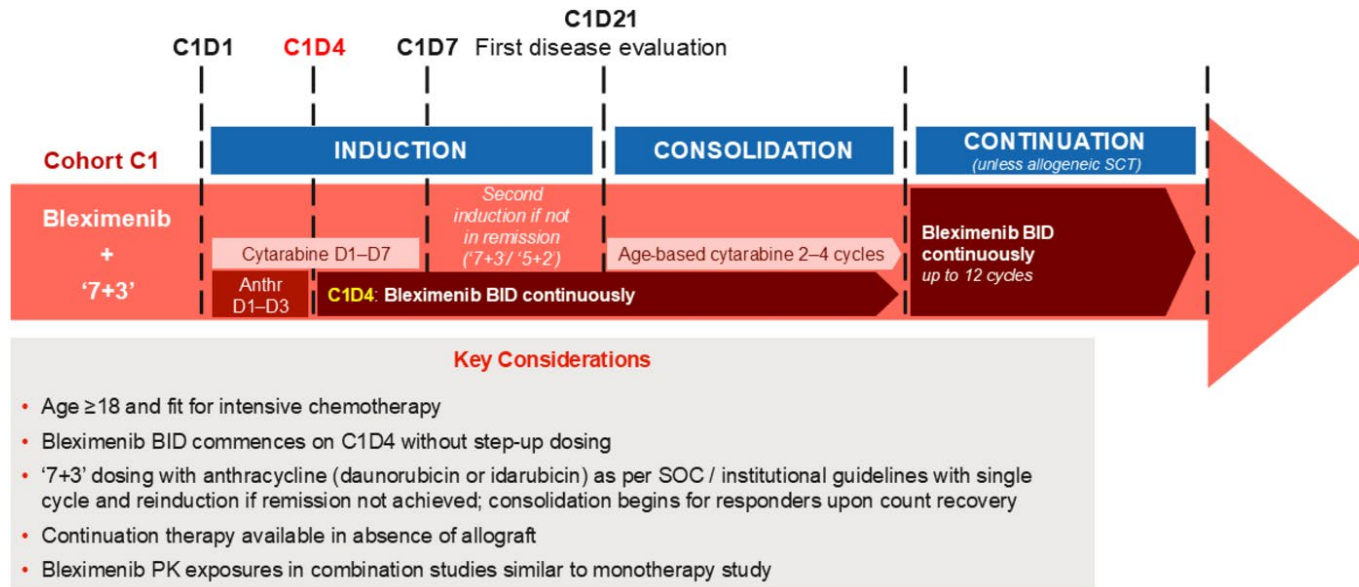
Ajout de thérapie ciblée Quizartinib

QuANTUM-WILD



Ajout de thérapie ciblée Inhibiteurs de Menin

3+7 + BLEXIMENIB dans les LAM *NPM1m* et *KMT2Ar* en 1L



Bleximenib 30-100 mg x2/jr à partir de J4 de l'induction puis en continu
 Induction 3+7 (daunorubicine 60 ou idarubicine 12 x3)
 Consolidation IDAC (jusqu'à 4)
 Maintenance jusqu'à 12 cycles
 AlloHSCT

N=44

Age médian 57 ans (19-71)

57% *NPM1m*, 43% *KMT2Ar*

ELN : 44%/28%/28% fav/int/défav

Safety : Mortalité J30/J60 : 0/2%

Toxicité attendue avec 3+7

Pas de SD, 4 allongements QTc (grade 1-2)

Durée aplasie : 30 jours

	N=24
RCc	87,5%
RC+RCh	75%
ORR	95,8%

4 patients traités à la dose de 100 mg x2/jr
 ont été allogreffés

Ajout de thérapie ciblée

Inhibiteurs de Menin

3+7 + REVUMENIB dans les LAM *NPM1m* et *KMT2Ar* en 1L

Critères d'inclusion :

18-75 ans

LAM ND *KMT2Ar*, *NPM1m* ou *NUP98r*

ECOG PS 0-2 (0-1 si > 65 ans)

Candidats pour chimio intensive

DL1 : Revumenib 110 mg x2/jr (220 si iCYP3A4 fort)

DL2 : Revumenib 160 mg x2/jr (270 si iCYP3A4 fort)

Induction 3+7 (daunorubicine ou idarubicine)

Consolidation HDAC x3

Maintenance jusqu'à progression

AlloHSCT

7 patients évaluable

Tous *KMT2Ar*, âge médian 37 ans

Safety :

1 arrêt de traitement pour AE durant induction

1 DLT (allongement QTc)

Réponse :

Taux de RC = 100%

100% MRD négative (6/6)

4 alloHSCT

Ajout de thérapie ciblée

Inhibiteurs de Menin

3+7 + ZIFTOMENIB dans les LAM *NPM1*m et *KMT2A*r en 1L

S130

Ziftomenib Combined With Intensive Induction (7+3) for Newly Diagnosed *NPM1*-m or *KMT2A*-r Acute Myeloid Leukemia (AML): Long-Term Results From the KOMET-007 Trial

Amer M Zeidan¹, Eunice Wang², Harry Erba³, Stephen Strickland⁴, Ghayas Issa⁵, Suresh K Balasubramanian⁶, Gail J Roboz⁷, Christine McMahon⁸, Marcello Rotta⁹, Yazan Madanat¹⁰, Keith Pratz¹¹, James S Blachly¹², Tara F Lin¹³, Gary Schiller¹⁴, Talha Badar¹⁵, Ivana Gojo¹⁶, Jessica K Altman¹⁷, James Mangan¹⁸, Mark Juckett¹⁹, Kiran Naqvi²⁰, Anjali Advani²¹, Leonard C. Alsfeld²², Jorge Cortes²³, Mohamad Khawandana²⁴, Kalyan Nadiminti²⁵, Hongling Zhang²⁶, Tianle Chen²⁶, Valerie Chamberlain Santos²⁶, Marcie Riches²⁶, Daniel Corum²⁶, Mollie Leoni²⁶, and Amir T Fathi²⁷

¹Yale University and Yale Comprehensive Cancer Center, New Haven, CT, USA; ²Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; ³Duke Cancer Institute, Durham, NC, USA; ⁴SCRi at TriStar Centennial, Nashville, TN, USA; ⁵Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ⁶Karmanos Cancer Institute, Wayne State University, Detroit, MI, USA; ⁷Weill Cornell Medicine and The New York Presbyterian Hospital, New York, NY, USA; ⁸Anschutz Medical Campus, Division of Hematology, University of Colorado School of Medicine, Aurora, CO, USA; ⁹Colorado Blood Cancer Center, Denver, CO, USA; ¹⁰The University of Texas Southwestern Medical Center, Dallas, TX, USA; ¹¹Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; ¹²The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; ¹³University of Kansas Medical Center, Kansas City, KS, USA; ¹⁴David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; ¹⁵Mayo Clinic, Jacksonville, FL, USA; ¹⁶Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA; ¹⁷Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL, USA; ¹⁸Moore Cancer Center, University of California, San Diego, CA, USA; ¹⁹Department of Hematology, University of Minnesota, Minneapolis, MN, USA; ²⁰Chao Family Comprehensive Cancer Center, University of California Irvine Health, Orange, CA, USA; ²¹Cleveland Clinic, Cleveland, OH, USA; ²²Ochsner MD Anderson Cancer Center, New Orleans, LA, USA; ²³Georgia Cancer Center, Augusta, GA, USA; ²⁴University of Oklahoma Health Sciences Center, Stephenson Cancer Center, Oklahoma City, OK, USA; ²⁵Carbone Cancer Center, University of Wisconsin-Madison, Madison, WI, USA; ²⁶Kura Oncology, Inc., San Diego, CA, USA; ²⁷Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

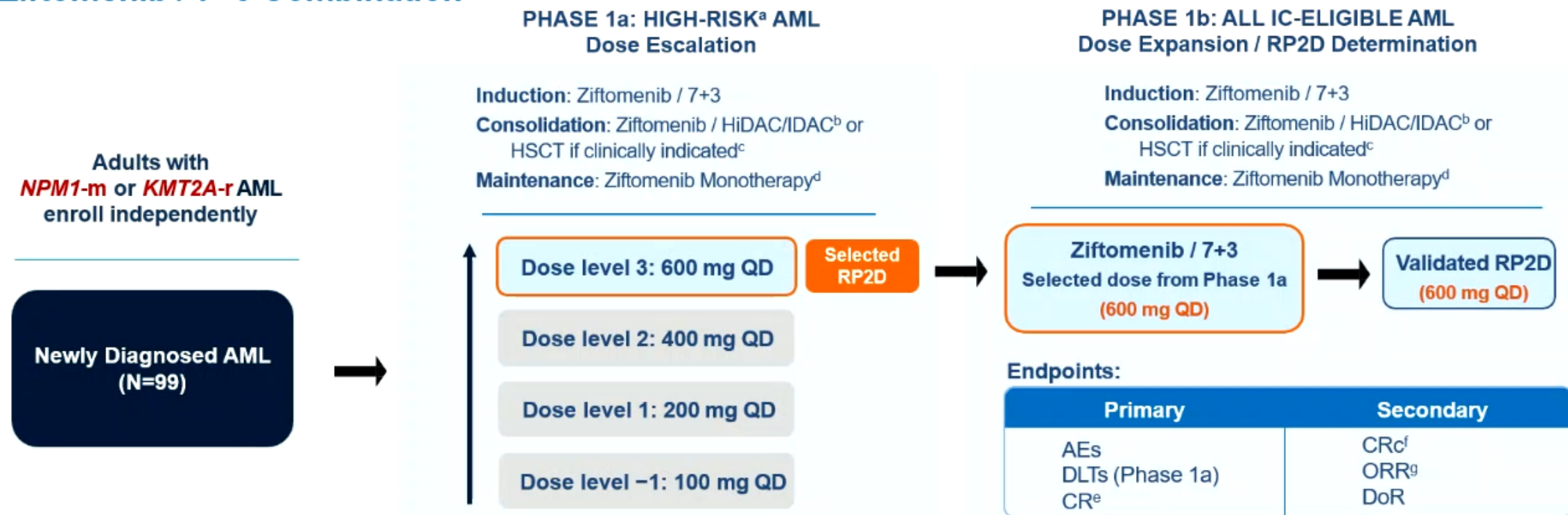


Slides can be accessed through this Quick Response (QR) code.

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KOMET-007: Ongoing Combination Trial of Ziftomenib in Newly Diagnosed AML

Ziftomenib / 7+3 Combination



- Ziftomenib started on Cycle 1 Day 8 and administered continuously thereafter; cytarabine was administered on Cycle 1 Days 1–7 and daunorubicin on Cycle 1 Days 1–3; re-induction cycles allowed based on bone marrow biopsy results

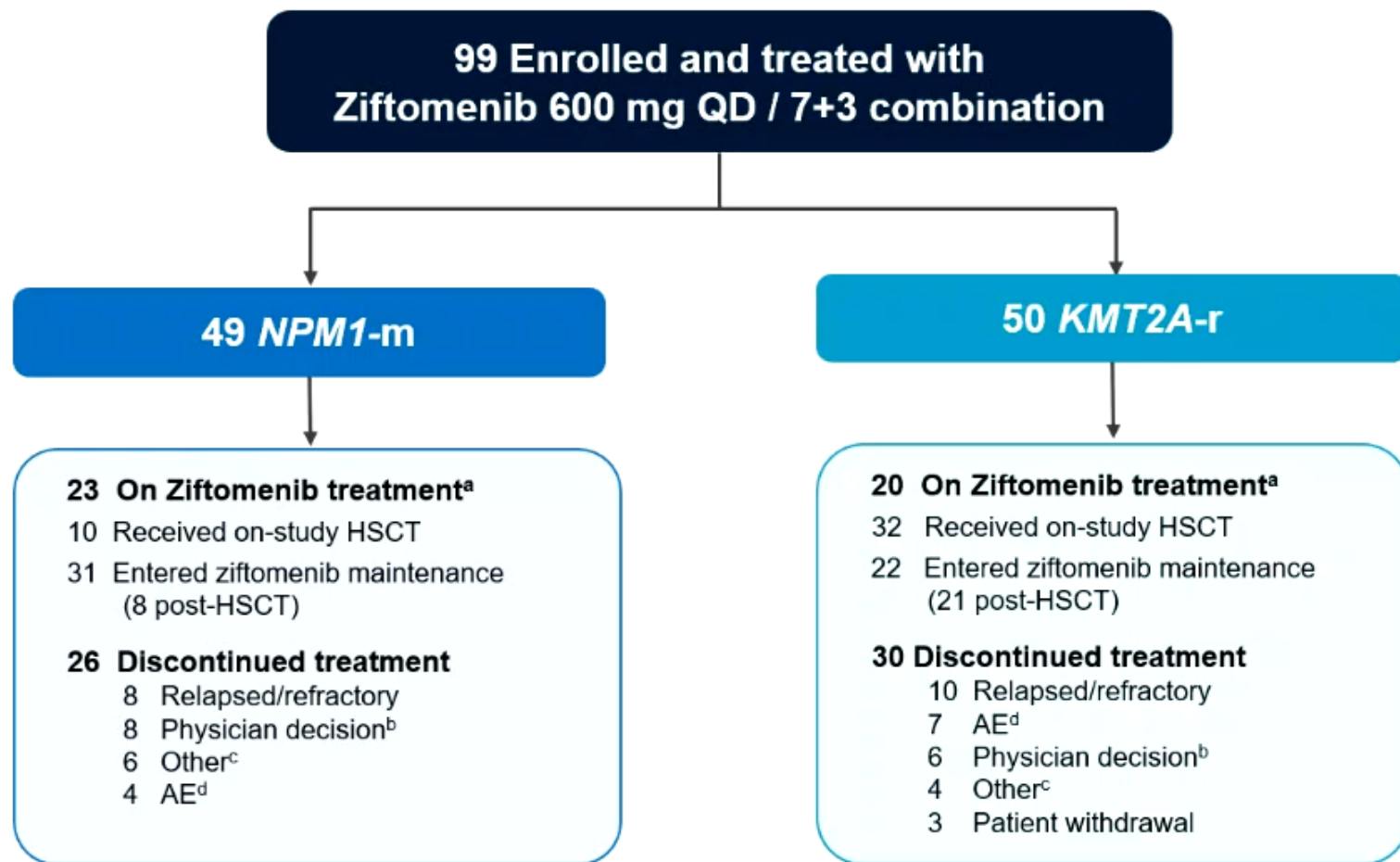
Here, we present updated safety and clinical activity in all patients with newly diagnosed AML treated at the ziftomenib RP2D of 600 mg QD in combination with standard doses of 7+3 across phase 1a/b

^aHigh-risk defined as *KMT2A*-r AML, or *NPM1*-m AML with adverse-risk cytogenetics per ELN criteria, age ≥ 60 years, and/or treatment-related AML regardless of age; ^bHiDAC, IDAC or VVXEOS[®] were permitted; ^cFor HSCT, ziftomenib was held;

^dZiftomenib 600 mg monotherapy for up to 2 years; ^eper ELN 2022 criteria; ^fCR, CRh, or CRi; ^gCRc or MLFS

7+3, cytarabine/daunorubicin; AE, adverse event; CR / CRh / CRi, complete remission with full / partial / incomplete hematologic recovery; CRc, composite complete remission; DLT, dose-limiting toxicity; DoR, duration of remission; HiDAC, high-dose cytarabine; HSCT, hematopoietic stem cell transplantation; IC, intensive chemotherapy; IDAC, intermediate-dose cytarabine; MLFS, morphologic leukemia-free state; ORR, objective response rate; RP2D, recommended phase 2 dose

KOMET-007 Patient Populations: Newly Diagnosed AML



- As of Apr 10, 2026, **99 patients** (49 *NPM1-m*, 50 *KMT2A-r*) with newly diagnosed AML were enrolled and treated with ziftomenib 600 mg orally once daily and 7+3
- Median follow-up was **17.6 months** for *NPM1-m* and **11.0 months** for *KMT2A-r*
- 90% (44/49) of *NPM1-m* and 62% (31/50) of *KMT2A-r* patients were still on-study

^aPatients who had not discontinued ziftomenib as of the data cutoff date; ^bPhysician decisions included: *NPM1-m*: decision to withdraw patient from study (n=1), myocarditis of uncertain etiology (n=1), patient graft-versus-host disease status (n=1), patient commencing alternative treatment (n=5); *KMT2A-r*: patient unable to return to site for treatment (n=1), patient started cranio-spinal irradiation (n=1), nonspecific symptoms (predominantly pruritus) (n=1), failure to meet eligibility criteria for post-HSCT maintenance therapy (n=1), commencing alternative treatment (n=2); ^cOther reasons included: *NPM1-m*: patient refusal to continue study treatment (n=1), maintenance off trial (n=1), patient declined to adhere to birth control requirements (n=1), patient proceeded to off-study transplant (n=3); *KMT2A-r*: patient proceeded with chemotherapy+donor lymphocyte infusion (n=1), patient decided not to continue with ziftomenib (n=1), patient proceeded to transplant (n=2); ^dAdverse events included: *NPM1-m*: arthralgia, ischemic enteritis, cerebral hemorrhage, drug-induced liver injury (all n=1); *KMT2A-r*: multiple organ dysfunction syndrome (n=1), sepsis (n=1), staphylococcal sepsis (n=1), clostridial sepsis (n=1), disseminated mucormycosis (n=1), cardiac arrest (n=1), differentiation syndrome (n=1)

Data cutoff: Apr 10, 2026. HSCT, hematopoietic stem cell transplantation

Clinical Activity of Ziftomenib with 7+3

n (%)	<i>NPM1</i> -m (N=49)	<i>KMT2A</i> -r (N=50)	All Patients (N=99)
CRc	47 (96)	45 (90)	92 (93)
ORR	48 (98)	46 (92)	94 (95)
CR	46 (94)	41 (82)	87 (88)
CRh	1 (2)	1 (2)	2 (2)
CRi	0	3 (6)	3 (3)
MLFS	1 (2)	1 (2)	2 (2)
PR	0	0	0
NR	1 (2)	3 (6)	4 (4)
NE	0	1 (2)	1 (1)
CR MRD negativity (local), n/m (%) ^a	39/46 (85)	30/35 (86)	69/81 (85)
CRc MRD negativity (local), n/m (%) ^a	40/47 (85)	32/39 (82)	72/86 (84)
Median time to CR MRD negativity, months (range)	1.5 (0.5–12.2)	0.9 (0.5–2.8)	1.2 (0.5–12.2)
Median time to CRc MRD negativity, months (range)	1.5 (0.5–12.2)	0.9 (0.5–2.8)	1.1 (0.5–12.2)

Central Molecular MRD Negativity: Newly Diagnosed *NPM1*-m AML

n/N (%)	Central MRD (Threshold <0.1%)	Central MRD (Threshold <0.01%)
CRc MRD negativity rate ^a	31/39 (79)	22/39 (56)
Median time to MRD negativity, months (range)	2.2 (0.7–2.6)	2.3 (0.8–3.1)
Timing of MRD negativity ^b :		
By Cycle 1	10/31 (32)	6/22 (27)
By Cycle 2	31/31 (100)	22/22 (100)
By Cycle 3	31/31 (100)	22/22 (100)

Grade ≥3 AEs of Interest

Differentiation syndrome (DS):

- 4 Gr3 DS cases (4%; 1 *NPM1*-m, 3 *KMT2A*-r); no Gr4
- All DS events successfully resolved with protocol-specified mitigation and 3 continued ziftomenib treatment

QTc prolongation:

- 3 Gr3 investigator-assessed QTc prolongation cases^g (3%; 1 *NPM1*-m, 2 *KMT2A*-r; none ziftomenib-related); no Gr4
- All QTc events successfully resolved and continued ziftomenib treatment

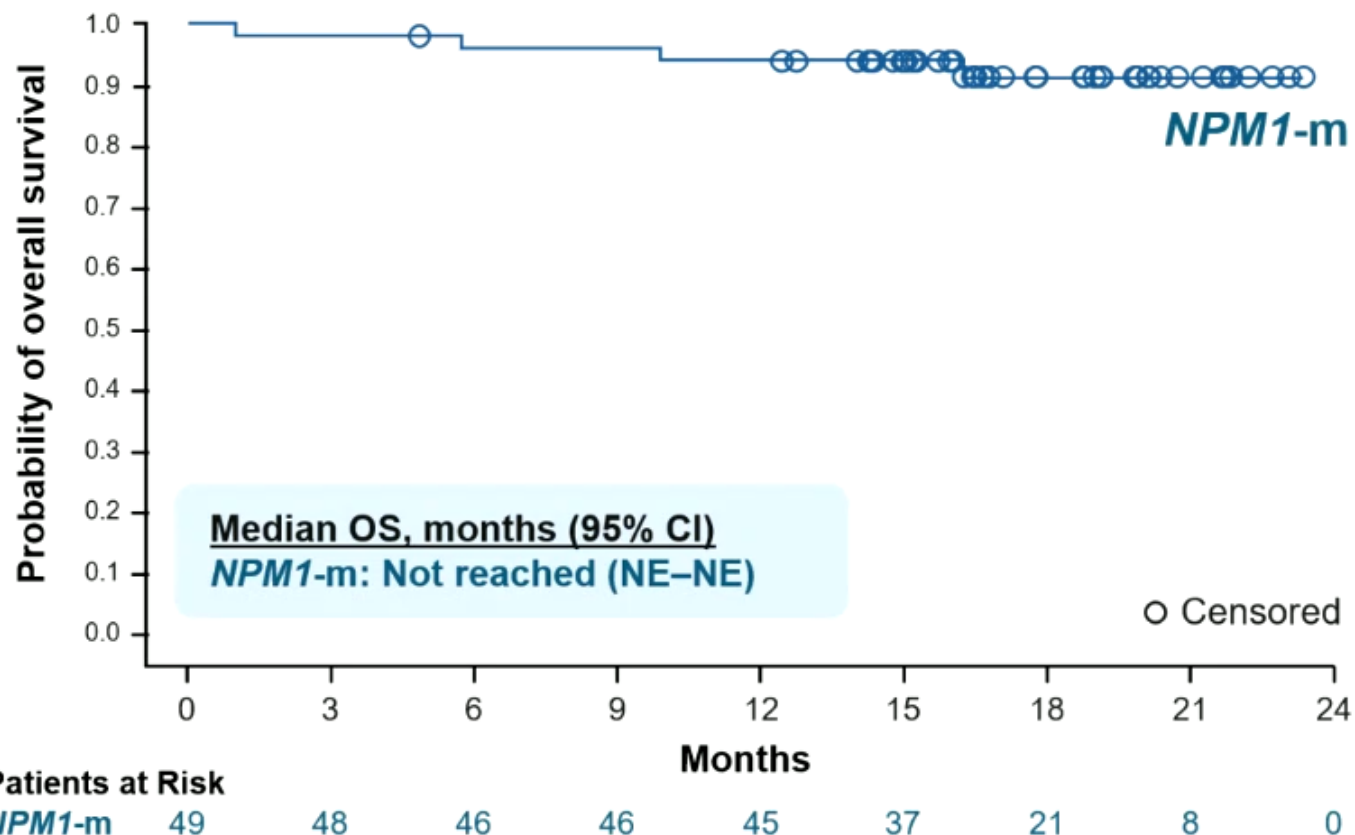
ANC and Platelet Recovery in CRc Responders

Median days (IQR), Cycle 1	<i>NPM1</i> -m (N=47)	<i>KMT2A</i> -r (N=45)	All Patients (N=92)
ANC $\geq 0.5 \times 10^9/L$	28 (21–32)	27 (25–29)	27 (23–30)
ANC $\geq 1.0 \times 10^9/L$	28 (27–35)	28 (26–35)	28 (26–35)
Platelets $\geq 50 \times 10^9/L$	23 (21–29)	26 (22–29)	25 (21–29)
Platelets $\geq 100 \times 10^9/L$	28 (24–33)	28 (26–30)	28 (25–33)

- Time to neutrophil and platelet recovery was comparable to that for intensive chemotherapy regimens^{1,2}

Overall Survival

NPM1-m



After a median follow-up of 17.6 months (range 1.0–23.5):

- Median OS was **not reached**
 - *NPM1-m*: 94% OS rate at 12 months
- Median age was 60 years
- 90% (44/49) of *NPM1-m* patients remained alive and continued on study^a
 - 60-day mortality: 2% (1/49)
- 12-month OS with intensive chemotherapy-based regimens varied from ~70–80% in younger/fit patients to ~45–55% in older adults¹⁻⁵

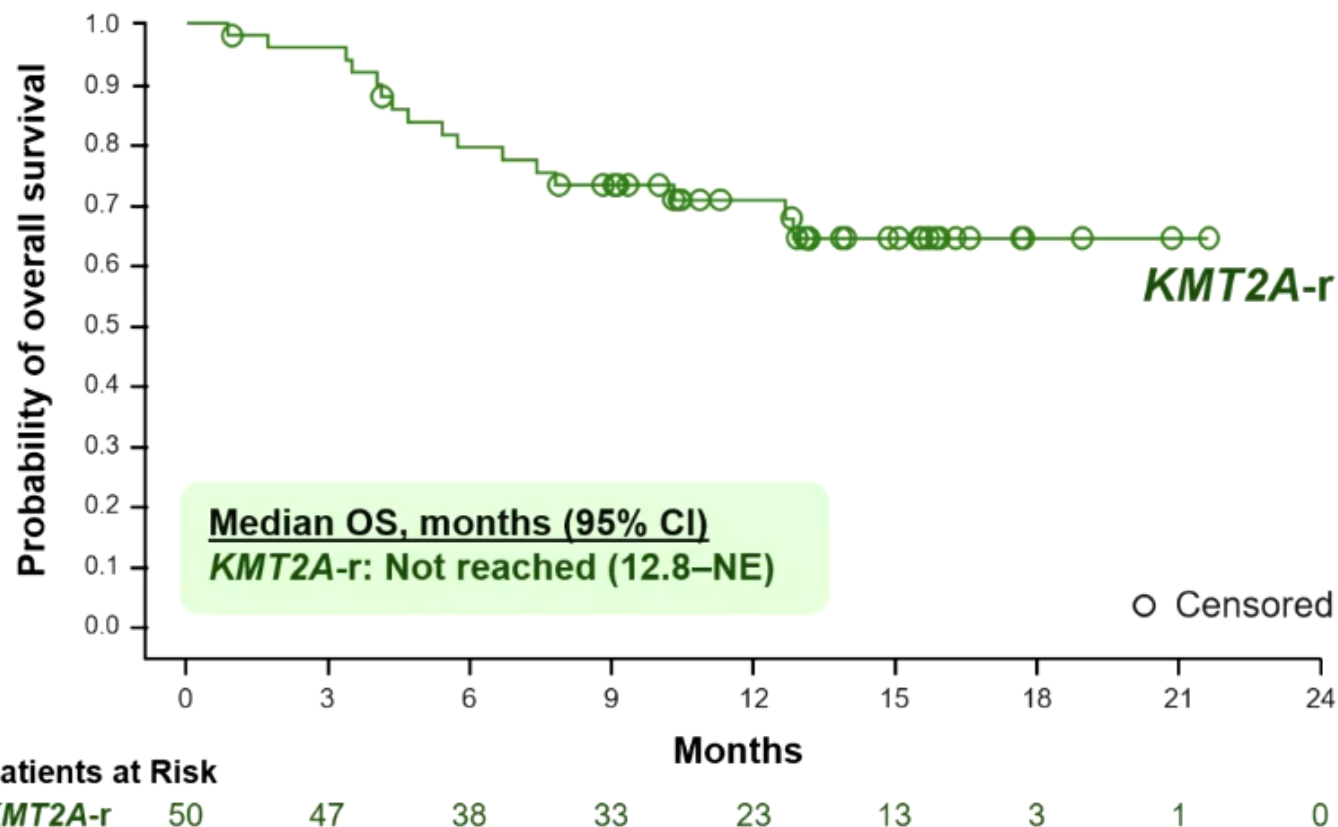
^aPatients on treatment or in long-term follow-up

Data cutoff: Apr 10, 2026. OS, overall survival

1. Othus et al. *Leukemia*. 2019; 33(2):371-378. 2. Othman et al. *Blood*. 2024; 144(7):714-728; 3. Lachowicz et al. *Blood Adv*. 2020; 4(7):1311–1320. 4. Hernández-Sánchez et al., *Leukemia*. 2026; 40(2):418-428. 5. Recher et al. *Leukemia*. 2022; 36(4):913-922.

Overall Survival

KMT2A-r



After a median follow-up of 11.0 months (range 0.9–21.9):

- Median OS was **not reached**
 - KMT2A-r: 71% OS rate at 12 months
- Median age was 43 years
- 62% (31/50) of KMT2A-r patients remained alive and continued on study^a
 - 60-day mortality: 4% (2/50)

^aPatients on treatment or in long-term follow-up

Data cutoff: Apr 10, 2026. OS, overall survival

Ajout de thérapie ciblée

Inhibiteurs de Menin

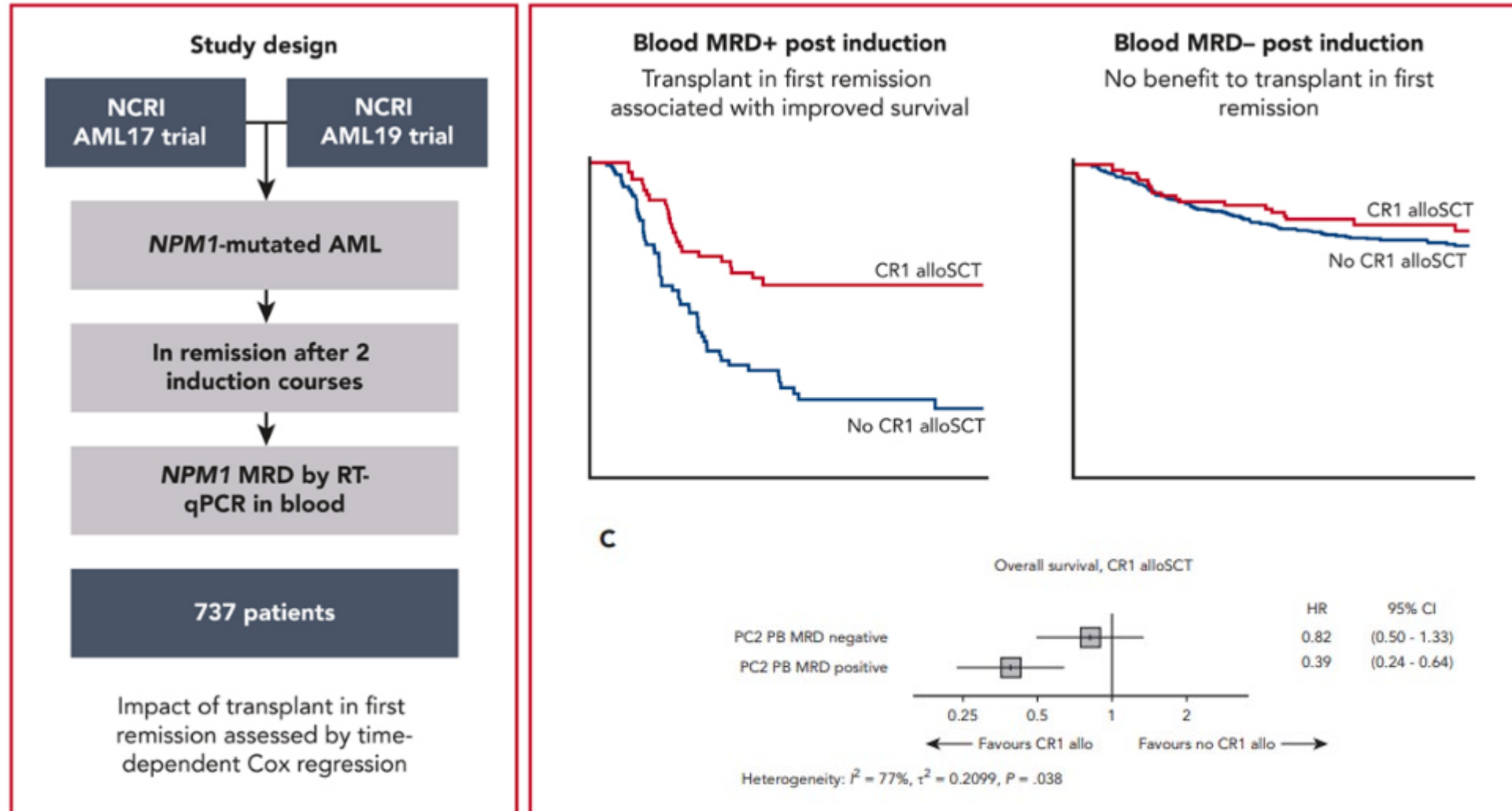
- **Phases 3 chimiothérapie intensive + iMENIN vs. Placebo en 1ere ligne :**
 - ALE-1002 (Bleximenib)
 - KO-MEN-017 (Ziftomenib)
 - SNDX-5613-0710 (Revumenib)
- D'autres iMenin en développement : Enzomenib, Vicrimenib...

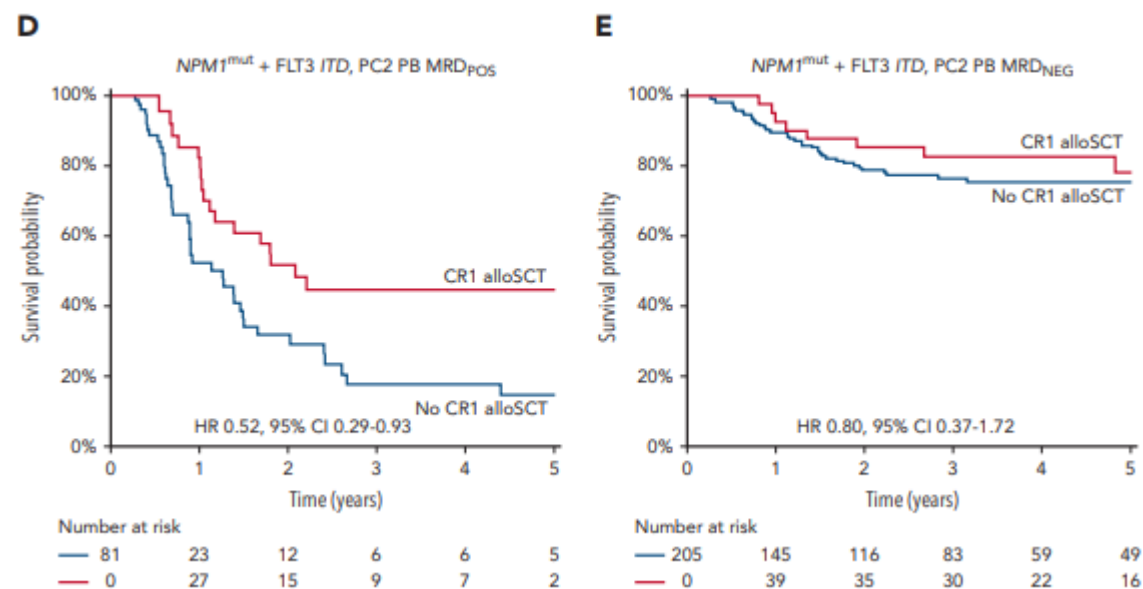
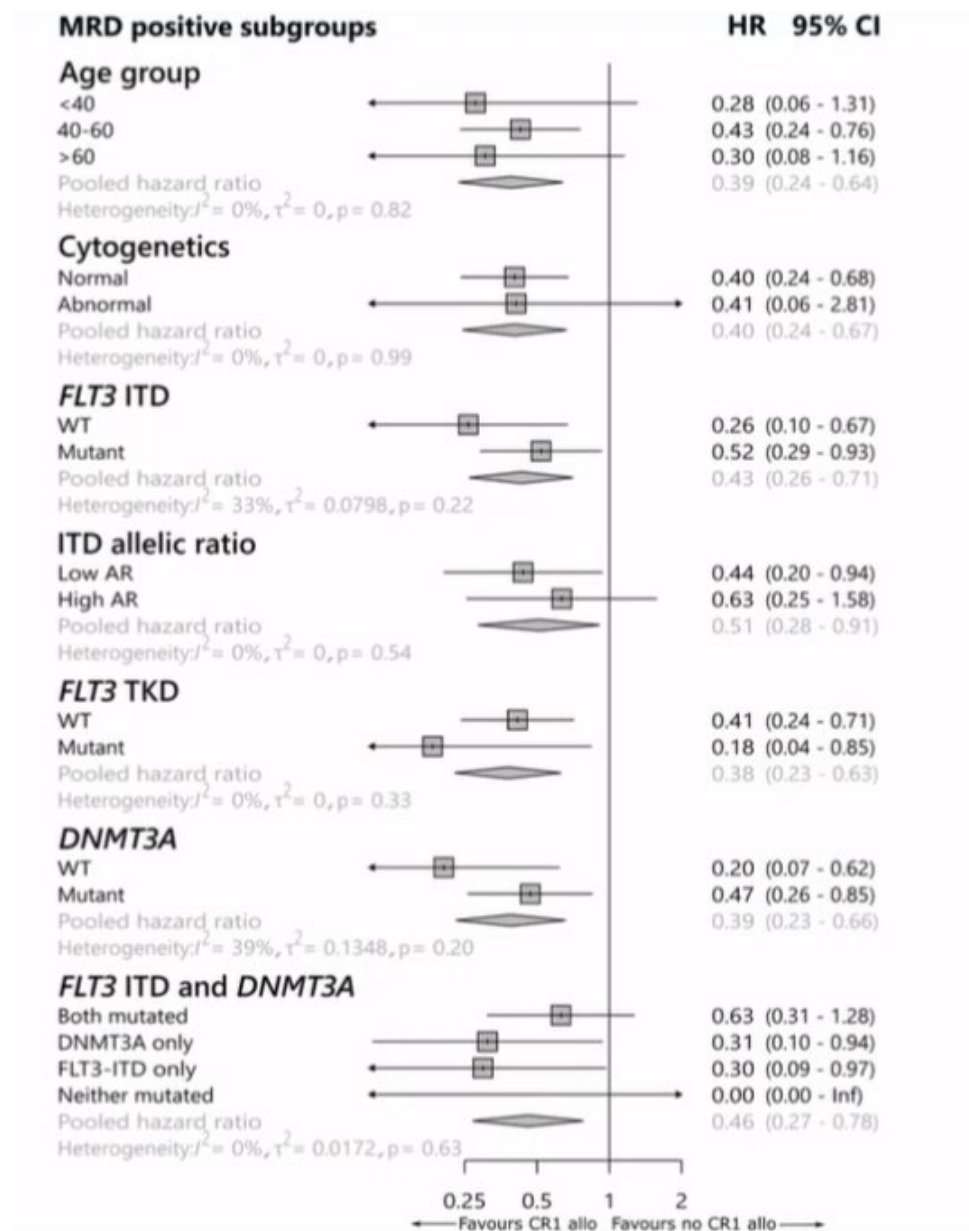
Comment continuer à améliorer les résultats de la chimiothérapie intensive ?

- Améliorer le 3+7 et les consolidations : ajout de thérapies ciblées
- **Stratifier les indications d'allogreffe en fonction de la MRD**

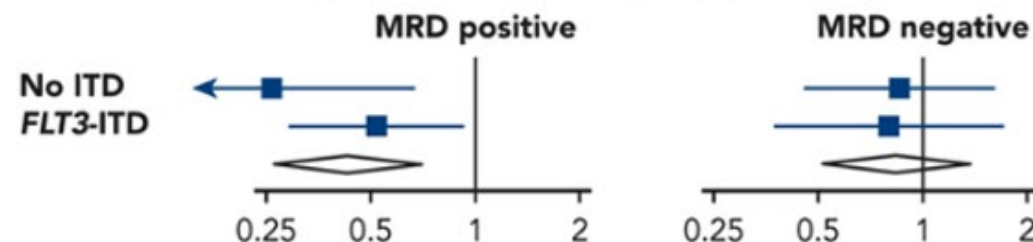
Traitement guidé par la MRD : indication d'alloH SCT en RC1

Essais AML17 et AML19, n = 737 LAM *NPM1*m en RC après 2 cycles, avec une MRD2 évaluable





Consistent findings in all examined subgroups, including *FLT3*-ITD:



Stratégie adoptée dans le protocole BIG-1 !

Traitement guidé par la MRD : peut-on se passer d'allogreffe dans les LAM intermédiaires avec MRD négative en CMF ?

RESOLVE

MRD guided treatment

The Study

The study is a multicenter randomized controlled pragmatic trial of standard intensity versus reduced intensity consolidation treatment in MRD-negative patients with AML or CLL (RESOLVE) **EU CT: 2024 – 512503 – 39 – 00**. The real-world nature of the study ensures broadly applicable results for all patients regardless of location, socioeconomic status, gender, sex, disability or ethnicity.

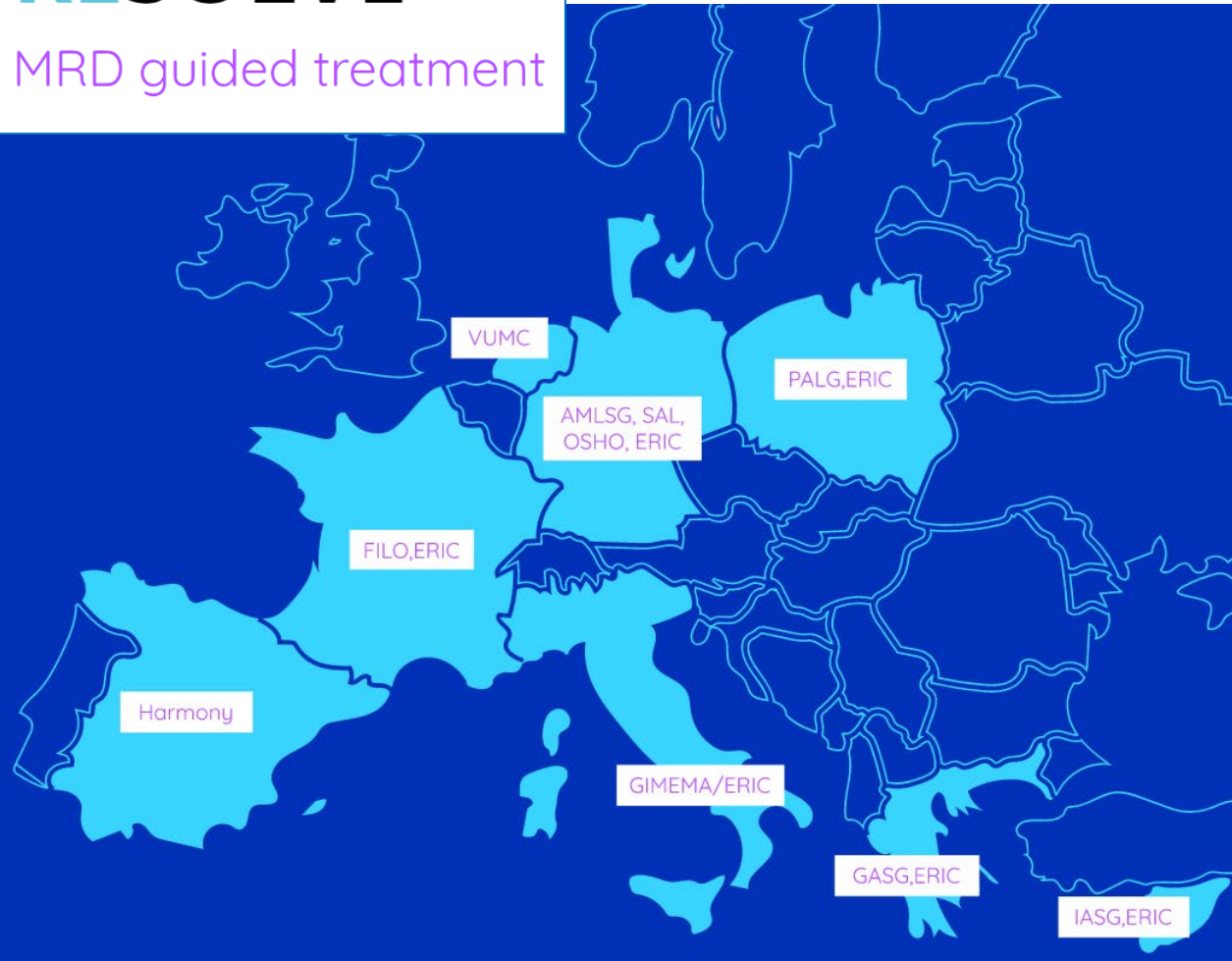
The study will be conducted in France, Germany, Greece, Israel, Italy, and Poland.

ALAN

CLLAN

EHA-SWG

ELN-DAVID



Où en est-on en France ?

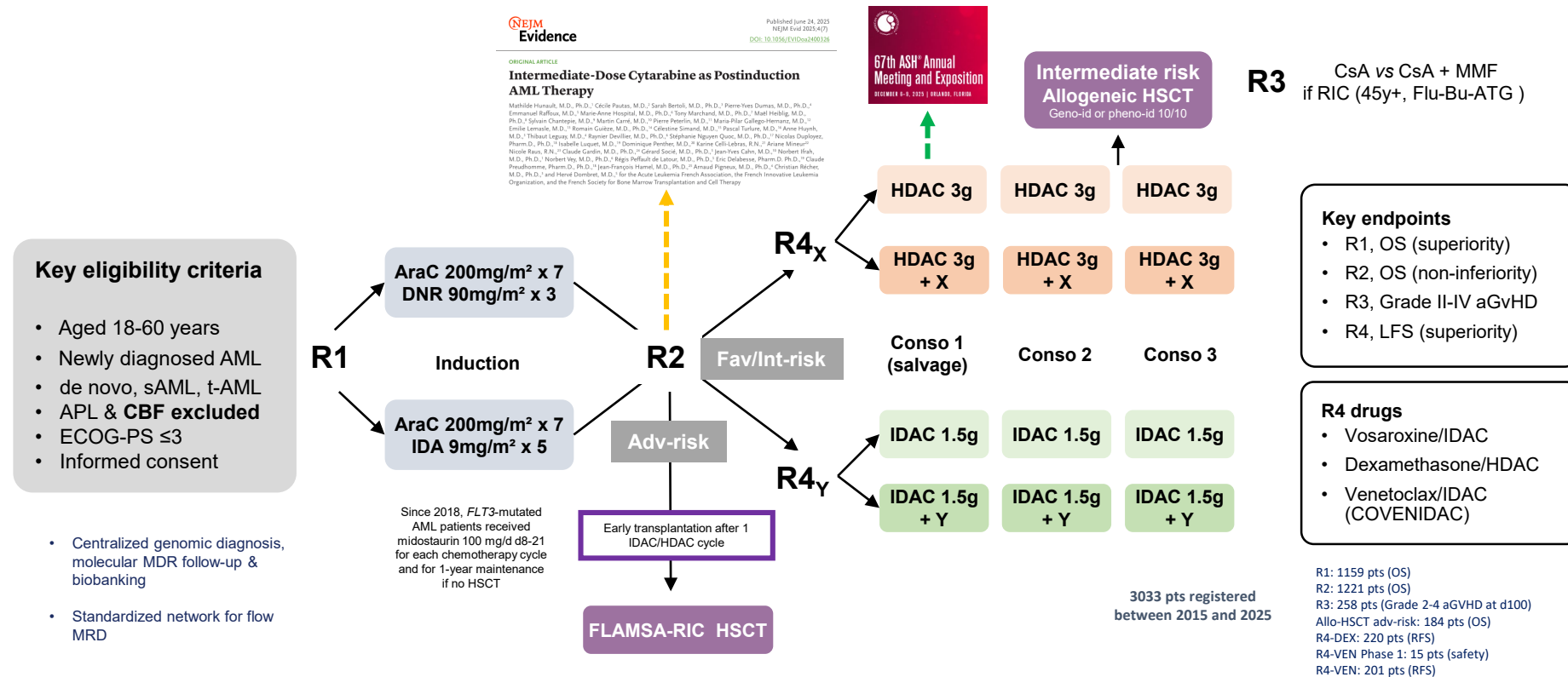
- Les enseignements du protocole BIG-1



- Le protocole BIG-2



Le protocole BIG-1 (NCT02416388)



R1 & R2: Hunault M, Pautas C, Bertoli S, et al. Blood (2023) 142 (Suppl 1): 967

R2: Hunault M, NEJM Evid 2025

R3: Forcade E, Devillier R, Hamel JF, et al. Blood (2024) 144 (Suppl 1): 4909

R4: Vey N, Orvain C, Recher C et al. Blood (2020) 136 (Suppl 1): 10-11.

Adv-risk: Peffault de Latour R, Forcade E, Huynh A, et al. Blood (2024) 144 (Suppl 1): 3483

Flow MRD: Plesa A, Mathis S, Dumezy F, et al. Blood (2024) 144 (Suppl 1): 226

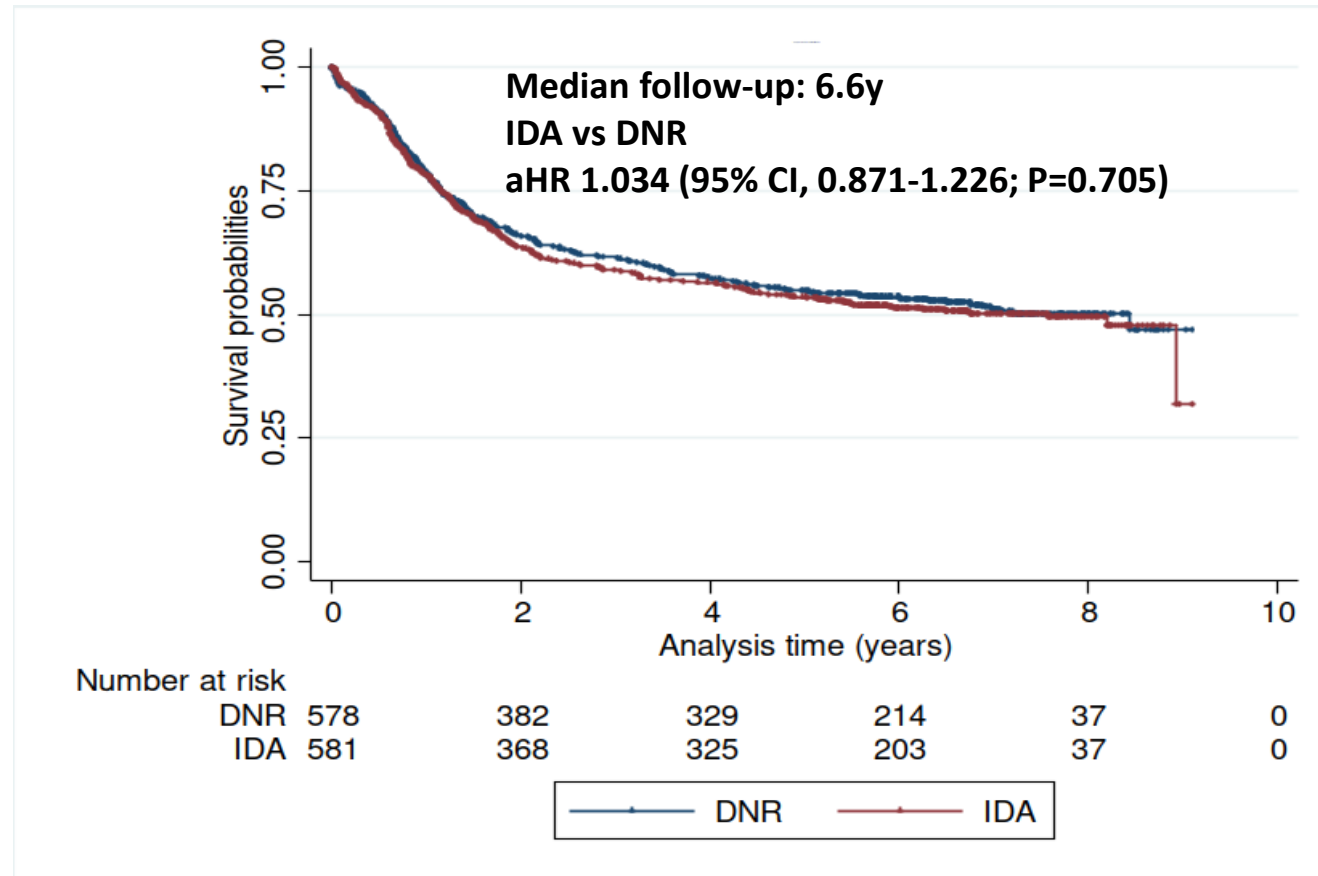
Le protocole BIG-1 (NCT02416388)

Response, n(%)	Daunorubicin N=578	Idarubicin N=581	All patients N=1159	sHR (95% CI)
CR/CRi	494 (85)	474 (82)	968 (84)	0.92 (0.81-1.04)
Cycle 1	415 (72)	428 (74)	843 (73)	
Cycle 2 (HDAC/IDAC)	65 (11)	37 (6)	102 (9)	
Cycle 2 (off protocol)	14 (2)	9 (2)	23 (2)	
No response	61 (11)	81 (14)	142 (12)	
Induction death	22 (4)	26 (4)	48 (4)	

Le protocole BIG-1 (NCT02416388)

ELN 2022 risk	Daunorubicin	Idarubicin	All patients
Favorable, n(%)	N=156	N=152	N=308
CR/CRi	152 (97)	149 (98)	301 (98)
- cycle 1	149 (96)	145 (95)	294 (95)
- cycle 2	2 (1)	4 (3)	6 (2)
No response	1 (1)	2 (1)	3 (1)
Induction death	3 (2)	1 (1)	4 (1)
Intermediate, n(%)	N=165	N=165	N=330
CR/CRi	144 (87)	138 (84)	282 (85)
- cycle 1	120 (73)	129 (78)	249 (75)
- cycle 2	24 (15)	9 (6)	33 (10)
No response	14 (9)	21 (13)	35 (11)
Induction death	7 (4)	6 (4)	13 (4)
Adverse, n(%)	N=230	N=234	N=464
CR/CRi	175 (76)	160 (68)	335 (72)
- cycle 1	125 (54)	131 (56)	256 (55)
- cycle 2	50 (22)	29 (12)	79 (17)
No response	43 (19)	55 (24)	98 (21)
Induction death	12 (5)	19 (8)	31 (7)

Le protocole BIG-1 (NCT02416388)

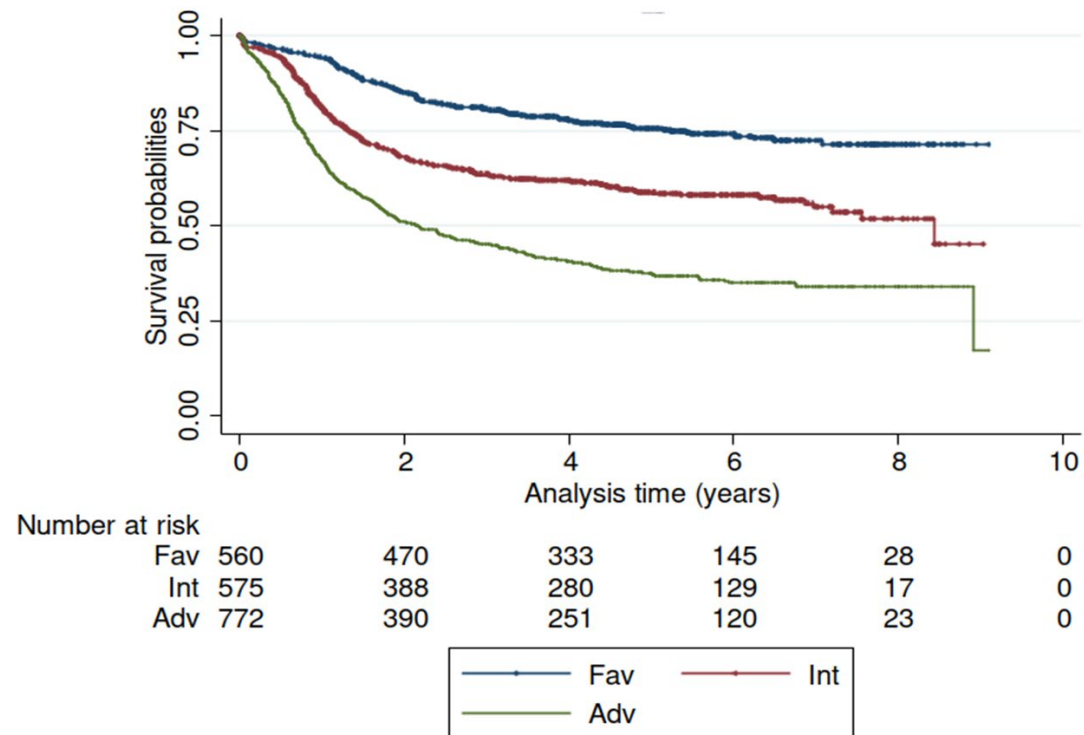


	OS	DNR	IDA
1-y		78%	78%
3-y		62%	59%
6-y		53%	51%
9-y		49%	48%

Adjusted on age, *de novo* vs secondary, sex, WBC, ELN 2022 risk, HDAC vs IDAC post-induction randomization and allo-HSCT

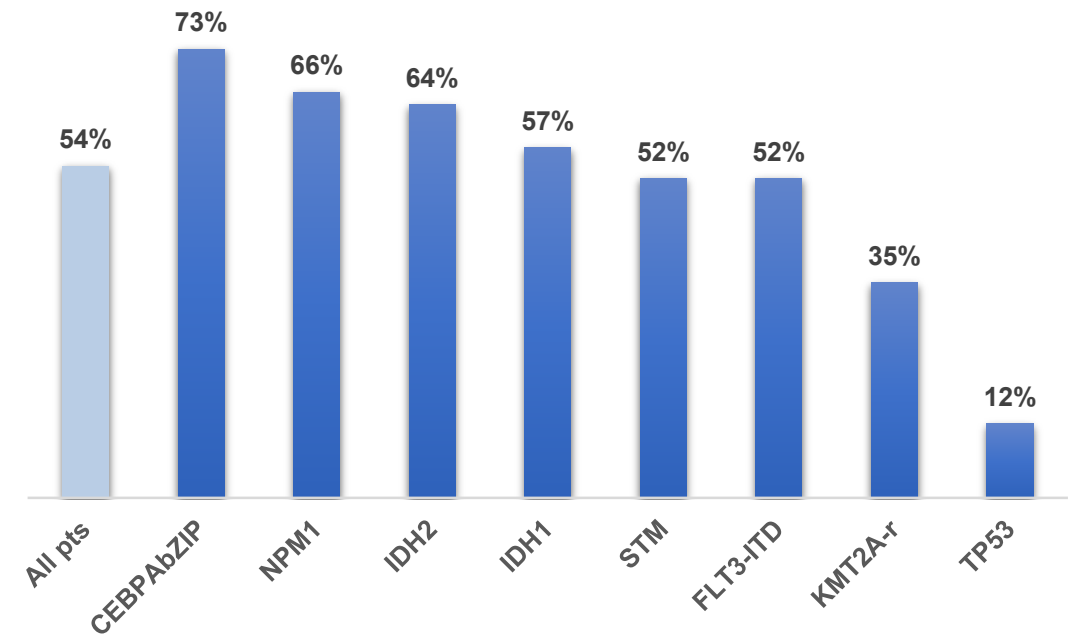
Le protocole BIG-1 (NCT02416388)

OS by ELN2022 risk



*CBF-AML not included

5y-OS by molecular subgroups



Le protocole BIG-1 (NCT02416388)

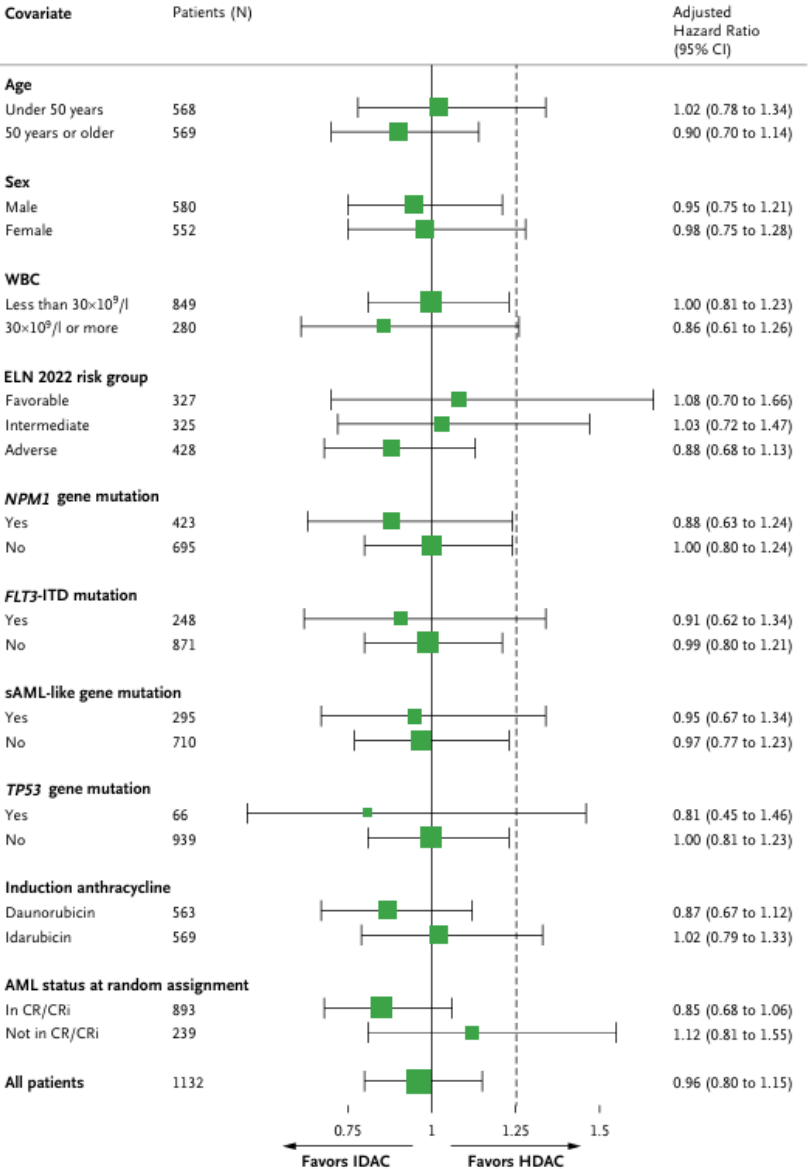
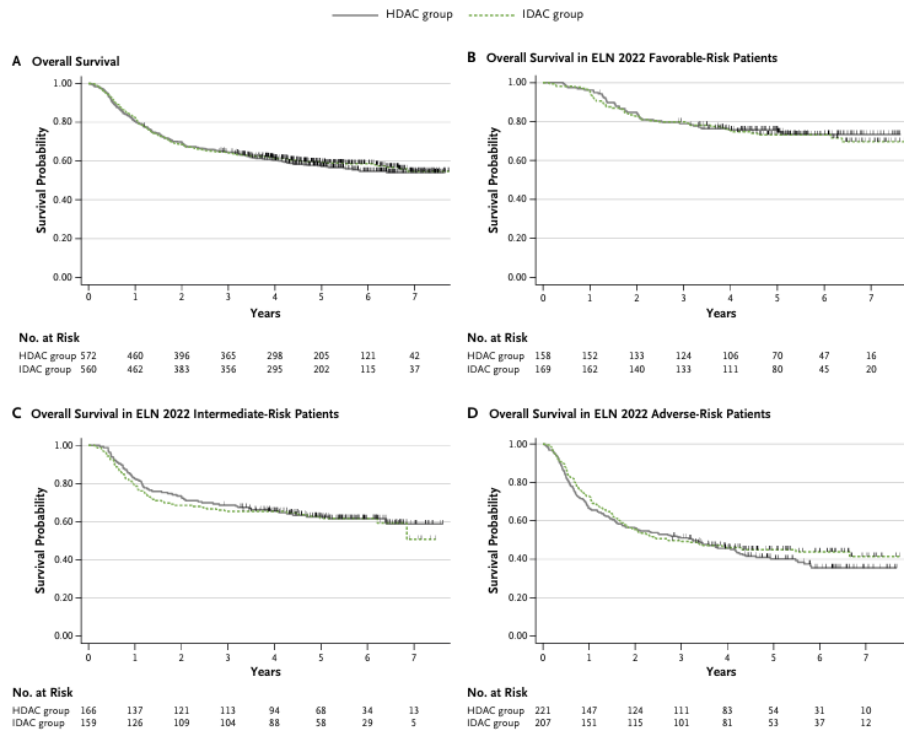
Events	Daunorubicin N=578	Idarubicin N=581	P
Mean number of days with fever $\geq 38.5^{\circ}\text{C}$, days (SD)	6.5 $\pm$ 5.9	6.5 $\pm$ 6.2	0.8817
Mean number of days with ANC < 0.5 G/L, days (SD)	21.3 $\pm$ 8.2	22.6 $\pm$ 9.4	0.0131
Mean number of days with platelet count < 20 G/L, days (SD)	12.5 $\pm$ 8.0	14.14 $\pm$ 9.6	0.0028
Mean number of days with IV antibiotics, days (SD)	21.1 $\pm$ 8.3	22.3 $\pm$ 9.1	0.0192
Mean number of days with IV antifungals, days (SD)	17.8 $\pm$ 11.0	18.4 $\pm$ 11.4	0.4103
Mean number of RBC unit transfusions, units per patient (SD)	8.7 $\pm$ 4.9	9.2 $\pm$ 4.5	0.0421
Mean number of platelet transfusions, episodes per patient (SD)	8.6 $\pm$ 7.4	9.3 $\pm$ 7.3	0.1186
Septic shock, N (%)	34 (6.0%)	44 (7.7%)	0.264
All grade fungal infection, N (%)	67 (11.8%)	104 (18.1%)	0.0029
All grade bacterial infection, N (%)	243 (42.9%)	270 (47.0%)	0.1557
Grade 3-4 cardiac toxicity, N (%)	32 (5.5%)	30 (5.2%)	0.7779
Grade 3-4 CNS adverse events, N (%)	9 (1.6%)	13 (2.2%)	0.396
Grade 3-4 cutaneous toxicity, N (%)	238 (41.2%)	261 (44.9%)	0.1978
Grade 3-4 hemorrhage, N (%)	45 (7.8%)	61 (10.5%)	0.1091
Grade 3-4 vomiting, N (%)	76 (13.5%)	87 (15.0%)	0.3714
Grade 3-4 diarrhea, N (%)	206 (35.6%)	229 (39.4%)	0.1845
Grade 3-4 mucositis, N (%)	107 (18.5%)	132 (22.7%)	0.0767
Grade 3-4 pneumopathy, N (%)	44 (7.61%)	47 (8.09%)	0.7627

Le protocole BIG-1 (NCT02416388)

ORIGINAL ARTICLE

Intermediate-Dose Cytarabine as Postinduction AML Therapy

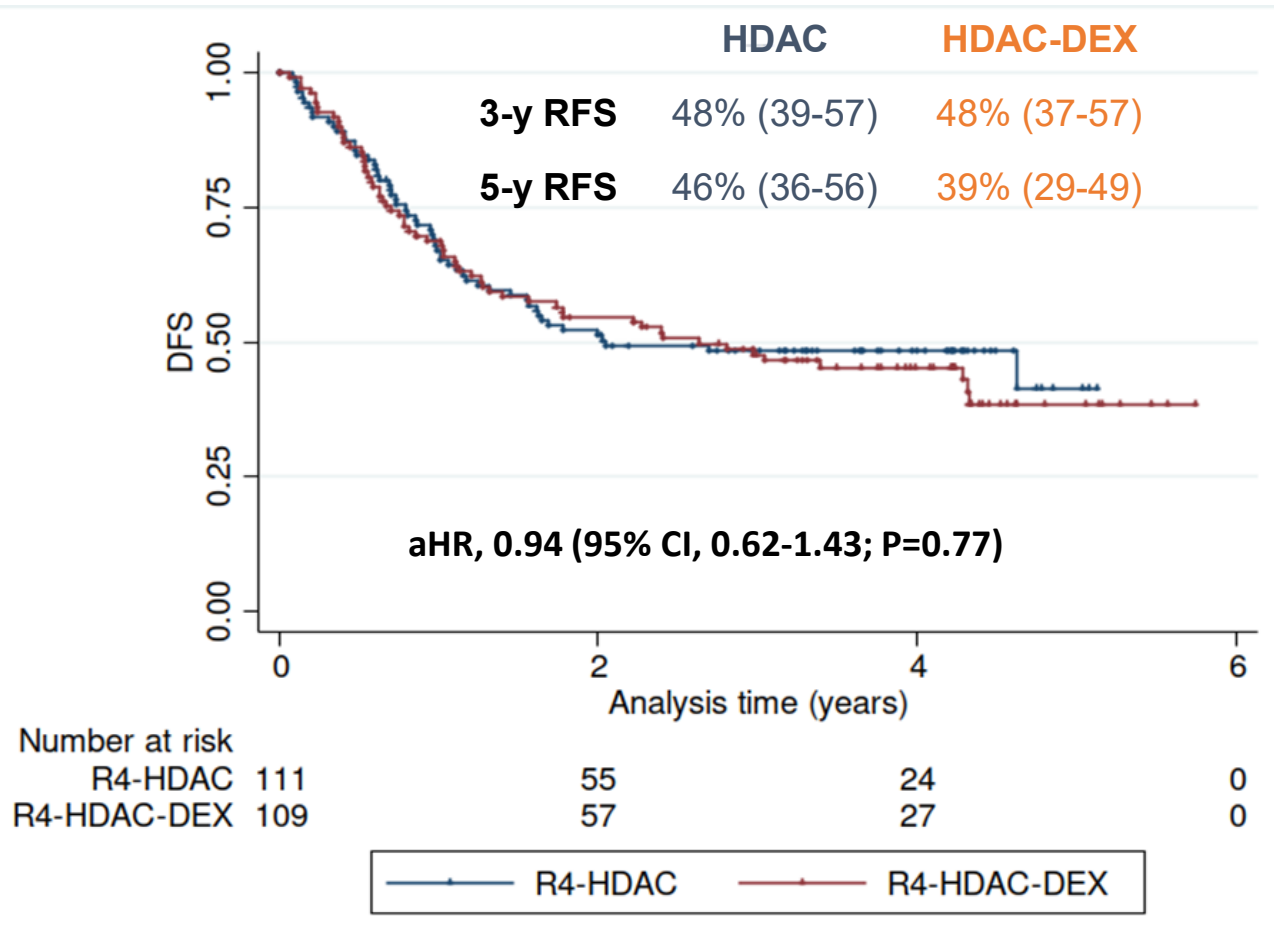
Mathilde Hunault, M.D., Ph.D.,¹ Cécile Pautas, M.D.,² Sarah Bertoli, M.D., Ph.D.,³ Pierre-Yves Dumas, M.D., Ph.D.,⁴ Emmanuel Raffoux, M.D.,⁵ Marie-Anne Hospital, M.D., Ph.D.,⁶ Tony Marchand, M.D., Ph.D.,⁷ Maël Heiblig, M.D., Ph.D.,⁸ Sylvain Chantepie, M.D.,⁹ Martin Carré, M.D.,¹⁰ Pierre Peterlin, M.D.,¹¹ Maria-Pilar Gallego-Hernanz, M.D.,¹² Emilie Lemasle, M.D.,¹³ Romain Guïèze, M.D., Ph.D.,¹⁴ Célestine Simand, M.D.,¹⁵ Pascal Turlure, M.D.,¹⁶ Anne Huynh, M.D.,¹⁷ Thibaut Leguay, M.D.,¹⁸ Raynier Devillier, M.D., Ph.D.,¹⁹ Stéphanie Nguyen Quoc, M.D., Ph.D.,¹⁷ Nicolas Duployez, Pharm.D., Ph.D.,¹⁸ Isabelle Luquet, M.D.,¹⁹ Dominique Penther, M.D.,²⁰ Karine Celli-Lebras, R.N.,²¹ Ariane Mineur²² Nicole Raus, R.N.,²³ Claude Gardin, M.D., Ph.D.,²⁴ Gérard Socié, M.D., Ph.D.,⁵ Jean-Yves Cahn, M.D.,¹⁰ Norbert Ifrah, M.D., Ph.D.,¹ Norbert Vey, M.D., Ph.D.,⁶ Régis Peffault de Latour, M.D., Ph.D.,⁵ Eric Delabesse, Pharm.D. Ph.D.,¹⁹ Claude Preudhomme, Pharm.D., Ph.D.,¹⁸ Jean-François Hamel, M.D., Ph.D.,²⁵ Arnaud Pigneux, M.D., Ph.D.,⁴ Christian Récher, M.D., Ph.D.,³ and Hervé Dombret, M.D.,⁵ for the Acute Leukemia French Association, the French Innovative Leukemia Organization, and the French Society for Bone Marrow Transplantation and Cell Therapy



Meilleure tolérance avec IDAC

- Durée de thrombopénie réduite
- Moins de transfusions (CGR, plaquettes)
- Moins de jours avec fièvre $\geq 38.5^{\circ}\text{C}$
- Moins d'hémorragies de grade 3/4
- Moins de nausées/vomissement de grade 3/4

Le protocole BIG-1 (NCT02416388)

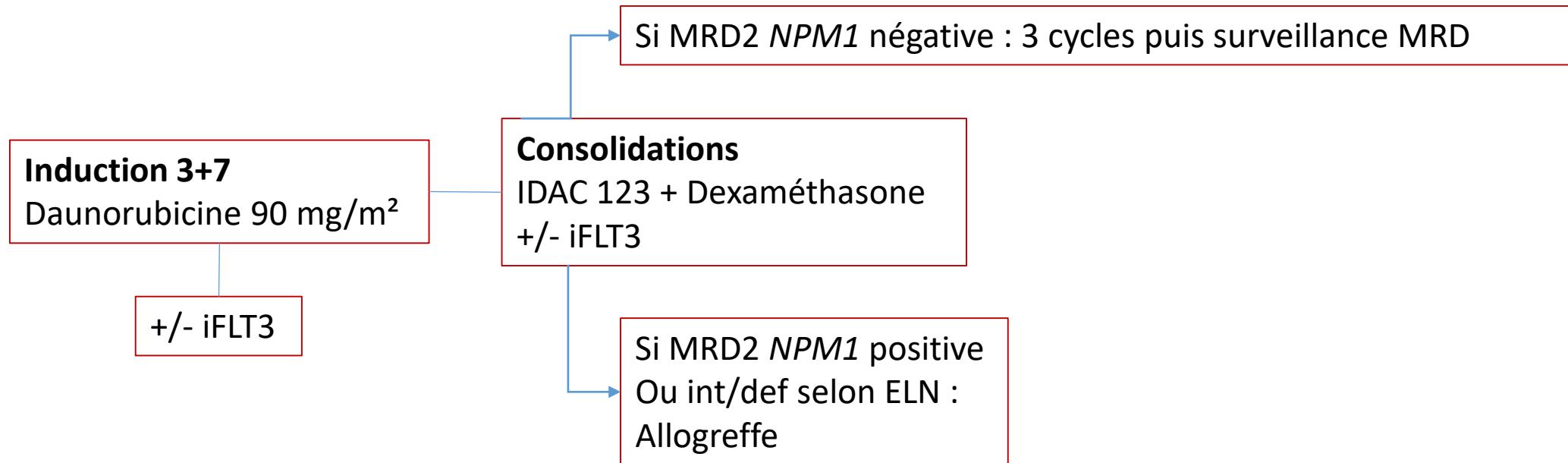


- Amélioration de la tolérance des consolidations par HDAC
- Diminution de la myélosuppression :
 - Diminution des durées de neutropénie et thrombopénie
 - Diminution du besoin transfusionnel (CGR et plaquettes)
- Moins de nausées/vomissements gr 3-4

Adjusted on age, sex, de novo vs secondary AML, WBC, CR1 (1 vs 2 cycles), ELN 2022 risk, *NPM1* mutation, induction with IDA vs DNR, CRP and allo-HSCT

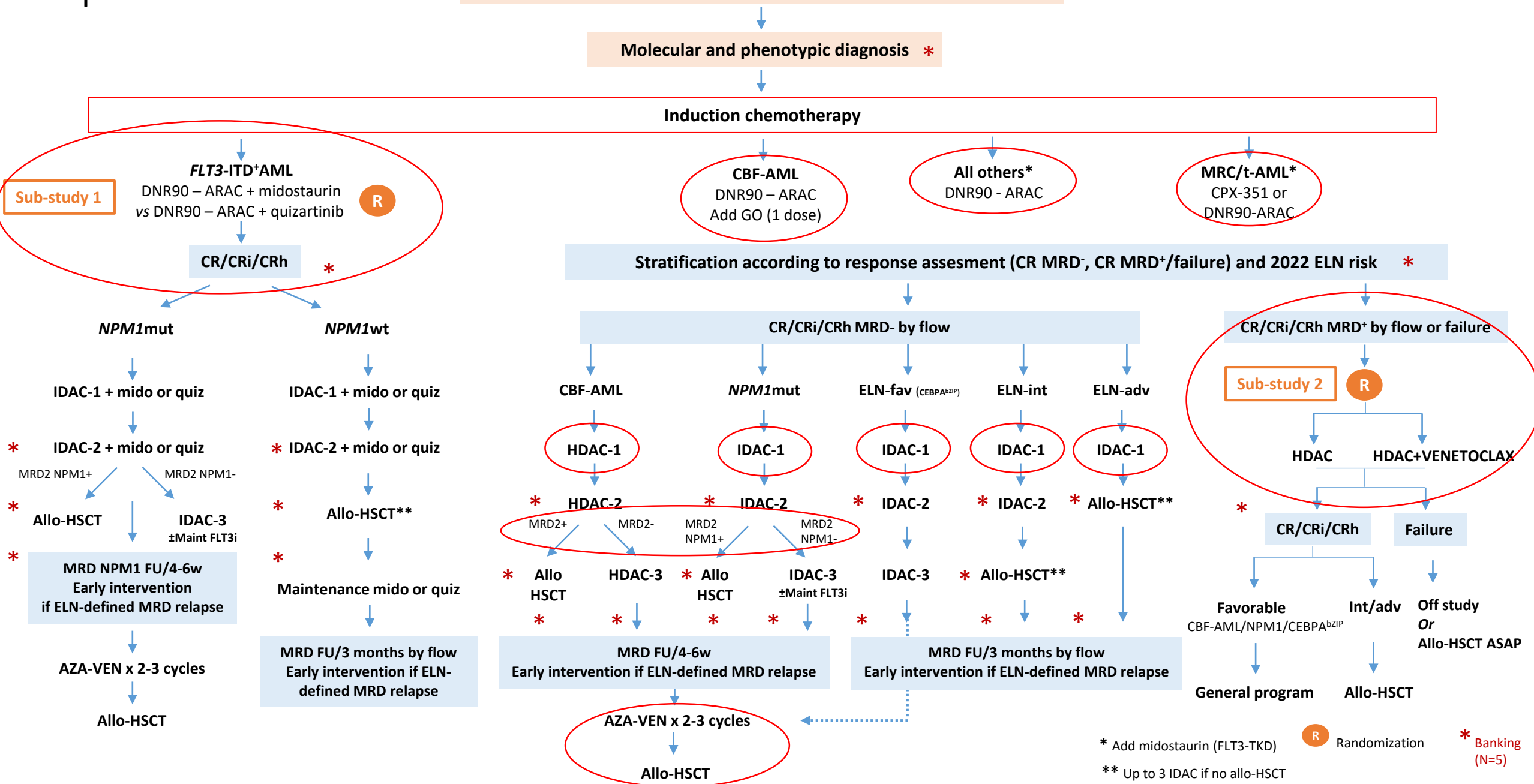
La chimiothérapie intensive en France en 2026 (sujet jeune)

« Le backbone BIG-1 »



Le protocole BIG-2

Newly diagnosed AML 18-60y except post-MPN AML or *BCR::ABL1*⁺ AML



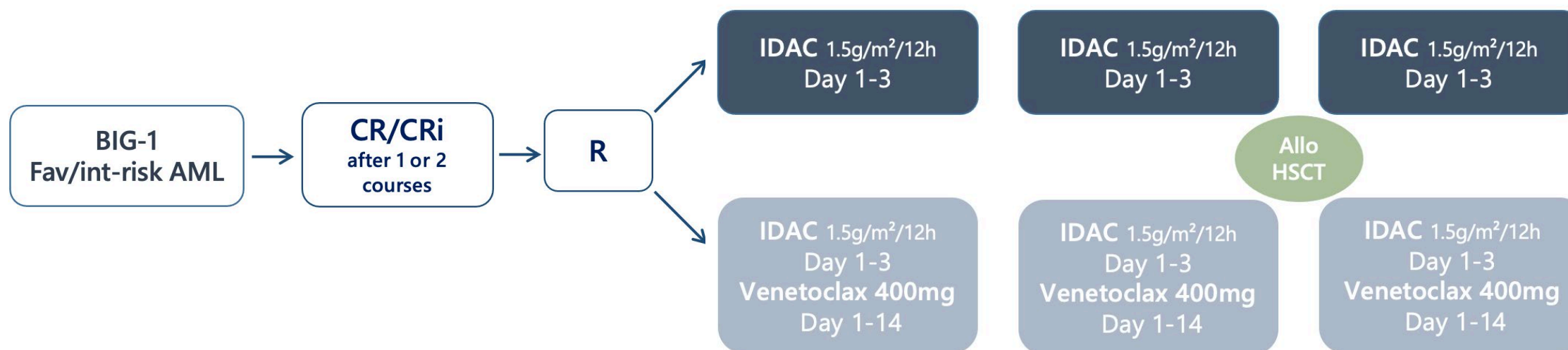
Comment continuer à améliorer les résultats de la chimiothérapie intensive ?

- **Ajout de Venetoclax en consolidation ?**
- **Pourquoi une seule thérapie ciblée ? Induction à 4 drogues**

Ajout de Venetoclax en consolidation

COVENIDAC – IDAC ± VEN post -induction

Adultes jeunes (18-60 ans) inclus dans le BIG-1, avec LAM fav/int-risk en 1ere RC/RCi



- **Primary endpoint:** Relapse-free Survival
- **Secondary endpoints:** OS, CIR, CID, RFS_{MRD}, EFS_{MRD}, CIR_{MRD}, QOL, alloHCT rate, DLT/safety
- Phase 1 completed (15 patients)*
- Phase 2 completed (201 patients randomized, last patient in 2025/01)

Pourquoi une seule thérapie ciblée ? Induction à 4 drogues

MIDOVEN

Days		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	..	
INDUCTION																															
Daunorubicin 60 mg/m ² /day																															..
Cytarabine 200 mg/m ² /day																															
Midostaurin 50 mg x 2/day																															
Posaconazole 300 mg/day					*					§																					
Schedule A (Ramp-up) Venetoclax (mg/day)									(20)	(50)	100	100	100	100	100																
Schedule B (Ramp-up) Venetoclax (mg/day)					(20)	(50)	100	100	100	100	100																				
Schedule C (Ramp-up) Venetoclax (mg/day)									(20)	(50)	100	100	100	100	100	100	100	100													
Schedule D (Ramp-up) Venetoclax (mg/day)					(20)	(50)	100	100	100	100	100	100	100	100																	

Days		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28		
CONSOLIDATIONS x 3, 35 days-cycles **																															
Cytarabine 1500 mg/m ² x 2/day ***																															
Midostaurin 50 mg x 2/day																															
Venetoclax 400 mg/day		400	400	400	400	400	400	400	400	400	400	400	400	400	400																

Days		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28		
MAINTENANCE x 12, 28-days cycles																															
Midostaurin 50 mg x 2/day																															
Venetoclax 400 mg/day		400	400	400	400	400	400	400	400	400	400	400	400	400	400																

Pourquoi une seule thérapie ciblée ? Induction à 4 drogues

VISTAML

Days		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	...
INDUCTION																														...
Daunorubicin 60 mg/m ² /day																														...
Cytarabine 200 mg/m ² /day																														...
Ivosidenib 500 mg D1-3 then 250 mg/day																														...
Posaconazole 300 mg/day					*					§																				...
Schedule A (Ramp-up)	Venetoclax (mg/day)								(20)	(50)	100	100	100	100	100															
Schedule B (Ramp-up)	Venetoclax (mg/day)				(20)	(50)	100	100	100	100	100																			
Schedule C (Ramp-up)	Venetoclax (mg/day)								(20)	(50)	100	100	100	100	100	100	100	100												
Schedule D (Ramp-up)	Venetoclax (mg/day)				(20)	(50)	100	100	100	100	100	100	100	100																
Days		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	...
CONSOLIDATIONS x 3, 35 days-cycles **																														...
Cytarabine 1500 mg/m ² x 2/day ***																														...
Ivosidenib 500 mg/day																														...
Venetoclax 400 mg/day		400	400	400	400	400	400	400	400	400	400	400	400	400	400															...
Days		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	...
MAINTENANCE x 12, 28-days cycles																														...
Ivosidenib 500 mg/day																														...
Venetoclax 400 mg/day		400	400	400	400	400	400	400	400	400	400	400	400	400	400															...

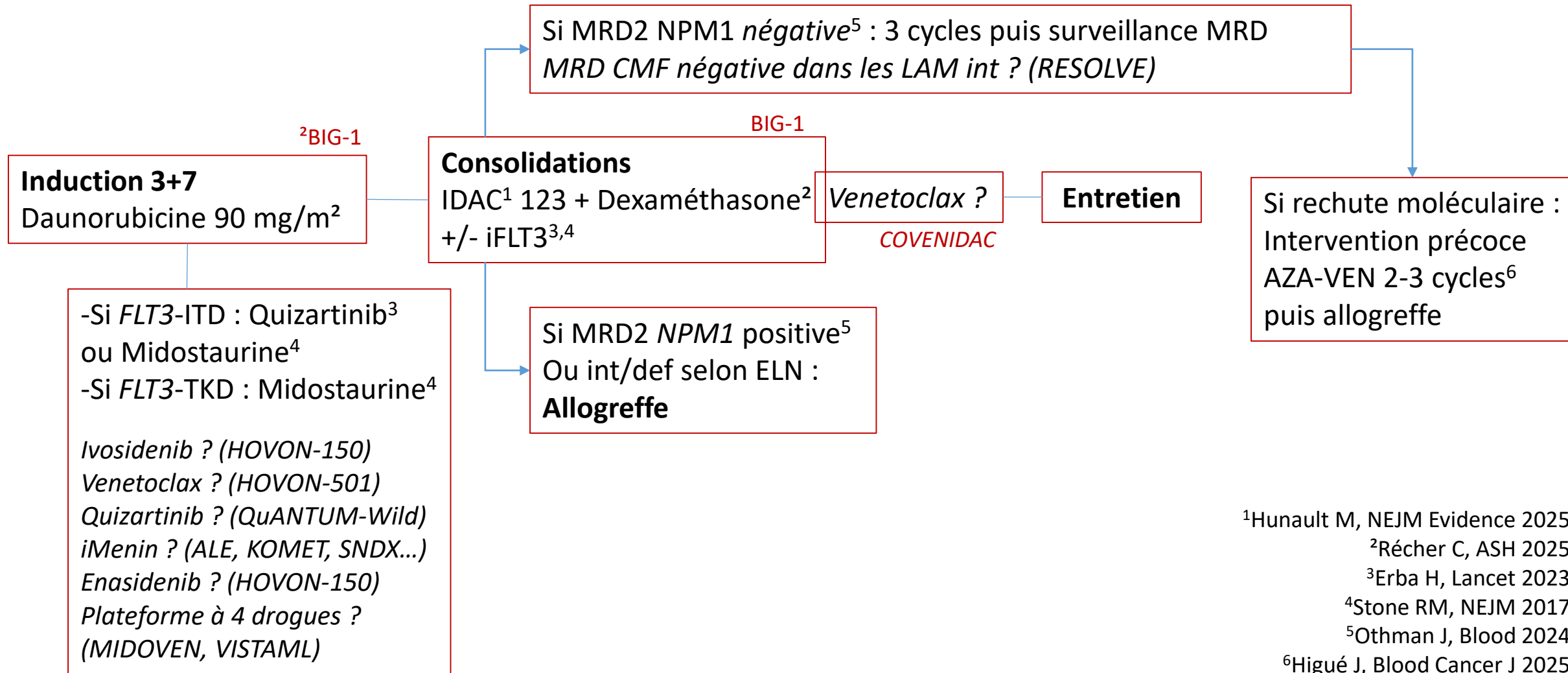
Déclinaison avec d'autres thérapies ciblées : Enasidenib ? iMenin ?...

PI : Pr PY Dumas

Chimiothérapie intensive – quoi d'autre ?

- Traitements d'**entretien** :
 - iFLT3
 - iIDH
 - *MIVONU*
- Généralisation du **Venetoclax pour les LAM en rechute/réfractaire**
- **Généralisation de la MRD**
 - Suivi moléculaire
 - Stratification des indications d'allogreffe
 - Détection des rechutes moléculaires et intervention précoce (AZA-VEN)
 - Implémentation de la MRD CMF
- **Allogreffe**
 - Plus de donneurs, plus d'interventions post-allogreffe
 - Allogreffe pour les LAM réfractaires ou en rechute (ASAP)
 - Amélioration des traitements de GVH

Le futur (*proche?*) de la chimiothérapie intensive en France (sujet jeune)



Les approches intensives vont-elles être challengées par l'association Azacitidine-Venetoclax ?

MYELOID NEOPLASIA

Comment on [Lu et al](#), page 2645

Are you ready for it? VEN-HMA for younger patients with AML

Tara L. Lin | University of Kansas Cancer Center

In this issue of *Blood*, [Lu et al](#) report results from a randomized clinical trial comparing outcomes of newly diagnosed younger patients with acute myeloid leukemia (AML) treated with venetoclax-decitabine (VEN-DEC) vs idarubicin-cytarabine (IA-12) induction and found noninferior response rates and superior safety with VEN-DEC.¹ Anthracycline-cytarabine induction has been the mainstay of AML treatment for over 50 years,² and the VIALE-A trial established the combination of venetoclax plus hypomethylating agent (VEN-HMA) as a new standard of care for older and unfit patients.³ Retrospective studies compared outcomes between the 2 approaches and demonstrated the feasibility and efficacy of VEN-HMA in younger patients,⁴⁻⁶ but, until this report, prospective, randomized data were lacking.

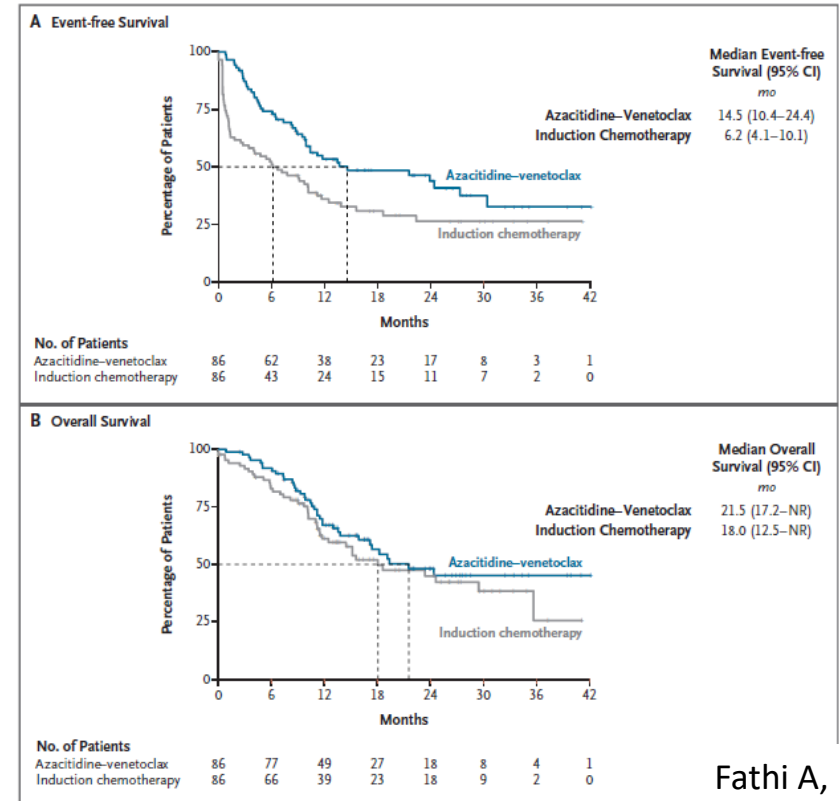
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

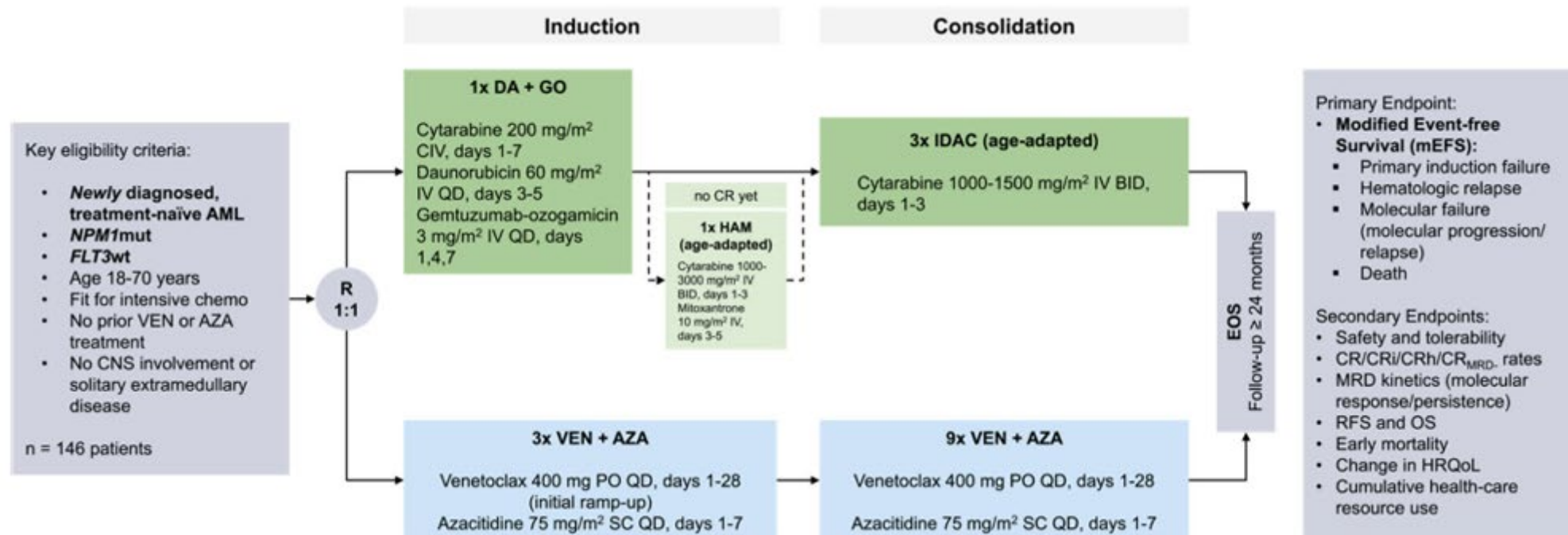
SEPTEMBER 3, 2026

VOL. 395 NO. 9

Azacitidine–Venetoclax or Induction Chemotherapy for Acute Myeloid Leukemia



VINCENT: A randomized-controlled trial evaluating venetoclax plus azacitidine versus intensive chemotherapy in patients with newly diagnosed, *NPM1*-mutated AML



CONCLUSION

- **Thérapie ciblée pour tous ?**
 - iFLT3 (lequel ?), iIDH1, VEN, QUIZ, iMenin... ?
- **Pas d'allogreffe en RC1 pour tous ?**
 - en cas de MRD2 négative dans les LAM *NPM1m*, y compris si *FLT3*-ITD / dans les CBF
 - MRD CMF ?
- **Améliorer le traitement des LAM réfractaires**
 - Sous-étude 2 du BIG-2
- La chimiothérapie intensive va-t-elle résister au traitement par AZA-VEN ? aux triplets ?