Qui admettre en réanimation en 2022
Le patient atteint de leucémie aiguë

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21ème Rencontre sur Urgences et Complications
Sévères chez le Patient Cancéreux

26/11/2022 Bruxelles

- **Faut il admettre tous les patients ?**

1. Quels qu'ils soient
2. Quelle que soit la maladie
3. Quel que soit le stade de traitement
4. Quelle que soit la complication aiguë

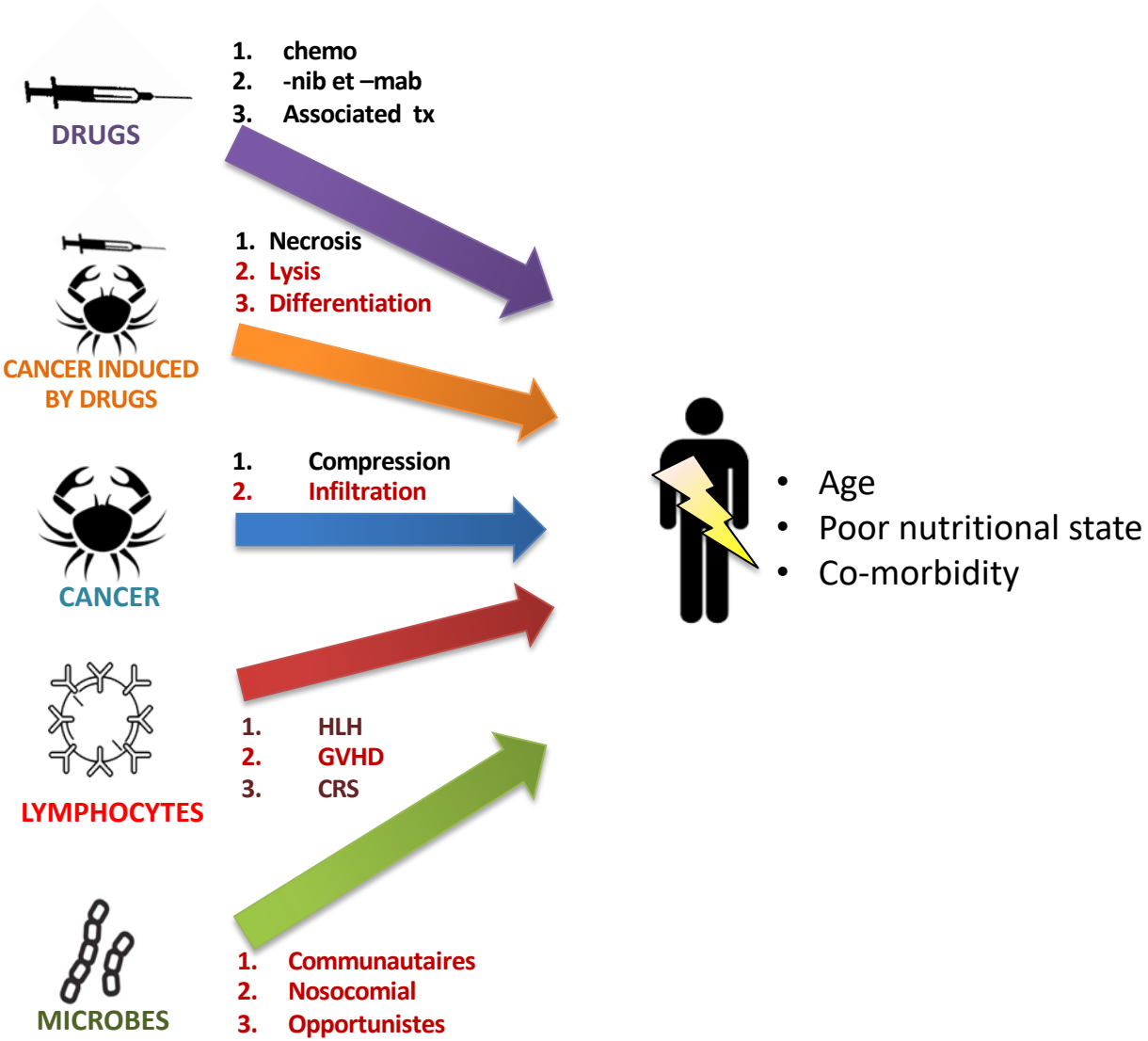
Hémopathies en réanimation

		30% Leucémies aigues (M)	30% Lymphomes agressifs	15% Myélome
50%	Respiratoire	Leucostase Infiltration pulmonaire OAP Sepsis Hémorragie	Syndrome d'activation macrophagique (SAM) Sepsis OAP infiltration pleuro-pulmonaire Médiasatin compressif	Sepsis OAP
30%	Choc	Sepsis Hemorragie anthracyclines	Sepsis SAM	Sepsis amylose cardiaque
30%	Métabolique Rénal	Syndrome de lyse tumorale Toxicité médicamenteuse	Syndrome de lyse tumorale Toxicité médicamenteuse	Tubulopathie des chaines legeres Toxicité médicamenteuses hyperviscosité
20%	Neurologique	leucostase Hémorragie Toxicité médicamenteuses	Toxicité médicamenteuse Localisation spécifique Sepsis	Toxicité médicamenteuses Sepsis Hyperviscosité

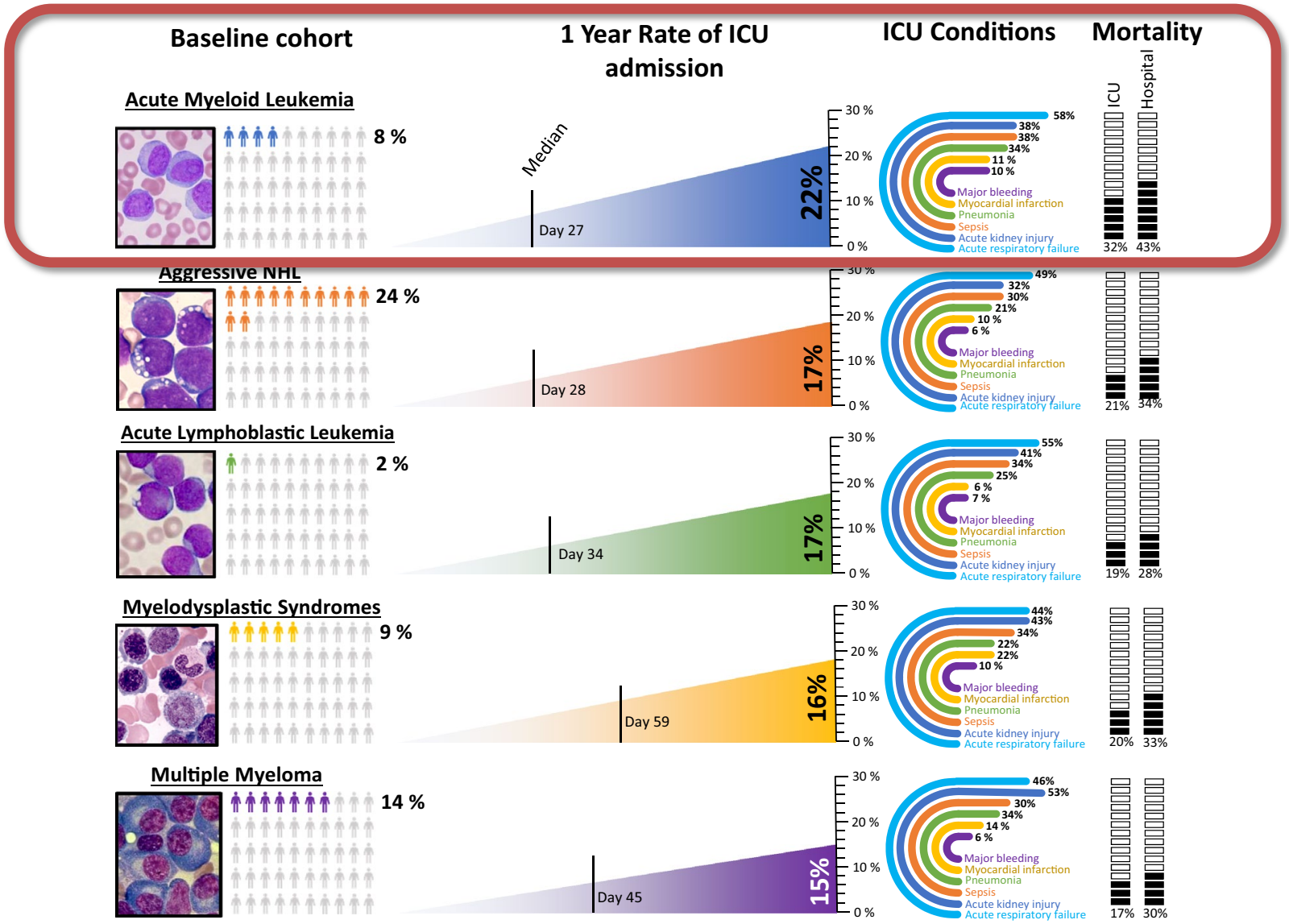
Spécificité de la réanimation hématologique

Sources d'agression multiples

Intervient dans un parcours de soin

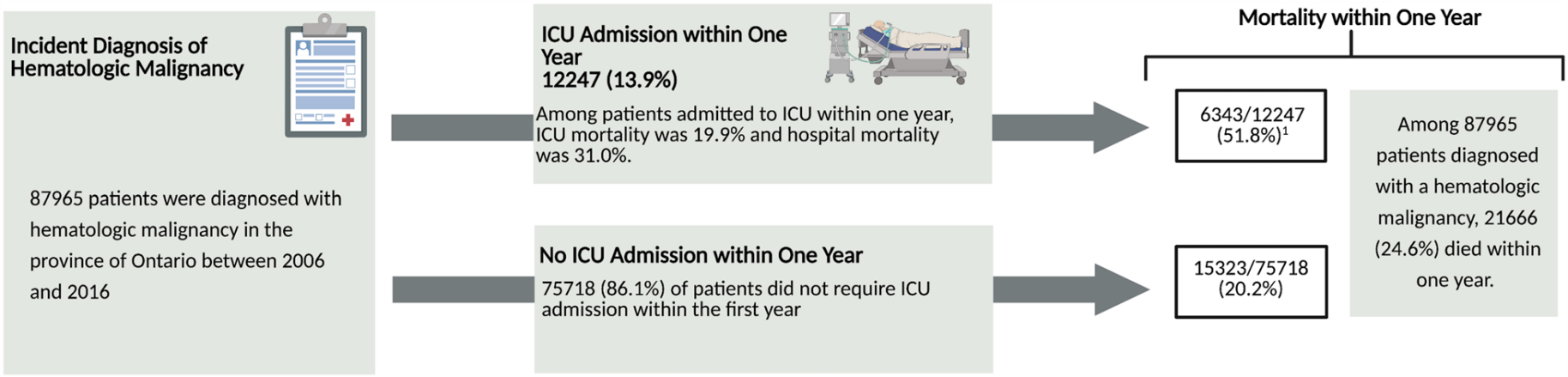


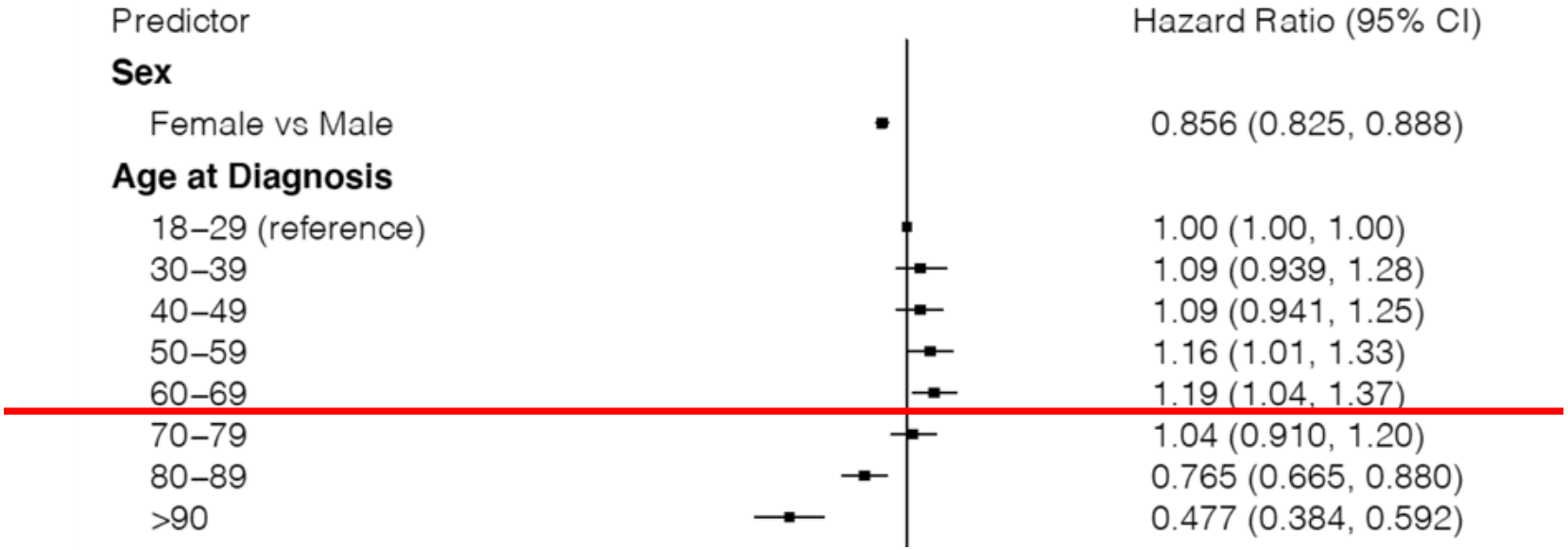
1 patient sur 4 admis en réanimation (1ere année)

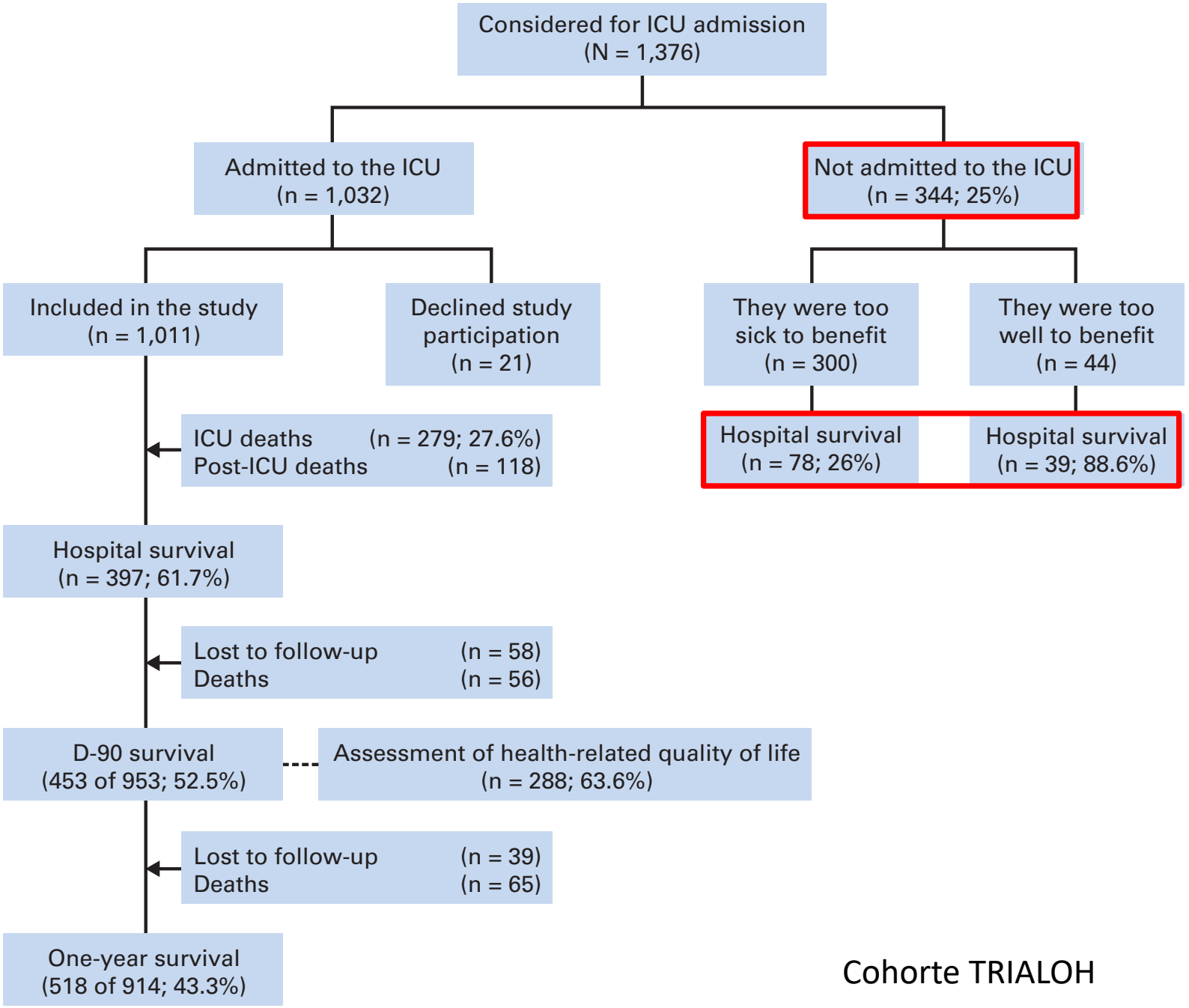


Ferreyro et al. ICM 2021

Quelle sélection en pratique ?

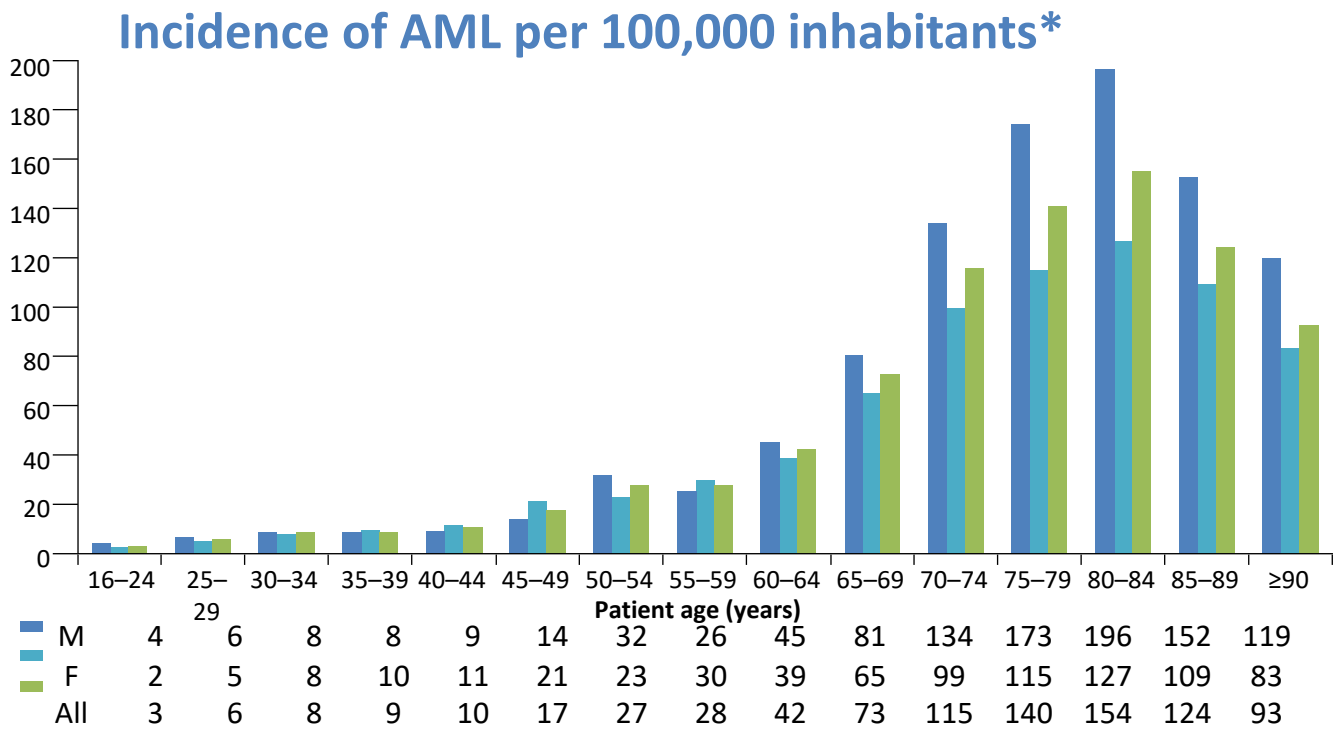






Cohorte TRIALOH

Les LAM sont des pathologies du sujet âgé

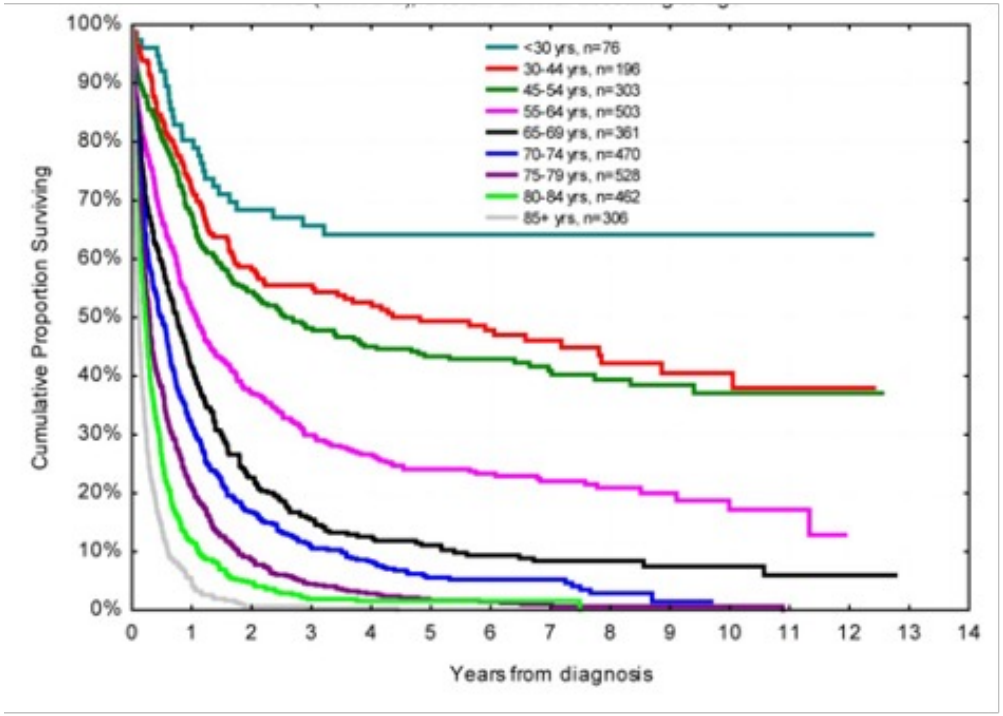


*Data from the Swedish Acute Leukemia Registry. M, male; F, female
Juliusson G *et al*. *Blood* 2009;113:4179–4187

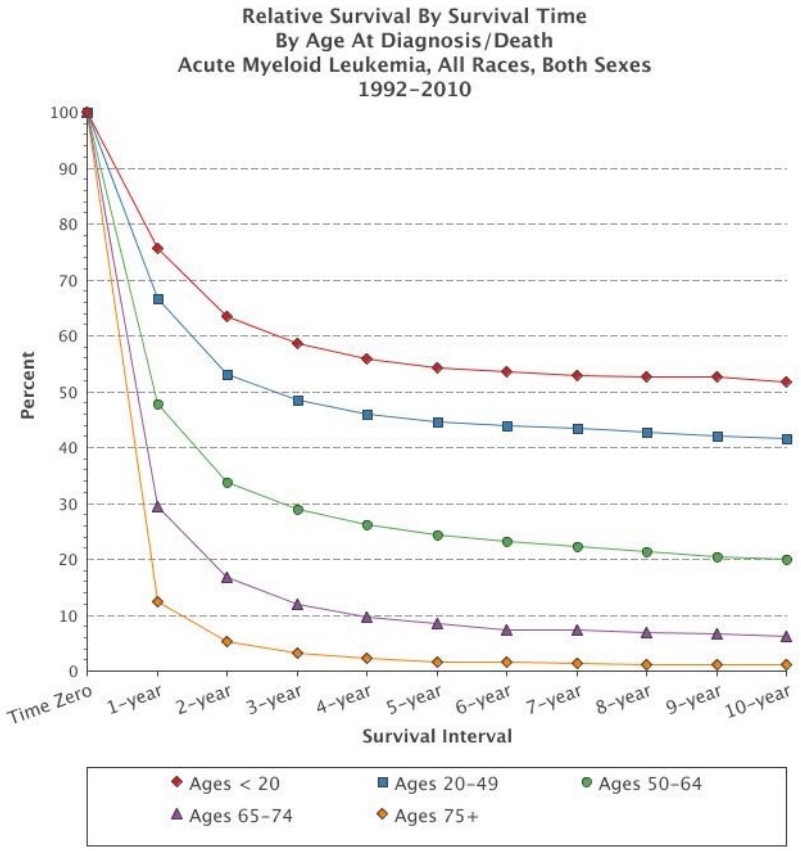
Median age at diagnosis: 69 years

La guérison : pas pour tous

Registre Suédois

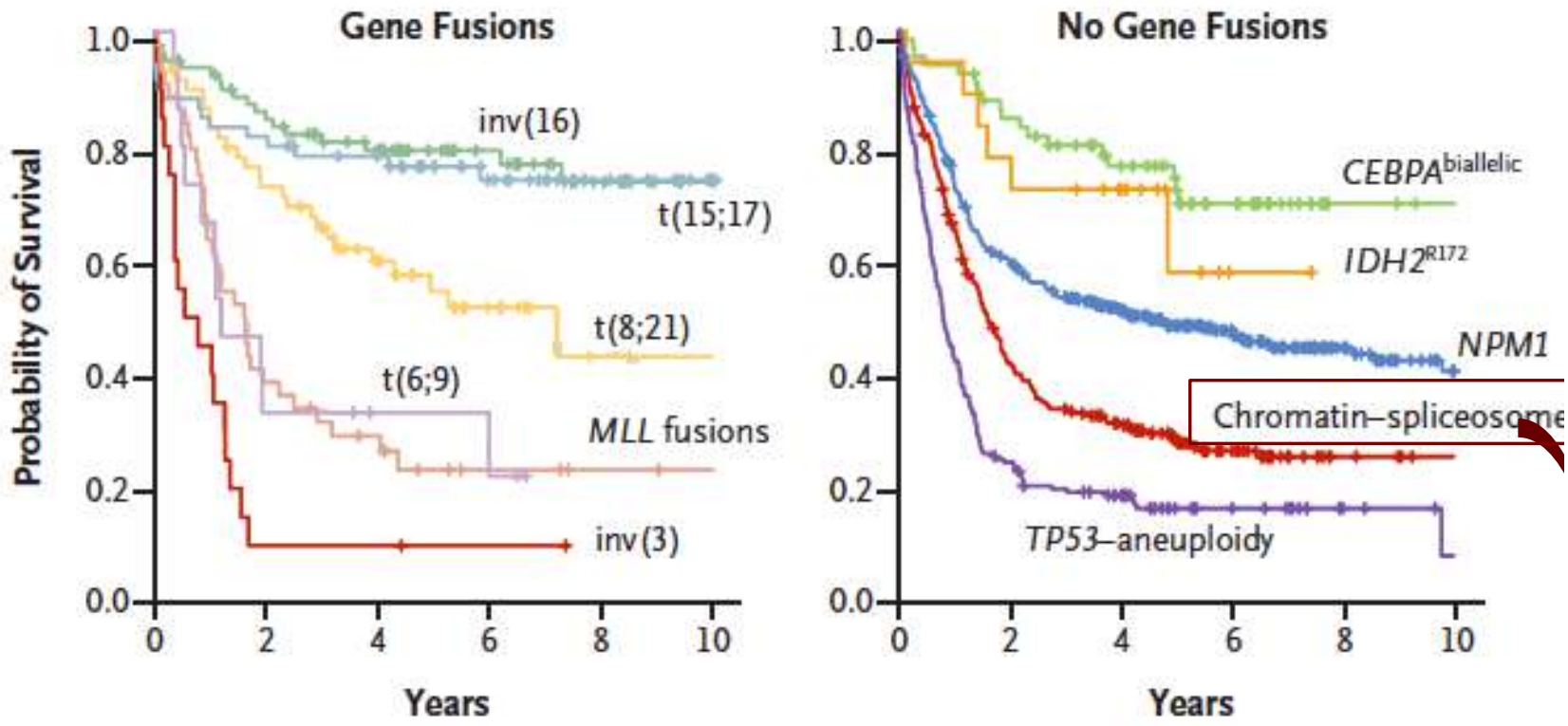


Registre SEER



Cancer sites include invasive cases only unless otherwise noted.
The annual survival estimates are calculated using monthly intervals.
Source: http://seer.cancer.gov/faststats/selections.php?series=age

Maladies hétérogènes



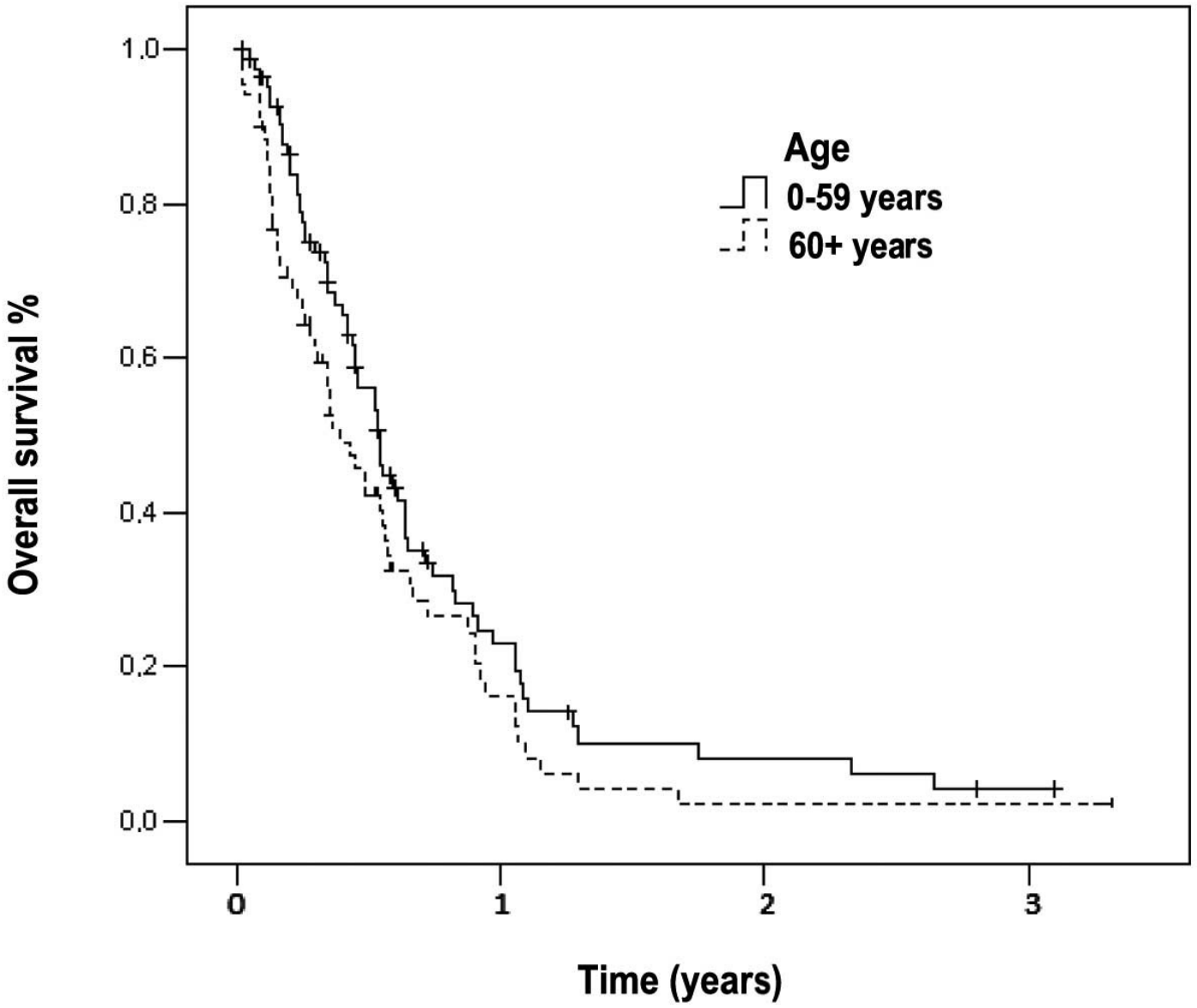
Maladies hétérogènes

Table 1 Main characteristics of AML patients with MK

Reference	Number of patients	Age (median, range)	MK frequency (%)	CR rate	OS	Comments
Breems et al[1]	1,975	NR, 15–60	9	48%	4% at 4 years	
Medeiros et al[9]	1,344	NR, 16–88	13	18%	3% at 4 years	Monosomies of 5 and 7 were the most common
Grimwade et al[7]	1,612	44, 16–59	6	NR	5% at 10 years	
Löwenberg et al[11]	813	67, 60–83	13	34%	4% at 2 years	
Lowenberg et al[10]	860	49, 18–60	10	52%	7% at 5 years	
Perrot et al[17]	186	68, 60–79	59	37%	7% at 2 years	
Haferlach et al[18]	824*	NR, 15–60	19	NR	Median 5.7 months	All cases were analyzed by multicolor FISH
Voutiadou et al[13]	549	53, 6–88	11.3	27%	8% at 3 years	Predominant monosomies were –5 and –7
Kayser et al[12]	1,058*	57, 17–84	30	32.5%	9% at 4 years	NPM1, FLT3-ITD, FLT3-D835 less frequent in MK+ group
Yang et al[19]	1,147*	NR, 15–88	18.5	25%	Median 5 months	Monosomies of 5 and 7 were the most frequent
Ahn et al[20]	369	47 (18–85)	6.2	34.8%	8.7% at 3 years	
Weinberg et al[21]	111	57 (17–83)	13	36%	Median 5.6 months	Most frequent chromosomes lost were 7 and 17
Manola et al[22]	140	13 (25–21)	12.1	NR	51.9% at 4 years	MK in children
Lu et al[23]	1,251	44 (15–89)	14.7	29.8%	Median 9 months	
Lazarevic et al[24]	1,893	71 (18–80)	18	59% in <60 years 41% in >60 years	NR	

Note: *AML patients with t (15;17), t (8;21), inv (16), and normal karyotype were excluded.

Abbreviations: AML, acute myeloid leukemia; FISH, fluorescence in situ hybridization; MK, monosomal karyotype; NR, not reported; OS, overall survival.


Overall survival %
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
Time (years)
Age
0-59 years
60+ years

Objectif thérapeutique

Stratégie ttt	Objectif	Enjeux
Curatif	Guérison	Toxicité / Futilisté
Palliatif actif	Durée de vie	Qualité de vie
Palliatif terminal	Symptômes	Qualité de la fin de vie

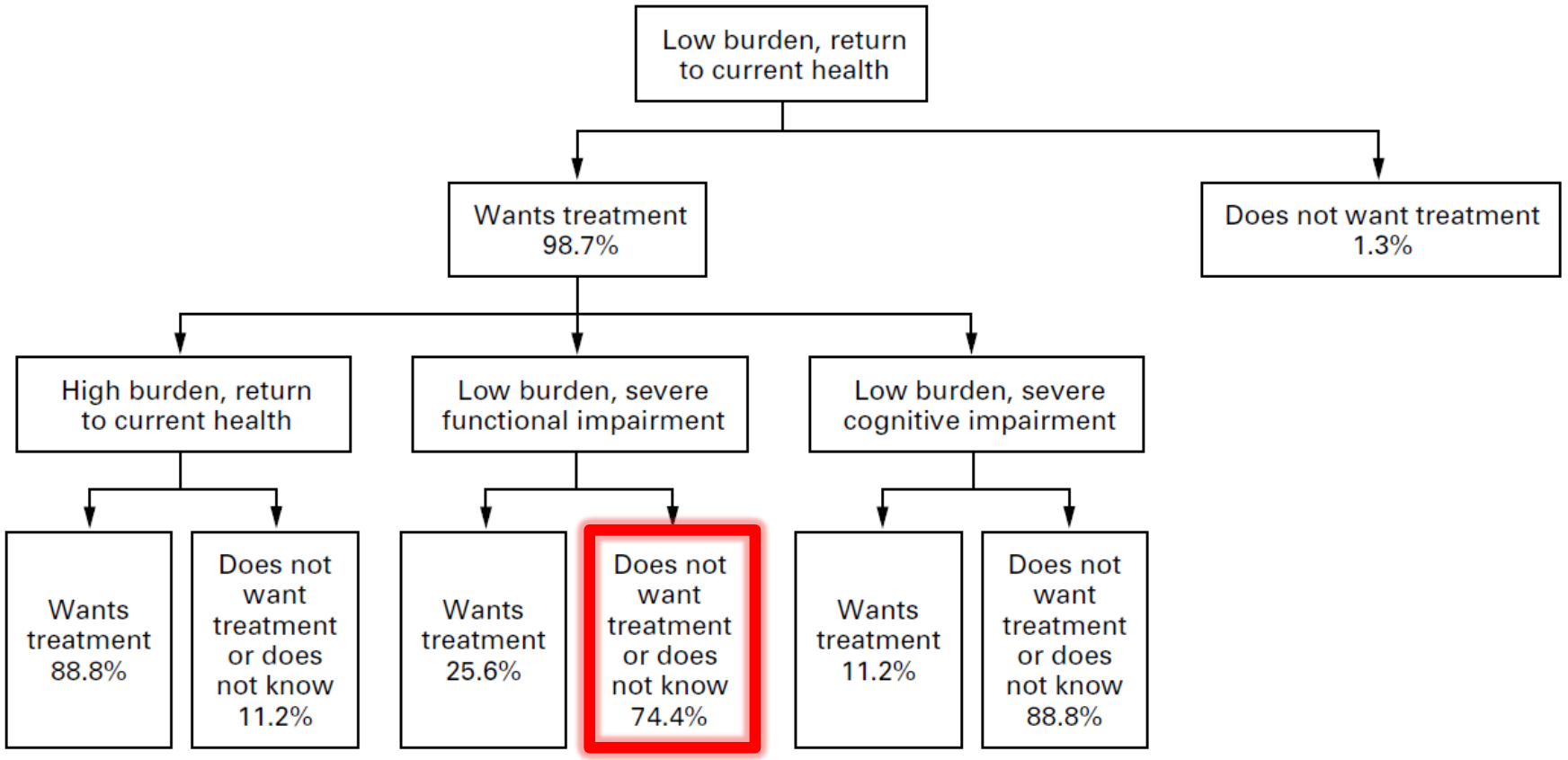
- **Définition Loyale et Réaliste**
  Avec le patient et ses proches
  Entre Hématologue et Réanimateur

Weeks et al. JAMA 1998
Weeks et al. NEJM 2012
Vaz-luis et al. Cancer 2017
Fried et al. NEJM 2002

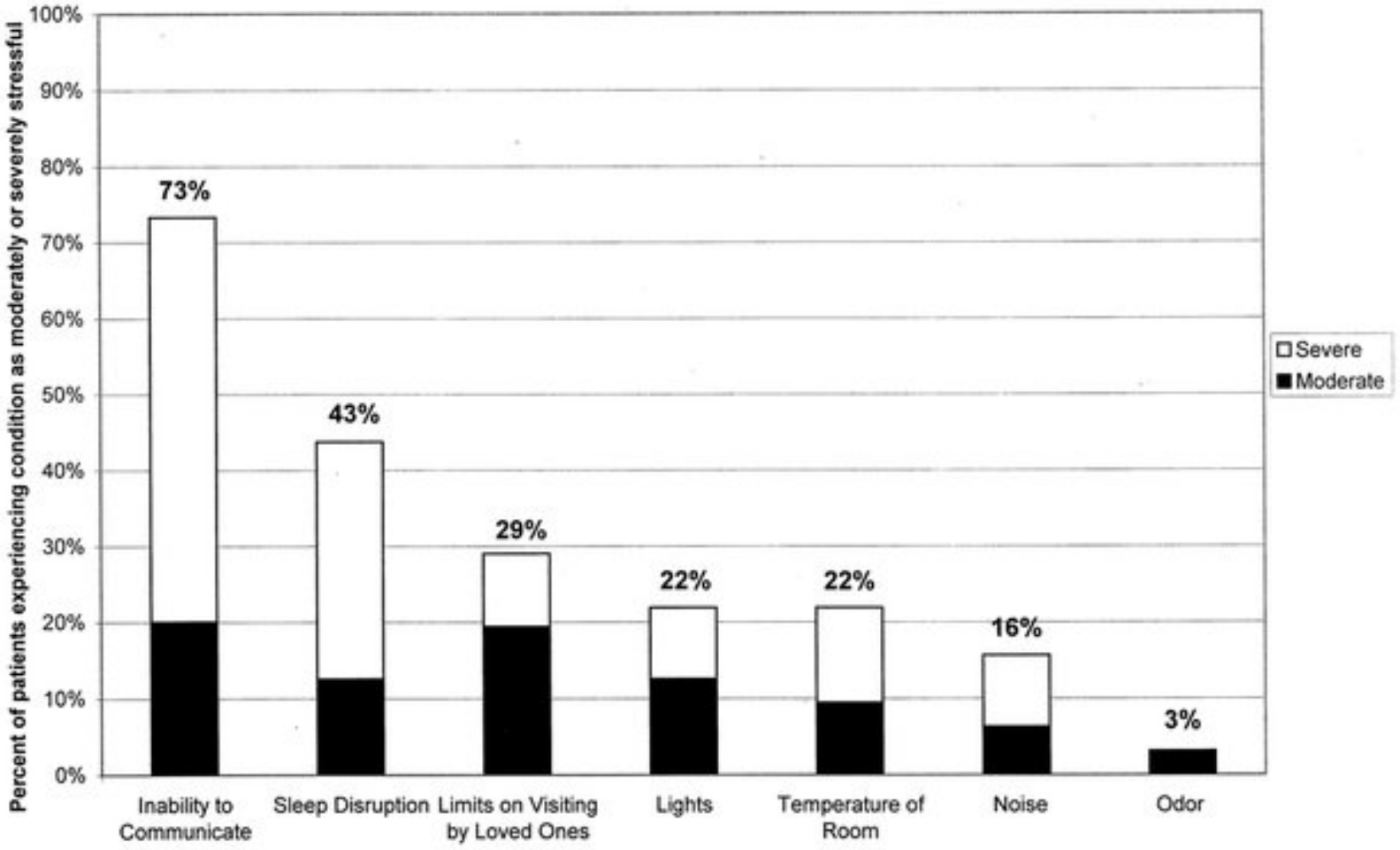
Special Article

UNDERSTANDING THE TREATMENT PREFERENCES OF SERIOUSLY ILL PATIENTS

TERRI R. FRIED, M.D., ELIZABETH H. BRADLEY, PH.D., VIRGINIA R. TOWLE, M.PHIL., AND HEATHER ALLORE, PH.D.



Stressful conditions for cancer patients in the intensive care unit



Judith E. Nelson et al., Critical CareMedicine 2001

Eligibilité pour une chimiothérapie intensive

Scores	Description
General status assessments	
Karnofsky performance status	Numbered scale (0 – 100) to classify patients according to functional impairment.
ECOG performance status	Numbered scale (0 – 5) to define functioning of clinical trial population.
Comprehensive geriatric assessment [1]	A comprehensive evaluation of cognitive and physical functions that may be used to improve risk stratification.
Comorbidity indexes	
Charlson (CCI) [2]	Method of classifying comorbidity to estimate risk of death from comorbid disease.
Sorror (HCT-CI) [3]	Simple, validated, reliable index of pre-SCT comorbidities that predicts non-relapse mortality and survival.
SIE/SIES/GITMO consensus [4]	A uniform and feasible characterisation of unfitness for intensive and non-intensive chemotherapy in AML.
Composite prognostic scores	
MRC-NCRI score [5]	A risk index based on regression coefficients of cytogenetics, age, WBC, PS and type of AML.
SWOG/MDACC [6]	Does not include the cytogenetic/molecular risk. “Age is primarily a surrogate for other covariates”.
German SAL score [7]	A web-based application for prediction of older AML outcomes.
Sorror AML model [8]	HCT-CI augmented by hypoalbuminemia, thrombocytopenia and LDH level + age + cytogenetic/molecular risk.
NCCN guidelines [9]	Treatment decision-making algorithm, which predicts the probability of achieving CR and the risk for an early death

1. Klepin HD, et al. *Blood*. 2013;121:4287-4294.
2. Charlson ME, et al. *J Chronic Dis*. 1987;40:373-383.
3. Sorror ML, et al. *Blood*. 2005;106:2912-2919.
4. Ferrara F, et al. *Leukemia*. 2013;27:997-999.
5. Wheatley K, et al. *Br J Haematol.* 2009;145:598-605
6. Walter RB, et al. *J Clin Oncol*. 2011;29:4417-4423.
7. Krug U, et al. *Lancet.* 2010;376:2000-2008
8. Sorror ML, et al. *JAMA*. 2017;[Epub ahead of print].
9. NCCN. Acute Myeloid Leukemia (Version 3.2017).

Evolution des stratégie

ETUDE VIALE-A: AZA+VEN vs AZA

The NEW ENGLAND JOURNAL of MEDICINE
AUGUST 13, 2020

Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia

C.D. DiNardo, B.A. Jonas, V. Pullarkat, M.J. Thirman, J.S. Garcia, A.H. Wei, M. Konopleva, H. Döhner, A. Letai, P. Fenaux,

Eligibility

Inclusion

- Patients with newly diagnosed confirmed AML
- Ineligible for induction therapy defined as **either**
  - ≥75 years of age
  - 18 to 74 years of age with at least one of the co-morbidities:
    - CHF requiring treatment or Ejection Fraction ≤50%
    - Chronic stable angina
    - DLCO ≤ 65% or FEV1 ≤ 65%
    - ECOG 2 or 3

Exclusion

- Prior receipt of any HMA, venetoclax, or chemotherapy for myelodysplastic syndrome
- Favorable risk cytogenetics per NCCN
- Active CNS involvement

Treatment

Randomization 2:1 N=433*

Venetoclax + Azacitidine (N=286)
Venetoclax 400 mg PO, daily, days 1–28 +
Azacitidine 75 mg/m² SC /IV days 1–7

Placebo + Azacitidine (N=145)
Placebo daily, days 1–28
+ Azacitidine 75 mg/m² SC /IV days 1–7

Endpoints

Primary

- Overall survival

Secondary

- CR+CRi rate
- CR+CRh rate
- CR+CRi and CR+CRh rates by initiation of cycle 2
- CR rate
- Transfusion independence
- CR+CRi rates and OS in molecular subgroups
- Event-free survival

Randomization Stratification Factors: Age (<75 vs. ≥75 years); Cytogenetic Risk (intermediate, Poor); Region

Venetoclax dosing ramp-up: Cycle 1 ramp-up Day 1: 100 mg, Day 2: 200 mg, Day 3 - 28: 400 mg; Cycle 2 → Day 1-28: 400 mg

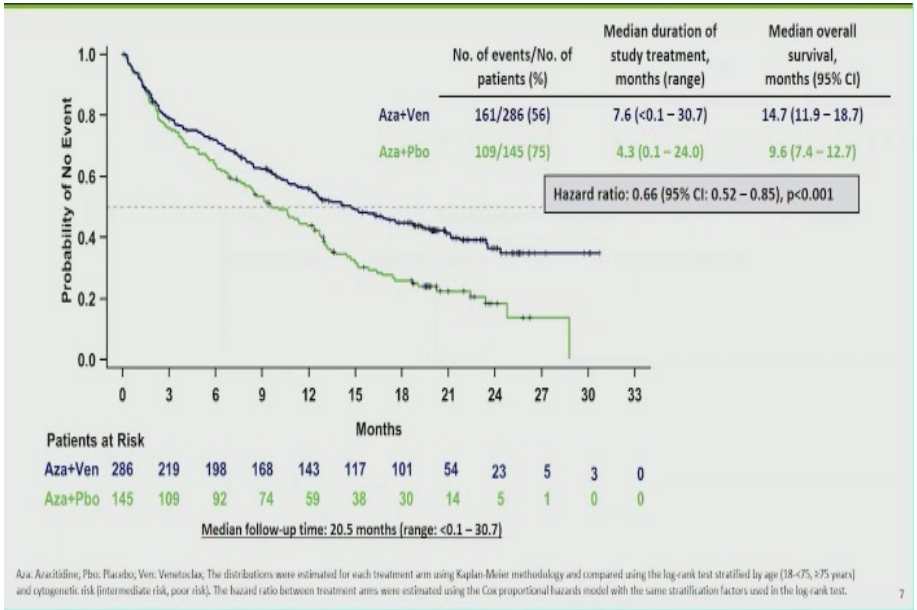
* 2 patients were not stratified by cytogenetic risk. They were excluded from efficacy analysis but included in the safety analysis. 6 patients who did not receive treatment were excluded from the safety analysis set.

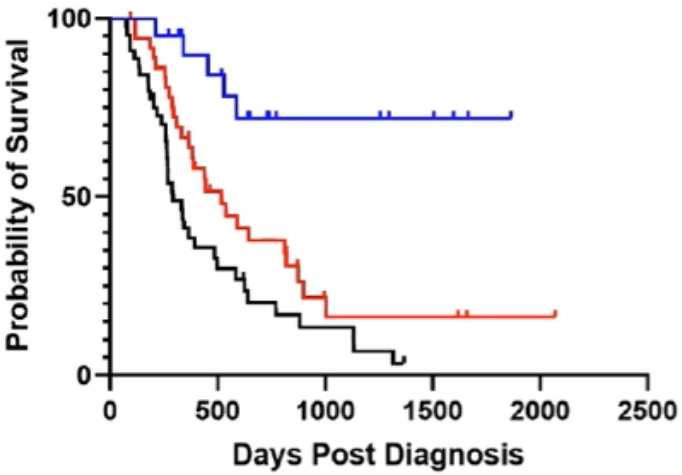
AML: Acute myeloid leukemia; CHF: Congestive heart failure; CNS: Central nervous system; CR: Complete remission; CRi: CR+ incomplete marrow remission; CRh: CR+ incomplete hematologic recovery; DCLO: diffusion lung capacity for carbon monoxide; ECOG: Eastern Cooperative Oncology Group; FEV1 : Forced expiratory volume; HMA: Hypomethylating agent; NCCN: National Comprehensive Cancer Network

4

Traitements +/- continus , traitements per os …

Survie Globale





HSCT

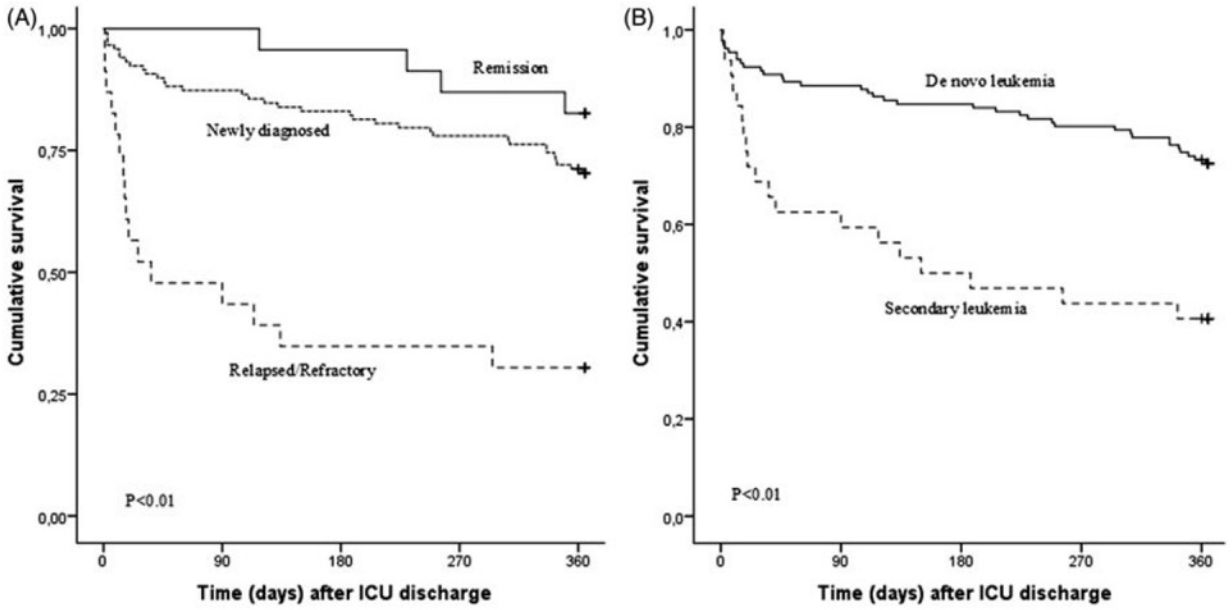
HSCT deferred

Not HSCT candidate, survived at least least 60 days from diagnosis

HCT vs HCT deferred *P* = .002

HCT deferred vs not HCT candidate survived 60 d *P* = .035

Survie après la réanimation



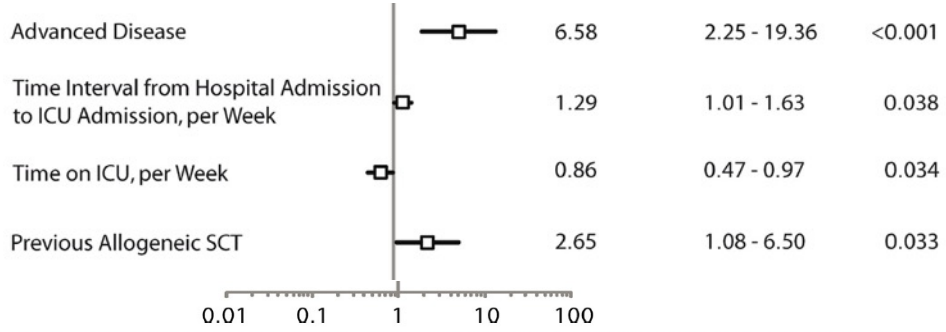


Fig 4. Hazard ratio (HR) plot of parameters associated with survival after ICU (intensive care unit) discharge. Abbreviations: SCT, stem cell/bone marrow transplantation; GCS, Glasgow Coma Scale; Hkt, hematocrit.

Tavares et al, *Leuk Lymph*, 2017

Pohlen et al, *PLoS One*, 2016

Les résultats de la réanimation dépendent de la quantité de défaillance

Intensive care in patients with newly diagnosed malignancies and a need for cancer chemotherapy*

Michael Darmon, MD; Guillaume Thiery, MD; Magali Ciroldi, MD; Sandra de Miranda, MD; Lionel Galicier, MD; Emmanuel Raffoux, MD; Jean-Roger Le Gall, MD; Benoît Schlemmer, MD; Élie Azoulay, MD, PhD

Crit Care Med 2005 Vol. 33, No. 11

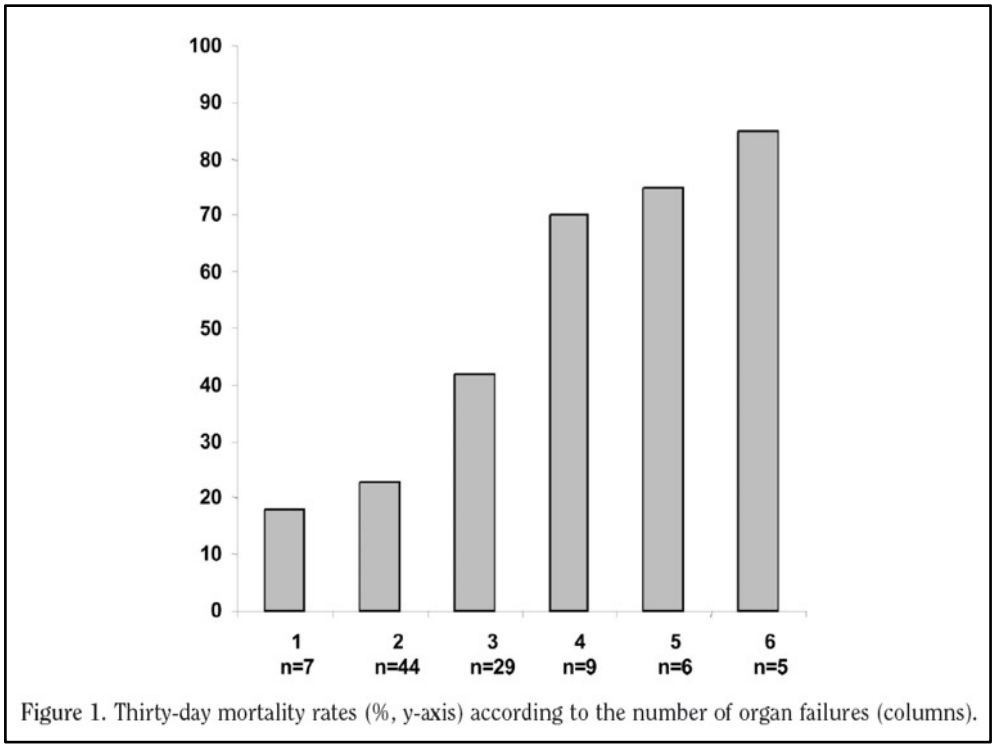


Figure 1. Thirty-day mortality rates (%, y-axis) according to the number of organ failures (columns).

Outcome of Critically Ill Allogeneic Hematopoietic Stem-Cell Transplantation Recipients: A Reappraisal of Indications for Organ Failure Supports

Frédéric Pène, Cécile Aubron, Elie Azoulay, François Blot, Guillaume Thiéry, Bruno Raynard, Benoît Schlemmer, Gérard Nitenberg, Agnès Buzyn, Philippe Arnaud, Gérard Socié, and Jean-Paul Mira

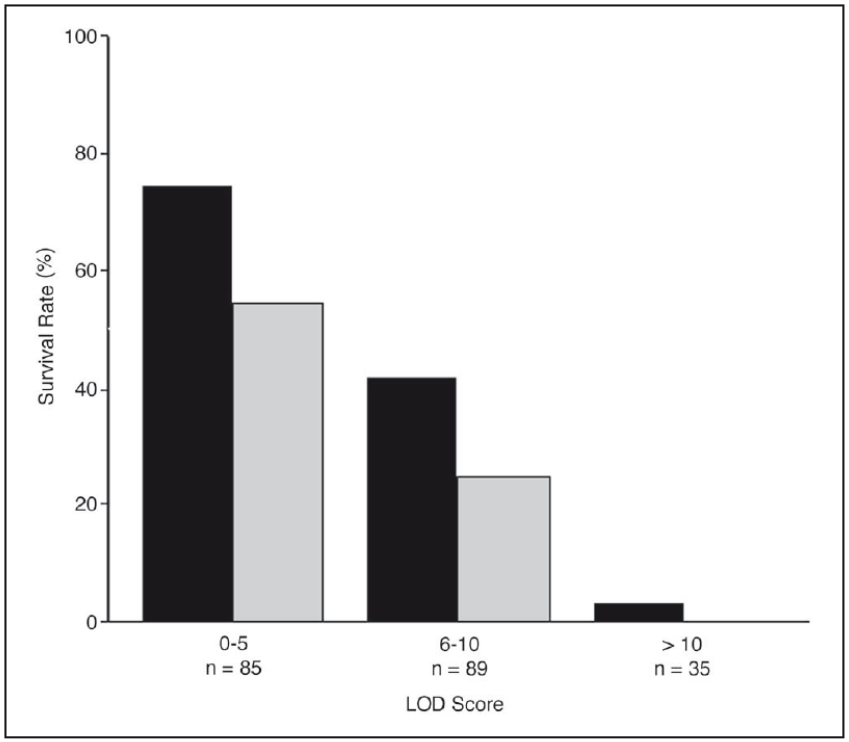


Fig 1. In–intensive care unit (ICU; black bars) and in-hospital (gray bars) survival rates according to the Logistic Organ Dysfunction (LOD) score at admission in the ICU.

Outcomes of Critically Ill Patients With Hematologic Malignancies: Prospective Multicenter Data From France and Belgium—A Groupe de Recherche Respiratoire en Réanimation Onco-Hématologique Study

Elie Azoulay, Djamel Mokart, Frédéric Pène, Jérôme Lambert, Achille Kouatchet, Julien Mayaux, François Vincent, Martine Nyunga, Fabrice Bruneel, Louise-Marie Laisne, Antoine Rabbat, Christine Lebert, Pierre Perez, Marine Chaize, Anne Renault, Anne-Pascale Meert, Dominique Benoit, Rebecca Hamidfar, Mercé Jourdain, Michael Darmon, Benoit Schlemmer, Sylvie Chevret, and Virginie Lemiale

Table 2. Hospital Mortality Associated With the Use of Life-Supporting Intervention Therapies in Five Predefined Subgroups

	Overall Cohort (N =1,011)		Patients Age < 60 Years (n =483)		Good Performance Status (n =816)*		Partial or Complete Remission (n =234)†		No Allogeneic BMT (n =866)		Dysfunction of Zero or One Organ (n =575)‡	
Life-Supporting Intervention	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total patients who died	397	39.3	169	34.9	284	34.8	78	33.3	319	36.8	115	20.0
Chemotherapy in the ICU	244		133		208		NA		244		141	
Patients who died	93	38.1	40	30.1	73	35.1			93	38.1	27	19.1
Noninvasive mechanical ventilation	318		148		244		71		260		142	
Patients who died	147	46.2	62	41.0	104	42.6	27	38.0	116	44.6	38	26.8
Invasive mechanical ventilation	484		228		378		106		415		73	
Patients who died§	293	60.5	126	55.0	214	56.6	57	53.8	244	58.8	23	31.5
Vasoactive drugs	518		233		394		126		438		101	
Patients who died§	298	57.5	122	52.4	213	54.1	57	45.2	247	45.9	22	21.8
Renal replacement therapy	262		126		206		20		231		64	
Patients who died§	155	59.2	73	58.0	111	53.9	11	55.0	131	56.7	12	18.8

Abbreviations: BMT, bone marrow transplantation; ICU, intensive care unit.
*Good performance status was defined as neither bedridden nor completely disabled.
†BMT patients were all considered in partial or complete remission.
‡Requiring invasive mechanical ventilation, vasoactive drugs, or renal replacement therapy.
§These patients received only one of the three following life-supporting interventions: invasive mechanical ventilation, vasoactive drugs, and renal replacement therapy.

Leukemia & Lymphoma, July 2012; 53(7): 1352–1359

ISSN: 1042-8194 print / 1029-2403 online
DOI: 10.3109/10428194.2011.649752

informa
healthcare

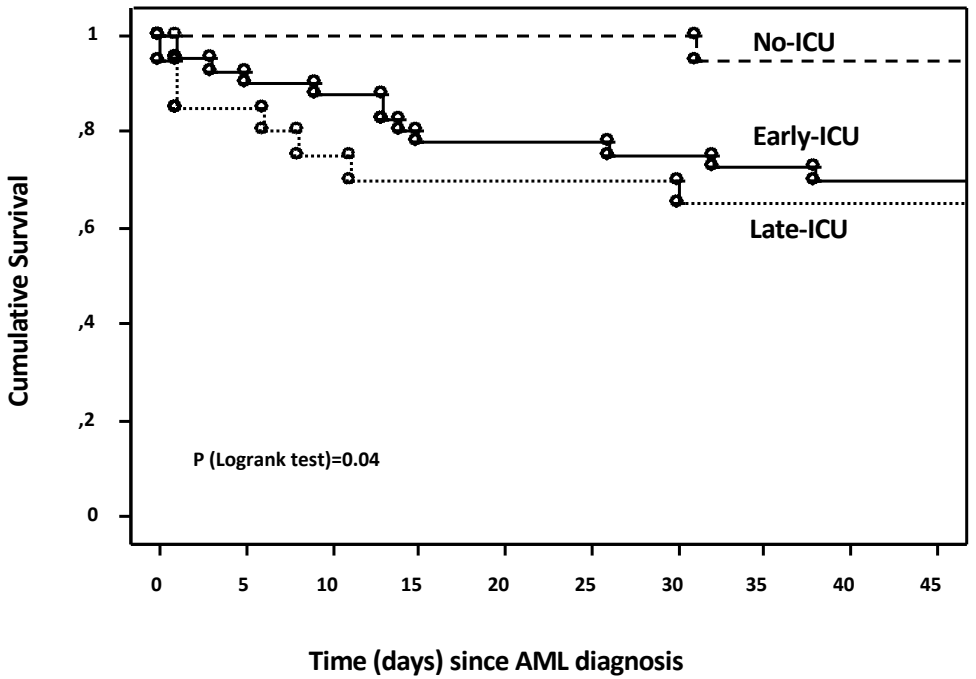
ORIGINAL ARTICLE: CLINICAL

Intensive care unit management of patients with newly diagnosed acute myeloid leukemia with no organ failure

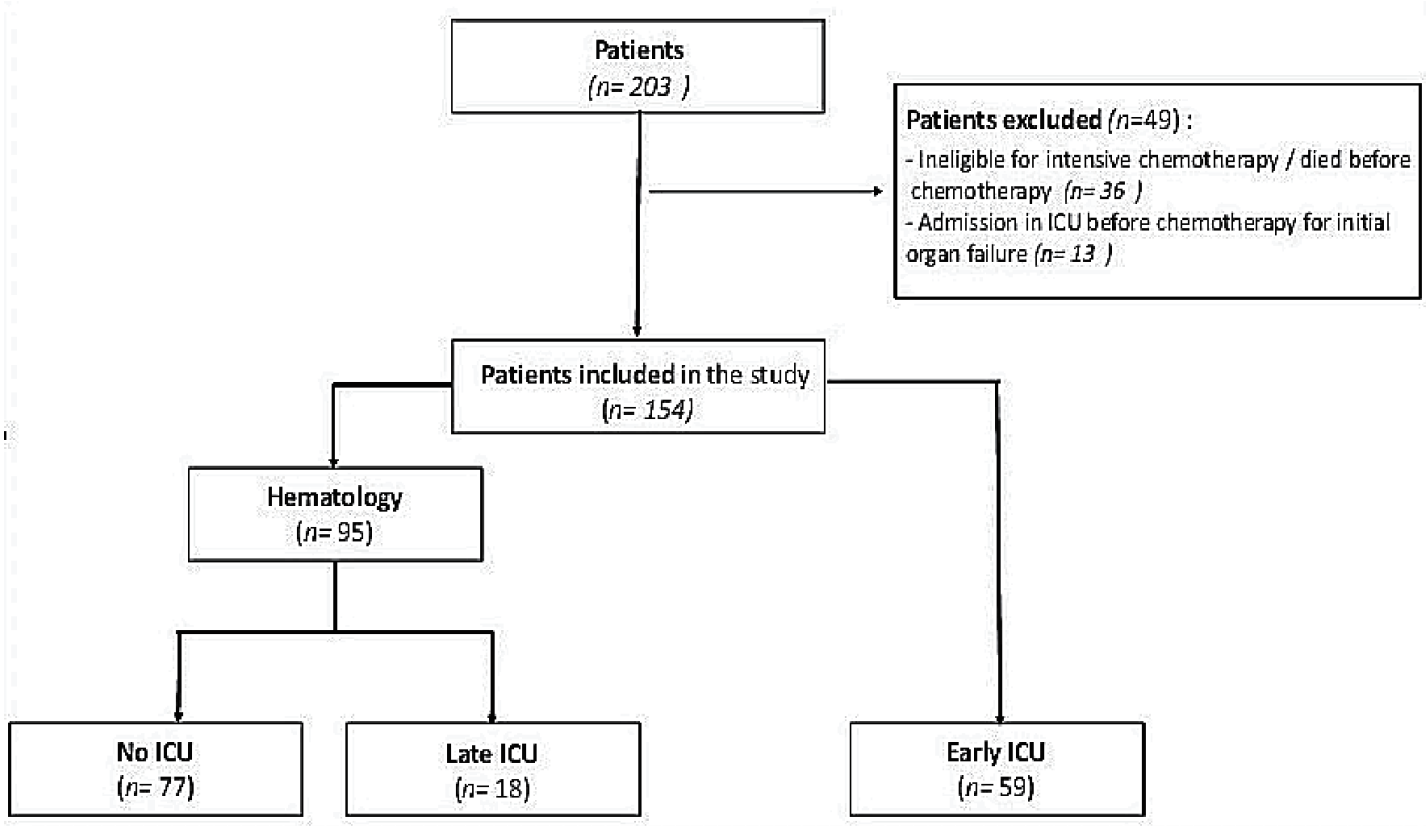
Etienne Lengliné, Emmanuel Raffoux, Virginie Lemiale, Michael Darmon, Emmanuel Canet, Nicolas Boissel, Benoît Schlemmer, Hervé Dombret & Elie Azoulay

Medical ICU and Hematology Departments, Hôpital Saint-Louis, AP-HP and UFR de Médecine, University Paris-7 Paris-Diderot, Paris, France

- Etude cas-contrôle rétrospective N =84
- Admission en réanimation **avant la survenue de défaillance**
- Appariement sur Age – FAB – Leucocytose avec patients admis en salle



Admission avant défaillance



Mortalité à J30: 28% 17%

Mottal et al. J Hematol 2020

Prognostic factors for intensive care unit admission, intensive care outcome, and post-intensive care survival in patients with *de novo* acute myeloid leukemia: a single center experience

Haematologica 2011;96(2):231-237.

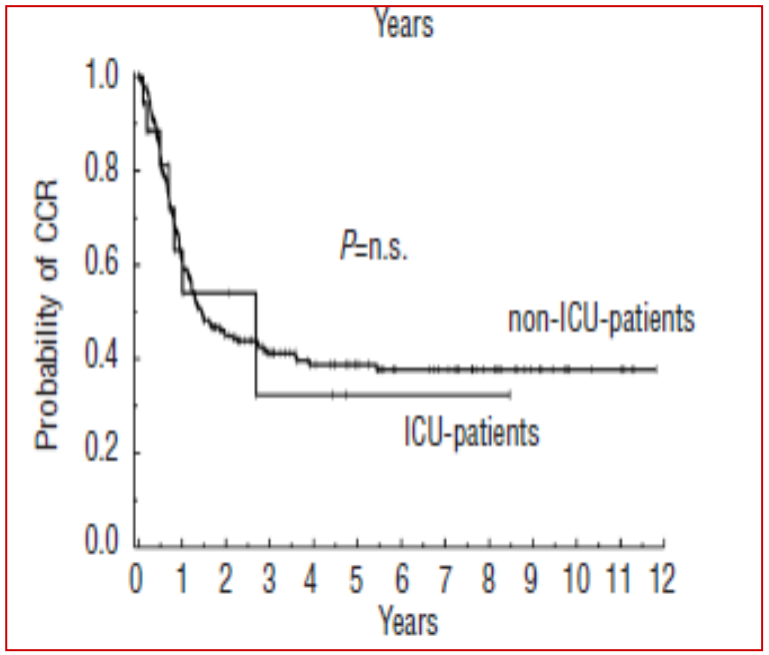
Peter Schellongowski,[1] Thomas Staudinger,[1] Michael Kundi,[2] Klaus Laczika,[1] Gottfried J. Locker,[1] Andja Bojic,[1] Oliver Robak,[1] Valentin Fuhrmann,[3] Ulrich Jäger,[4] Peter Valent,[4,5] and Wolfgang R. Sperr[1,4]

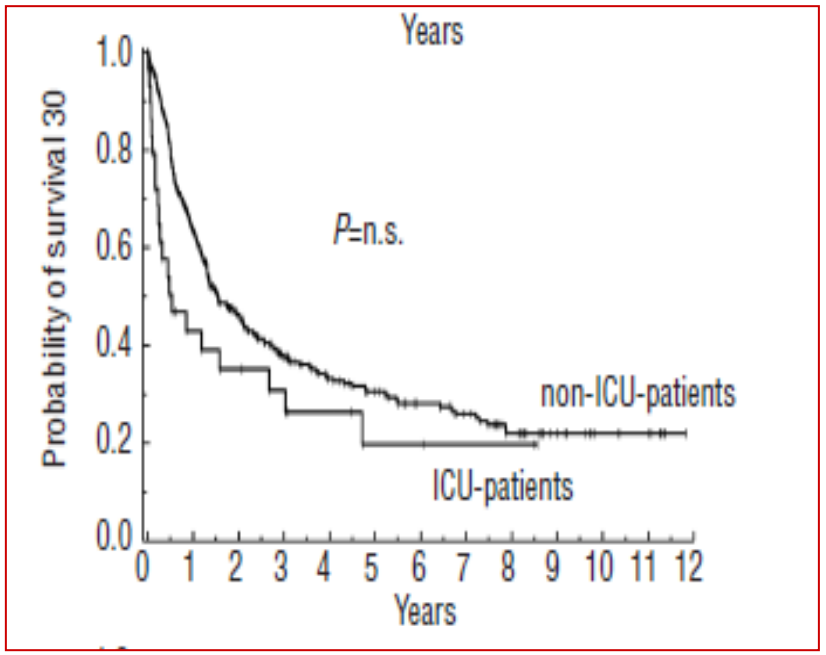
Survie / guérison post réanimation

406 new diagnosed AML patients

ICU required in 15%

Landmark analysis (Day 30 / Complete remission)





Survie après chimiothérapie

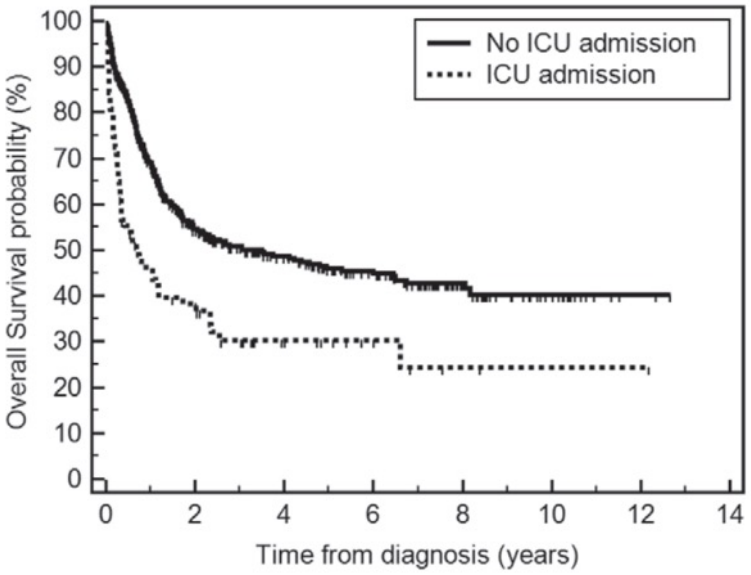


Figure 1. Overall survival of patients admitted to the ICU at any stage during induction or consolidation chemotherapy, compared to patients not admitted to the ICU at any phase of treatment ($p < 0.0001$).

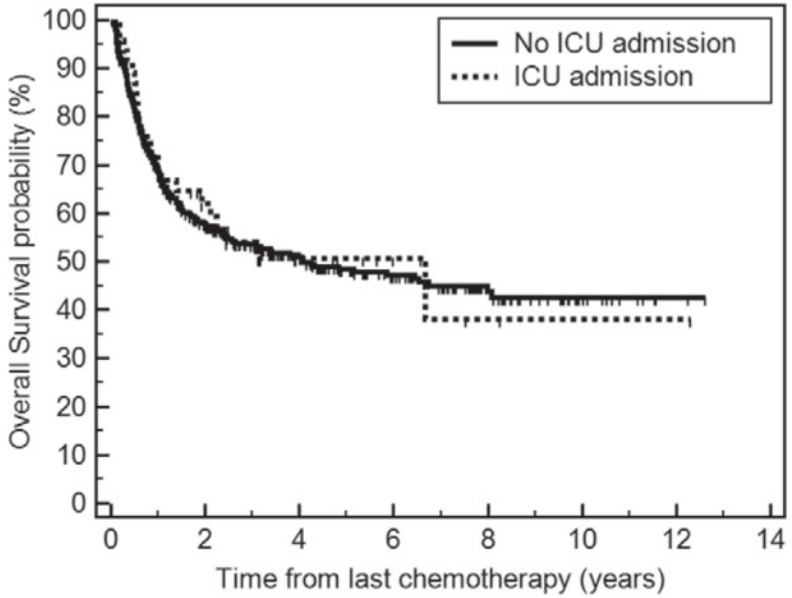
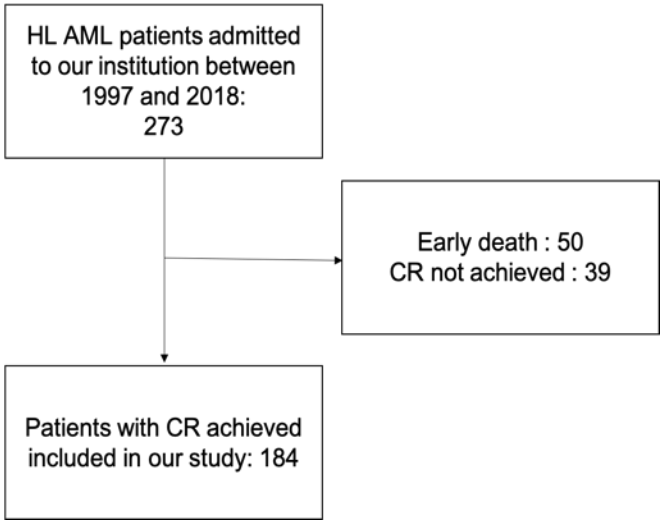


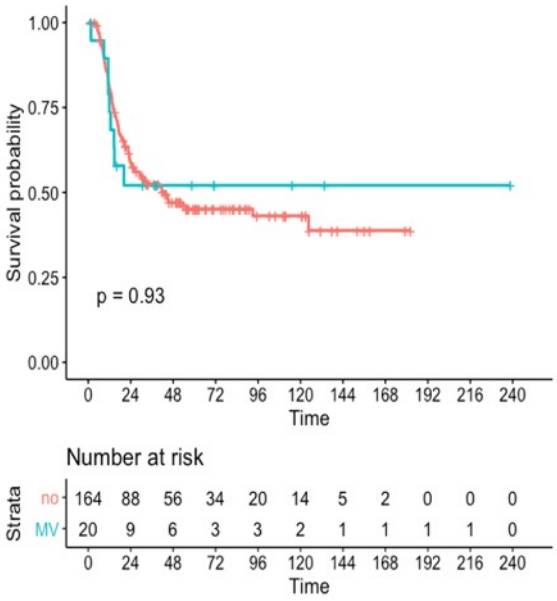
Figure 2. Landmark analysis showing overall survival of patients who survived all chemotherapy cycles administered, according to requirement for ICU admission ($p = 0.83$).

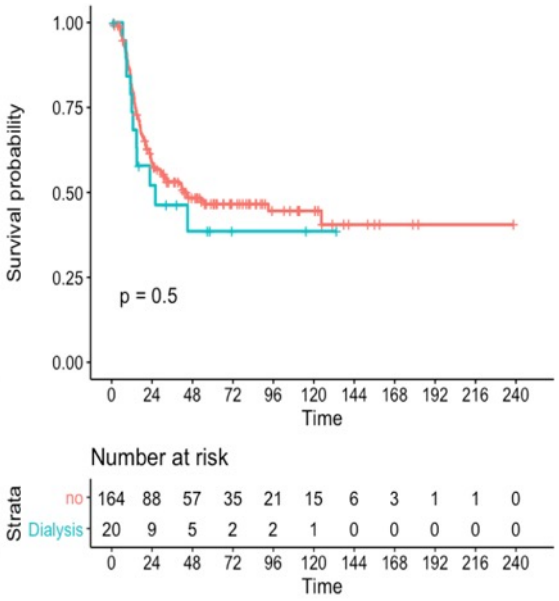
Jackson et al, *Leuk Lymph*, 2015

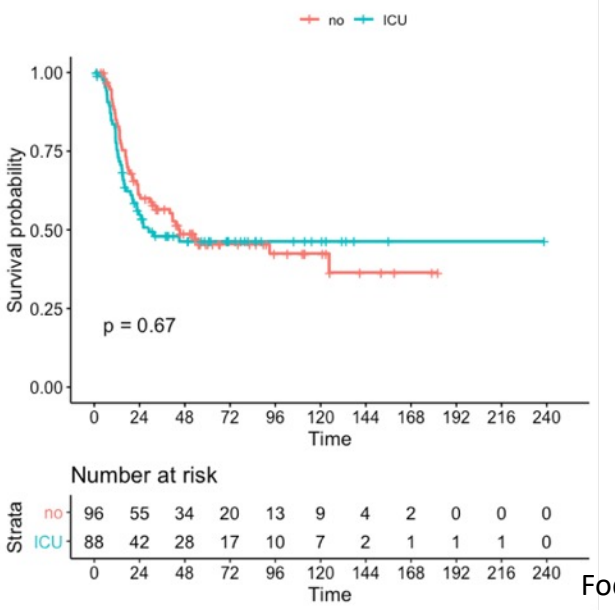
Devenir post rémission après traitements de suppléances vitales



- N=184 CR1 patients with >50 G/L WBC
- Median: **47 years old** IQR (32,5-60,5)
- **FAB M4/M5** : 63,3 %
- **Karyotype** (Fav/Interm/poor) : 15% / 70% / 15%
- **FLT3 ITD** = 30,4 % / **NPM1mut** = 40,3%
- **TLS** = 46% / **Hypoxemia** = 32%







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Conclusion(s)

1. Les LAM sont (quasi) incurables pour la majorité des patients
2. Le pronostic à long terme est difficile à évaluer au plan individuel et surtout a la phase initiale
3. Eligibilité à recevoir une chimio intensive au sommet de l'algorithme décisionnel
4. Admission large & précoce en cas de projet curatif sans impact défavorable pour les survivants