FRENCH INNOVATIVE
LEUKEMIA ORGANIZATION

DEXAML-02
A phase II study of dexamethasone added to induction and postremission therapy in older patients with newly diagnosed AML. A French Innovative Leukemia Organization (FILO) study.

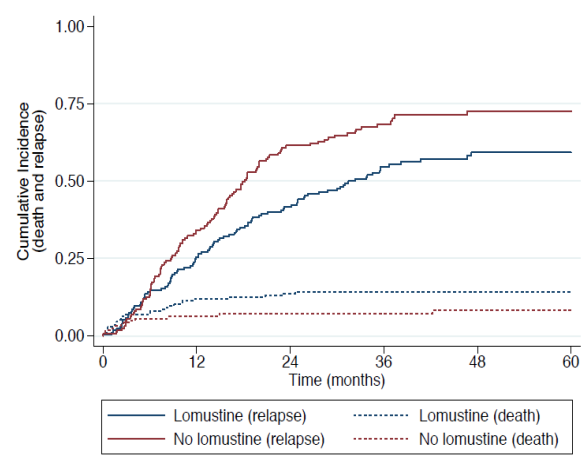
C. Récher, S. Bertoli, P. Peterlin, R. Guieze, Y. Desbrosses, Y. Hicheri, O. Benbrahim, M. Carre, M. Hunault-Berger, A. Banos, M. Bernard, E. Gyan, A. Saad, S. Chebrek, G. Roth Guepin, V. Dorvaux, L. Sanhes, M.P. Gallego Hernanz, C. Exbrayat, L. Vincent, C. Himberlin, L. Largeaud, E. Delabesse, F. Vergez, N. Vey, A. Mineur, C. Simand, I. Luquet and Arnaud Pigneux

Rencontres de Recherche Clinique, Dijon, 23/11/2022

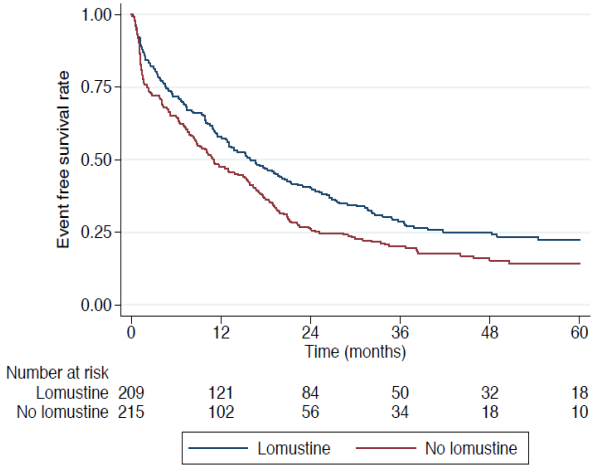
Background (1)

- **LAM-SA 2007**
  - Addition of Lomustine (CCNU) to Idarubicin-Cytarabine improves CR, CIR, EFS and OS in AML patients without unfavorable cytogenetics (Pigneux A, JCO 2018, *in press*)

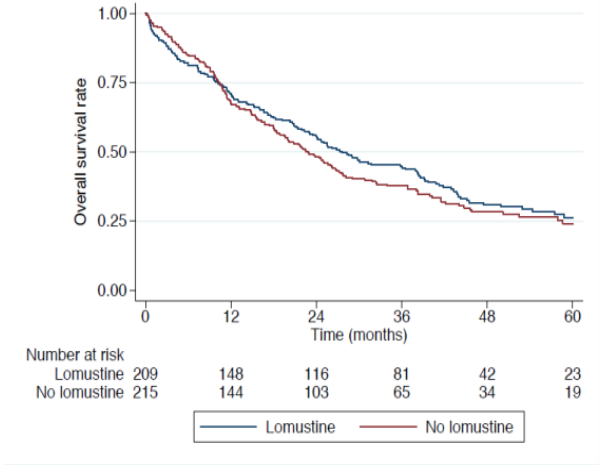
  - Response: ICL: CR/CRi (78.9/5.7%): 84.7% vs IC: (73/1.8%): 74.9% (OR, 1.86; 95%CI:1.15-3.04; P=0.01)
  - Induction failure (one course) : ICL : 8% vs 21% IC (P=0.001)
  - Induction death: ICL : 8% vs 4% IC (P=0.1)



CIR
41% (ICL) vs 61% (IC) (*P*= 0.003)



2y-EFS
41% (ICL) vs 26% (*P*=0.002)



2y-OS
56% (ICL) vs 48% (*P*=0.04)
Median OS : 30 vs 24 months

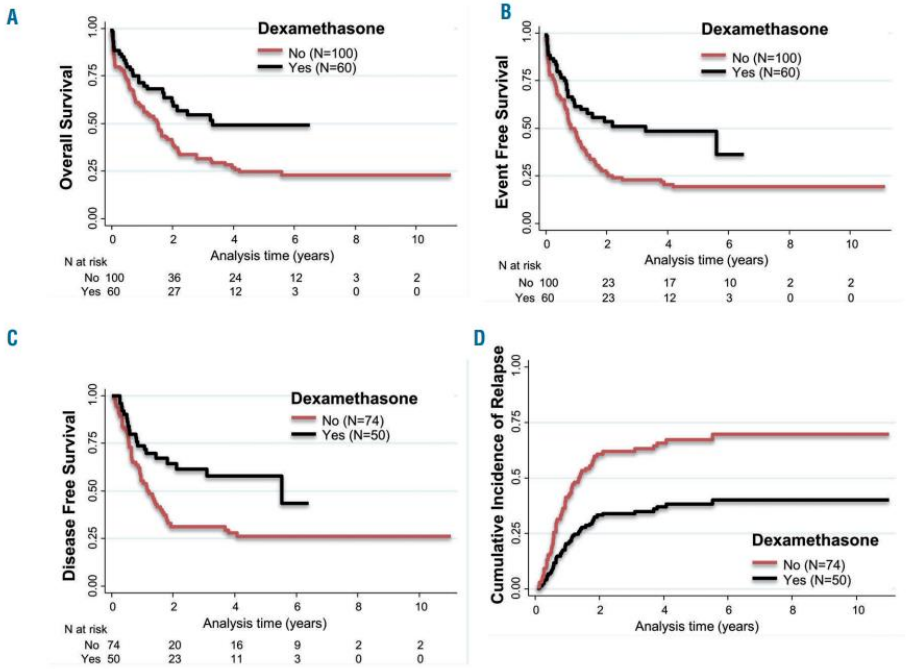
Background (2)

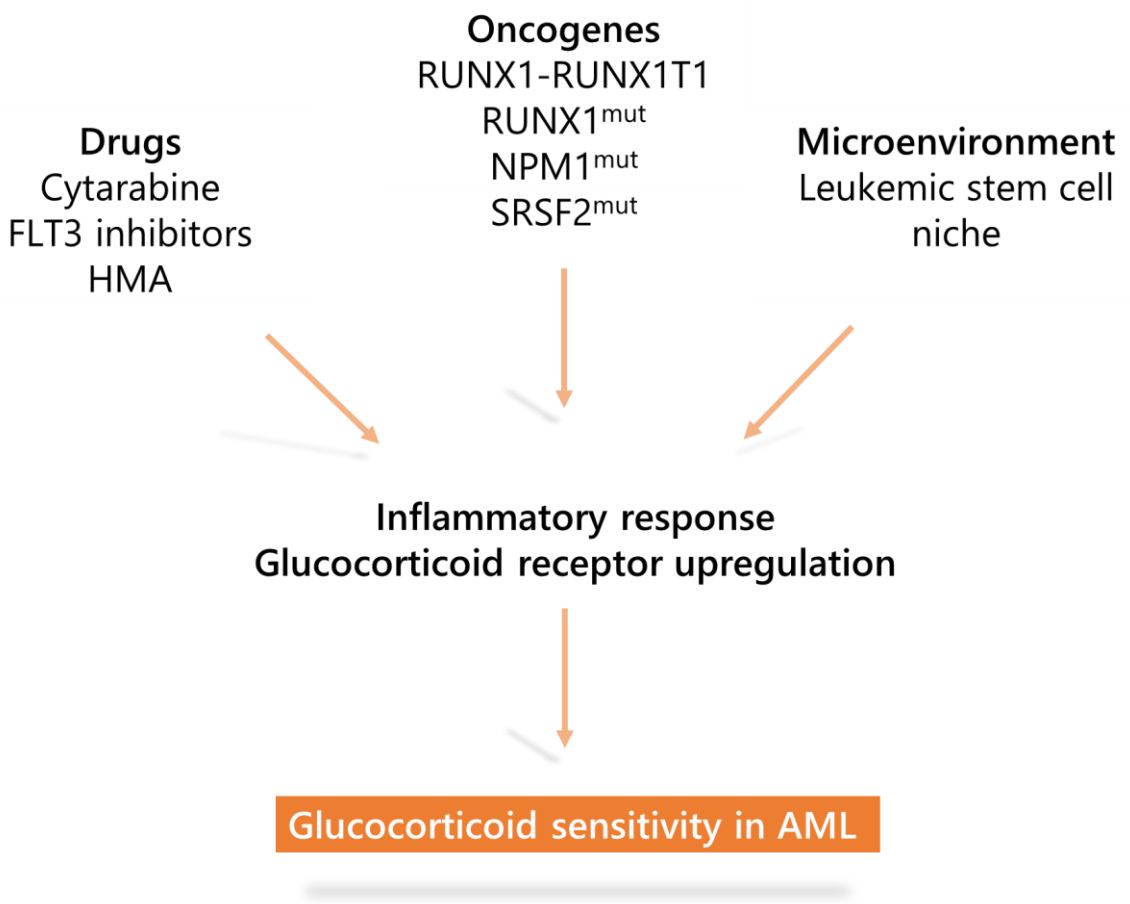
Dexamethasone in hyperleukocytic acute myeloid leukemia

Sarah Bertoli,[1,2,3]* Muriel Picard,[4]* Emilie Bérard,[5,6]* Emmanuel Griessinger,[7] Clément Larrue,[3] Pierre Luc Mouchel,[1,3] François Vergez,[2,3,8] Suzanne Tavitian,[1] Edwige Yon,[5] Jean Ruiz,[4] Eric Delabesse,[2,3,8] Isabelle Luquet,[8] Laetitia Karine Linares,[9,10,11] Estelle Saland,[3] Martin Carroll,[12] Gwenn Danet-Desnoyers,[12] Audrey Sarry,[1] Françoise Huguet,[1] Jean Emmanuel Sarry[3] and Christian Récher[1,2,3]

[1]Service d'Hématologie, Centre Hospitalier Universitaire de Toulouse, Institut Universitaire du Cancer de Toulouse Oncopole, France; [2]Université Toulouse III Paul Sabatier, France;

Haematologica 2018
Volume 103(6):988-998





Récher C, Frontiers in Oncology, 2021

Study criteria

Key inclusion criteria

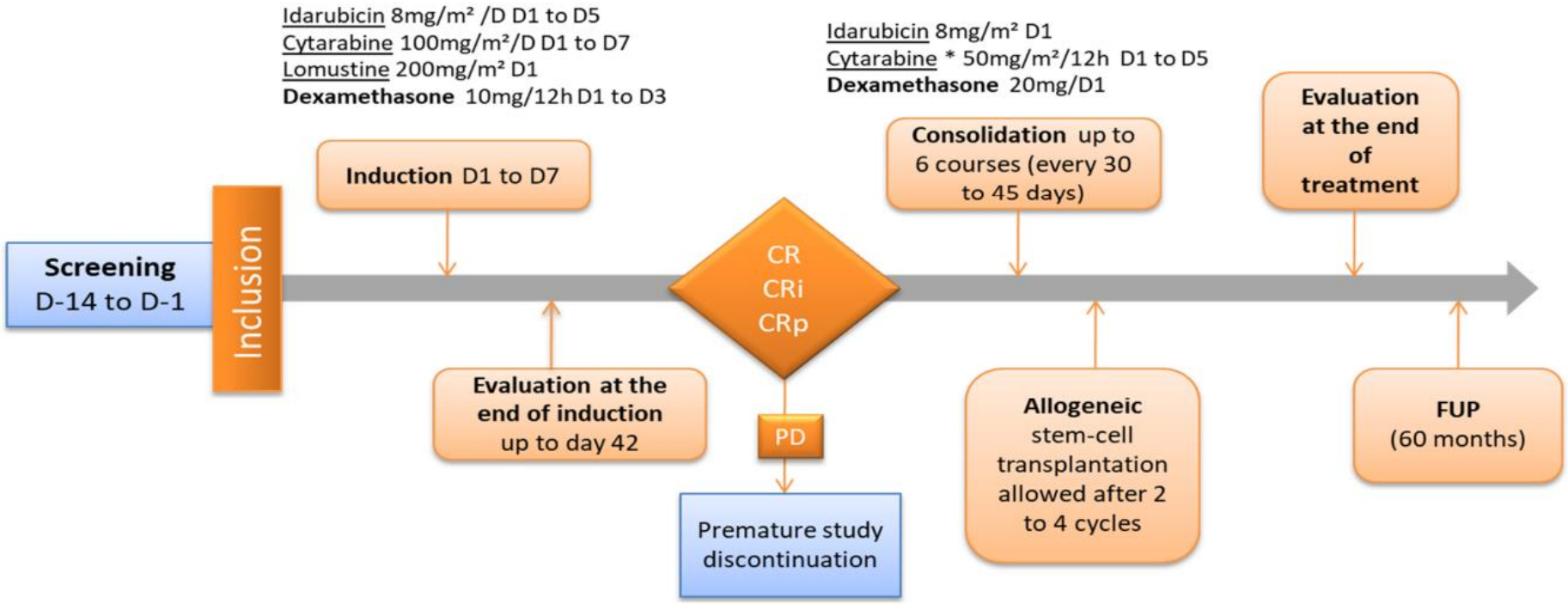
1. > 60 years of age.
2. Newly diagnosed AML according to the WHO 2016 either de novo AML or therapy-related AML
3. AML with favorable or intermediate cytogenetic risk.
4. Subjects should be eligible for intensive chemotherapy by Idarubicin, cytarabine, Lomustine.
5. ECOG < 3
6. SORROR ≤ 3

Key exclusion criteria

1. APL or acute megakaryocytic leukemia.
2. AML with adverse cytogenetic risk
3. AML arising from myelodysplastic syndromes, myeloproliferative disorders or CMML
4. AML with Philadelphia chromosome or with BCR::ABL1.
5. Known active central nervous system leukemia
6. Previous anti-AML treatment other than hydroxyurea.
7. Cumulative anthracycline dose equivalent to ≥550 mg/m²

Study design

- Non-randomized phase II multicenter trial
- Historical comparison with the LAM-SA 2007 trial (arm A) which had similar study criteria
- Primary endpoint: 2y-EFS (a 15% increase of EFS compared to this historical data (from 40% to 55%)

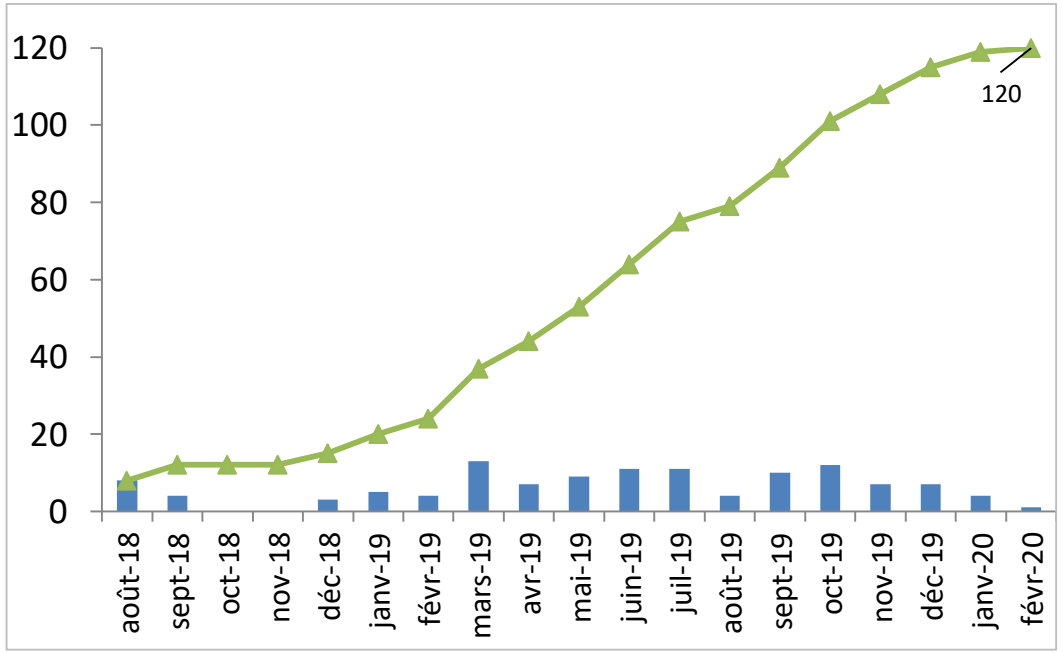


•NB1: the addition of midostaurin (50 mg orally twice daily, on days 8 through 21) in patients with FLT3-ITD or FLT3-TKD mutations is allowed according to standard recommendations of the product.

•NB2 : patients with CBF-AML could receive 2-3 cycles of intermediate doses of cytarabine (IDAC) instead of 6 cycles of mini-consolidations according to investigator choice:

Study population

- 120 patients enrolled
- 6 patients excluded : adverse karyotype (n=3), HCT-CI ≥3 (n=2), CNS disease (n=1)
- Median FU: 32 months (IQR, 28-35)
- 21 patients received an allogeneic-SCT in CR1

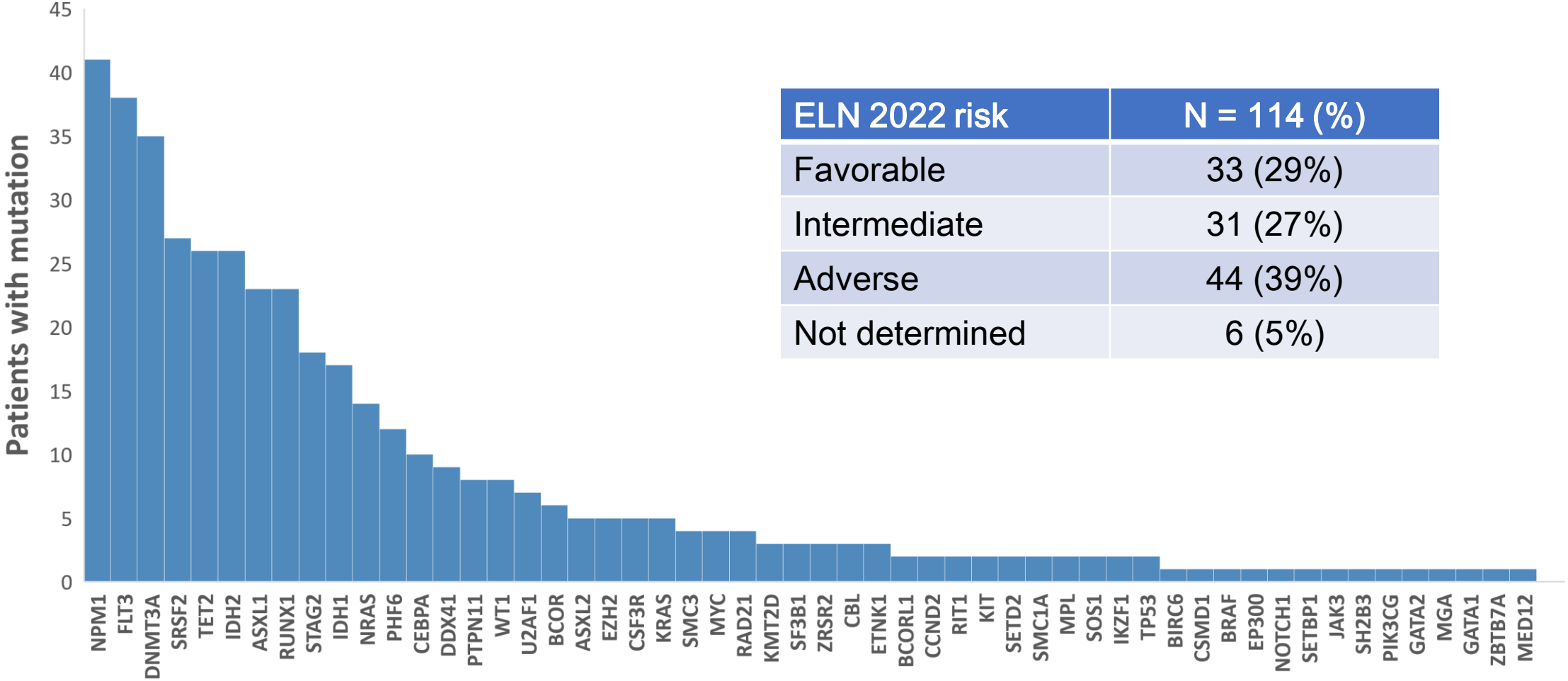


Patient characteristics

Variable	Statistic	Total N=114
Gender	**n/missing**	**114/0**
Male	n (%)	72 (63.2)
Age (years)	n /missing	114/0
	Median [Min;Max]	70.00 [61.00; 80.00]
ECOG	**n/missing**	**114/0**
0	n (%)	46 (40.4)
1	n (%)	59 (51.8)
2	n (%)	9 (7.9)
HCT-CI*	**n/missing**	**114/0**
0	n (%)	59 (51.8)
1	n (%)	31 (27.2)
2	n (%)	11 (9.6)
3	n (%)	9 (7.9)
4	n (%)	4 (3.5)
AML STATUS	**n/missing**	**114/0**
De novo	n (%)	108 (94.7)
t-AML	n (%)	6 (5.3)
WBC (G/L)	**n /missing**	**114/0**
	Median [IQR]	4.99 [2.22;11.06]
	Min ; Max	0.64 ; 137.00

Variable	Statistic	Total N=114
Cytogenetic risk	**n/missing**	**114/0**
Favorable	n (%)	5 (4.4)
Intermediate normal	n (%)	76 (66.7)
Intermediate abnormal	n (%)	32 (28.1)
Not determined	n (%)	1 (0.9)
Missing	n (%)	0 (0.0)
ELN2022	**n/missing**	**114/0**
Favorable	n (%)	33 (28.9)
Intermediate	n (%)	31 (27.2)
Adverse	n (%)	44 (38.6)
not determined	n (%)	6 (5.3)
Missing	n (%)	0 (0.0)
NPM1 mutation	**n/missing**	**114/0**
No	n (%)	71 (62.3)
Yes	n (%)	43 (37.7)
Missing	n (%)	0 (0.0)
FLT3 mutation	**n/missing**	**111/3**
No	n (%)	73 (65.8)
Yes	n (%)	38 (34.2)
Missing	n (%)	3 (2.6)

ELN 2022 risk classification



ELN 2022 risk	N = 114 (%)
Favorable	33 (29%)
Intermediate	31 (27%)
Adverse	44 (39%)
Not determined	6 (5%)

E. Delabesse; L. Largeaud

Response to induction

Response	All patients - n (%)
CR	77 (67.5)
CRi	7 (6.1)
CRp	11 (9.7)
CR/CRi/CRp	**95 (83.3)**
Refractory	14 (12.3)
Toxic death	5 (4.4)

Adverse events during induction

	Statistic	Total N=114 (%)
Grade 3-4 infections	n/missing	114/0
Yes	n (%)	53 (46.5)
Grade 3-4 mucositis	n/missing	114/0
Yes	n (%)	20 (17.5)
Grade 3-4 GI events	n/missing	114/0
Yes	n (%)	9 (7.9)
Grade 3-4 hepatic events	n/missing	114/0
Yes	n (%)	14 (12.3)
Grade 3-4 hyperglycemia	n/missing	114/0
Yes	n (%)	12 (10.5)
Grade 3-4 pulmonary events	n/missing	114/0
Yes	n (%)	8 (7.0)
Grade 3-4 cardiac events	n/missing	114/0
Yes	n (%)	7 (6.1)
Grade 3-4 bleeding events	n/missing	114/0
Yes	n (%)	5 (4.4)

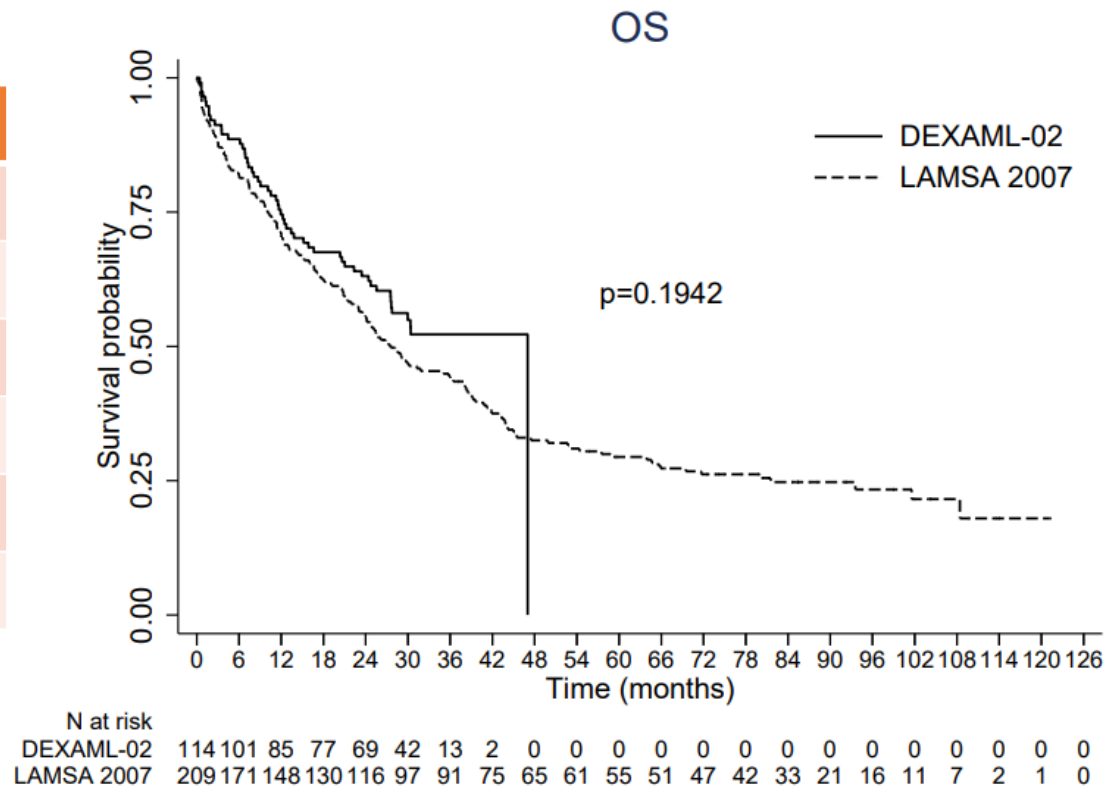
	Early deaths - n (%)
Day-30	4 (3.5%)
Day-60	9 (7.9%)

Overall survival

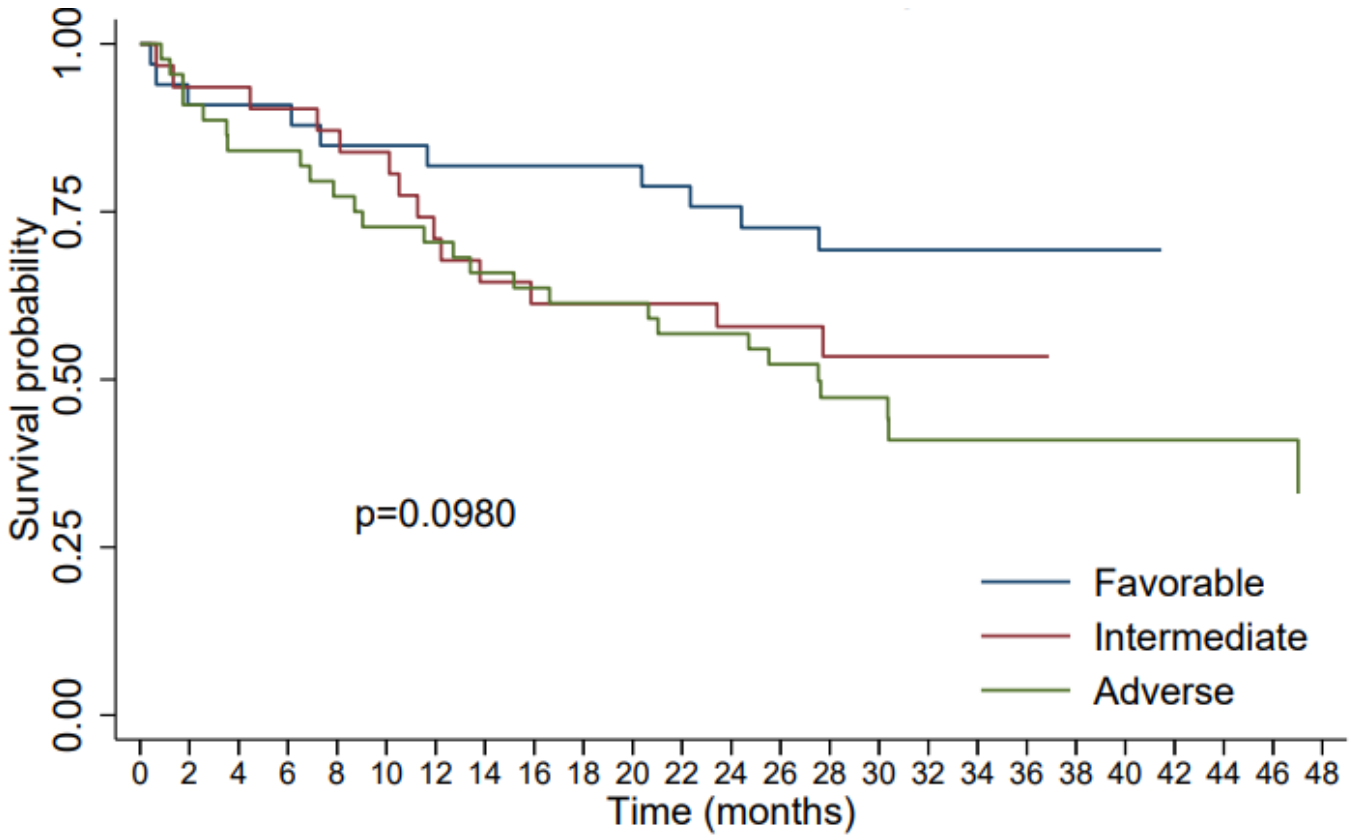
	DEXAML-02
Median FU (months, IQR)	32 (28.2-35.5)
Median OS (months, IQR)	**47.0 (11.9-47.0)**
1-y OS (95%CI)	74.5% (65.5-81.6)
2y-OS	63.1% (53.5-71.2)
3-y OS	52.2 (42.2-61.3)
5y-OS	-

OS (DEXAML-02 vs. LAMSA-2007)

	DEXAML-02	LAM-SA 2007*
Median FU (months, IQR)	32 (28.2-35.5)	86.7 (78.1-88.9)
Median OS (months, IQR)	**47.0 (11.9-47.0)**	**27.6 (10.2-81.5)**
1-y OS (95%CI)	74.5% (65.5-81.6)	70.8% (64.1-76.5)
2y-OS	63.1% (53.5-71.2)	55.5% (48.5-61.9)
3-y OS	52.2 (42.2-61.3)	44.4% (37.6-51.0)
5y-OS	-	29.4% (23.3-35.8)



OS according to ELN 2022 risk classification



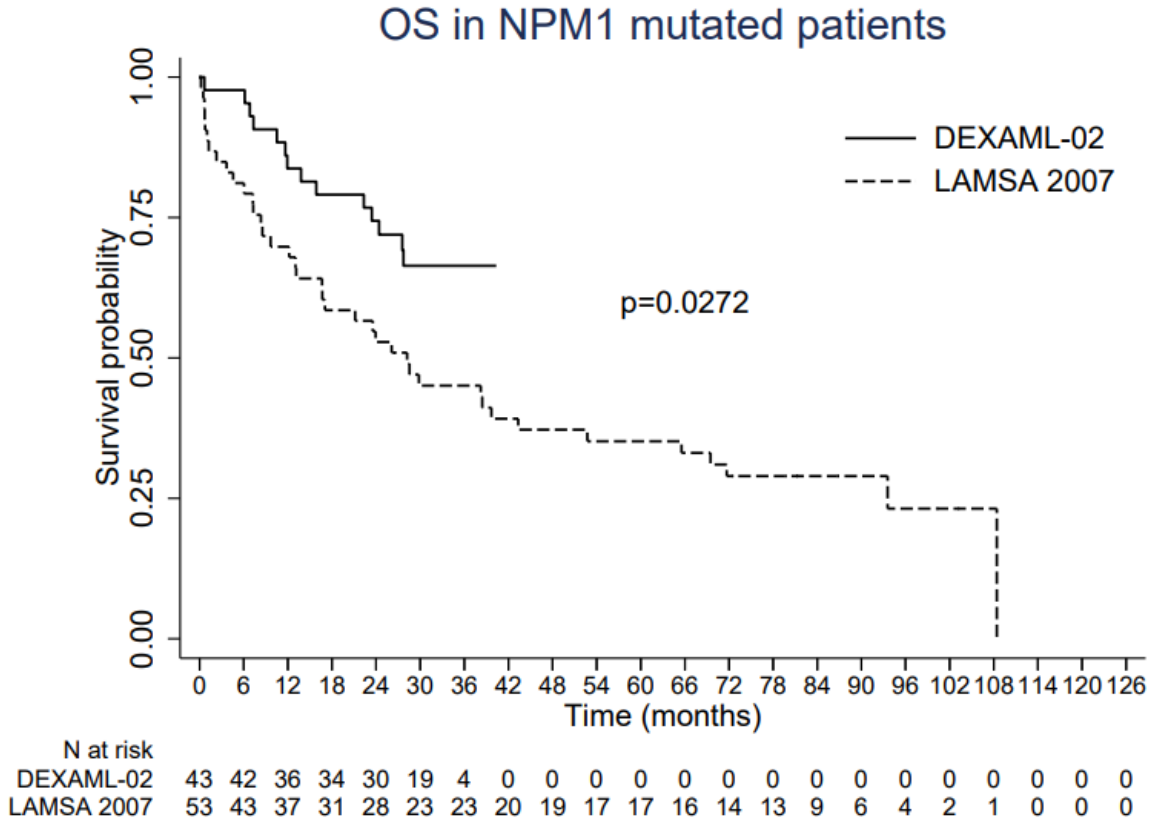
N at risk																								
Favorable	33	30	30	30	28	28	27	27	27	27	27	26	24	23	21	18	10	6	4	2	2	0	0	0	0
Intermediate	31	29	29	28	27	26	22	20	19	19	18	18	17	16	11	8	8	6	2	0	0	0	0	0	0
Adverse	44	40	37	37	34	32	31	29	28	27	27	25	25	22	18	15	11	9	7	5	4	2	1	1	0

DEXAML-02 in patients with *NPM1* mutation

Response	All patients - n (%)	NPM1 mut - n (%)
CR	77 (67.5)	38 (88.4)
CRi	7 (6.1)	2 (4.7)
CRp	11 (9.7)	1 (2.3)
CR/CRi/CRp	**95 (83.3)**	41 (95.4)
Refractory	14 (12.3)	1 (2.3)
Toxic death	5 (4.4)	1 (2.3)

DEXAML-02 in patients with *NPM1* mutation

	DEXAML-02	LAM-SA 2007
Median OS (months, IQR)	NR (23.4-NR)	28.2 (8.3-93.6)
1y-OS (95%CI)	83.7% (68.9-91.9)	69.8% (55.5-80.3)
2y-OS	74.4% (58.6-84.9)	52.8 % (38.6-65.2)
3y-OS	66.4% (49.8-78.6)	45.1% (31.4-57.8)
5y-OS	-	35.2 (22.6-48.0)



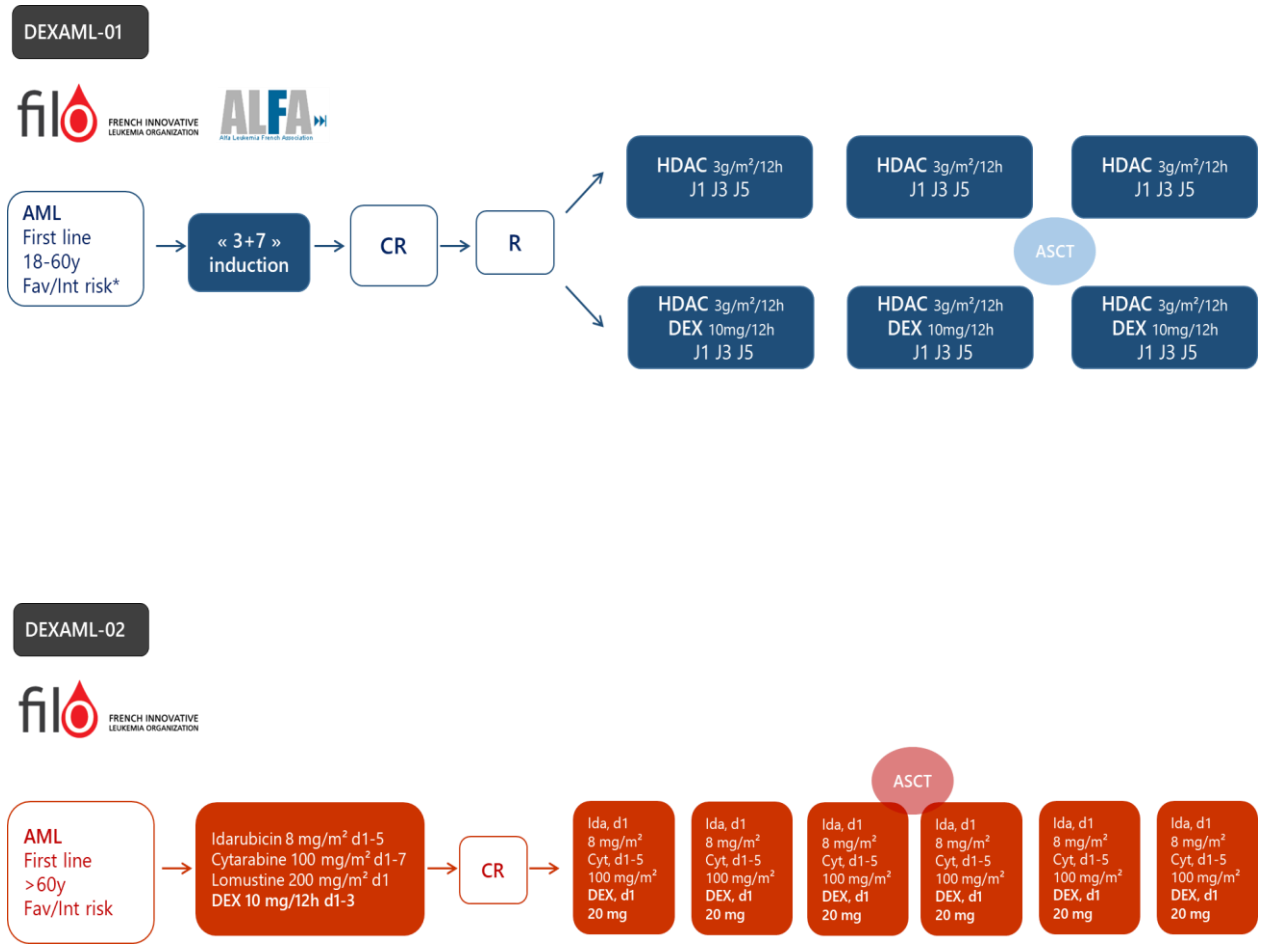
Preliminary conclusion

- In older AML patients who are eligible for intensive treatment, adding dexamethasone to induction and consolidation chemotherapy is feasible and associated with a high response rate after a single induction cycle and encouraging overall survival compared to a historical cohort.

- Patients with *NPM1* mutation may particularly benefit from dexamethasone.

- Theoretically, this finding deserves confirmation in a phase 3 randomized trial.

Programmes DEXAML



Merci de votre attention….sans vous, on ne peut rien faire!