V JORNADA ONCOFARMA

Actualización en el manejo de la Leucemia Mieloide Aguda en el paciente adulto y pediátrico

GEDEFO Centro - Canarias y Cataluña - Baleares

MANEJO DE LA LEUCEMIA MIELOIDE AGUDA EN PRIMERA LÍNEA EN EL PACIENTE ADULTO

José Luis López Lorenzo

Hospital Universitario Fundación Jiménez Díaz, Madrid

ORGANIZA:

sefh Sociedad Española de Farmacia Hospitalaria

fefh Fundación Española de Farmacia Hospitalaria

gedefo Grupo de Farmacia Oncológica de la sefh

MANEJO DE LA LEUCEMIA MIELOIDE AGUDA (LAM) EN PRIMERA LÍNEA EN EL PACIENTE ADULTO

José Luis López Lorenzo

Hematólogo

Fundación Jiménez Díaz- Madrid

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WEBINAR V JORNADA ONCOFARMA

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Agenda

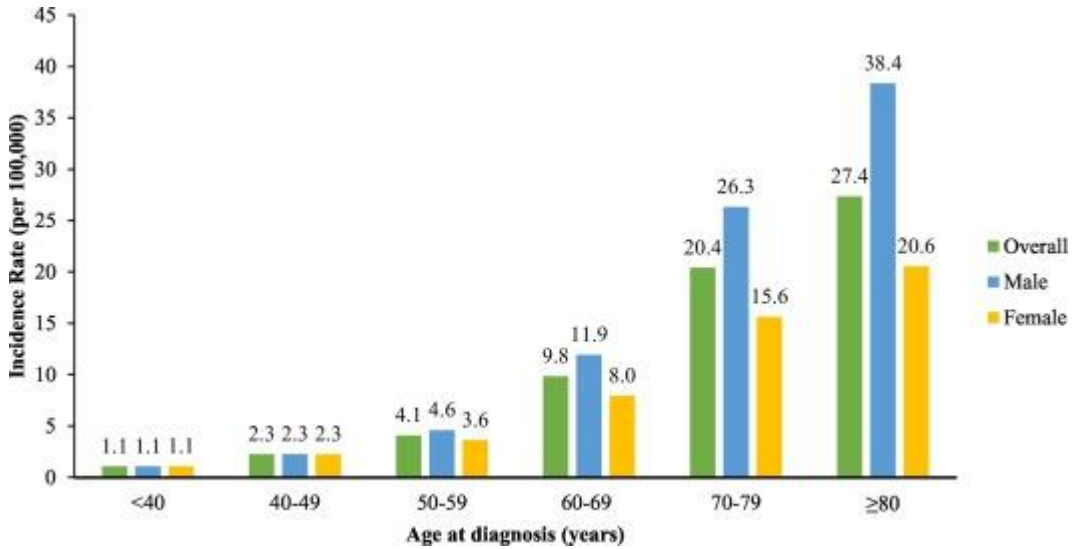
- Introducción a la LAM
- Tratamiento de primera línea de la LAM
  - ➢Paciente candidato a quimioterapia intensiva
  - ➢Paciente NO candidato a quimioterapia intensiva

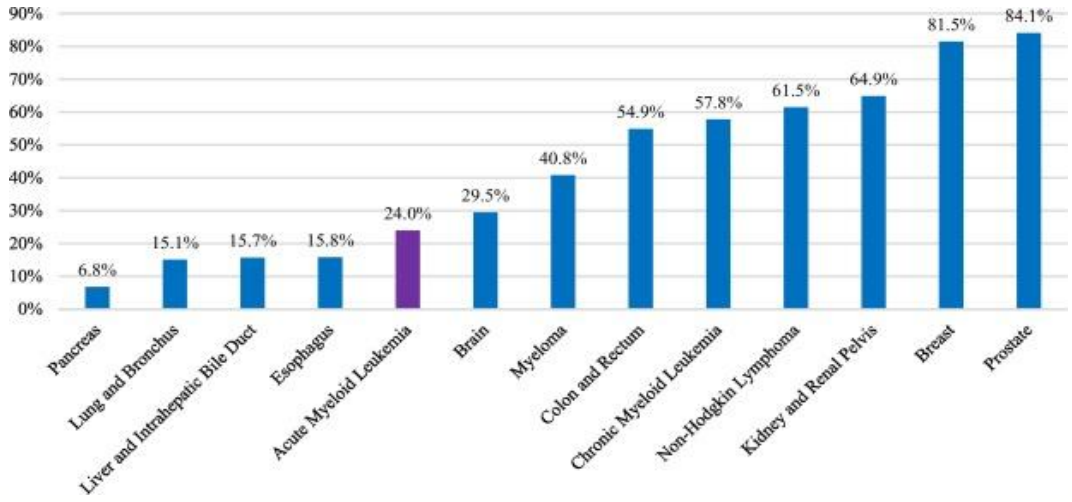
Introducción a la LAM

- Epidemiologia
- Patogénesis
- Clasificación
- Diagnóstico
- Pronóstico

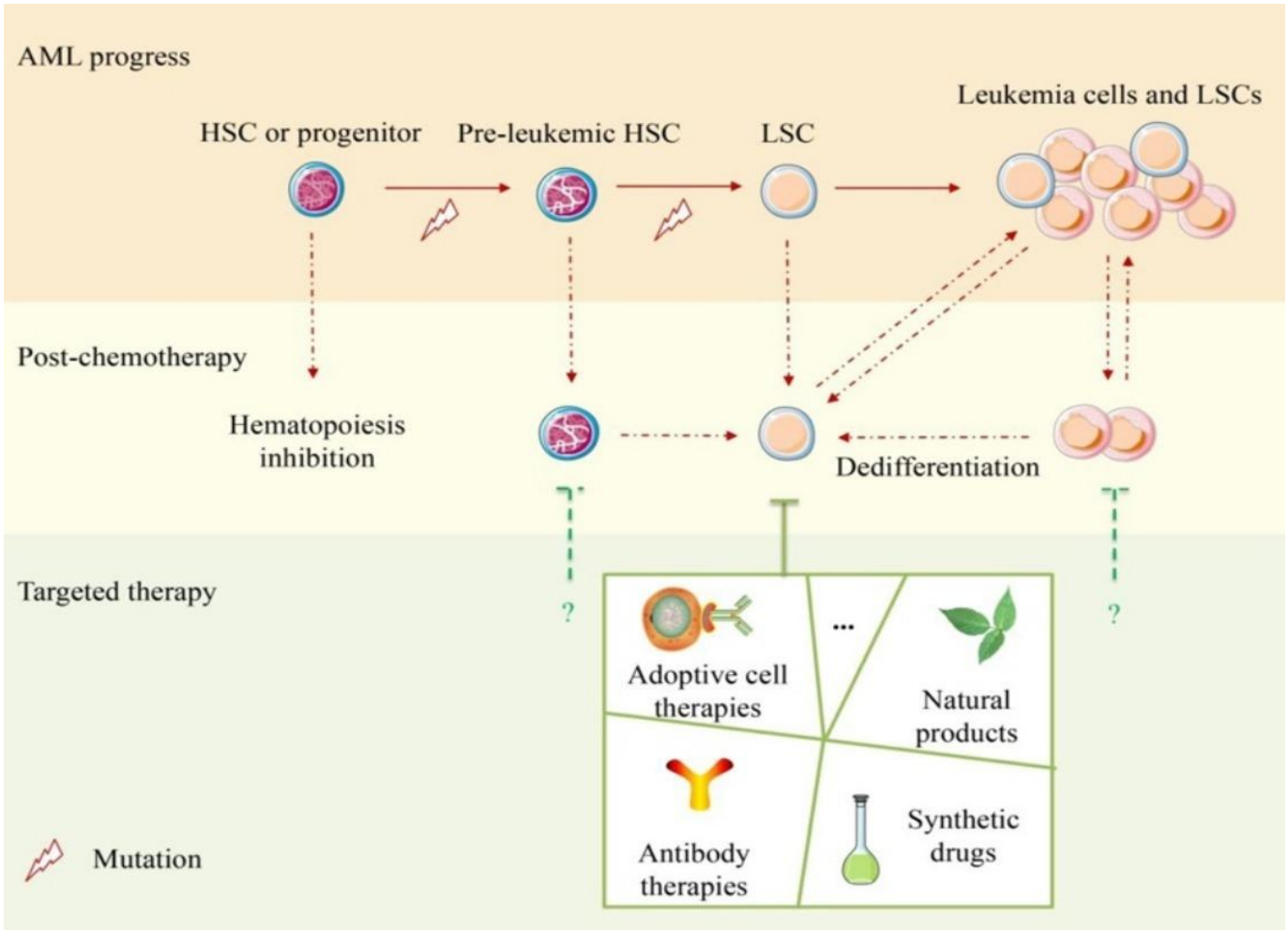
EPIDEMIOLOGIA

- 3-5/100.000 habitantes
- Media 68 años
- SG a 5 años 24%





Patogenesis



Patogenia

- Enfermedad clonal
- Lesión genetica. > 100 alteraciones. Protooncogenes, genes supresores tumorales y genes responsables de integridad genoma.
- Enfermedad epigenetica: microRNA, metilacion y acetilacion.
- Anomalias cromosomicas detectables
- Mutaciones puntuales

Patogenia

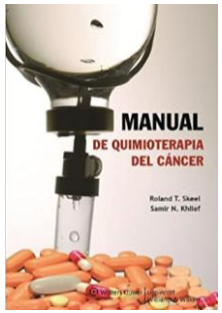
DESCONOCIDA

HEREDITARIAS

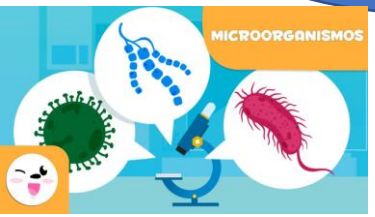
EXPOSICIONES AMBIENTALES

CAUSA

QUIMIOTERAPIA



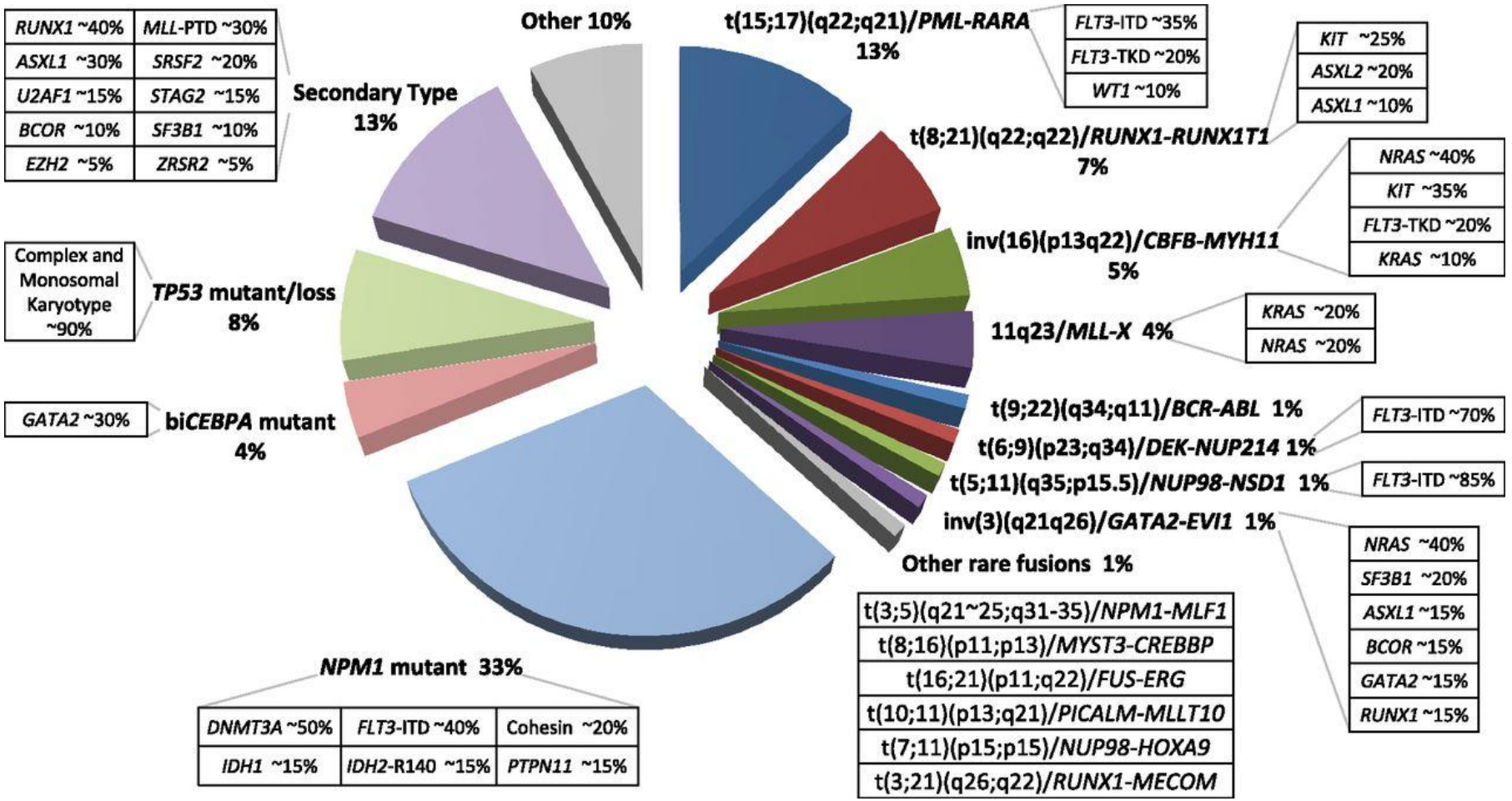
INFECCIONES??



OTRAS CAUSAS??

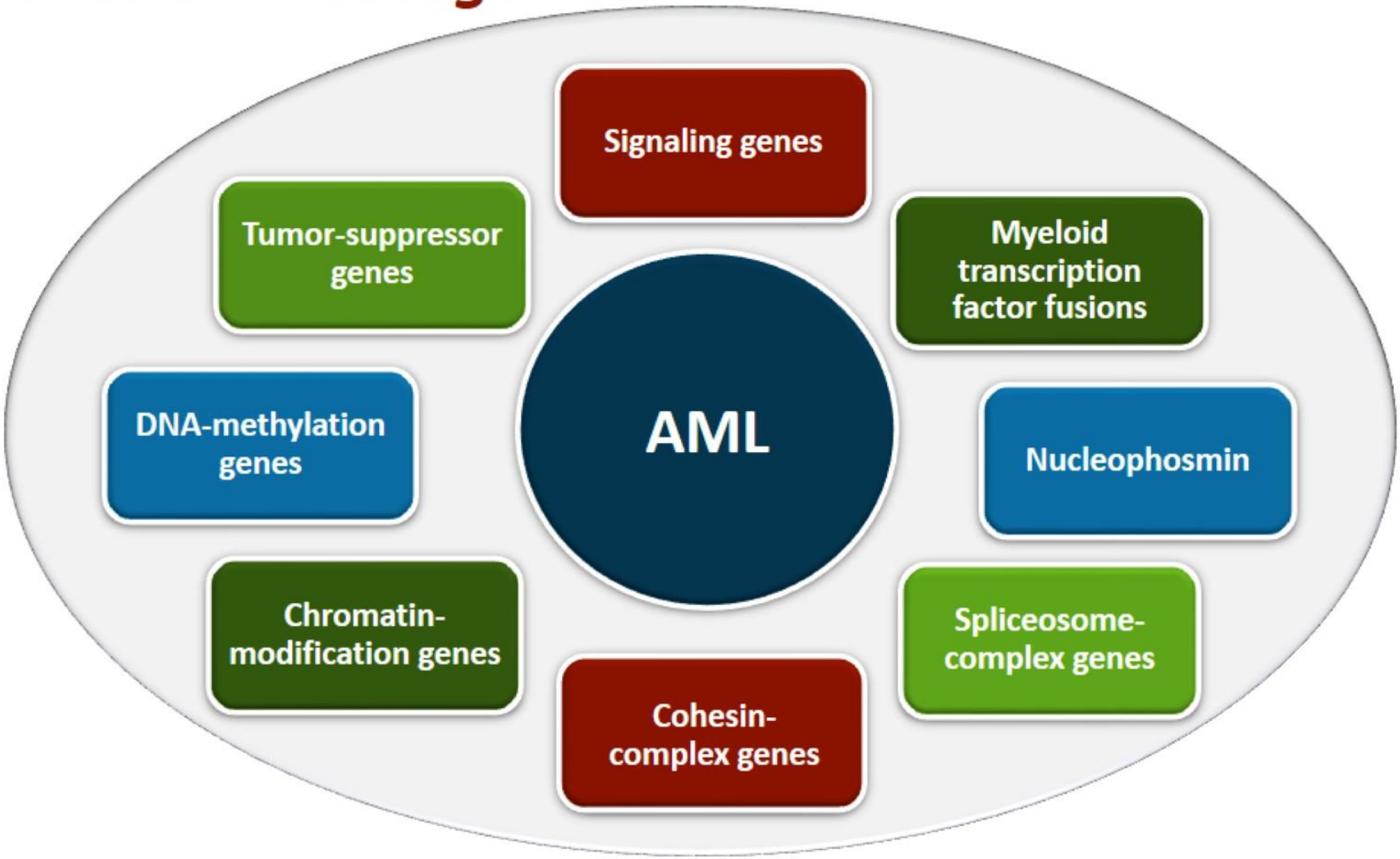
RADIOTERAPIA

Alteraciones citogeneticas y moleculares en la LMA adulto joven



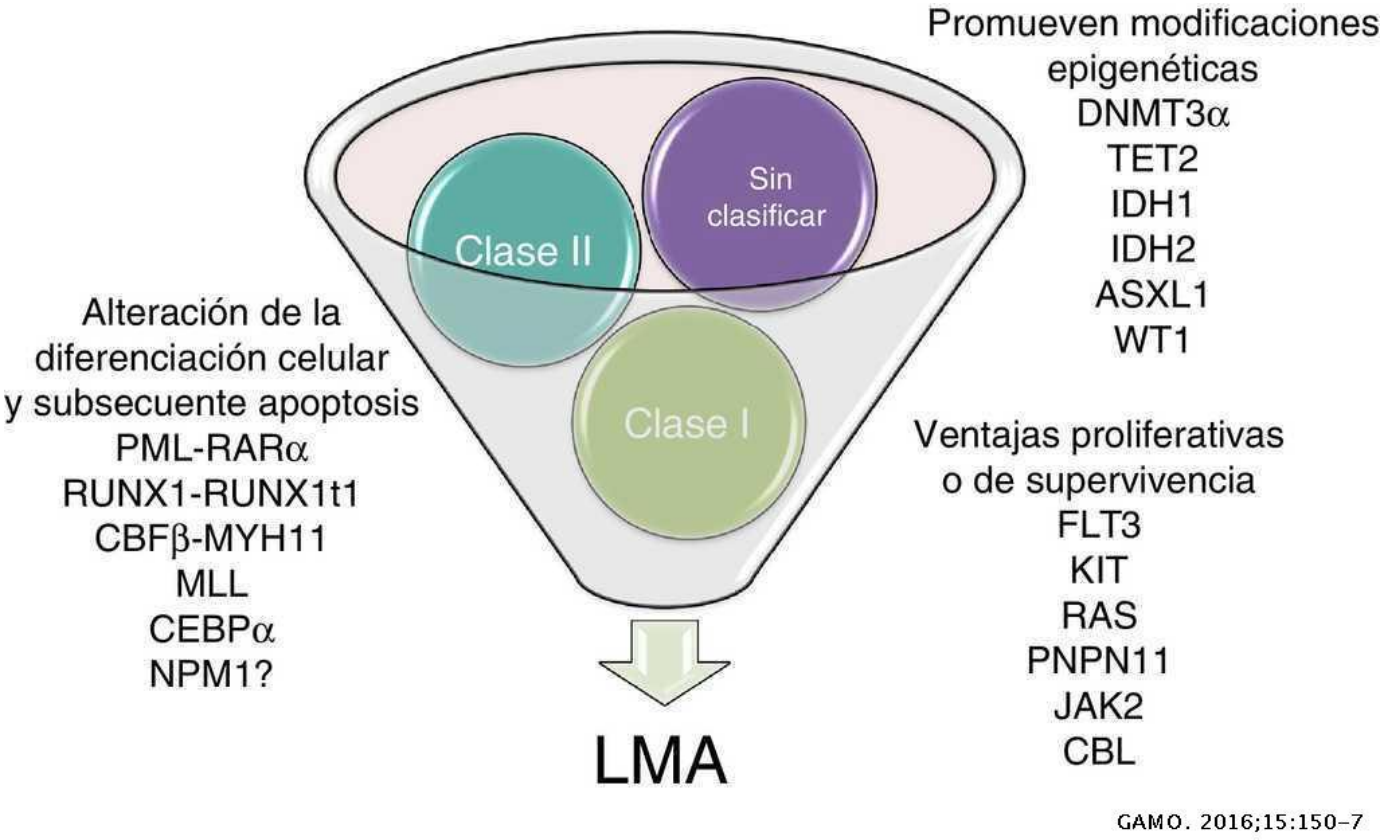
David Grimwade,Adam Ivey,Brian J. P. Huntly, Molecular landscape of acute myeloid leukemia in younger adults and its clinical relevance, Blood, 2016, Figure 1

Genetic Mutations in AML
Functional Categories



Döhner H, et al. *N Engl J Med* 2015;373:1136-1152.

Patogenesis



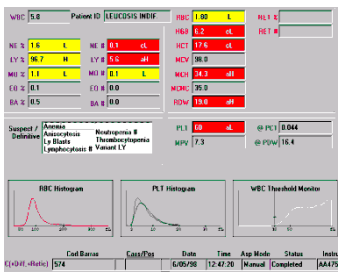
GAMO. 2016;15:150–7

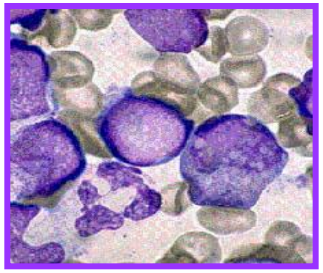
DIAGNÓSTICO DE LA LMA

CLÍNICA

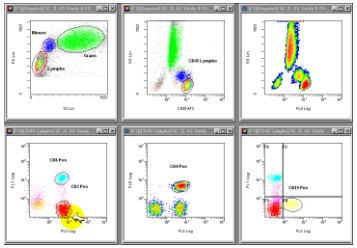
MORFOLOGÍA

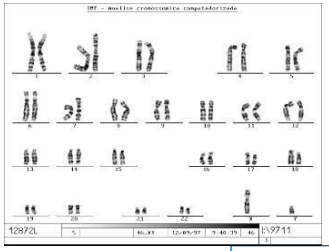
CITOQUÍMICA





DIAGNÓSTICO





CITOMETRÍA DE FLUJO

CITOGENÉTICA + FISH

BIOLOGÍA MOLECULAR

Clasificación actual

Table 1. Myeloid neoplasms with germ line predisposition, AML and related precursor neoplasms, and acute leukemias of ambiguous lineage (WHO 2016)

Myeloid neoplasms with germ line predisposition (see Table 2)	
AML and related neoplasms	**AML and related neoplasms (cont'd)**
AML with recurrent genetic abnormalities	Acute myelomonocytic leukemia
AML with t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*	Acute monoblastic/monocytic leukemia
AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*	Pure erythroid leukemia#
Acute promyelocytic leukemia with *PML-RARA**	Acute megakaryoblastic leukemia
AML with t(9;11)(p21.3;q23.3); *MLLT3-KMT2A*†	Acute basophilic leukemia
AML with t(6;9)(p23;q34.1); *DEK-NUP214*	Acute panmyelosis with myelofibrosis
AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2,MECOM(EVI1)*	Myeloid sarcoma
AML (megakaryoblastic) with t(1;22)(p13.3;q13.3); *RBM15-MKL1*‡	Myeloid proliferations related to Down syndrome
Provisional entity: AML with *BCR-ABL1*	Transient abnormal myelopoiesis
AML with mutated *NPM1*§	Myeloid leukemia associated with Down syndrome
AML with biallelic mutations of *CEBPA*§	Blastic plasmacytoid dendritic cell neoplasm
Provisional entity: AML with mutated *RUNX1*	**Acute leukemias of ambiguous lineage**
AML with myelodysplasia-related changes‖	Acute undifferentiated leukemia
Therapy-related myeloid neoplasms¶	MPAL with t(9;22)(q34.1;q11.2); *BCR-ABL1***
AML, NOS	MPAL with t(v;11q23.3); *KMT2A* rearranged
AML with minimal differentiation	MPAL, B/myeloid, NOS
AML without maturation	MPAL, T/myeloid, NOS
AML with maturation	

Clasificación OMS 2016

LMA CON ANOMALIAS GENETICAS RECURRENTES
T(8, 21), inv16,t(15,17), t(6.9) t(9.11)t(3,3),NPM1 ,

LMA NO ESPECIFICADA DE OTRO MODO
Basado en morfologia

LMA CON CAMBIOS RELACIONADOS CON MIELODISPLASIA

LMA ASOCIADAS A PREDISPOSICION LINEA GERMINAL

LMA RELACIONADA CON TERAPIA

SARCOMA MIELOIDE, LMA ASOCIADA A SD DOWN, LEUCEMIAS AMBIGUAS

Pronóstico

Factores clínicos:

- ✓Edad
- ✓Estado general
- ✓Tratamientos previos
- ✓Enfermedades hematologicas

Factores citog/moleculares:

- ✓**Cariotipo**
- ✓**Mutaciones**

Table 5. 2017 ELN risk stratification by genetics

Risk category*	Genetic abnormality
Favorable	t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*
	inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*
	Mutated *NPM1* without *FLT3*-ITD or with *FLT3*-ITD^{low}†
	Biallelic mutated *CEBPA*
Intermediate	Mutated *NPM1* and *FLT3*-ITD^{high}†
	Wild-type *NPM1* without *FLT3*-ITD or with *FLT3*-ITD^{low}† (without adverse-risk genetic lesions)
	t(9;11)(p21.3;q23.3); *MLLT3-KMT2A*‡
	Cytogenetic abnormalities not classified as favorable or adverse
Adverse	t(6;9)(p23;q34.1); *DEK-NUP214*
	t(v;11q23.3); *KMT2A* rearranged
	t(9;22)(q34.1;q11.2); *BCR-ABL1*
	inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2,MECOM(EVI1)*
	−5 or del(5q); −7; −17/abn(17p)
	Complex karyotype,§ monosomal karyotype‖
	Wild-type *NPM1* and *FLT3*-ITD^{high}†
	Mutated *RUNX1*¶
	Mutated *ASXL1*¶
	Mutated *TP53*#

Genetic Risk Group	Frequency	Survival	ELN 2017 Subset
Favorable	15%	65-75%	▪ t(8;21)(q22;q22); *RUNX1-RUNX1T1* ▪ inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11* ▪ Mutated *NPM1* without *FLT3*-ITD or *FLT3*-ITD ^{low} ▪ Biallelic mutated *CEBPA*
Intermediate	55%	50-55%	▪ Mutated *NPM1* and *FLT3*-ITD ^{high} ▪ Wild-type *NPM1* without *FLT3*-ITD or *FLT3*-ITD ^{low} (without adverse-risk genetic lesions) ▪ t(9;11)(p22;q23); *MLLT3-MLL* ▪ Any cytogenetics not classified as favorable or adverse
Adverse	30%	20-25%	▪ t(6;9)(p23;q34); *DEK-NUP214* ▪ t(v;11)(v;q23); *MLL (KMT2A)* rearranged ▪ Inv(3)(q21q26.2) or t(3;3)(q21;q26.2); *RPN1-EVI1 (GATA2, MECOM (EVI1)* ▪ t(9;22)(q34.1;q11.2) *BCR-ABL1* ▪ Monosomy 5 or del(5q); monosomy 7; monosomy 17; abnormal 17p ▪ Complex karyotype(≥ 3 abnormalities) or monosomal karyotype ▪ Wild-type *NPM1* and *FLT3*-ITD ^{high} ▪ Mutated *RUNX1* ▪ Mutated *ASXL1* ▪ Mutated *TP53*

Döhner H, et al. *Blood.* 2017;129(4):424-447.

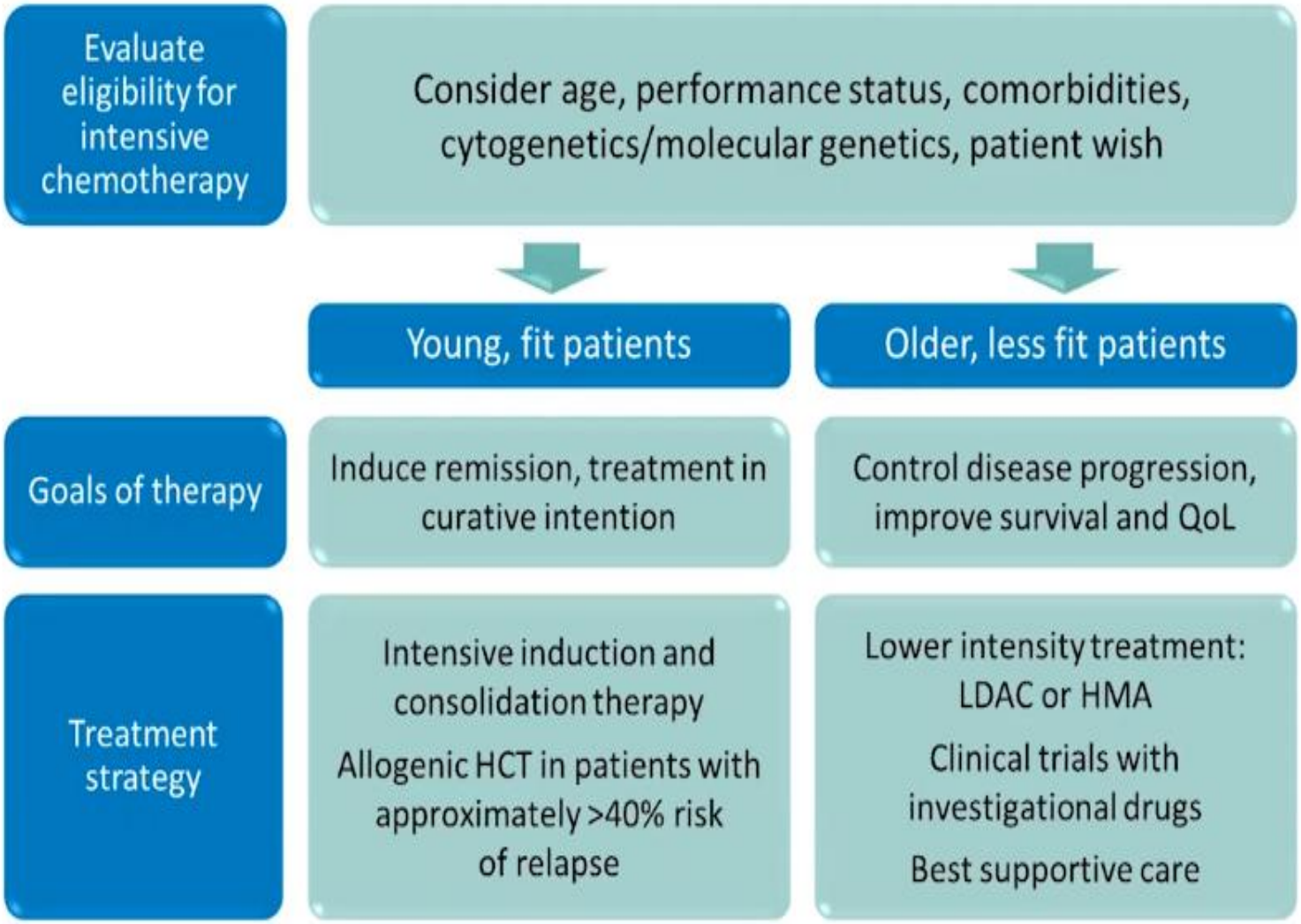
TRATAMIENTO LMA

- SOPORTE
  - ✓TRANSFUSIONES
  - ✓SD LISIS TUMORAL
  - ✓INFECCIONES….
- TRATAMIENTO DIRIGIDO A ERRADICAR LA LEUCEMIA
  - ➢QUIMOTERAPICO CLASICO
  - ➢TRASPLANTE HEMATOPOYETICO
  - ➢TRATAMIENTOS DIRIGIDOS A DIANAS ESPECIFICAS

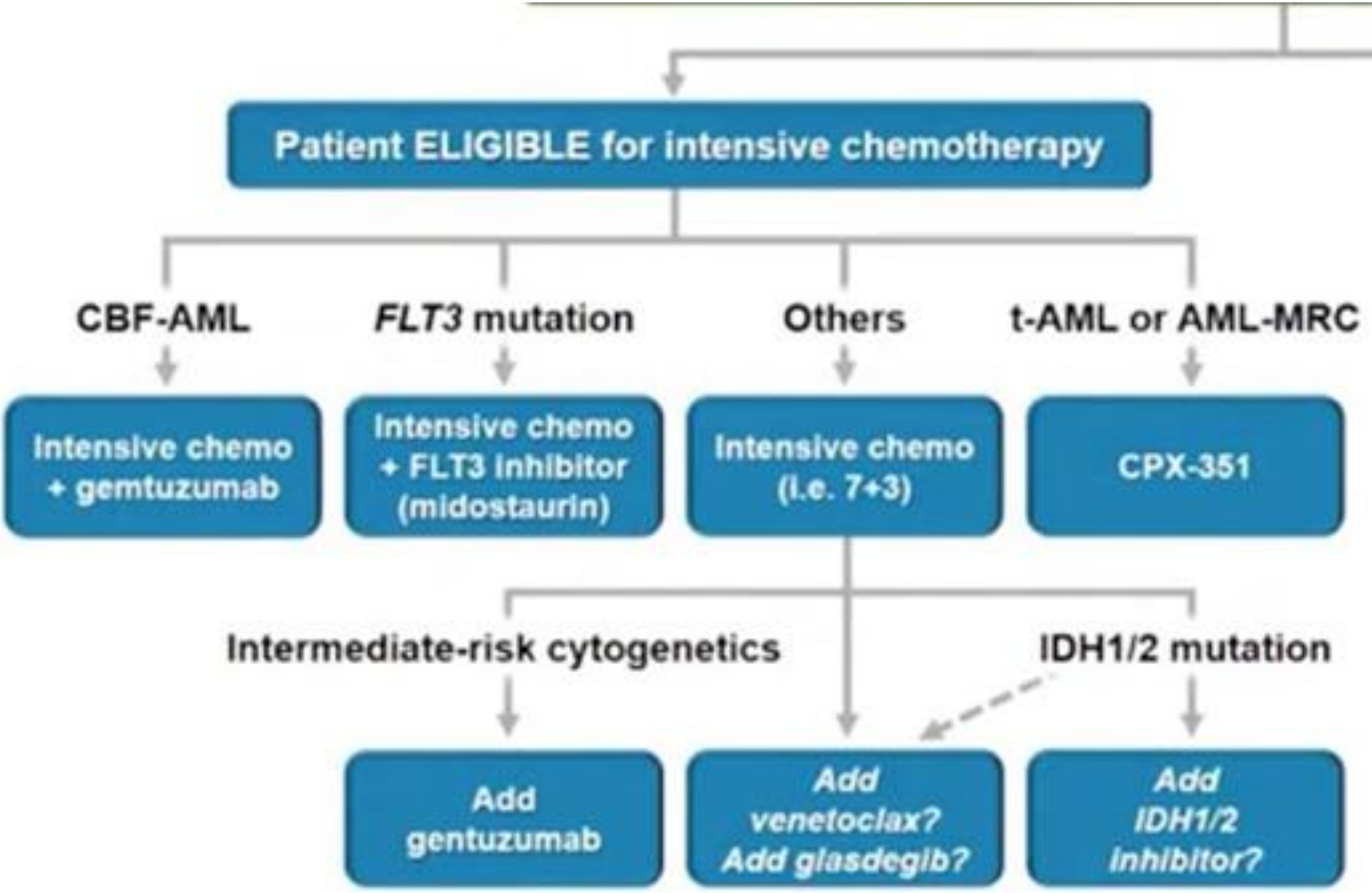
TRATAMIENTO ANTILEUCEMICO

- INTENSIVO
  1. TTO INDUCCION
  2. TTO POSTREMISION
     - ➢ QUIMIOTERAPIA
     - ➢ AUTOTRASPLANTE
     - ➢ ALOTRASPLANTE
     - ➢ MANTENIMIENTO
- BAJA INTENSIDAD
  - ✓DOSIS BAJAS ARAC, HIPOMETILANTES, NUEVOS FARMACOS

Vision actual del tratamiento de primera línea



Döhner H, *et al. Blood* 2017; **129(4)**

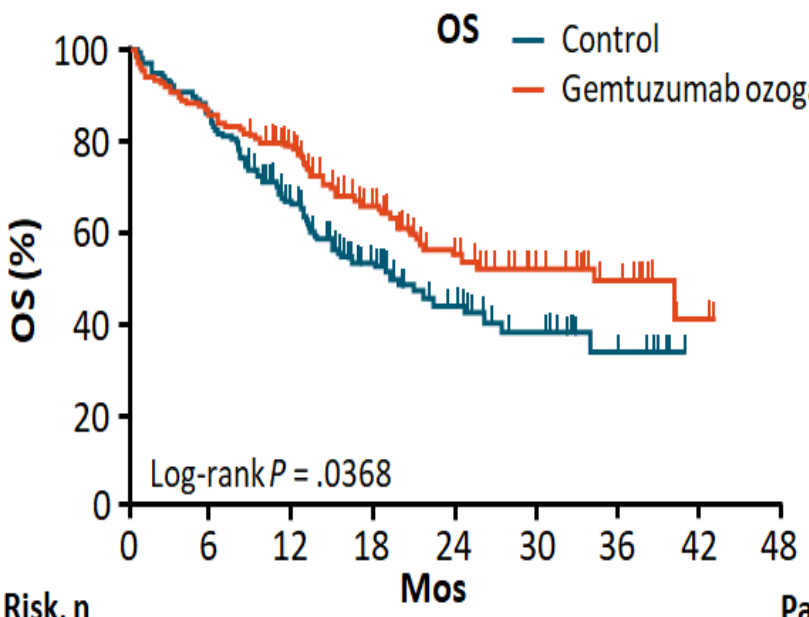

Patient ELIGIBLE for intensive chemotherapy
CBF-AML
FLT3 mutation
Others
t-AML or AML-MRC
Intensive chemo + gemtuzumab
Intensive chemo + FLT3 inhibitor (midostaurin)
Intensive chemo (i.e. 7+3)
CPX-351
Intermediate-risk cytogenetics
IDH1/2 mutation
Add gentuzumab
Add venetoclax? Add glasdegib?
Add IDH1/2 inhibitor?

Novedades en tratamiento LMA

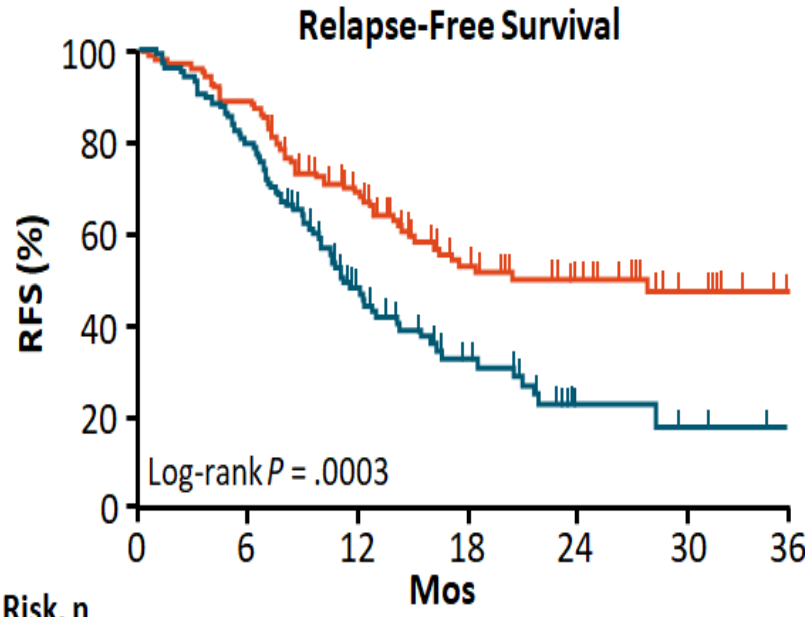
- Gemtuzumab ozogamicina
- Midostaurina
- CPX351
- *"Venetoclax"*

Standard Induction Chemotherapy ± Gemtuzumab Ozogamicin for Newly Diagnosed CD33+ AML

- Gemtuzumab ozogamicin 3 mg/m^2 on Days 1, 4, 7 of induction and Day 1 of each consolidation cycle



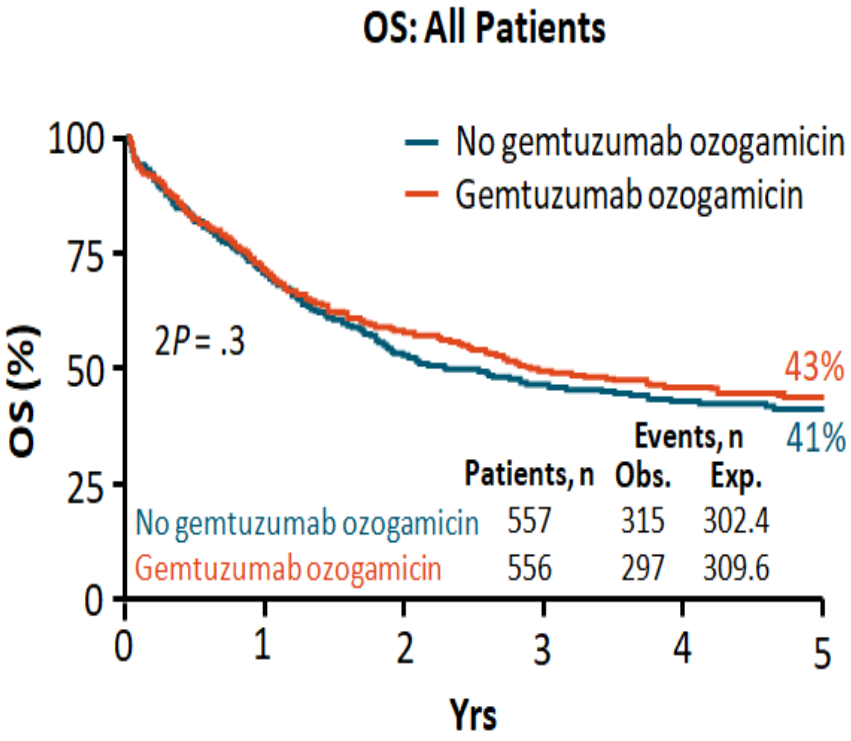
Patients at Risk, n									
Control	139	117	82	45	26	16	6	0	0
Gemtuzumab ozogamicin	139	118	98	66	43	25	16	4	0

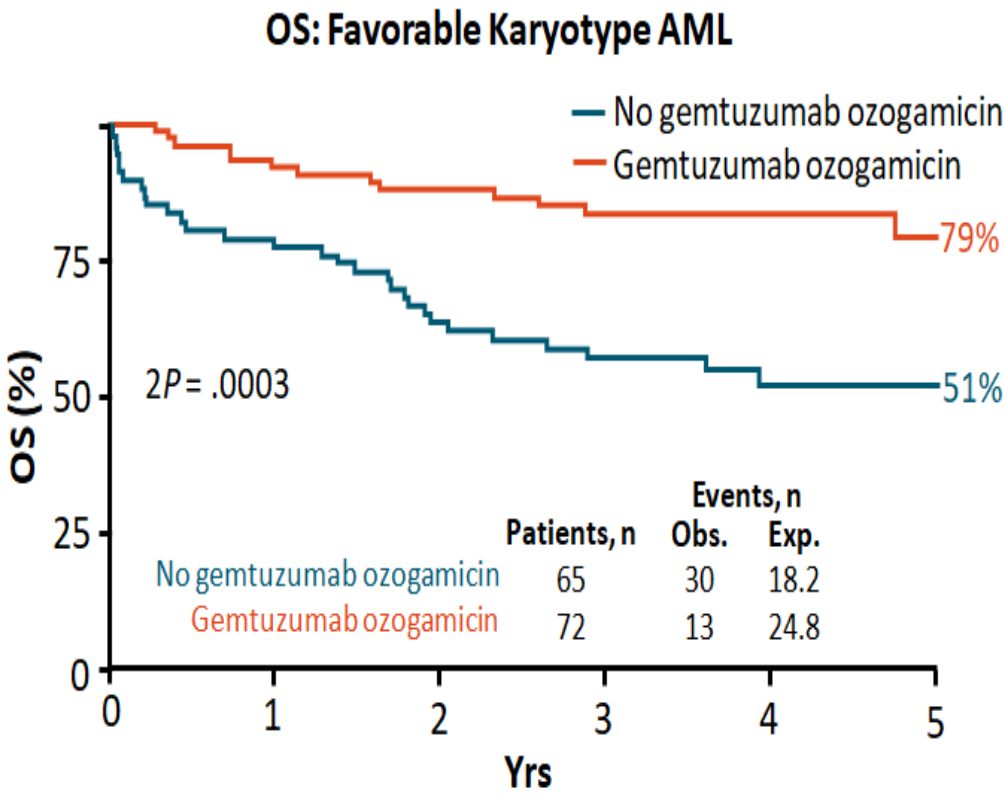


Patients at Risk, n							
Control	104	83	39	19	6	3	1
Gemtuzumab ozogamicin	113	101	68	41	29	16	8

Castaigne. Lancet. 2012;379:1508.

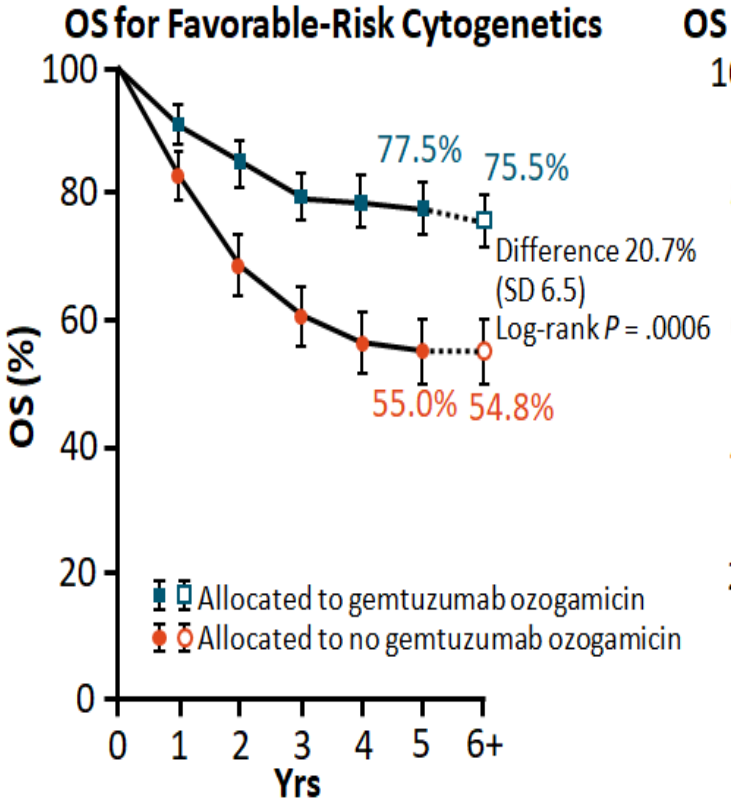
AML15: Addition of Gemtuzumab Ozogamicin to Cytarabine-Based Induction Chemotherapy in AML

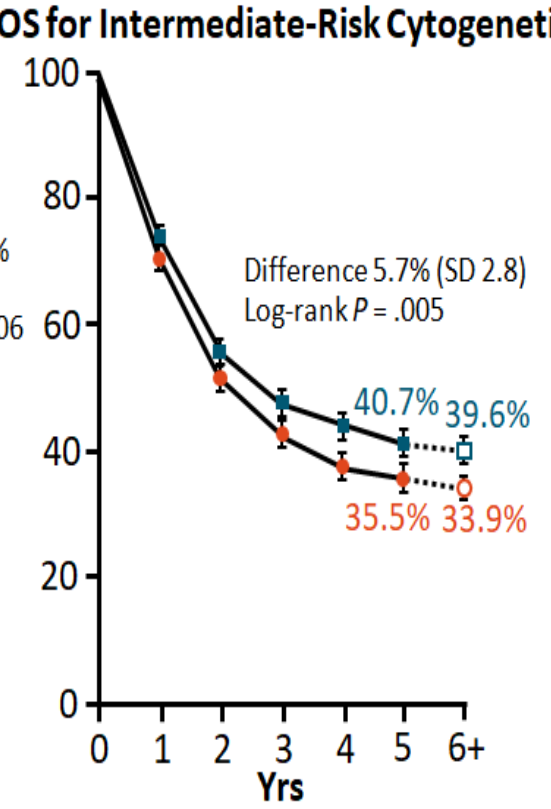


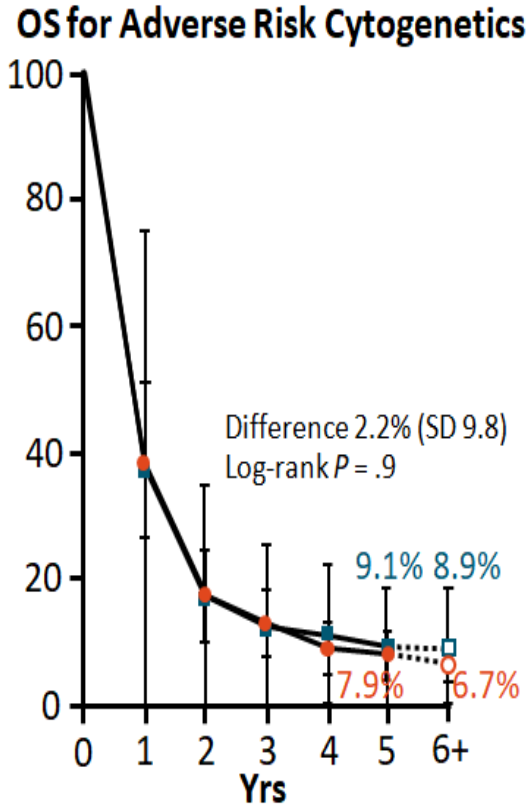


Burnett. J Clin Oncol. 2011;29:369.

Addition of Gemtuzumab Ozogamicin to Induction Therapy: Meta-analysis of 5 Randomized Trials







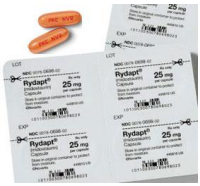
Annual Event Rates	Yrs 1-5	Yrs 6+
Gemtuzumab ozogamicin	5.8% SD 1.1	2.3% SD 1.3
No gemtuzumab ozogamicin	14.1% SD 1.9	0% SD 0

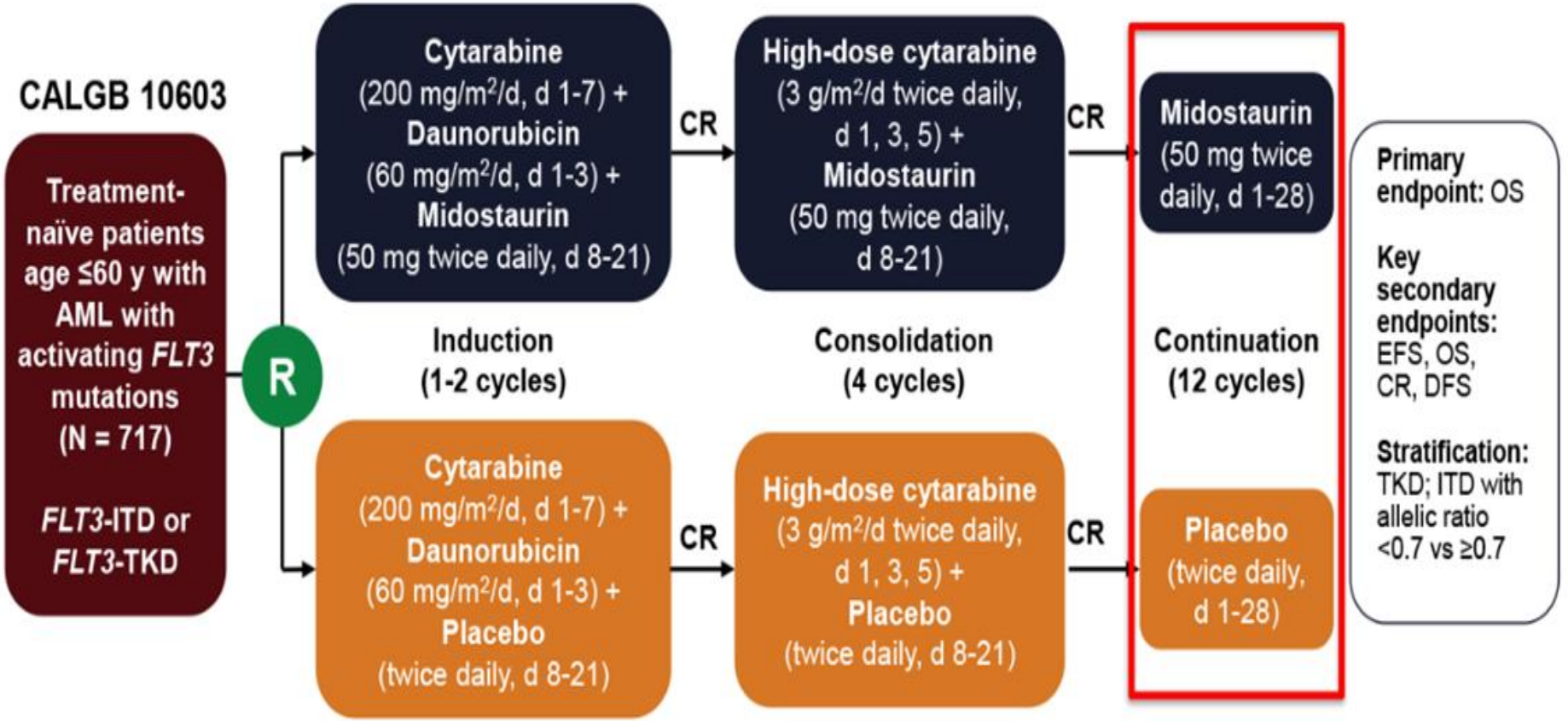
Yrs 1-5	Yrs 6+
22.4% SD 1.0	2.7% SD 0.9
26.2% SD 1.1	4.9% SD 1.3

Yrs 1-5	Yrs 6+
73.8% SD 4.6	2.4% SD 2.4
76.7% SD 4.8	21.1% SD 10.5

Hills. Lancet Oncol. 2014;15:986.

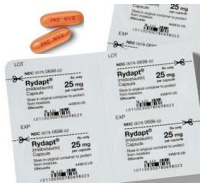
Phase 3 RATIFY Study: Chemotherapy ± Midostaurin in Newly Diagnosed AML[1]



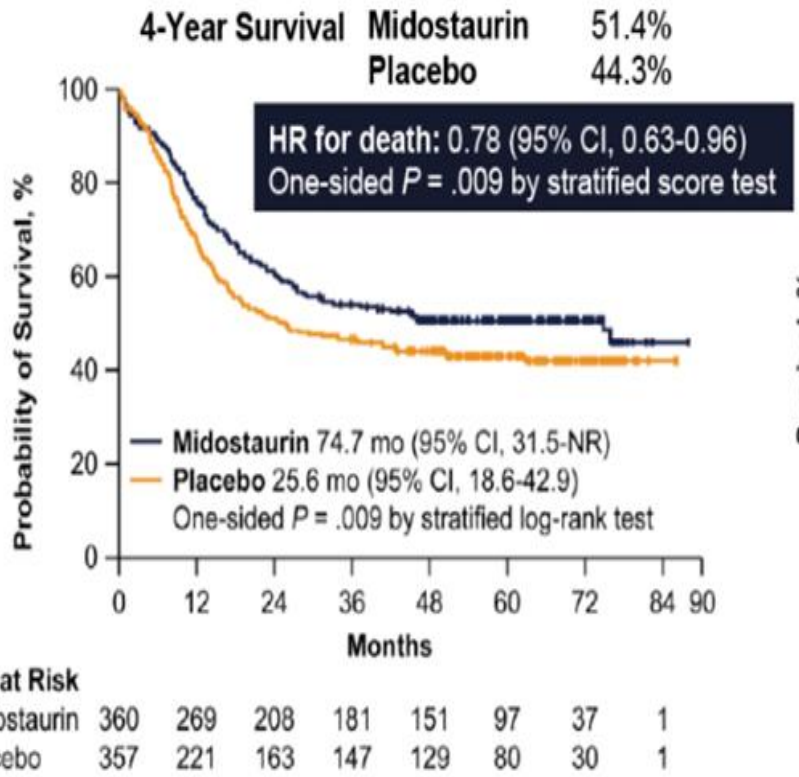


Stone RM, et als . Midostaurin plus Chemotherapy for Acute Myeloid Leukemia with a FLT3 Mutation. N Engl J Med. 2017 Aug 3;377(5):454-464.

RATIFY/C10603 Overall Survival



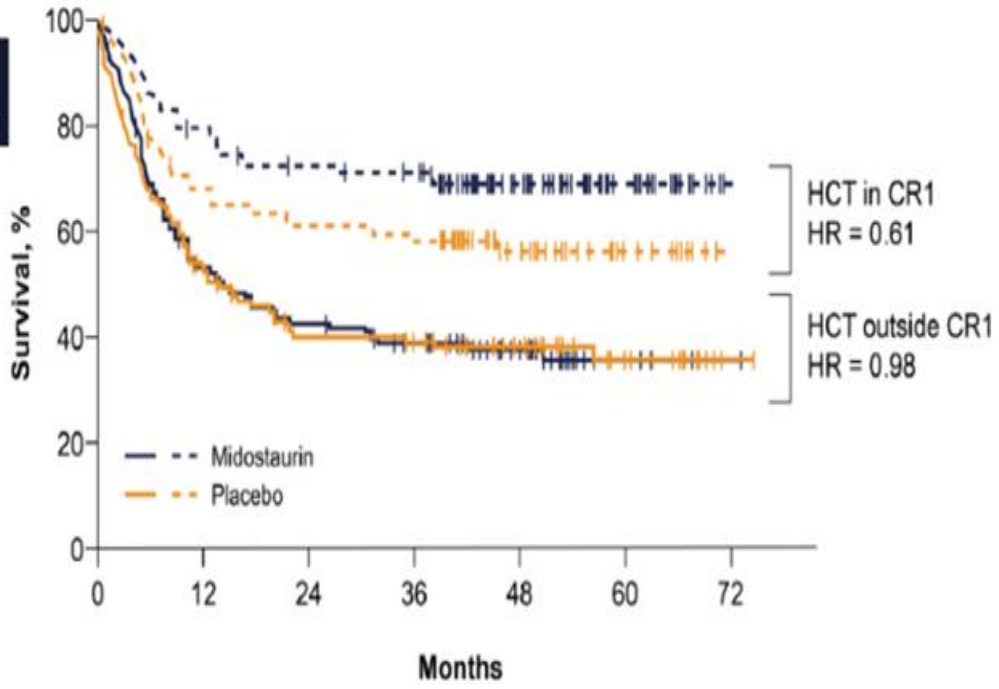
All Patients[1]



No. at Risk

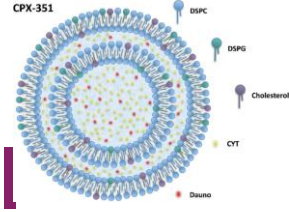
Midostaurin	360	269	208	181	151	97	37	1
Placebo	357	221	163	147	129	80	30	1

Transplanted Patients[2]



Stone RM, et als . Midostaurin plus Chemotherapy for Acute Myeloid Leukemia with a FLT3 Mutation. N Engl J Med. 2017 Aug 3;377(5):454-464.

Vyxeos liposomal está autorizado por procedimiento centralizado, pero no se encuentra comercializado en España.



Ensayo 301 datos a 5 años: Diseño del estudio

Criterios de elegibilidad
- No tratado previamente para LMAs/de alto riesgo
- 60-75 años de edad
- Capaz de tolerar QI
- ECOG PS 0-2

Vyxeos Liposomal (n=153)
- LMA con historia de SMD
  - Hipometilantes previos
  - No Hipometilantes previos
- LMA con historial de LMMC
- LMA *de novo* con CRMD

7+3 (n=156)

Inducción (1-2 ciclos)

Pacientes en CR/CRi: **Consolidación** (1-2 ciclos)

Seguimiento
- Muerte
- 5 años

Este análisis muestra los datos de seguimiento de los pacientes a 5 años

Vyxeos liposomal

1ª Inducción
100 unidades/m². Días 1,3 y 5

Re-Inducción
100 unidades/m². Días 1 y 3

1ª y 2ª Consolidación
65 unidades/m². Días 1 y 3

1 unidad de Vyxeos liposomal = 1mg citarabina + 0,44mg daunorubicina

7+3

100 mg/m²/día citarabina (C)+ 60 mg/m² daunorubicina (D)

1ª Inducción
7 + 3

Re-Inducción
5 + 2

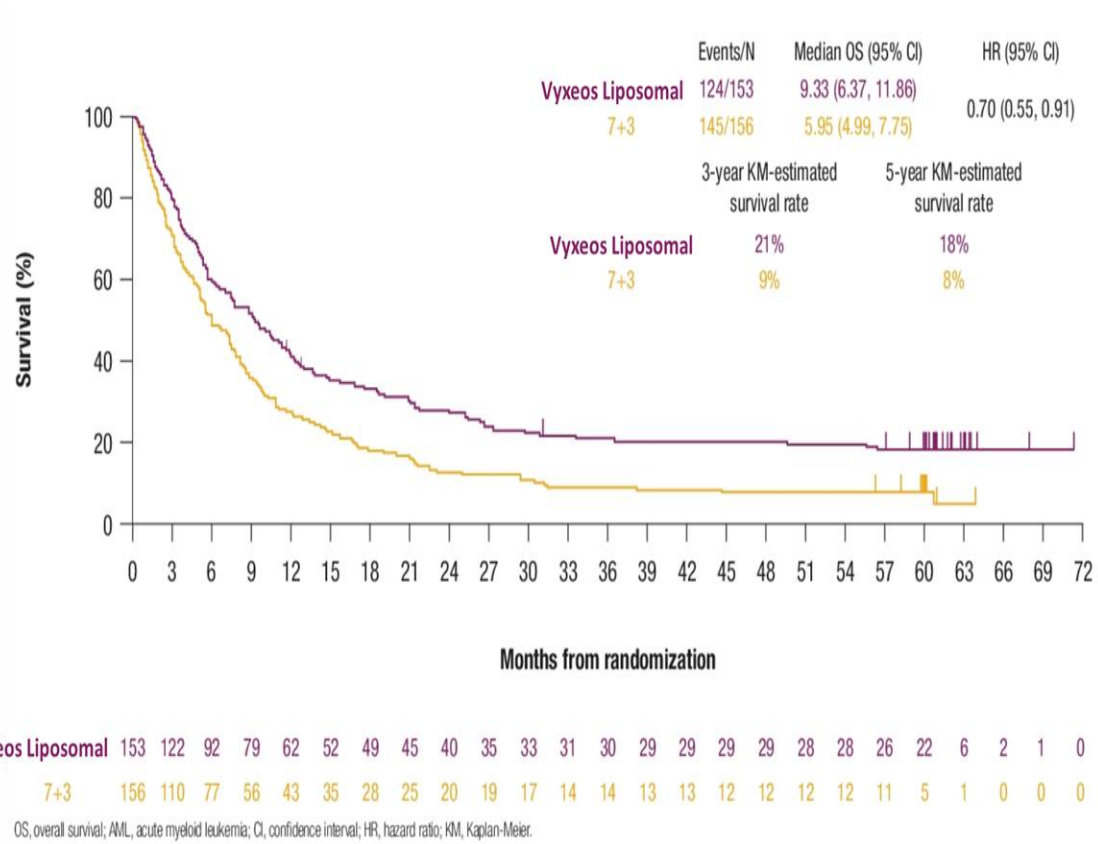
1ª y 2ª Consolidación
5 + 2

Lancet JE, et al. J Clin Oncol 2018;36(26):2684-2692. Lancet JE, et al. J Clin Oncol 38: 2020 (suppl; abstr 7510)

Vyxeos liposomal está autorizado por procedimiento centralizado, pero no se encuentra comercializado en España.

Ensayo 301 datos a 5 años: Supervivencia global

La SG de los pacientes tratados con Vyxeos liposomal fue superior a la observada en los pacientes tratados con 7+3



OS, overall survival; AML, acute myeloid leukemia; CI, confidence interval; HR, hazard ratio; KM, Kaplan-Meier.

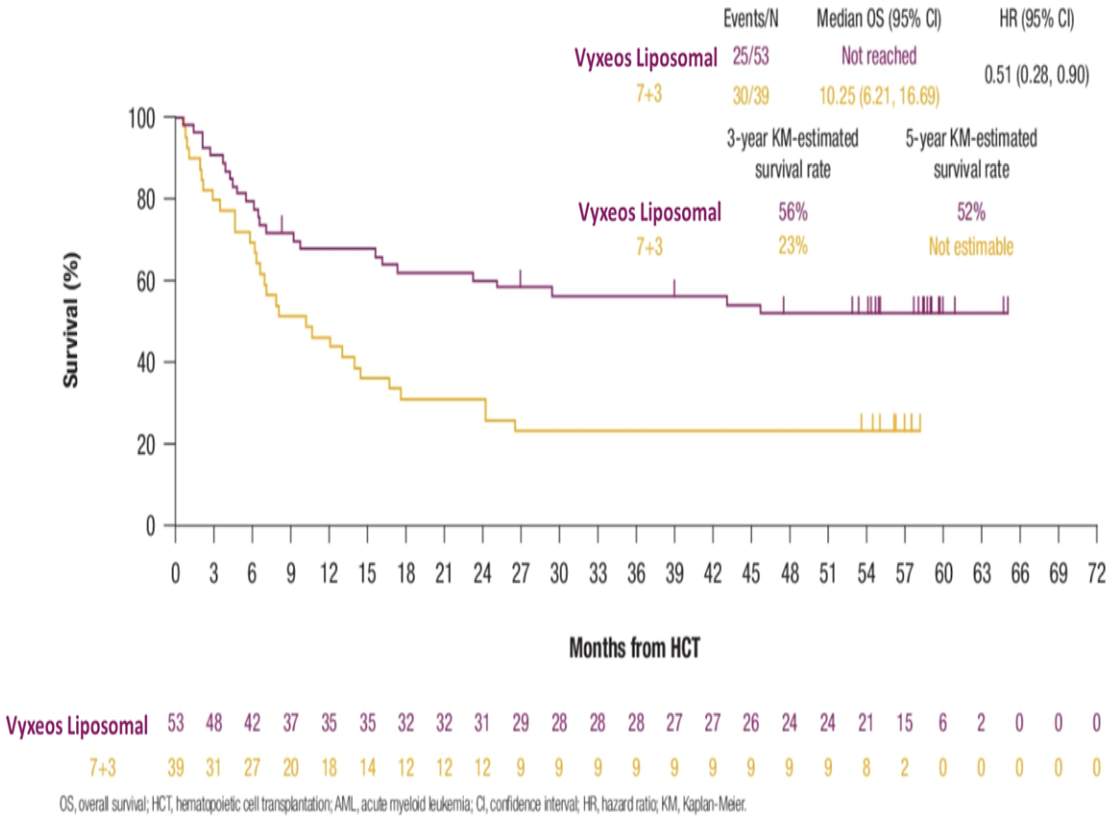
- **SG a tres años:**
  - 21% con Vyxeos liposomal
  - 9% con 7+3
- **SG a cinco años:**
  - 18% con Vyxeos liposomal
  - 8% con 7+3

Lancet JE, et al. J Clin Oncol 2018;36(26):2684-2692.
Lancet JE, et al. J Clin Oncol 38: 2020 (suppl; abstr 7510)

Vyxeos liposomal está autorizado por procedimiento centralizado, pero no se encuentra comercializado en España.

Ensayo 301 datos a 5 años: Supervivencia global desde la fecha del TPH

La mediana de SG de los pacientes tratados con Vyxeos liposomal no se alcanzó



- Un 35% (53/153) de los pacientes tratados con Vyxeos liposomal se sometieron a TPH vs. un 25% (39/156) con 7+3.
- La mediana de SG de los pacientes tratados con Vyxeos liposomal no se alcanzó, vs. 7+3 cuya mediana de supervivencia fue de 10.25 meses.
- La mayoría de los pacientes que se sometieron a TPH alcanzaron CR o CRi (77% con Vyxeos liposomal vs. 62% tratados con 7+3).

Lancet JE, et al. J Clin Oncol 2018;36(26):2684-2692. Lancet JE, et al. J Clin Oncol 38: 2020 (suppl; abstr 7510)

VIALE-A Study Design

(NCT02993523)

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

DiNardo CD, et als Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia. N Engl J Med. 2020 Aug 13;383(7):617-629.

Baseline Characteristics

Characteristic	Aza+Ven n = 286	Aza+Pbo n = 145
Median age, (range) years	76 (49–91)	76 (60–90)
≥75 years, n (%)	174 (61)	87 (60)
AML type, n (%)		
De novo	214 (75)	110 (76)
Secondary	72 (25)	35 (24)
Secondary AML, n (%)		
Post MDS, CMML	46 (64)	26 (74)
Therapy-related AML	26 (36)	9 (26)
AML with myelodysplasia related changes, n (%)		
Yes	92 (32)	49 (34)
No	194 (68)	96 (66)
ECOG performance status, n (%)		
0 – 1	157 (55)	81 (56)
2 – 3	129 (45)	64 (44)

Characteristic	Aza+Ven n = 286	Aza+Pbo n = 145
Bone marrow blast count, n (%)		
<30%[#]	85 (30)	41 (28)
≥30 – <50%	61 (21)	33 (23)
≥50%	140 (49)	71 (49)
Cytogenetic risk category, n (%)		
Intermediate	182 (64)	89 (61)
Poor	104 (36)	56 (39)
Somatic mutations, n/N analyzed (%)		
IDH1/2	61/245 (25)	28/127 (22)
FLT3	29/206 (14)	22/108 (20)
NPM1	27/163 (17)	17/86 (20)
TP53	38/163 (23)	14/86 (16)

[#]Bone marrow blast counts were between 20 – <30%

AML: Acute myeloid leukemia; Aza: Azacitidine; CMML: Chronic myelomonocytic leukemia; MDS: Myelodysplastic syndrome; Ven: Venetoclax

Data cut off: 04 Jan 2020

Courtney D DiNardo, et als. 14 June 2020. EHA 25 Annual Congress

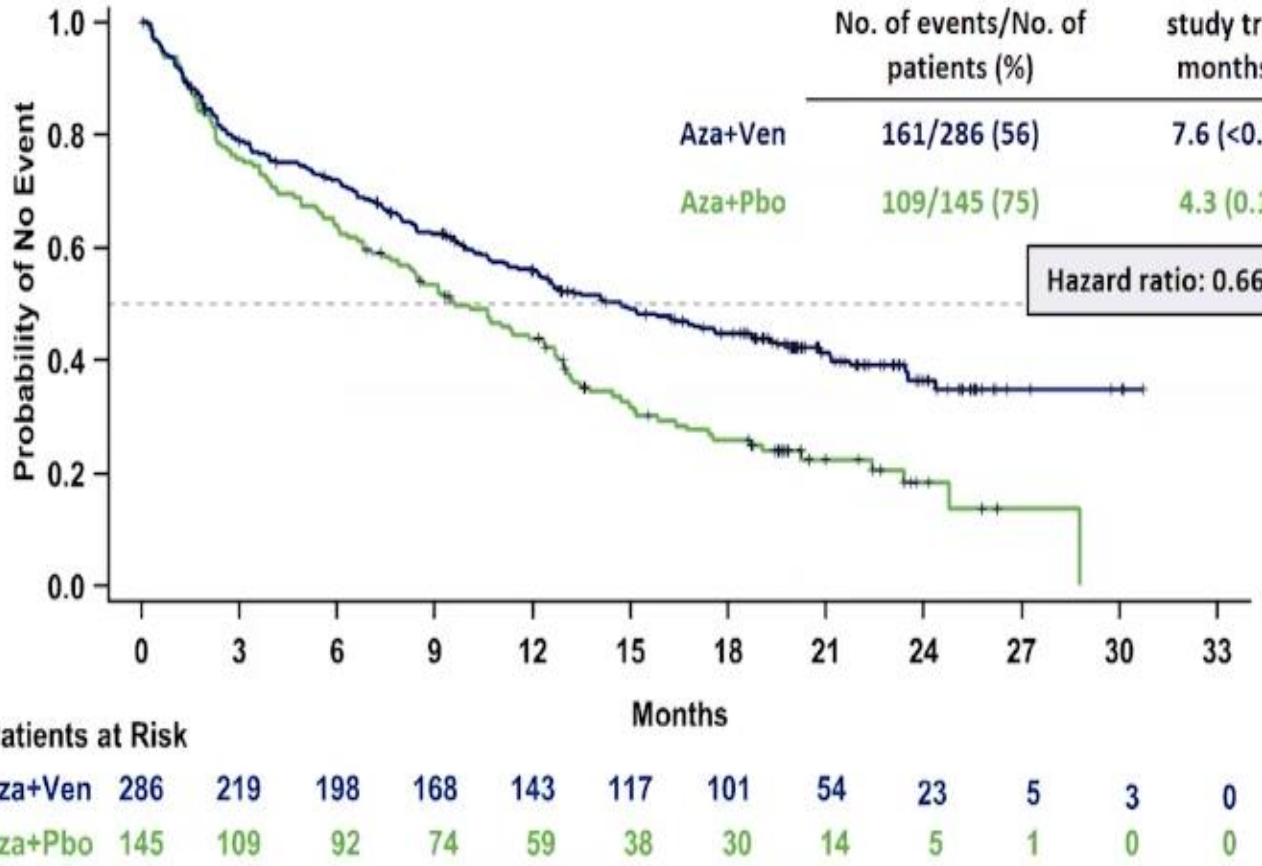
Patient Disposition

Characteristic	Aza+Ven n = 286	Aza+Pbo n = 145
Duration of follow-up, median (range), months	20.7 (0.0 – 30.7)	20.2 (0.2 – 28.8)
Active on treatment, n (%)	77 (27)	18 (12)
Discontinued treatment[1], n (%)	209 (73)	127 (88)
Adverse event	5 (2)	5 (3)
Disease progression/morphologic relapse	120 (42)	62 (43)
Withdrew consent	26 (9)	22 (15)
Lost to follow-up	1	0
Physician's decision	17 (6)	9 (6)
Death during treatment	39 (14)	23 (16)
Non-compliance	0	1 (1)
Other reason	1 (<1)	5 (3)
Discontinued study[2], n (%)	173 (61)	112 (77)
Death in survival follow-up	161 (56)	109 (75)
Other	12 (4)	3 (2)

[1] Patients who discontinued treatment for reasons other than death were followed for survival; [2] Patients who were no longer observed for survival follow-up;
2 patients in Aza+Ven arm and 1 patient in the Aza+Pbo arm underwent transplantation after discontinuing study treatment

Courtney D DiNardo, et als. 14 June 2020. EHA 25 Annual Congress

Overall Survival



	No. of events/No. of patients (%)	Median duration of study treatment, months (range)	Median overall survival, months (95% CI)
Aza+Ven	161/286 (56)	7.6 (<0.1 – 30.7)	14.7 (11.9 – 18.7)
Aza+Pbo	109/145 (75)	4.3 (0.1 – 24.0)	9.6 (7.4 – 12.7)

Hazard ratio: 0.66 (95% CI: 0.52 – 0.85), p<0.001

Patients at Risk

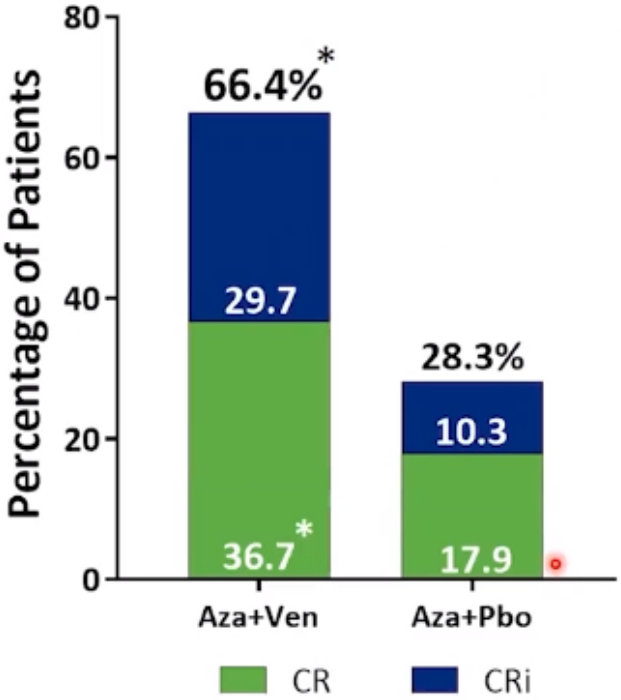
Aza+Ven	286	219	198	168	143	117	101	54	23	5	3	0
Aza+Pbo	145	109	92	74	59	38	30	14	5	1	0	0

Median follow-up time: 20.5 months (range: <0.1 – 30.7)

Aza: Azacitidine; Pbo: Placebo; Ven: Venetoclax; The distributions were estimated for each treatment arm using Kaplan-Meier methodology and compared using the log-rank test stratified by age (18-<75, ≥75 years) and cytogenetic risk (intermediate risk, poor risk). The hazard ratio between treatment arms were estimated using the Cox proportional hazards model with the same stratification factors used in the log-rank test.

Courtney D DiNardo, et als. 14 June 2020. EHA 25 Annual Congress

Composite Response Rate (CR+CRi)



	No. of treatment cycles, median (range)	Median time to CR/CRi, Months (range)	*CR+CRi by initiation of Cycle 2, n (%)
Aza+Ven (n=286)	7.0 (1.0 – 30.0)	1.3 (0.6 – 9.9)	124 (43.4)
Aza+Pbo (n=145)	4.5 (1.0 –26.0)	2.8 (0.8 – 13.2)	11 (7.6)

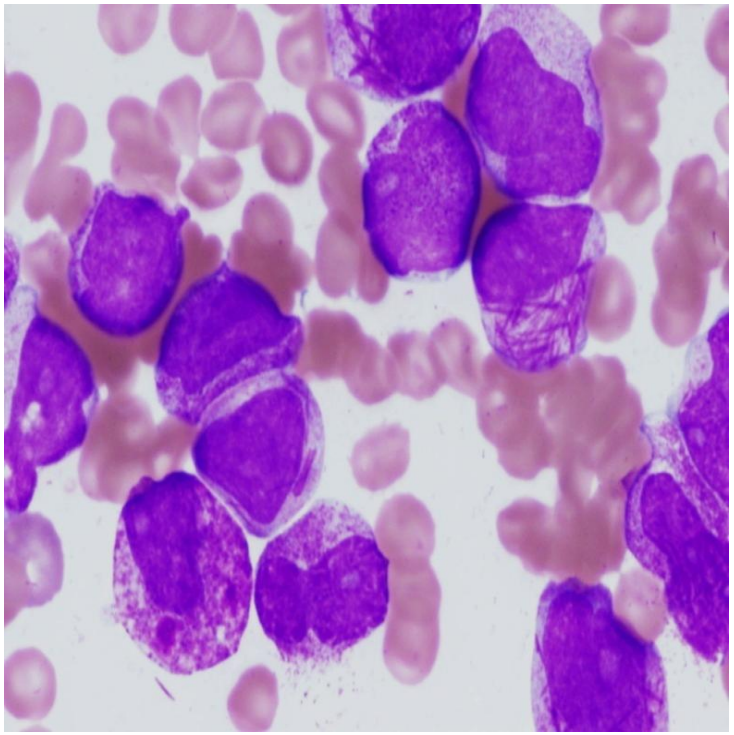
*CR+CRi rate, CR rate, and CR+CRi by initiation of cycle 2 are statistically significant with p<0.001 by CMH te

za: Azacitidine; Pbo: Placebo; Ven: Venetoclax; CR: Complete remission; CRi: CR with incomplete-count recovery; CR was defined as absolute neutrophil count >10^3/μL, platelets >10^5/μL, red cell transfusion ndependence (TI), and bone marrow with <5% blasts; CRi was defined as all criteria for CR, except for neutropenia ≤10^3/μL or thrombocytopenia ≤10^5/μL.
R + CRi rate was compared using Cochran-Mantel-Haenszel (CMH) test stratified by age (18 – < 75, ≥ 75) and cytogenetic risk (intermediate, poor).

DiNardo CD, et als Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia. N Engl J Med. 2020 Aug 13;383(7):617-629.

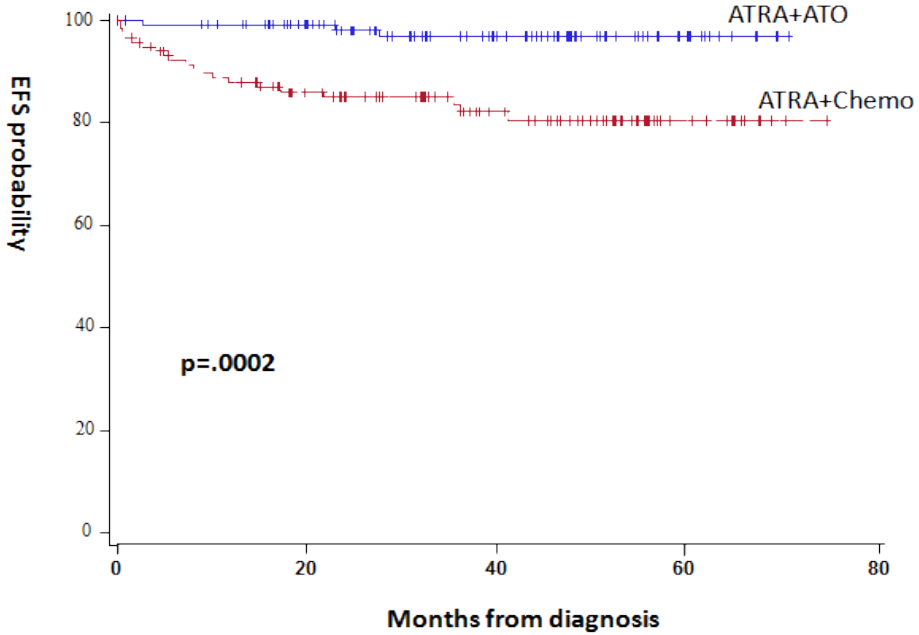
Leucemia Aguda Promielocitica

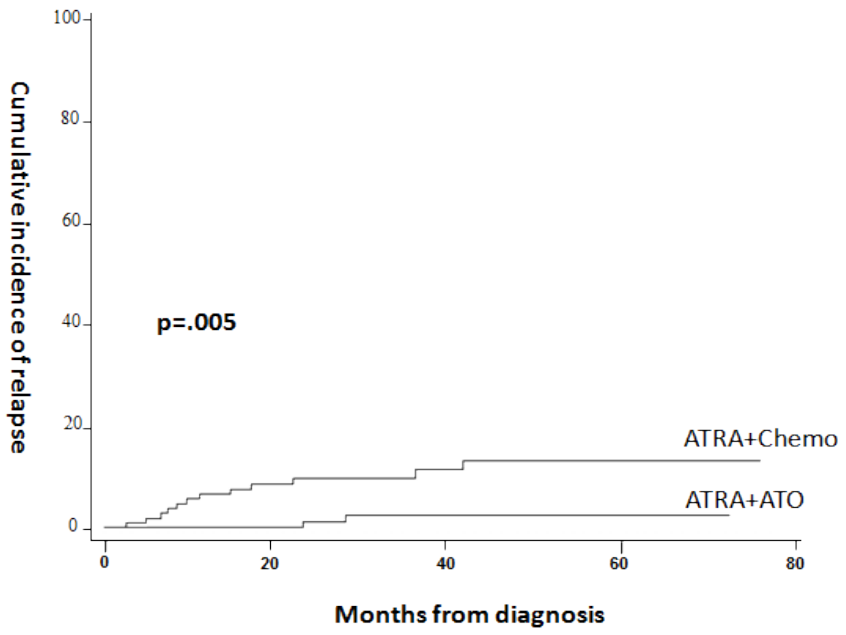
- **10-15% de LMA adulto; 20-30% en hispanoamericanos**
- **Leucopenia**
- **Coagulopatía**
- **t(15;17)**
- **Sensible a las antraciclinas**
- ***Transcrito fusion PML-RARα***
- **Retinoico produce diferenciacion**
- **Trioxido arsenico produce apoptosis**



Improved Outcome with ATRA-Arsenic Trioxide Compared to ATRA-Chemotherapy in Non-High Risk Acute Promyelocytic Leukemia Italian-German APL0406 Trial

Prospective, open-label, randomized trial
N 276 low & intermediate risk
CR 100 % vs 97%
OS 99.1 % vs 94.4%





Uwe Platzbecker, et als. Improved Outcome with ATRA-Arsenic Trioxide Compared to ATRA-Chemotherapy in Non-High Risk Acute Promyelocytic Leukemia – Updated Results of the Italian-German APL0406 Trial on the Extended Final Series, Blood, 2014, Figure 1

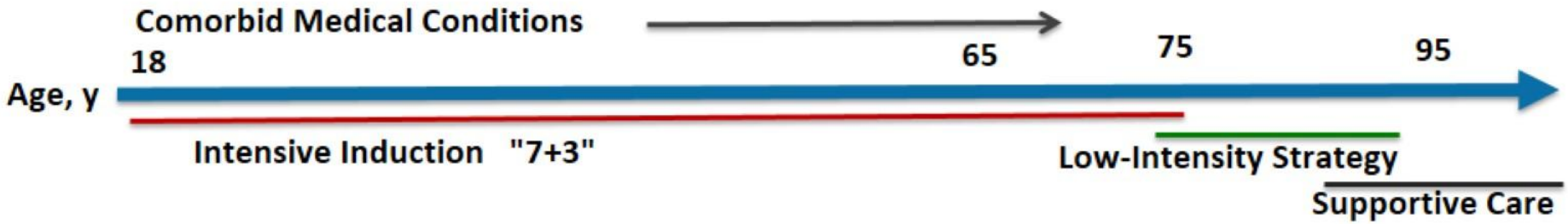
Mensajes finales

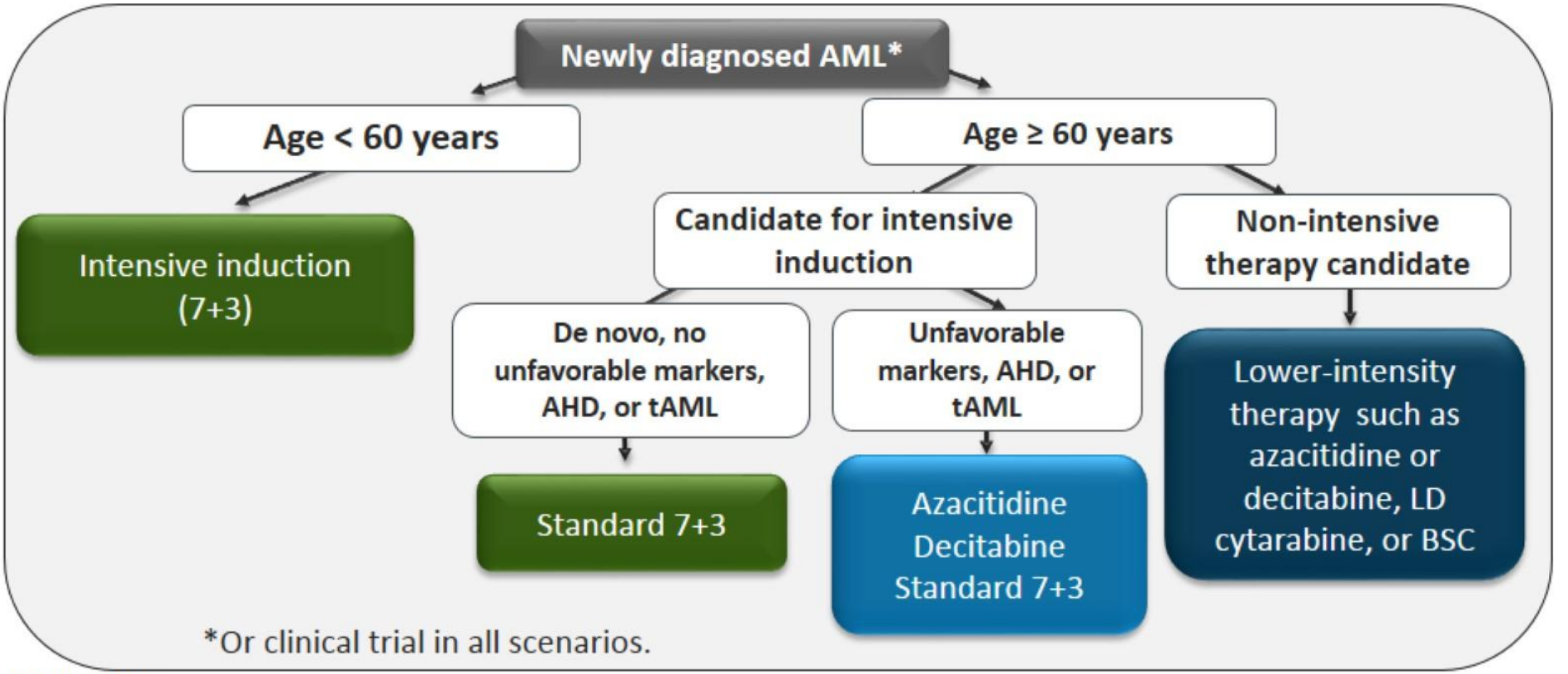
- **Grandes avances biológicos en conocimiento enfermedad**
- **Aparición de nuevos fármacos con repercusión limitada en la evolución /control de la enfermedad**
- **Grandes esperanzas en un futuro completamente diferente, quizás similar al cambio que hemos visto en LPA**

¡ GRACIAS!

- **Se agradecen preguntas….**

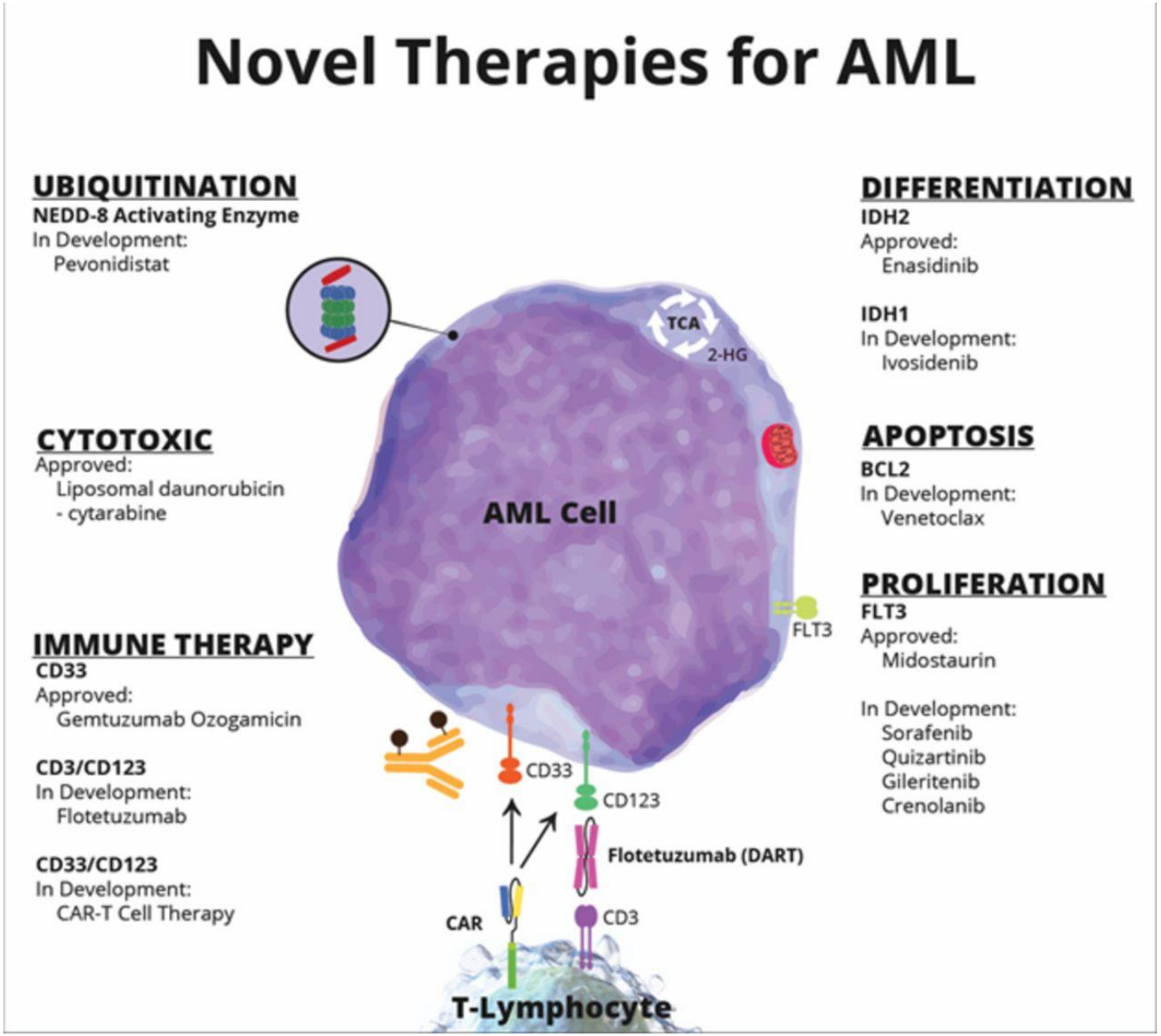
Treating Newly Diagnosed AML
Current Paradigms





NCCN website.

Novel Therapies for AML



Julian R Davis et al. J Investig Med 2018;66:1088-1095

FIGURE. Immune and Molecular Targeted Approaches in Acute Myeloid Leukemia