



Esperienza di pratica clinica paziente FIT a rischio intermedio

Dott.ssa Lara Aprile
ASL Taranto – P.O. S.G Moscati

Table 10. Selected treatment options for patients fit for intensive chemotherapy

Fit for intensive chemotherapy	Induction	Consolidation*	Maintenance
AML with <i>FLT3</i> mutation	Daunorubicin 60 mg/m ² IV d1-3; or idarubicin 12 mg/m ² IV d1-3; and cytarabine 100-200 mg/m ² /d CIV d1-7; plus midostaurin 50 mg q12h PO d8-21 Re-induction: either 2nd cycle "7 + 3" or regimen containing higher dose of cytarabine, each plus midostaurin, preferable the latter in patients with no response to 1st cycle	3-4 cycles of IDAC 1000-1500 mg/m ² IV (500-1000 mg/m ² if ≥60 y old) over 3h q12h d1-3; plus midostaurin 50 mg q12h PO d8-21 (in all cycles)†	Midostaurin 50 mg q12h PO d1-28, q4 wk, over 12 cycles‡
Non- <i>FLT3</i> mutant§	Daunorubicin 60 mg/m ² IV d1-3, idarubicin 12 mg/m ² IV d1-3, or mitoxantrone 12 mg/m ² IV d1-3; and cytarabine 100-200 mg/m ² /d CIV d1-7 Re-induction: either 2nd cycle "7 + 3" or regimen containing higher dose of cytarabine, preferable the latter in patients with no response	3-4 cycles of IDAC 1000-1500 mg/m ² IV (500-1000 mg/m ² if ≥60 y old) over 3h q12h d1-3	Oral azacitidine 300 mg PO daily d1-14, q4 wk, until disease progression
Other options 			
Gemtuzumab ozogamicin (GO) for CD33-positive AML, favorable (or intermediate) cytogenetic risk	Daunorubicin 60 mg/m ² IV d1-3 and cytarabine 100-200 mg/m ² /d CIV d1-7; plus GO 3 mg/m ² (maximum dose 5 mg) IV, d1, 4, 7. GO is also widely administered on day 1 of induction only. Re-induction (if not in CR/CRh/CRi) may be with daunorubicin 60 mg/m ² IV d1-2 and cytarabine 1000 mg/m ² IV (500-1000 mg/m ² if ≥60 y old) over 3h q12h d1-3 without GO	2-4 cycles of IDAC 1000-1500 mg/m ² IV (500-1000 mg/m ² if ≥60 y old) over 3h q12h d1-3. GO 3 mg/m ² may be added on d1 (in up to 2 cycles). Consider omitting GO if allogeneic HCT is planned to reduce the risk of veno-occlusive disease.	
CPX-351 for AML with myelodysplasia-related changes or therapy-related AML¶	CPX-351 100 U/m ² (daunorubicin 44 mg/cytarabine 100 mg) IV d1, 3, 5 Re-induction (if not in CR/CRh/CRi): CPX-351 100 U/m ² IV d1, 3 only	1-2 cycles of CPX-351 65 U/m ² (daunorubicin 29 mg/cytarabine 65 mg) IV d1, 3	

RISCHIO INTERMEDIO

GO vs NO GO

C'è realmente un vantaggio nell'uso del GO?

Qual è il mio obiettivo nella gestione di pz con LAM a rischio intermedio???



Benefit of GO according to ELN classification and the existence of signaling mutation

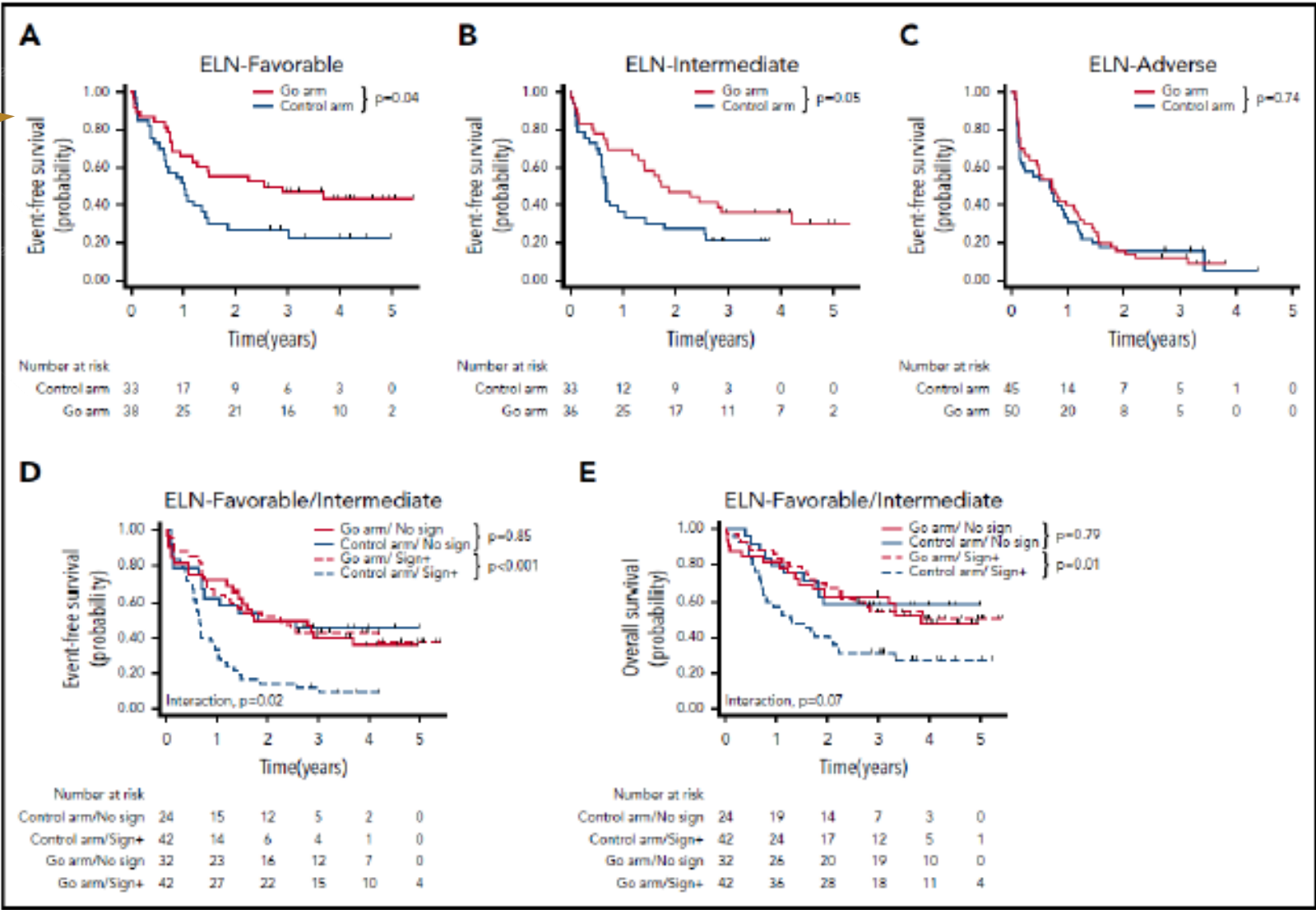
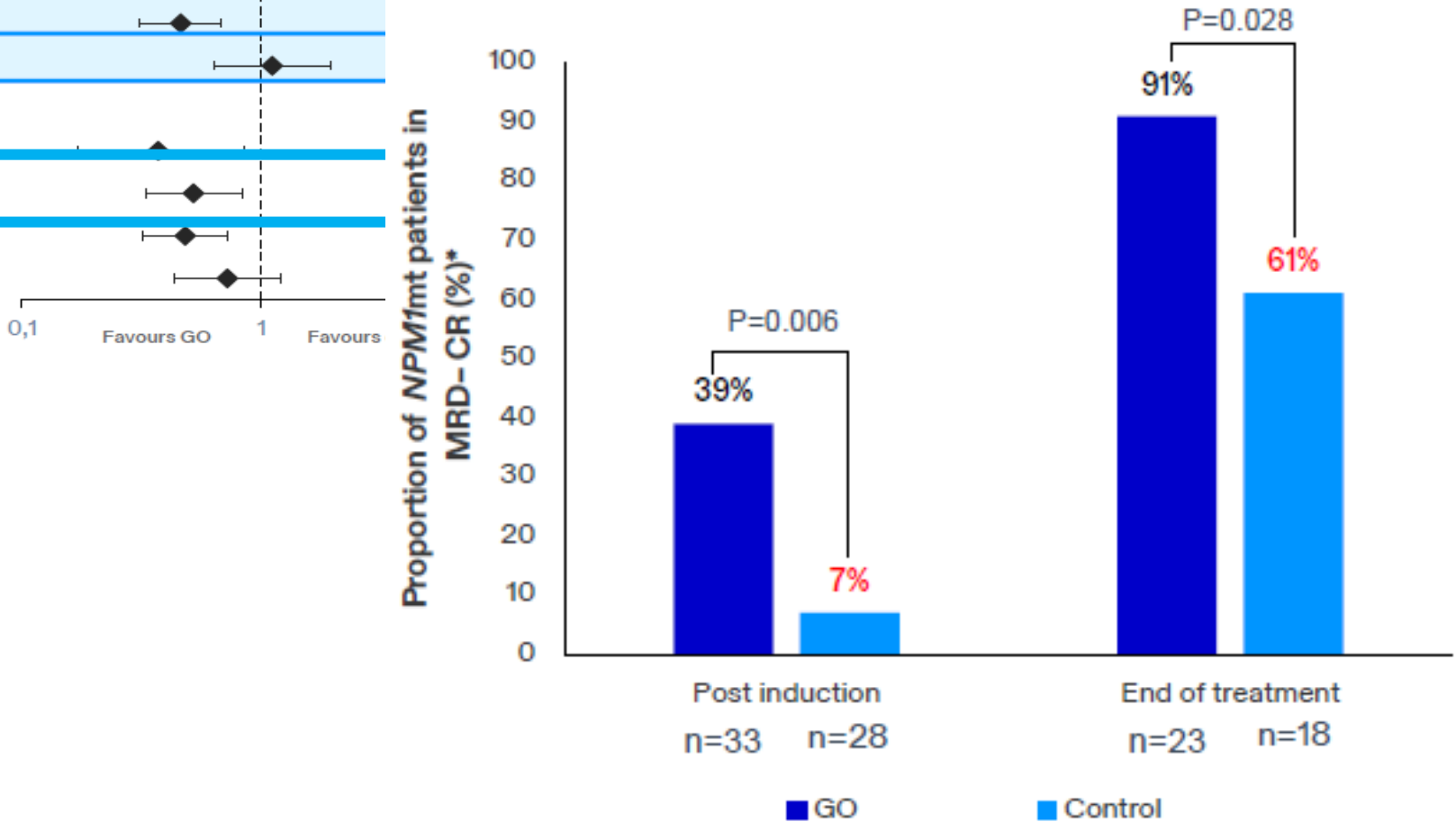


Figure 1. Benefit of GO according to ELN classification and the existence of signaling mutation. (A-C) EFS according to ELN 2017 subgroups. EFS (D) and OS (E) according to protocol arm and the existence of signaling mutations.

ALFA-0701: Event-free survival by subgroup (cont'd)

Subgroup ¹		Hazard ratio (95% CI)
Primary EFS		0.56 (0.42–0.76)
CD33 expression		
<30%		0.52 (0.24–1.15)
≥30%		0.55 (0.37–0.83)
<70%		0.65 (0.36–1.15)
≥70%		0.50 (0.31–0.79)
Cytogenetics		
Favourable/intermediate		
Adverse		
Risk based on ELN		
Favourable		
Intermediate		
Favourable/intermediate		
Poor/adverse		

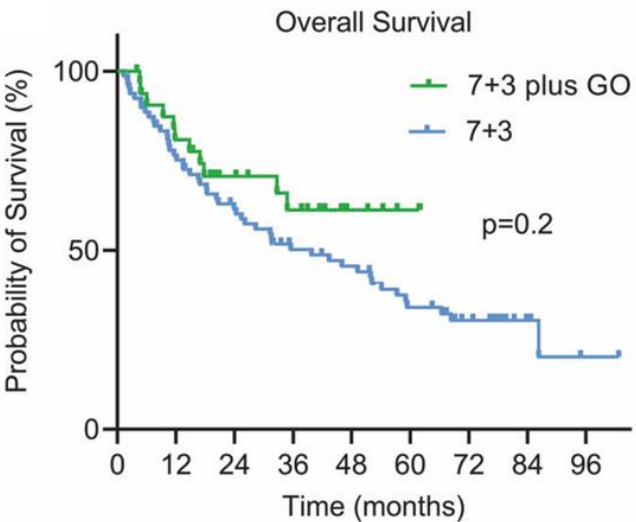
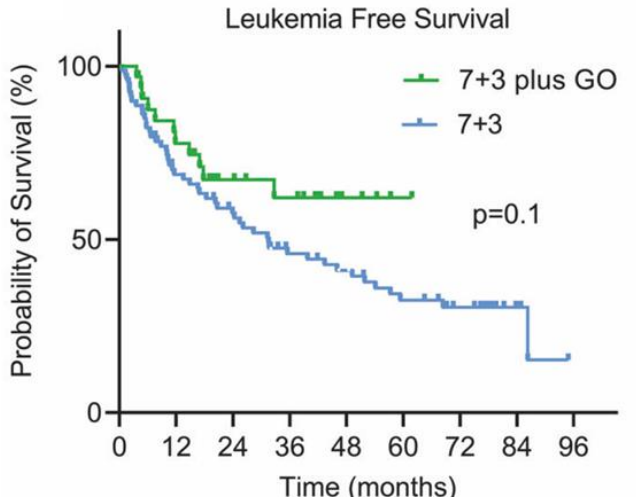
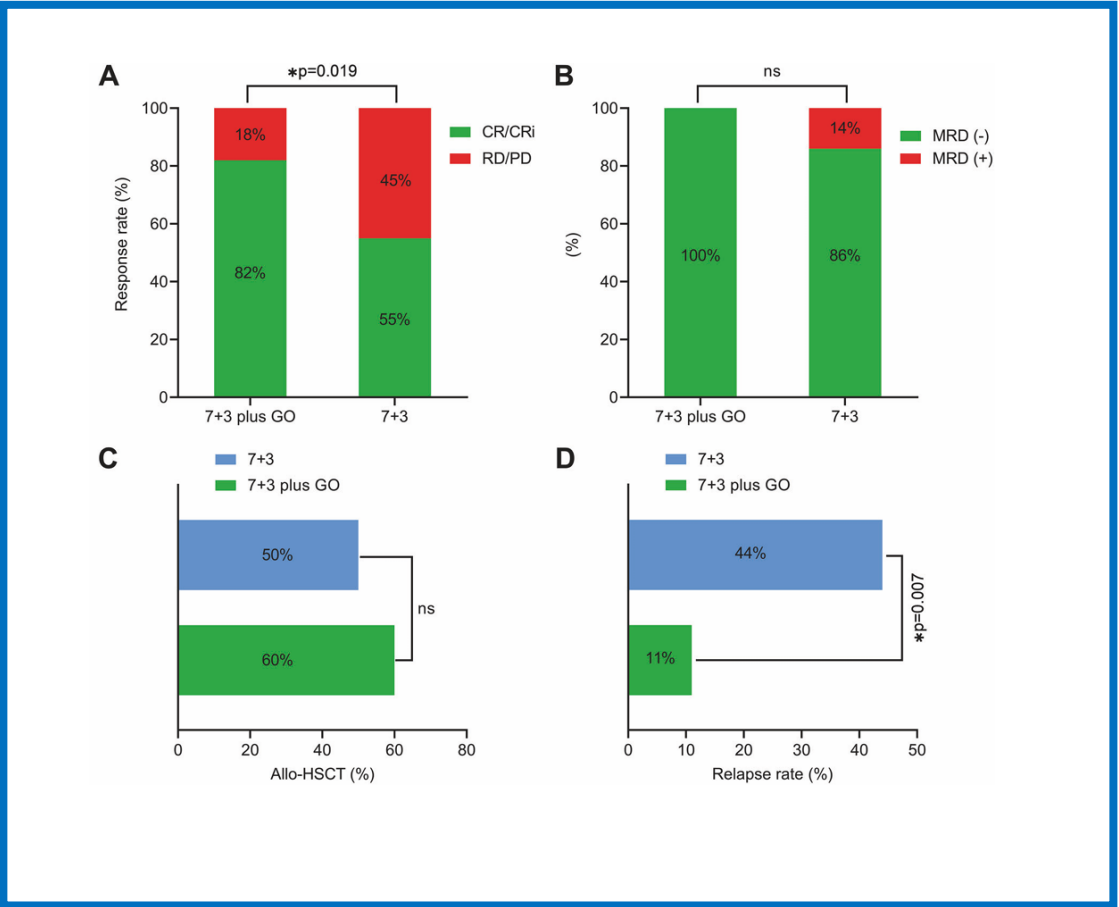
Adapted from: Lambert et al. 2019. (Suppl.)



Gemtuzumab nel rischio citogenetico intermedio

Studio retrospettivo - 113 pazienti

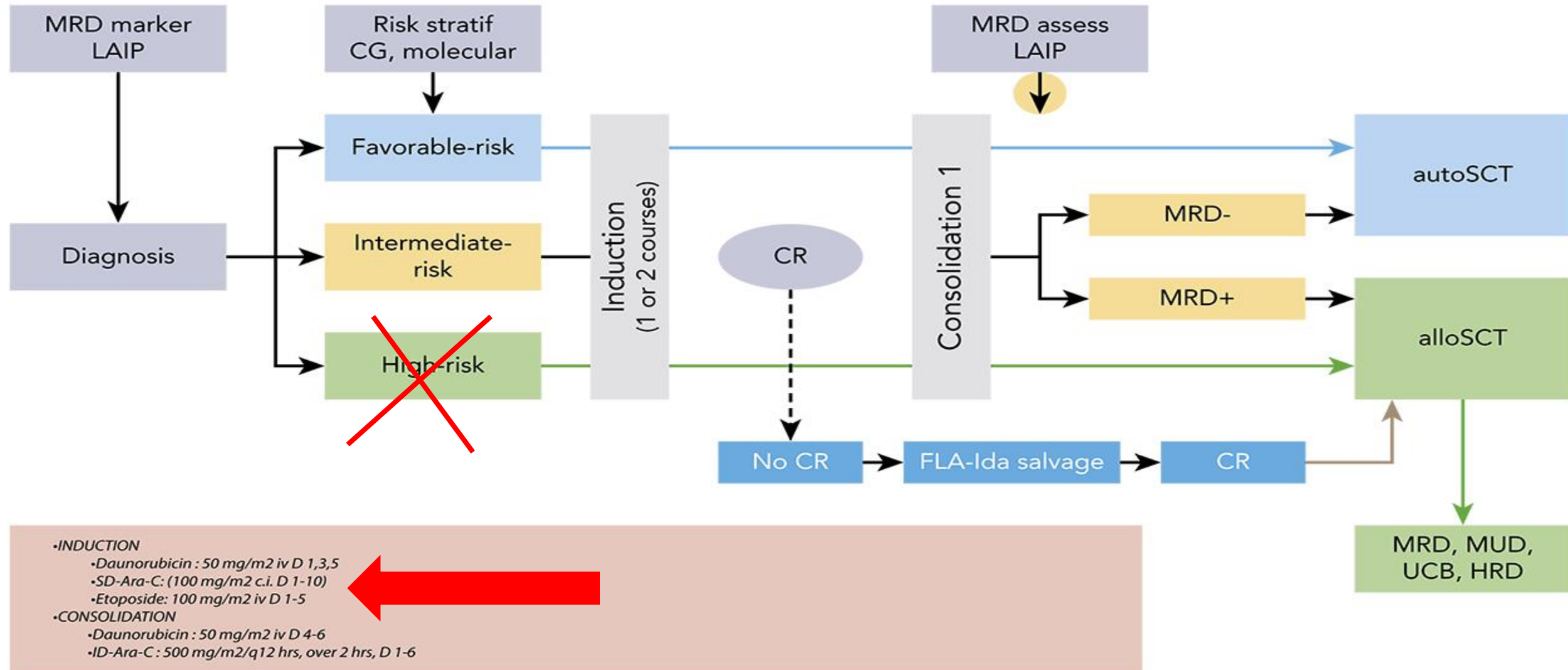
Group/Variables	7 + 3	7 + 3 plus GO	p-value
n (%)	80 (71)	33 (29)	
Follow-up (mo), median (range)	24.3 (4–62.0)	29.8 (1.3–102.7)	
Accrual dates, range (mo/yr)	1/2018–8/2021	1/2015–6/2022	
Age (y), median (range)	57 (19–73)	59 (22–87)	ns
≥60 y, n (%)	15 (45)	38 (48)	ns
Female/Male, n (%)	18 (55)/15 (45)	37 (46)/43 (54)	ns
AML subtype			ns
pAML, n (%)	68 (85)	30 (91)	ns
sAML, n (%)	8 (10)	2 (6)	ns
tAML, n (%)	4 (5)	1 (3)	ns
Mortality			
30-day, n (%)	1 (1.3)	0 (0)	ns
60-day, n (%)	3 (3.8)	0 (0)	ns
Conditioning chemotherapy prior to allo-HSCT (%)			
Myeloablative regimens	9	20	ns
Reduced-intensity regimens	91	80	ns
Gene mutations (%)			
ASXL1	14	6	ns
DNMT3A	5	33	0.0001
FLT3 (ITD/TKD)	11	12	ns
IDH1/2	15	36	0.02
NPM1	23	3	0.01
KRAS/NRAS	23	21	ns
RUNX1	14	9	ns
TP53	3	3	ns
Molecular risk stratification per ELN 2022			
Favorable, n (%)	15 (19)	8 (24)	ns
Intermediate, n (%)	29 (37)	10 (30)	ns
Adverse, n (%)	34 (44)	15 (46)	ns



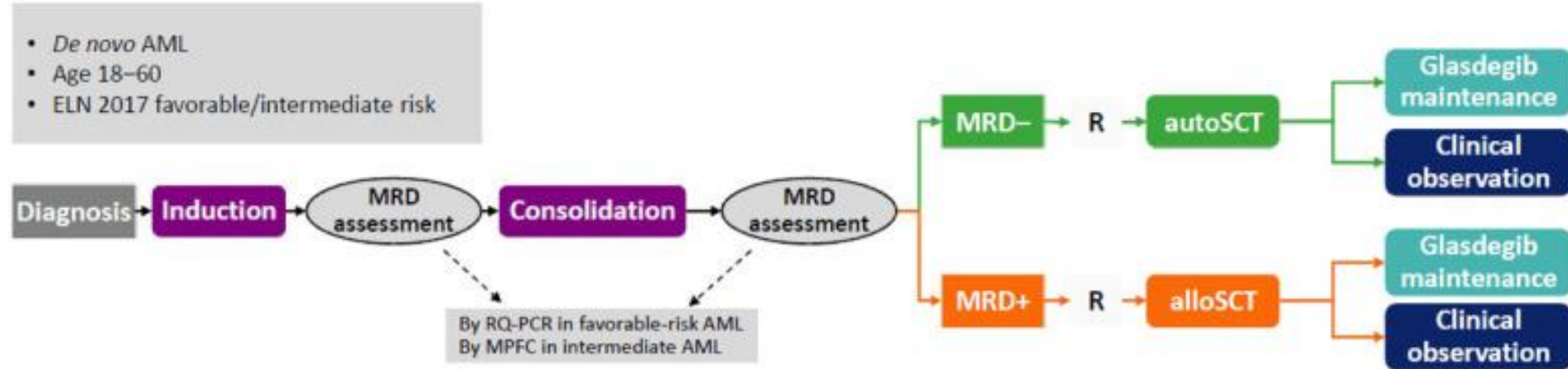
GIMEMA AML 1310 → AML 1819

Nei pazienti IR la scelta trapiantologica MRD-driven supera il valore prognostico sfavorevole della MRD+

AML1310 Study Design



P505 GIMEMA AML1819 TRIAL: GEMTUZUMAB OZOGAMICIN PLUS INTENSIVE CHEMOTHERAPY IMPACTS ON THE LEVEL OF POST-CONSOLIDATION MEASURABLE RESIDUAL DISEASE (MRD) IN ACUTE MYELOID LEUKEMIA



Two co-primary endpoints:

1. % MRD-negative after consolidation treatment
2. Disease-free survival in patients randomized to glasdegib maintenance or clinical observation

Induction

- GO: 3 mg/m² D1, 4, 7*
- Daunorubicin : 60 mg/m² D1–3
- Ara-C: 200 mg/m² D1–7

Consolidation

- GO: 3 mg/m² D1*
- Daunorubicin : 50 mg/m² D4–6
- Ara-C: 500 mg/m² BID, D1–6

Maintenance post-transplant

- Glasdegib 100 mg/day, orally, for up to 1 year or until toxicity/relapse

AML1819	145 pt	CR+CRi 107 (74%)	96 post CONS	F-u 17,4 m 1yOS
Età	53 (18-61)			
M/F %	52/48			
Low-ELN 2017	76 (52%)	63 (83%)	47/58 (81%)MRD neg 11/58 (19%) MRD pos	83,1%
Int-ELN 2017	69 (48%)	44 (64%)	24/38 (63%)MRD neg 14/38 (37%) MRD pos	72,1%

“With all the limits of such a comparison, we also found that the proportion of patients being MRD negative after consolidation was higher in AML1819 trial than in AML1310 one, in which no GO was added to chemotherapy. Such a finding has practical implications since, in AML1819 trial, a lower fraction of patients is submitted to ASCT”

RISCHIO INTERMEDIO

GO vs NO GO

C'è realmente un vantaggio nell'uso del GO?

Qual è il mio obiettivo nella gestione di pz con LAM a rischio intermedio???



GIMEMA AML1819 !!!

2022 ad oggi: 3 pz «RISCHIO ELN 2017 INTERMEDIO» trattati con GO fuori di protocolli clinici

1 CR avviato a Allo-BMT in MMR pos

2 NR avviati a Allo-BMT in CR2 -> 1 CR

1 aza-ven

Table 5. 2017 ELN risk stratification by genetics

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

Table 6. 2022 ELN risk classification by genetics at initial diagnosis*

Risk category†	Genetic abnormality
Favorable	- t(8;21)(q22;q22.1)/<i>RUNX1::RUNX1T1</i>†,‡ - inv(16)(p13.1;q22) or t(16;16)(p13.1;q22)/<i>CBFB::MYH11</i>†,‡ - Mutated <i>NPM1</i>†,§ without <i>FLT3</i>-ITD - bZIP in-frame mutated <i>CEBPA</i>
Intermediate	- Mutated <i>NPM1</i>†,§ with <i>FLT3</i>-ITD - Wild-type <i>NPM1</i> with <i>FLT3</i>-ITD (without adverse-risk genetic lesions) - t(9;11)(p21.3;q23.3)/<i>MLLT3::KMT2A</i>†,¶ - Cytogenetic and/or molecular abnormalities not classified as favorable or adverse
Adverse	- t(6;9)(p23.3;q34.1)/<i>DEK::NUP214</i> - t(v;11q23.3)/<i>KMT2A</i>-rearranged# - t(9;22)(q34.1;q11.2)/<i>BCR::ABL1</i> - t(8;16)(p11.2;p13.3)/<i>KAT6A::CREBBP</i> - inv(3)(q21.3;q26.2) or t(3;3)(q21.3;q26.2)/<i>GATA2, MECOM(EVI1)</i> - t(3q26.2;q)/<i>MECOM(EVI1)</i>-rearranged -5 or del(5q); -7; -17/abn(17p) - Complex karyotype,** monosomal karyotype†† - Mutated <i>ASXL1</i>, <i>BCOR</i>, <i>EZH2</i>, <i>RUNX1</i>, <i>SF3B1</i>, <i>SRSF2</i>, <i>STAG2</i>, <i>U2AF1</i>, and/or <i>ZRSR2</i>‡‡ - Mutated <i>TP53</i>*

rischio ELN 2017 INTERMEDIO	14/34
PS $\leq$ 2	14/14
Età mediana	51 anni (25-75)
M/F	5/9
citogenetica	9/14 normale 1/14 T9;11 1/14 T8;21 non isolata
NPM+	1/14
FLT3-ITD	0/14

DATI REP

Dargenio et al. Leuk.Res. 2025

6/14 Allo-BMT	8/14 NO Allo-BMT
6/6 MMR+	6/8 CR -> 3/6 MMR neg -> 3/3 VIVI IN CR
1/6 CR2	3/6 MMR + follow-up troppo breve

1 pz 75 anni
1 RC MMRneg (NPM)ad oltre 12 mesi
1 pz 8;21 non isolata

1 pz II linea ->aploBMT
1 Allo-BMT in CR1
1 MMR neg viva in CR

Nome: XXXXXXXXXX

Data di nascita: 14.07.53

Provenienza: Ematologia AMBULATORIO

Data analisi: 19.02.2026

Status: ctr. post-1° consolidamento

Diagnosi: LAM CBFbeta-MYH11+*

*fenotipo all'esordio: CD117+CD33+^{interm}CD13+HLA-DR+CD34+CD15+(38%) cyMPO+

Materiale inviato: sangue midollare

cellularita'(WBC/ul) = 6837 ←

Medico richiedente: Dott.ssa DI CARLO

qualita' campione: modesta ←

STUDIO IMMUNO - FENOTIPICO in citometria a flusso

Metodica utilizzata: Immunofluorescenza diretta

Eventi totali acquisiti: 303729 ←

Eventi CD45+: 173544

LOD (Limit of Detection)= 0.007

LOQ (Limit of Quantitation)= 0.016

Campione diluito (↑linfociti, ↑PMN) ←

GRAZIE DELL'ATTENZIONE

Dott.ssa Lara Aprile
ASL Taranto – P.O. S.G Moscati