Clinical use of MRD testing

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Disclosure of Adriano Venditti

	Research funding	Consultancy	Invited speaker
Celgene			√
Daiichi Sankyo		√	√
Jazz Pharmaceuticals		√	√
Abbvie		√	√
Helsinn		√	
Janssen		√	√
Novartis		√	
Sandoz	√		
Merus		√	
Amgen		√	
Astellas		√	

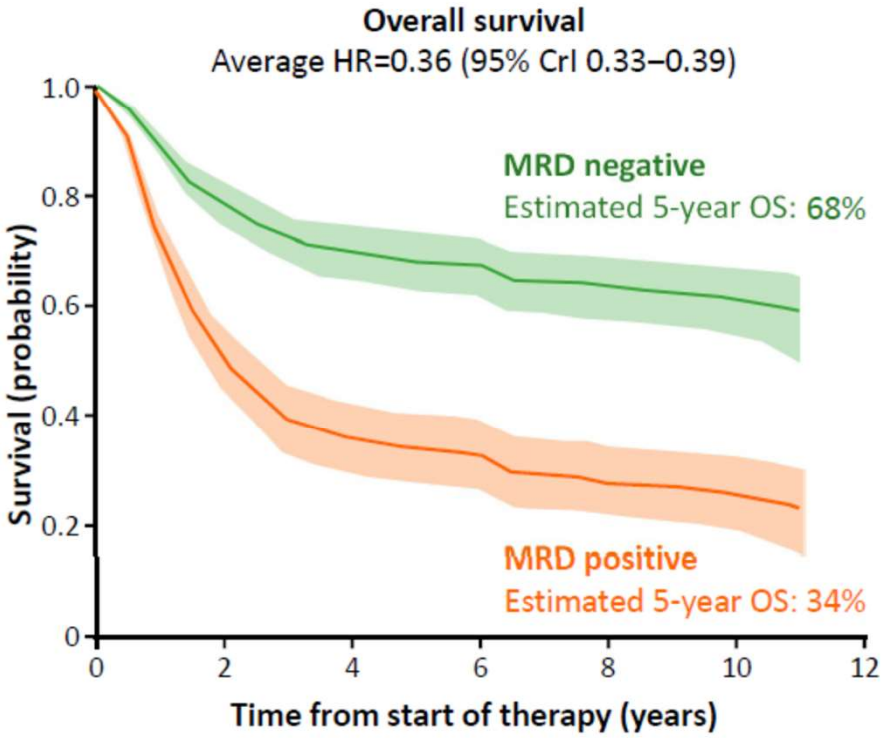
Mesurable Residual Disease (MRD)

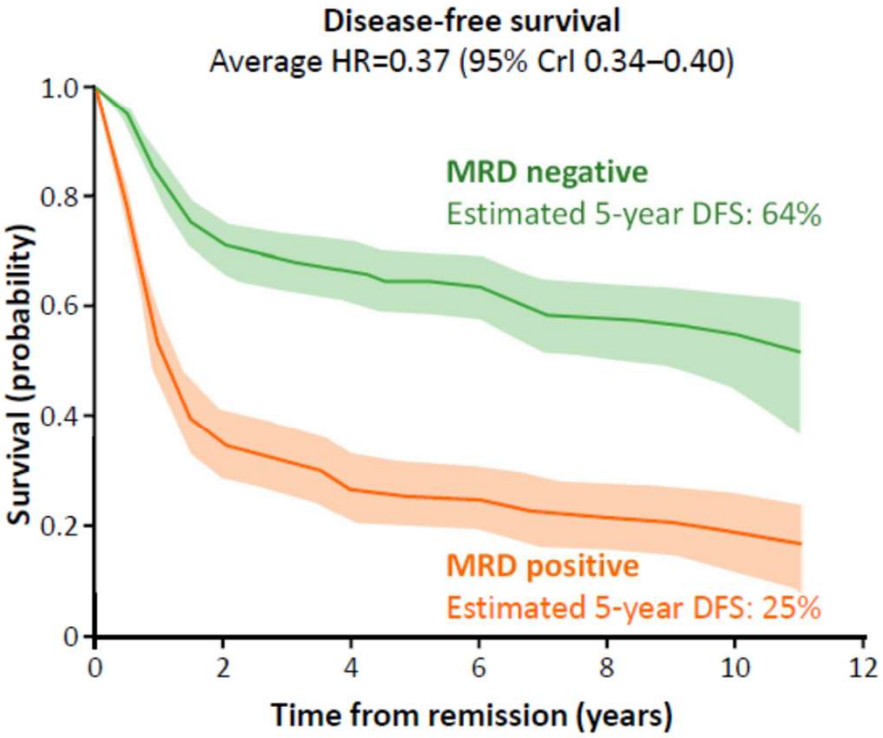
MRD denotes the presence of leukemia cells that survives despite mCR and causes relapse

Walter R et al. Leukemia https://doi.org/10.1038/s41375-021-01230-4

Estimate OS and DFS stratified by MRD status

Systematic review and meta-analysis of 81 publications including 11,151 patients

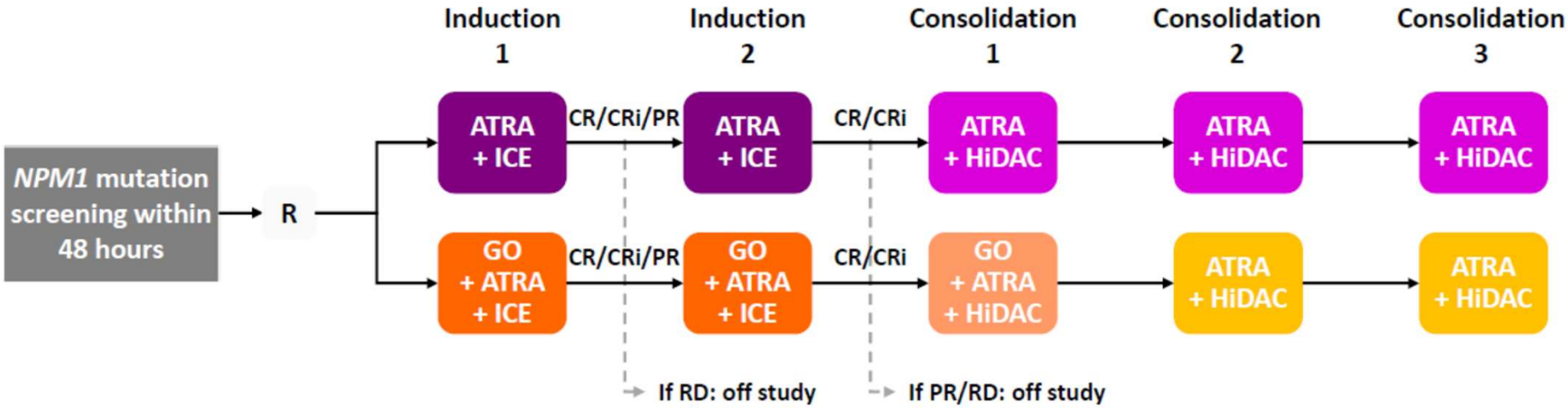




Short NJ et al. JAMA Oncol. 2020;6(12):1890-1899

AMLSG 09-09 trial – Study design

Phase 3 trial of chemotherapy + ATRA ± GO in patients with AML and *NPM1* mutation

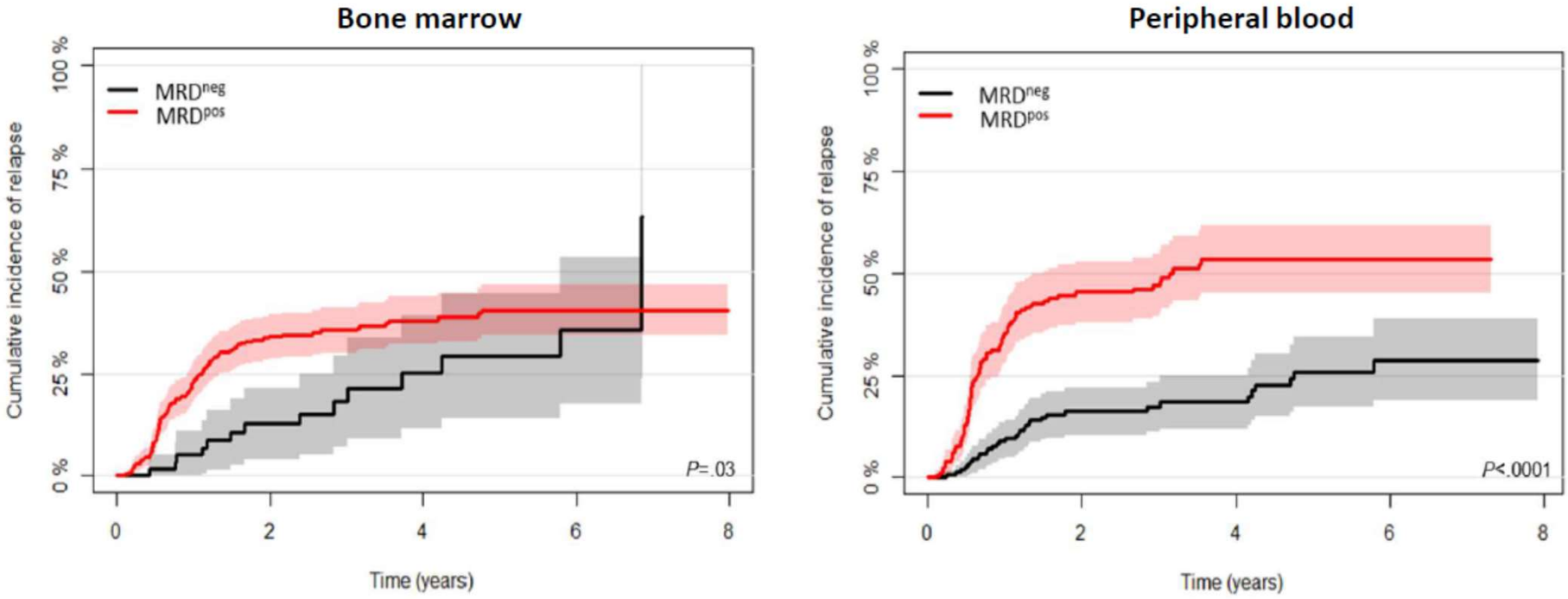


Kapp-Schwoerer S, et al. Blood 2020;136(26):3041-3050

AMLSG 09-09 trial – Impact of *NPM1*^{mut} MRD status after 2 cycles

Phase 3 trial of chemotherapy + ATRA ± GO in patients with AML and *NPM1* mutation

MRD negativity assessed by RT-qPCR and defined as no transcript detected or at least 3-log reduction

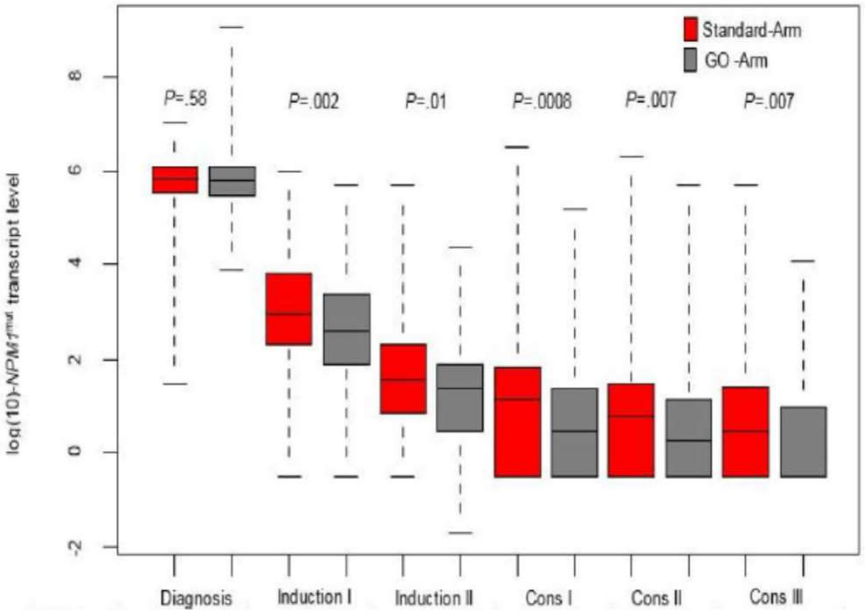


Kapp-Schwoerer S, et al. Blood 2020;136(26):3041-3050

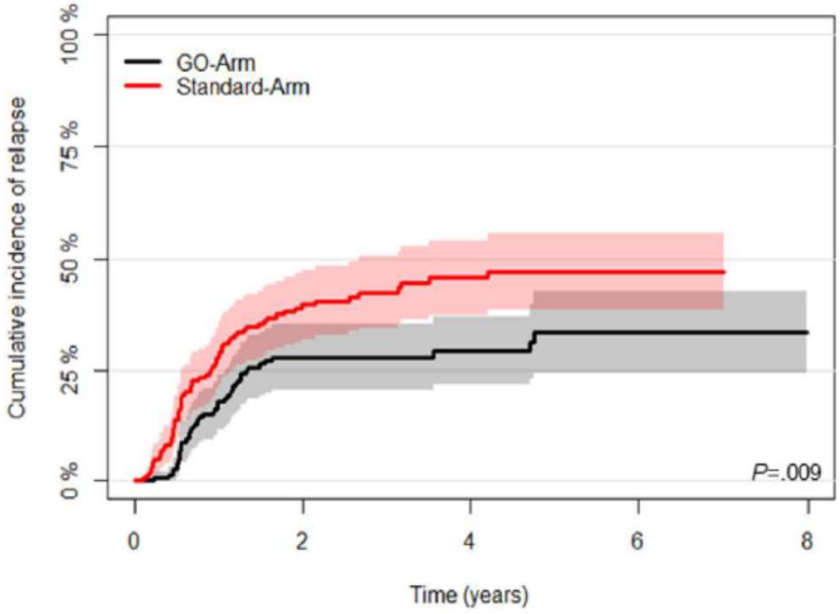
AMLSG 09-09 trial – Impact of GO on *NPM1*^{mut} levels and CIR

Phase 3 trial of chemotherapy + ATRA ± GO in patients with AML and *NPM1* mutation

Kinetics of the *NPM1*^{mut} transcript levels in the bone marrow



CIR after 2 induction cycles in patients with still detectable MRD in the bone marrow



Kapp-Schwoerer S, et al. Blood 2020;136(26):3041-3050

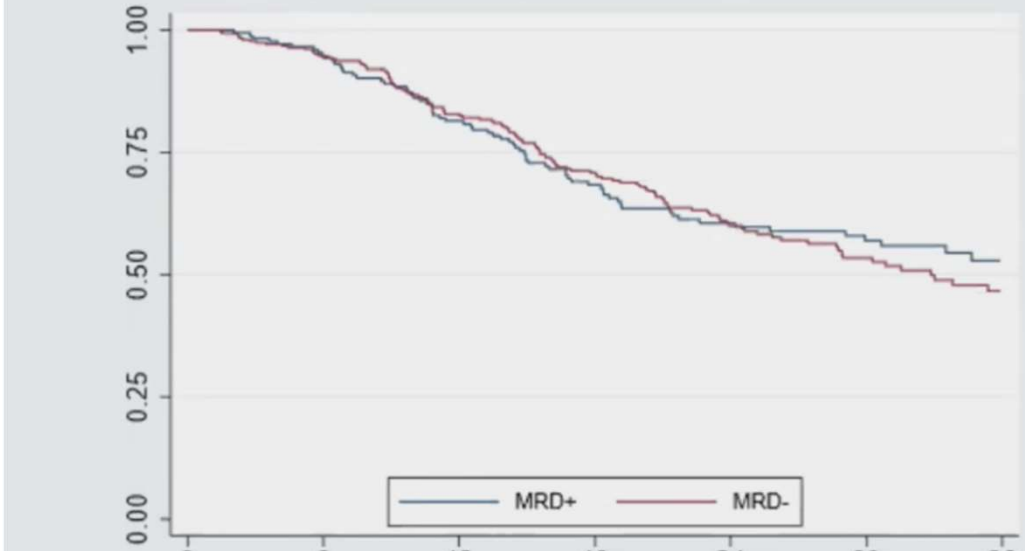
UK NCRI AML18 TRIAL (older pts with AML)

EUROPEAN HEMATOLOGY ASSOCIATION

EHA25 VIRTUAL

Survival by post Course 1 MRD in CR/CRi patients

Overall survival by post-course 1 MRD status in CR/CRi patients



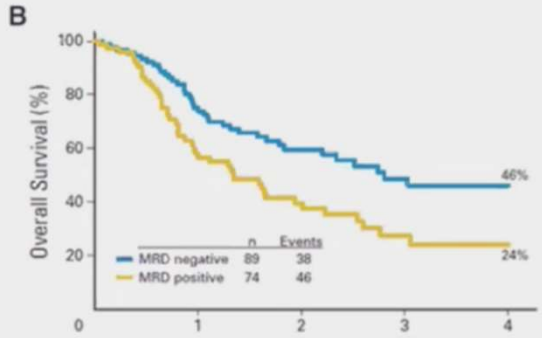
Number at risk							
MRD+	178	164	136	102	77	56	0
MRD-	315	279	228	179	109	66	0

3year OS, 51.1% MRD+ vs 46.6% MRD-

HR: 1.03, 95% CI: 0.77-1.37, p 0.84

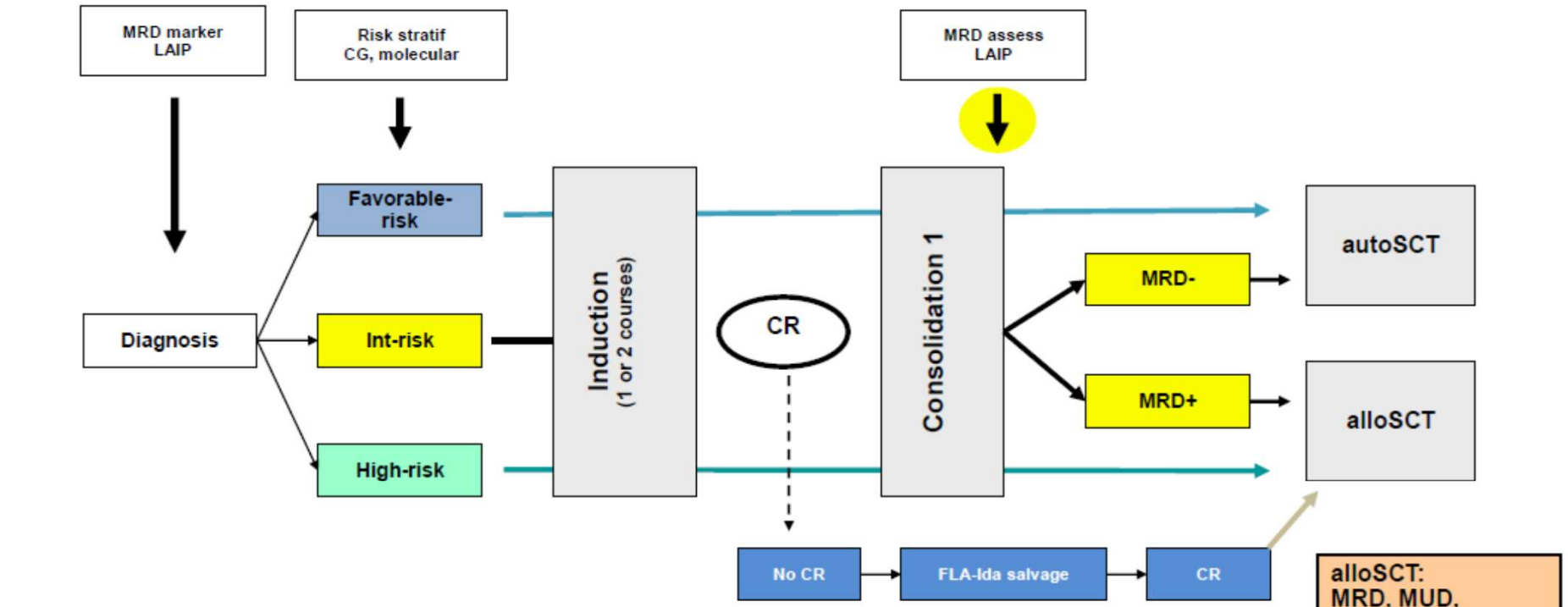
AML16

3 year OS 24% MRD+ vs 46% MRD -



Russell N, et al. EHA Library. 06/12/20; 294955; S135

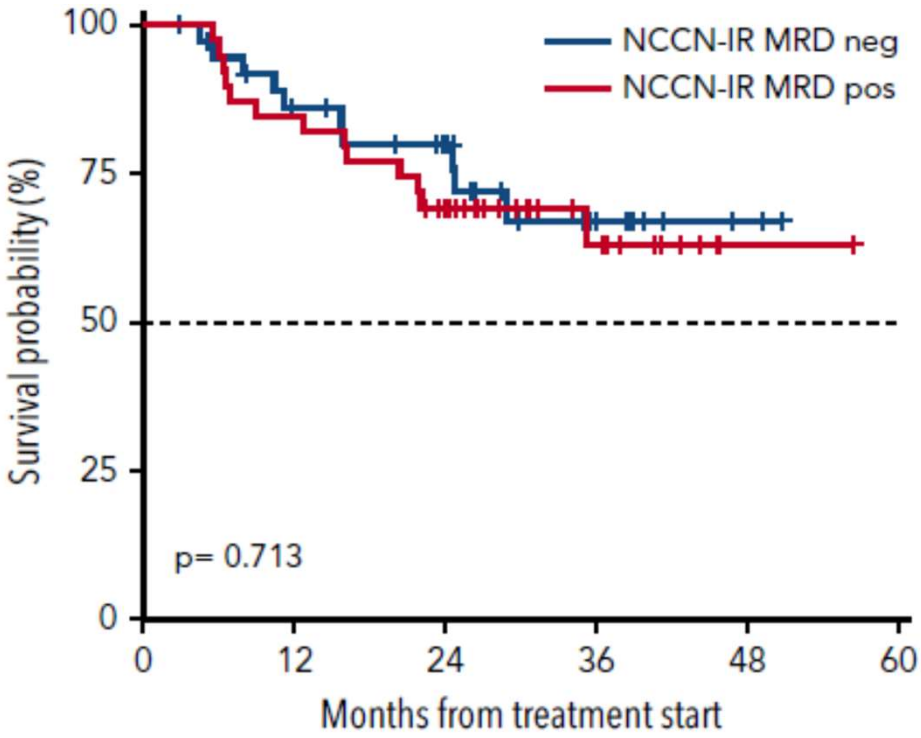
AML1310 Study Design

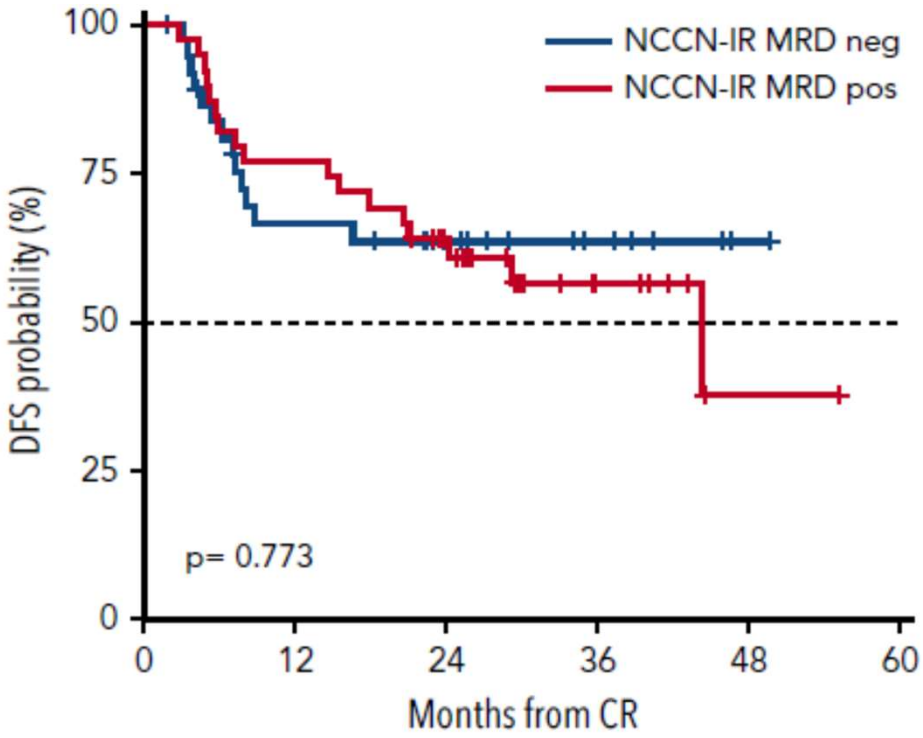


- *INDUCTION*
  - *Daunorubicin : 50 mg/m2 iv D 1,3,5*
  - *SD-Ara-C: (100 mg/m2 c.i. D 1-10)*
  - *Etoposide: 100 mg/m2 iv D 1-5*
- *CONSOLIDATION*
  - *Daunorubicin : 50 mg/m2 iv D 4-6*
  - *ID-Ara-C : 500 mg/m2/q12 hrs, over 2 hrs, D 1-6*

Venditti A et al. Blood 2019;134(12):935-945

GIMEMA AML1310 Trial
Survival estimates of pts with IR-AML

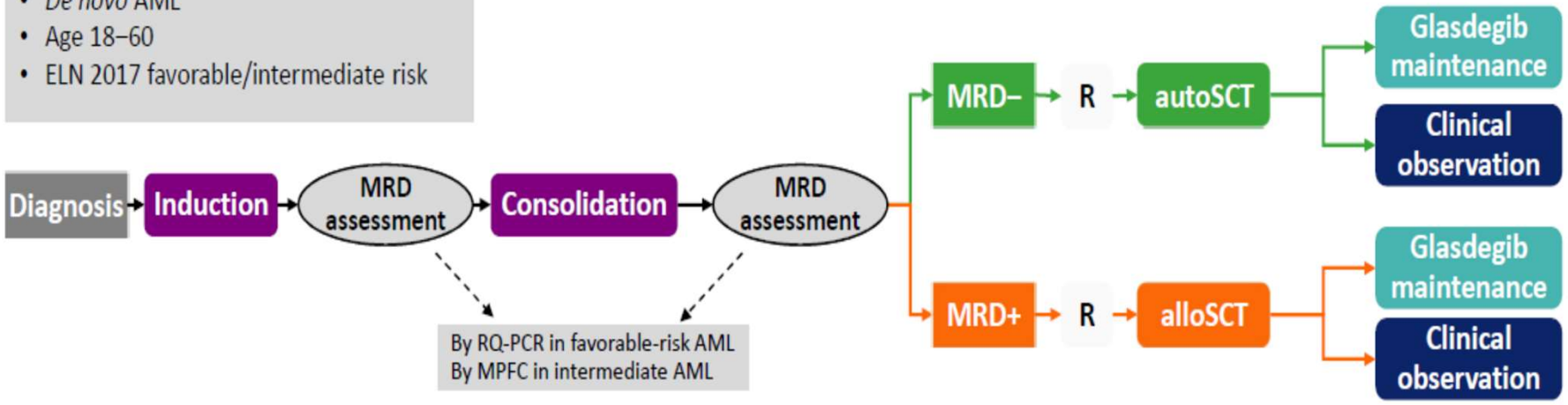




Venditti A et al. Blood 2019;134(12):935-945

GIMEMA AML1819 Trial

- *De novo* AML
- Age 18–60
- ELN 2017 favorable/intermediate risk



Two co-primary endpoints:

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

Induction	Consolidation	Maintenance post-transplant
• GO: 3 mg/m^2 D1, 4, 7*	• GO: 3 mg/m^2 D1*	• Glasdegib 100 mg/day, orally, for up to 1 year or until toxicity/relapse
• Daunorubicin : 60 mg/m^2 D1–3	• Daunorubicin : 50 mg/m^2 D4–6	
• Ara-C: 200 mg/m^2 D1–7	• Ara-C: 500 mg/m^2 BID, D1–6	

fondazione GIMEMA onlus
per la promozione e lo sviluppo della ricerca scientifica sulle malattie ematologiche. FRANCO MANDELLI

* Flat dose capped at 5 mg.

Impact of Conditioning Intensity of Allogeneic Transplantation for Acute Myeloid Leukemia With Genomic Evidence of Residual Disease

Christopher S. Hourigan, DM, DPhil[1]; Laura W. Dillon, PhD[1]; Gege Gui, ScM[1]; Brent R. Logan, PhD[2]; Mingwei Fei, MSc[2]; Jack Ghannam, BS[1]; Yuesheng Li, PhD[1]; Abel Licon, MS[3]; Edwin P. Alyea, MD[4]; Asad Bashey, MD[5]; H. Joachim Deeg, MD[6]; Steven M. Devine, MD[7]; Hugo F. Fernandez, MD[8]; Sergio Giralt, MD[9]; Mehdi Hamadani, MD[10]; Alan Howard, PhD[7]; Richard T. Maziarz, MD[11]; David L. Porter, MD[12]; Bart L. Scott, MD[6]; Erica D. Warlick, MD[13]; Marcelo C. Pasquini, MD[2]; and Mitchell E. Horwitz, MD[14]

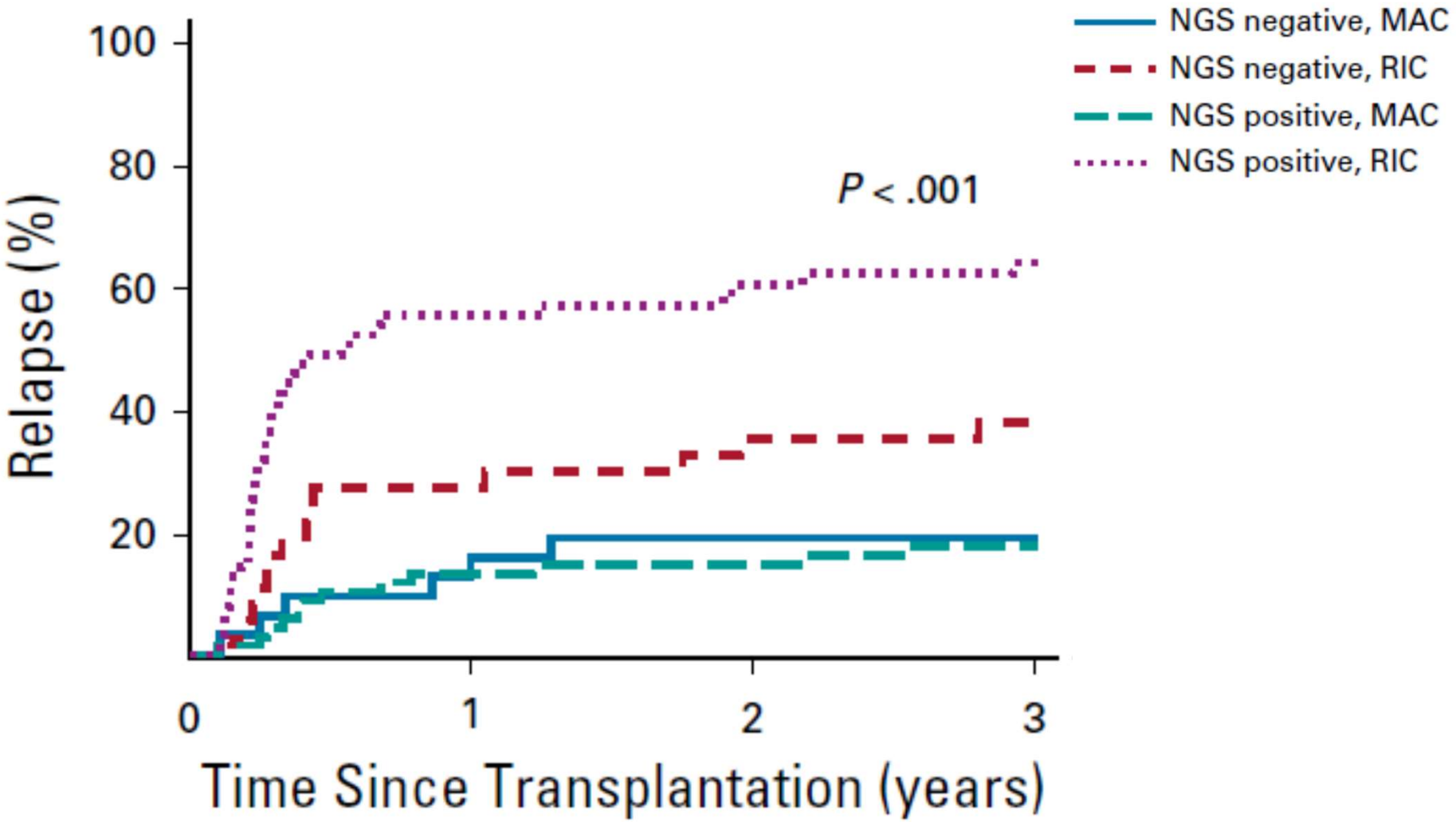
Hourigan CS et al. JCO 2020;38(12):1273-1283

Patients Characteristics

Characteristic	MAC, No. (%)	RIC, No. (%)	Total, No.
No. of patients	95	95	190
Age			
Median (range)	54.9 (21.9-66)	54.7 (21.9-65.9)	
≤ 50	28 (29.5)	27 (28.4)	55
> 50	67 (70.5)	68 (71.6)	135
Sex			
Female	44 (46.3)	51 (53.7)	95
Male	51 (53.7)	44 (46.3)	95
HCT-CI			
0	33 (34.7)	33 (34.7)	66
1-2	33 (34.7)	30 (31.6)	63
> 2	29 (30.5)	32 (33.7)	61

Hourigan CS et al. JCO 2020;38(12):1273-1283

Outcome according to MRD level prior to the ASCT and the conditioning regimen received



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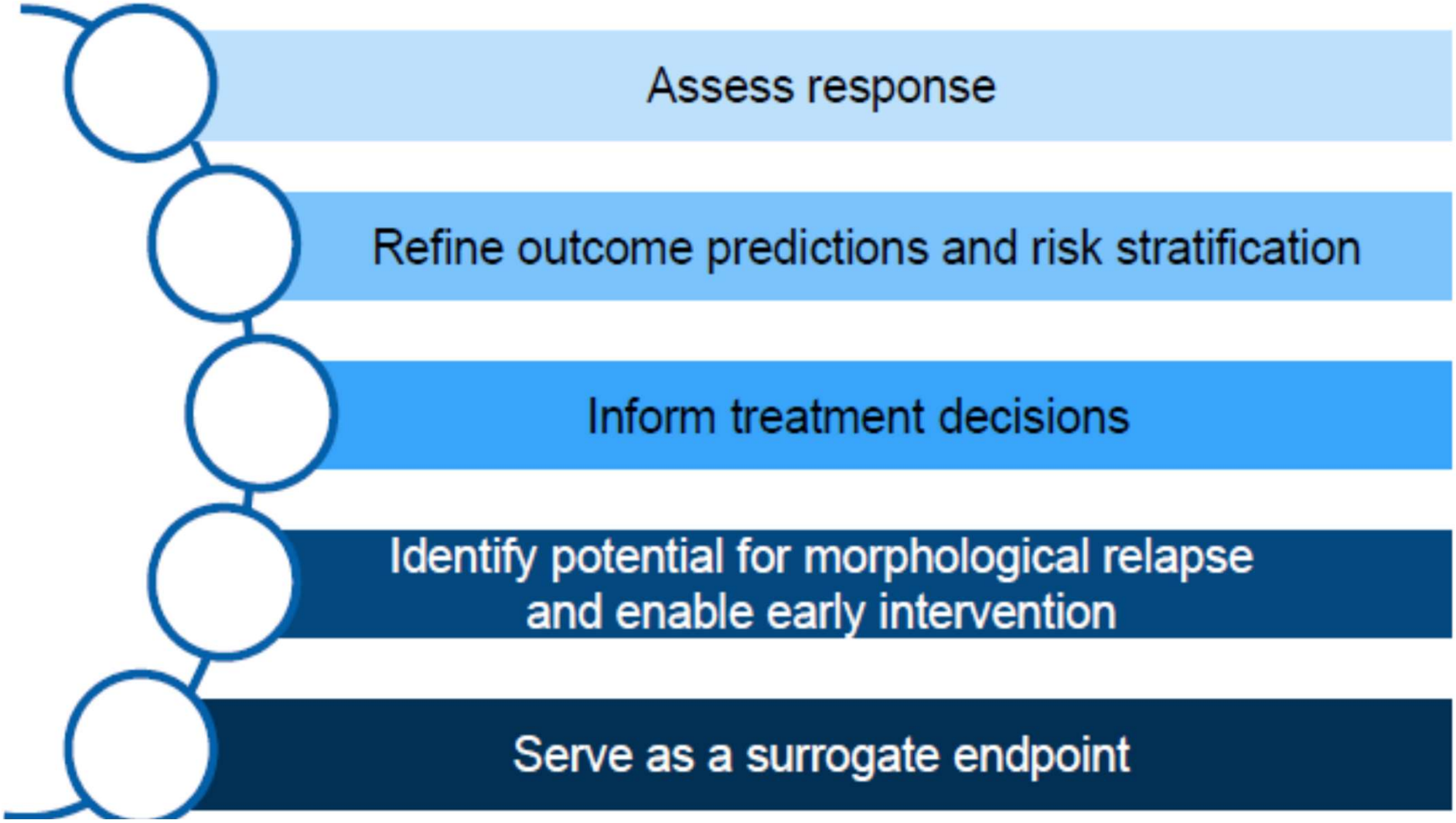
MRD Applications



HARMONY

Research Project Proposal

Project Title:
(Max. 150 characters)

Measurable residual disease as surrogate marker for survival in AML: an individual patient-level correlation

Aim:

To assess MRD status after 2 cycles of CHT as a potential surrogate endpoint, by the collaborative MRD AML group consisting of AML trial groups (HOVON-SAKK, AMLSG, UK-NCRI, GIMEMA, SAL, ALFA, Polish AML Group), pharmaceutical companies within the HARMONY project, by performing a prospectively planned, pooled analysis of individual patient data from prospective randomized controlled trials of upfront treatment of AML