FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

L'attuale approccio clinico al paziente con **Sindrome Mielodisplastica**

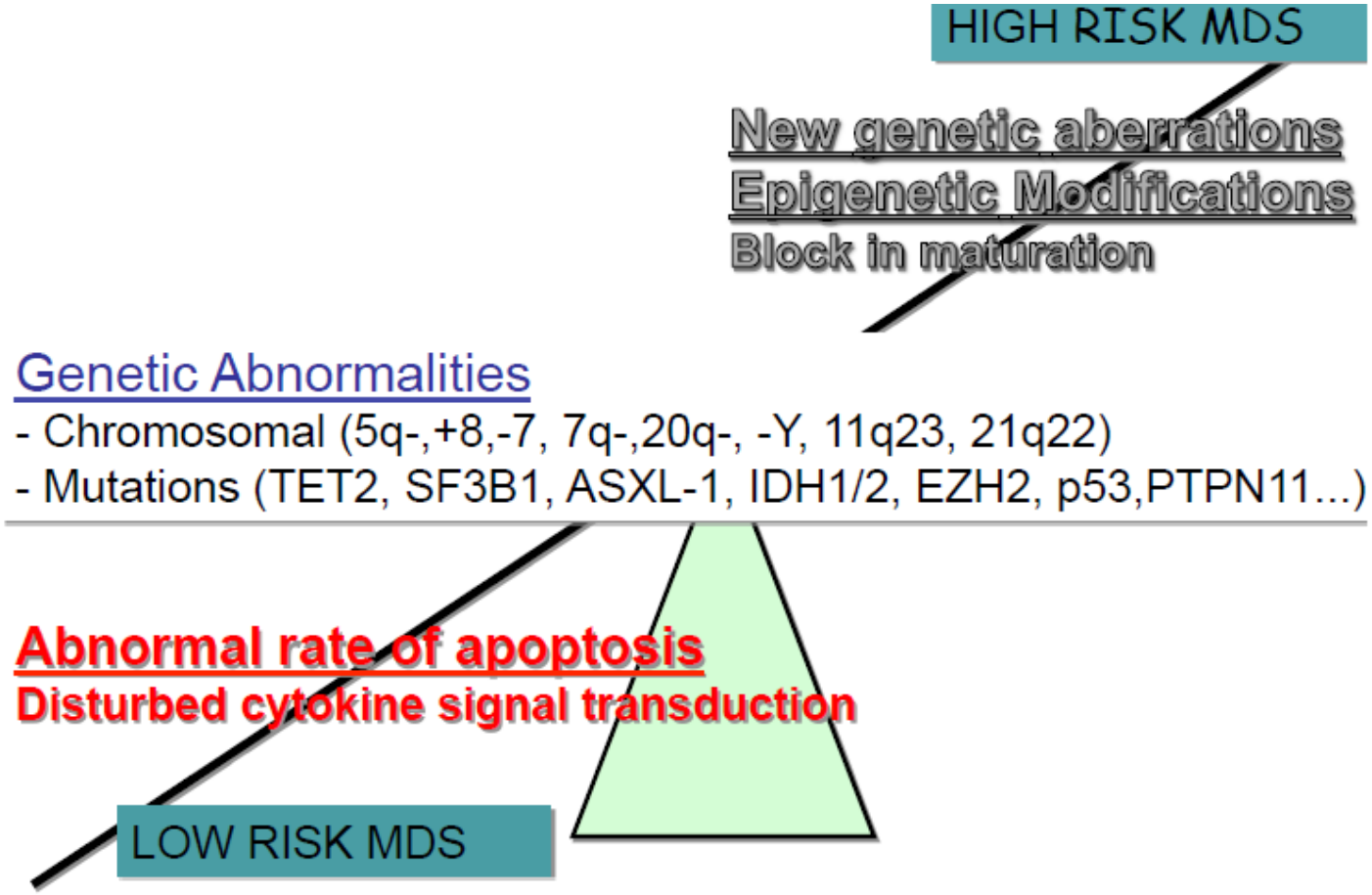
Ottimizzazione del Trattamento con Ipometilanti

Antonella Poloni

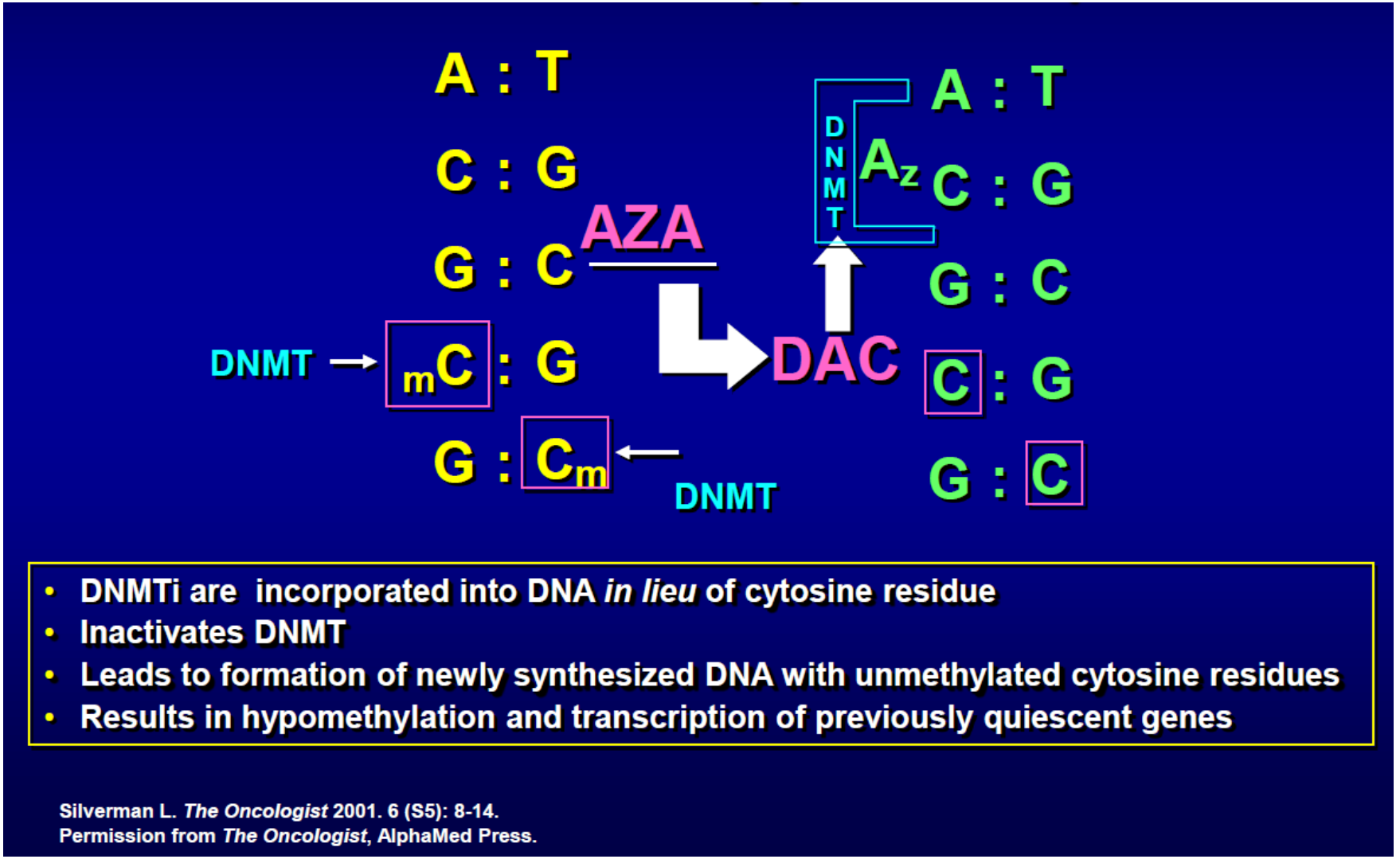
Clinica di Ematologia

Ancona

Pathogenesis of MDS



DNA Methyltransferase Inhibitor Induced DNA Hypomethylation

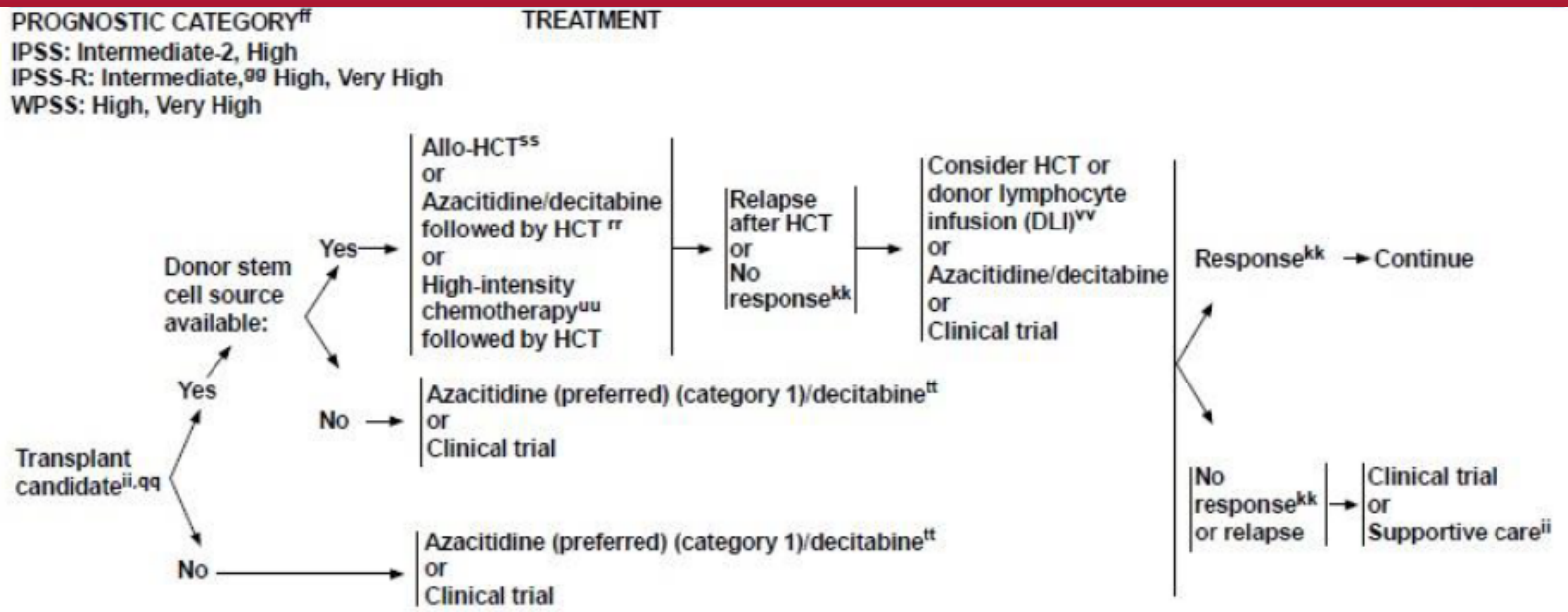


- DNMTi are incorporated into DNA *in lieu* of cytosine residue
- Inactivates DNMT
- Leads to formation of newly synthesized DNA with unmethylated cytosine residues
- Results in hypomethylation and transcription of previously quiescent genes

Silverman L. *The Oncologist* 2001. 6 (S5): 8-14.
Permission from *The Oncologist*, AlphaMed Press.

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) MDS

Version I.2016



[ff]Presence of comorbidities should also be considered for evaluation of prognosis. See Comorbidity Indices in the Discussion.

[gg]Given its more accurate risk stratification, the IPSS-R categorization is preferred although the other systems also have good value. IPSS-R Intermediate patients may be managed as very low/low risk or high/very high risk depending on additional prognostic factors such as age, performance status, serum ferritin levels, and serum LDH levels.

[ii]See Supportive Care (MDS-B).

[kk]Response should be evaluated based on IWG criteria: Cheson BD, Greenberg PL, Bennett JM, et al. Clinical application and proposal for modification of the International Working Group (IWG) response criteria in myelodysplasia. Blood 2006;108:419-425.

[qq]Based on age, performance status, major comorbid conditions, psychosocial status, patient preference, and availability of caregiver. Patients may be taken immediately to transplant or bridging therapy can be used to decrease marrow blasts to an acceptable level prior to transplant.

[rr]Azacitidine, decitabine, or other therapy may also be used as a bridge to transplant while awaiting donor availability. However, these agents should not be used to delay available HCT.

[ss]HCT: Allogeneic-matched sibling including standard and reduced-intensity preparative approaches or MUD.

[tt]While the response rates are similar for both drugs, survival benefit from a phase III randomized trial is reported for azacitidine and not for decitabine. Azacitidine or decitabine therapy should be continued for at least 4 to 6 cycles to assess response to these agents. In patients who have clinical benefit, continue treatment with hypomethylating agent as maintenance therapy.

[uu]High-intensity chemotherapy:
- Clinical trials with investigational therapy (preferred), or
- Standard induction therapy if investigational protocol is unavailable or if it is used as a bridge to HCT.

[vv]Consider second transplant or DLI immuno-based therapy for appropriate patients who had a prolonged remission after first transplant.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

MDS-11

blood
2013 122: 2943-2964
doi:10.1182/blood-2013-03-492884 originally published online August 26, 2013

Diagnosis and treatment of primary myelodysplastic syndromes in adults: recommendations from the European LeukemiaNet

Luca Malcovati, Eva Hellström-Lindberg, David Bowen, Lionel Adès, Jaroslav Cermak, Consuelo del Cañizo, Matteo G. Della Porta, Pierre Fenaux, Norbert Gattermann, Ulrich Germing, Joop H. Jansen, Moshe Mittelman, Ghulam Mufti, Uwe Platzbecker, Guillermo F. Sanz, Dominik Selleslag, Mette Skov-Holm, Reinhard Stauder, Argiris Symeonidis, Arjan A. van de Loosdrecht, Theo de Witte and Mario Cazzola

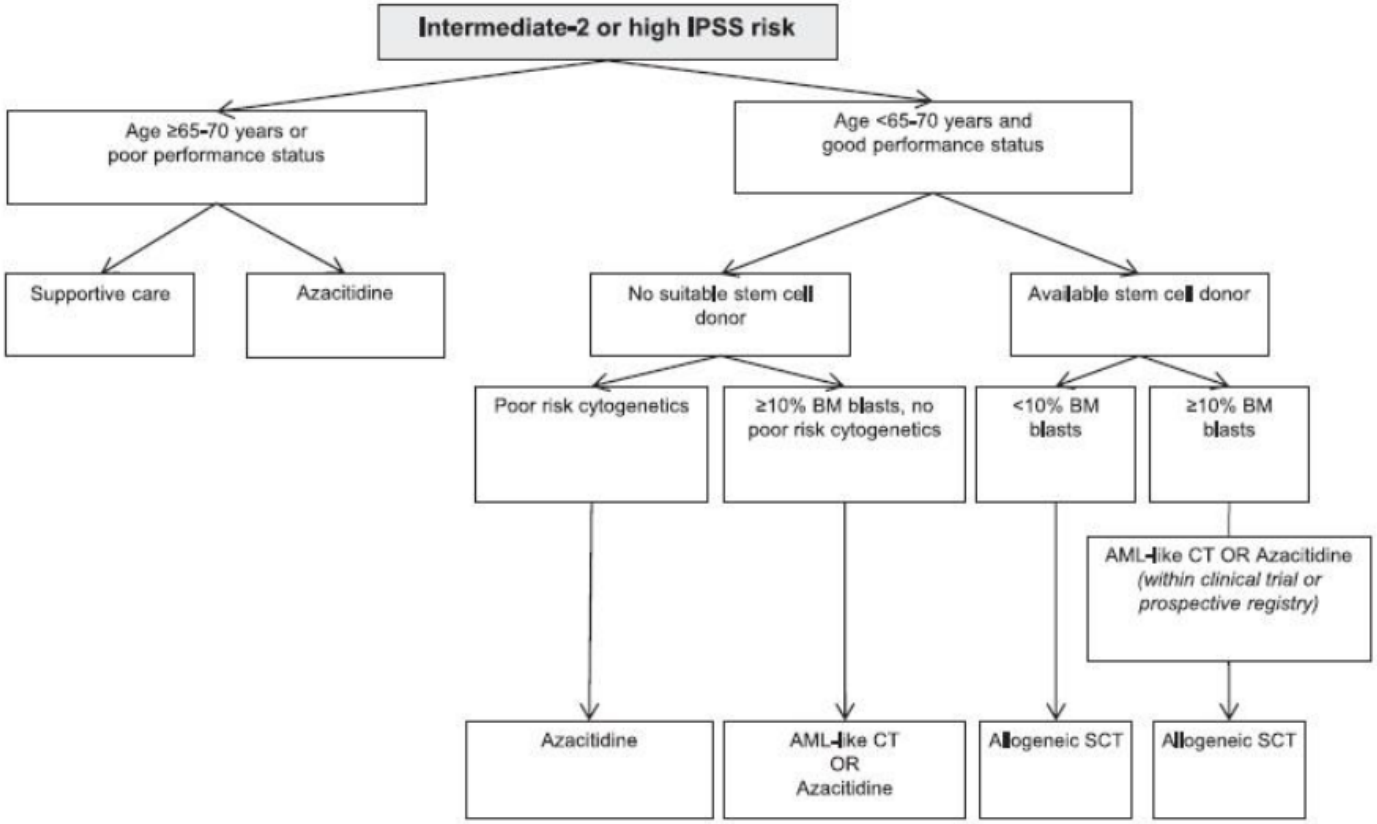


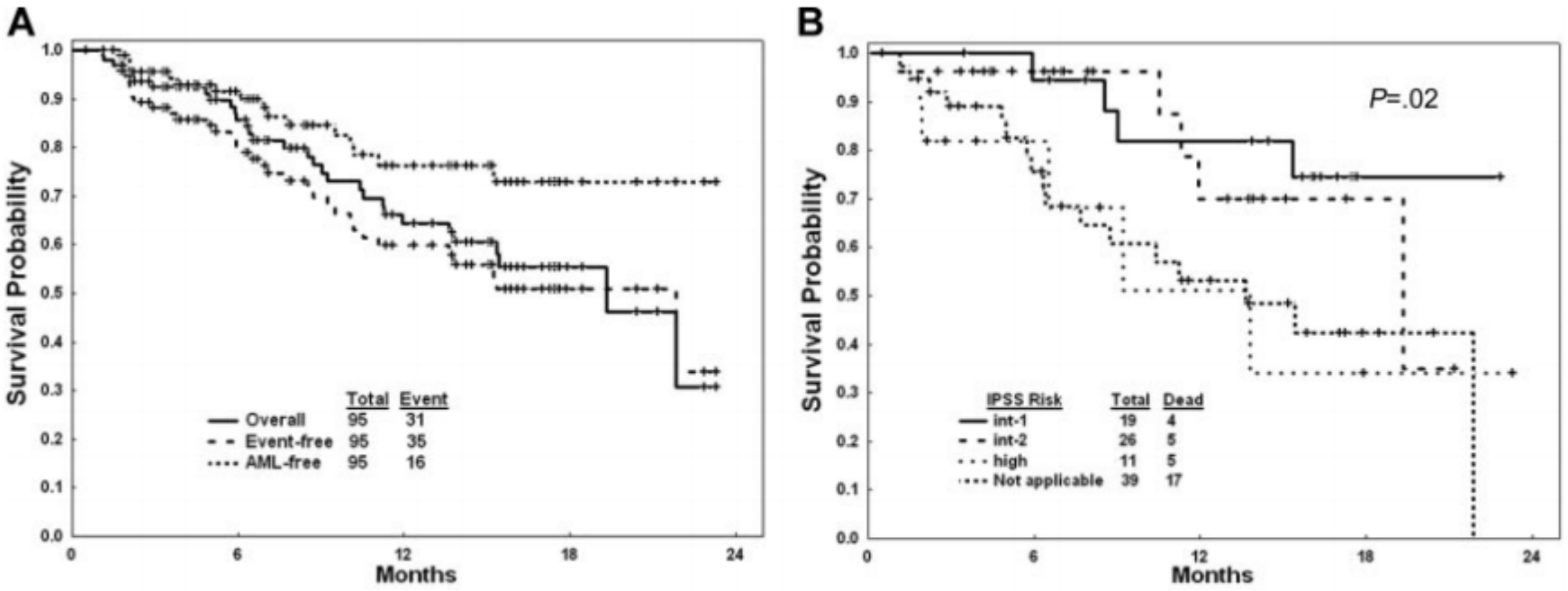
Figure 3. Therapeutic algorithm for adult patients with primary MDS and intermediate-2 or high IPSS score. CT, chemotherapy.

Azacitidine and Decitabine in MDS

Author	N° of Patients	Therapy	Response (ORR)	Survival (OS) (months)
Silverman et al., 2002: CALGB 9221	191	AZA vs BSC	AZA: 60% BSC: 5%	AZA: 20 BSC: 14 Accounting for crossover: AZA: 18 BSC: 11
Fenaux et al., 2009: AZA-001	358	AZA vs CCR	AZA: 49% CCR: 41%	AZA: 24 CCR: 15
Kantarjian et al., 2006: D-0007	170	DAC vs BSC	DAC: 30% BSC: 7%	DAC: 14 BSC: 14.9
Lubbert et al., 2011: EORTC-06011	233	DAC vs BSC	DAC: 34% BSC: 2%	DAC: 10.1 BSC: 8.5

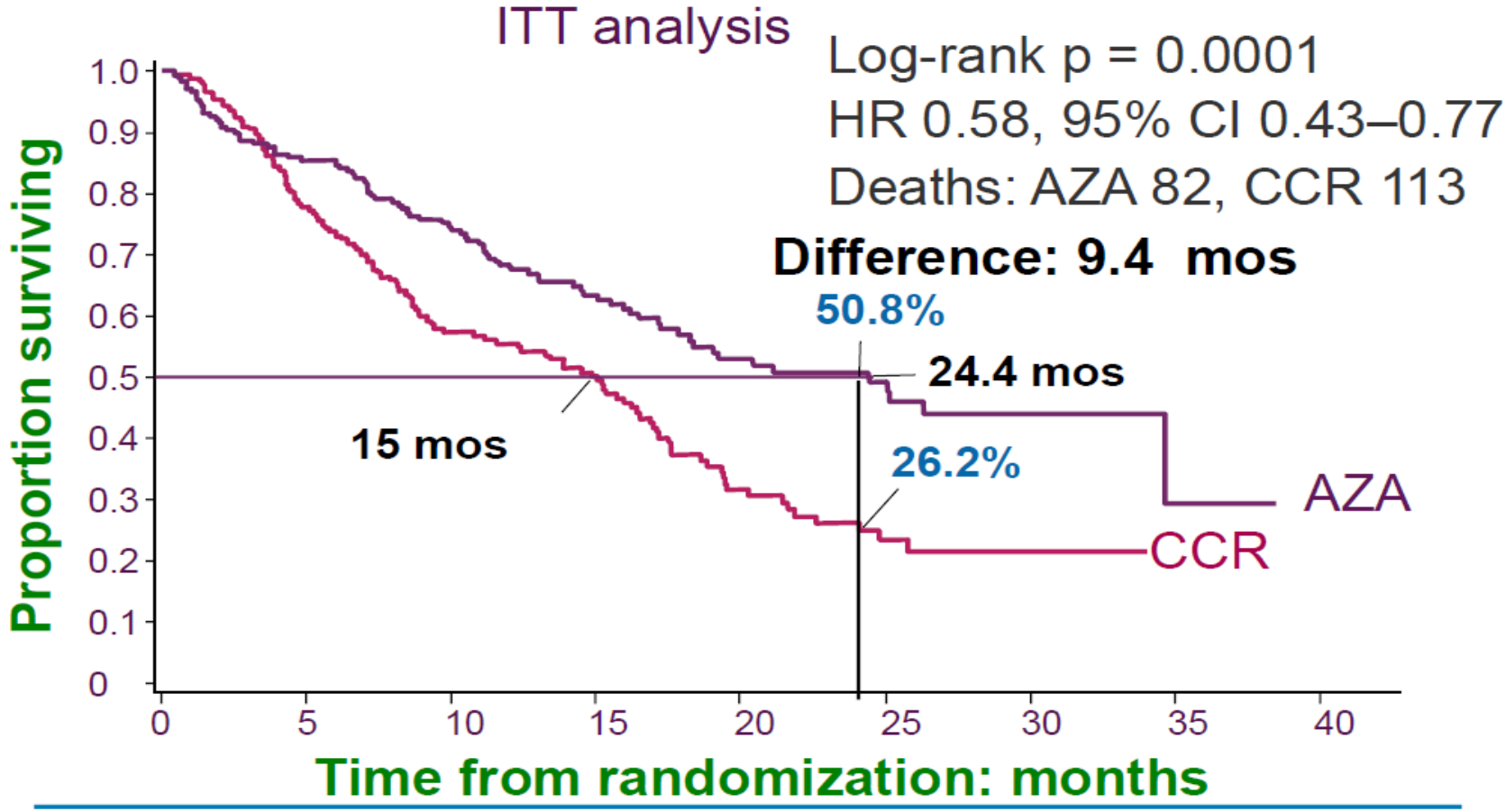
AZA: azacitidine; DAC: decitabine; BSC: Best supportive care; CCR: Conventional care regimens; ORR: Overall response rate; OS: Overall survival.

Decitabine in MDS



(A) Survival (solid line); event-free survival, AML or death; dashed line); and duration of freedom from AML (dotted line). (B) Survival in IPSS risk groups and in CMML

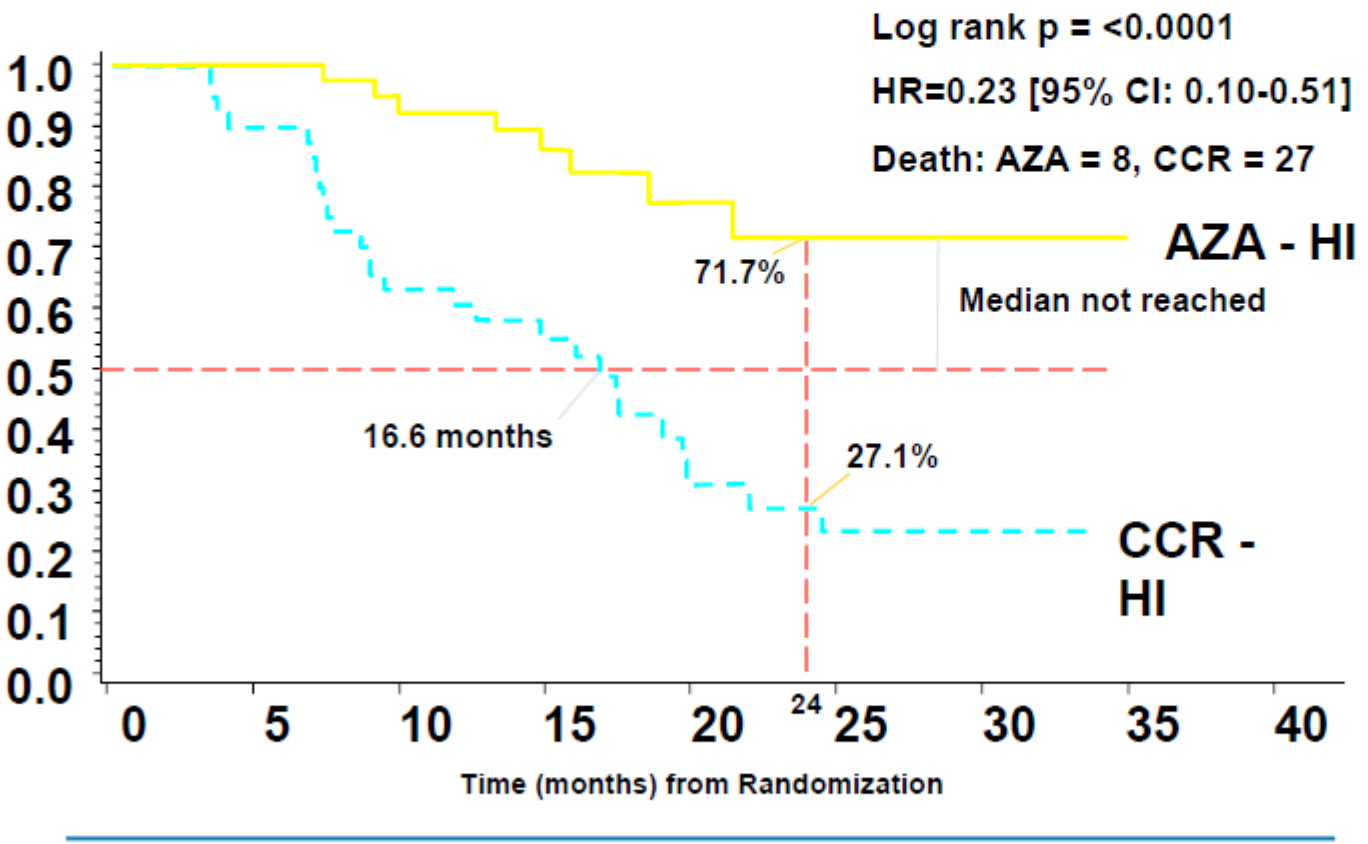
Overall survival: AZA vs CCR



CI, confidence interval; ITT, intention-to-treat.

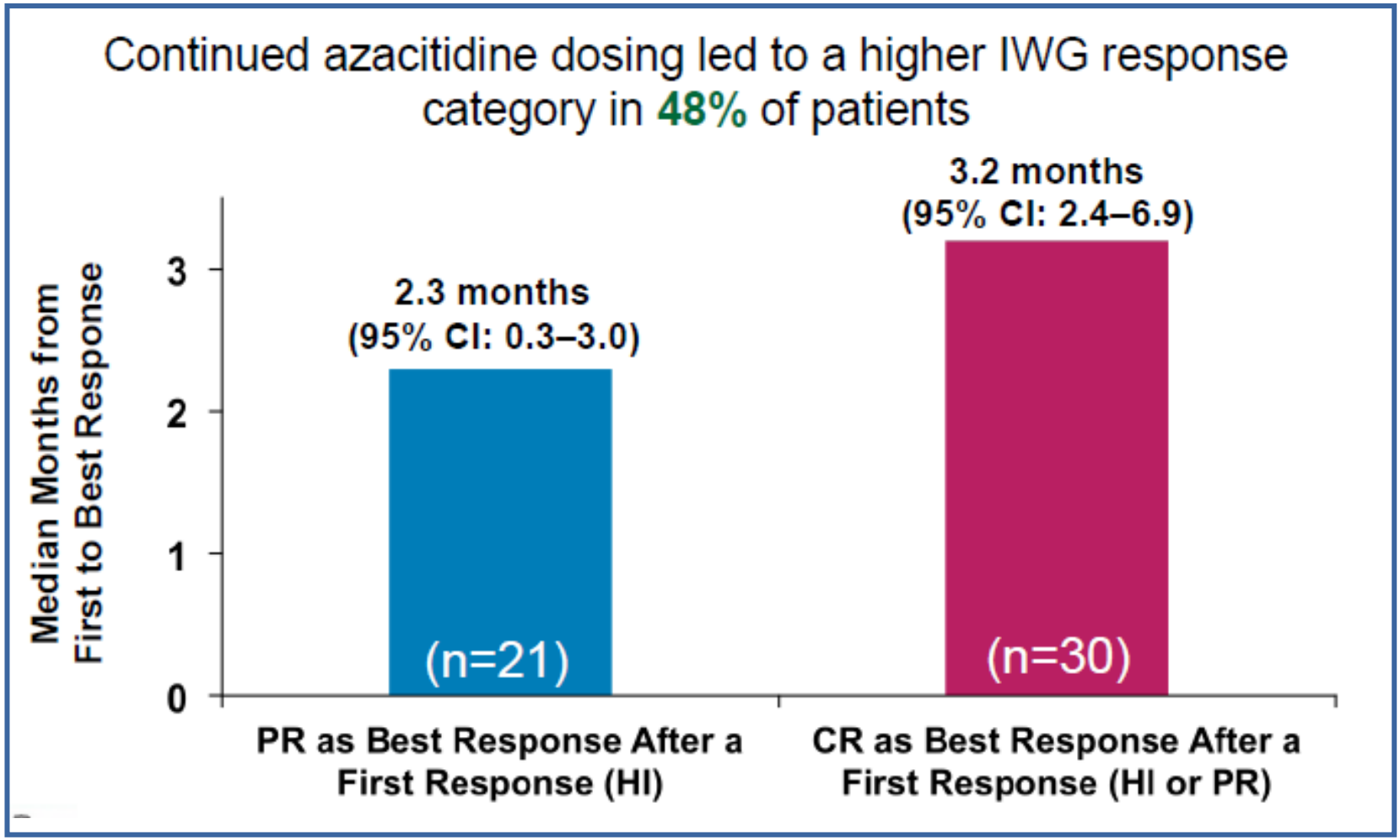
Fenaux P, et al. Lancet Oncol. 2009;10:223-32.

AZA vs CCR: OS in Pts with Best Response of HI

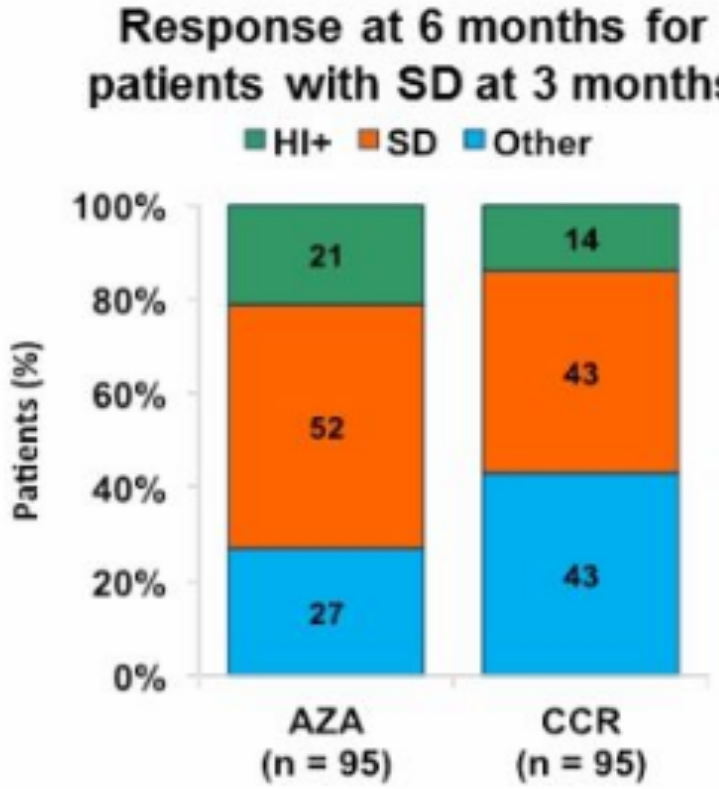


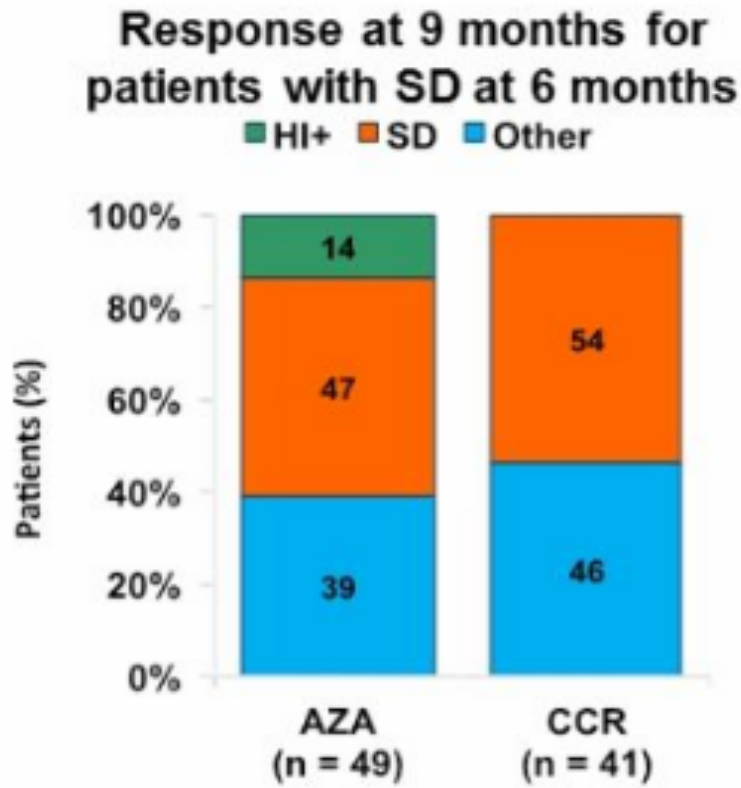
Gore S, et al, Haematologica. 2013 Jul;98(7):1067-72.

AZA-001: time from first to best response



AZA-001: Multivariate Analysis: Continued AZA Improved Responses Beyond Stable Disease



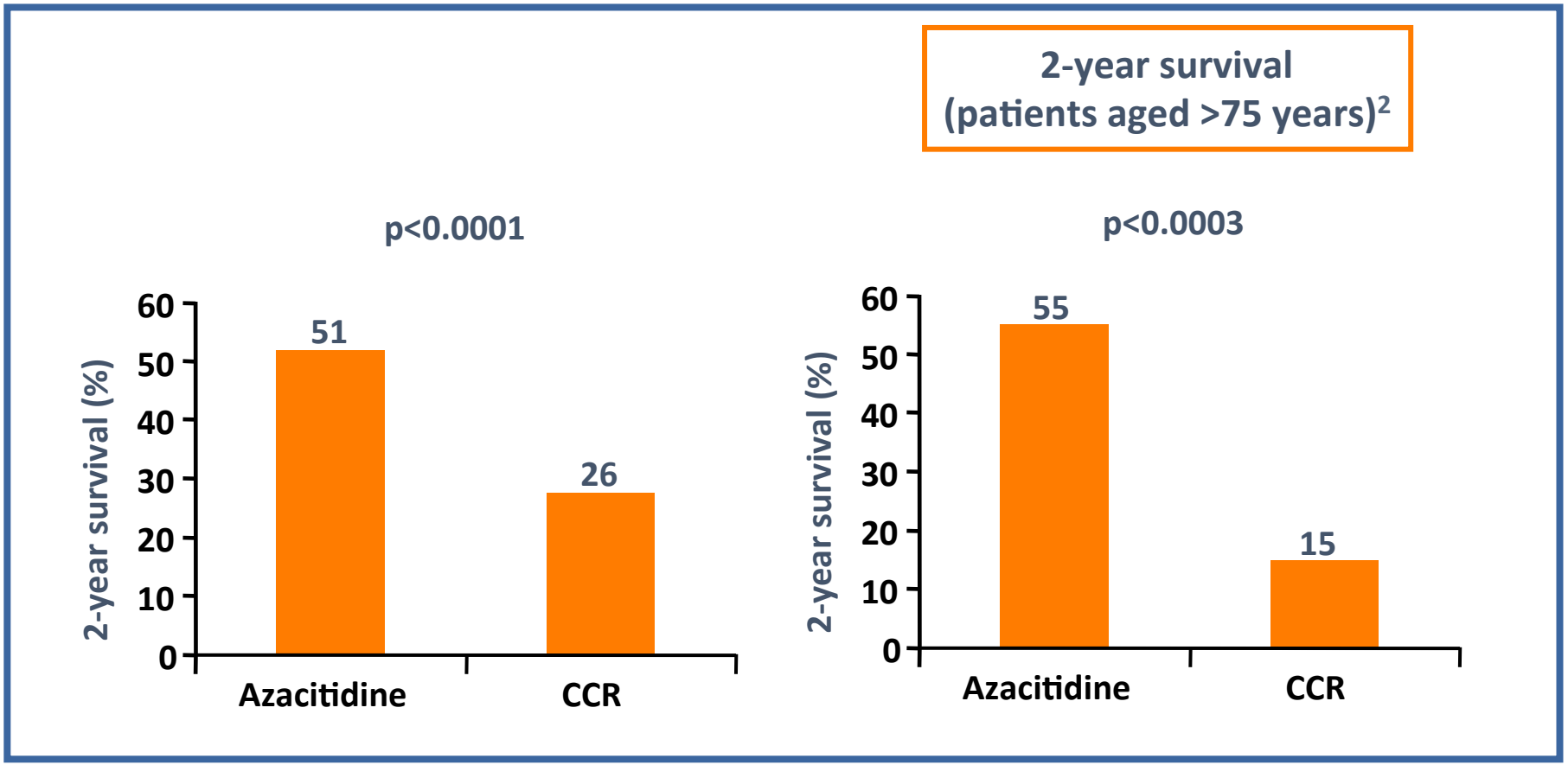


- 21% of AZA-treated patients compared with 14% of CCR-treated patients with SD at 3 months achieved an HI⁺ by 6 months
- 14% of AZA-treated patients compared with 0% of CCR-treated patients with SD at 6 months achieved an HI⁺ by 9 months

AZA, azacitidine; CCR, conventional care regimen; CR, complete response/remission; HI, hematologic improvement; HI+, CR, PR, and/or HI; OS, overall survival; PR, partial response/remission; SD, stable disease

Gore S, et al, Haematologica. 2013 Jul;98(7):1067-72.

La 5-aza è utilizzabile anche nei «very elderly»



Fenaux P, et al. Lancet Oncol 2009;
Seymour, Crit Rev Oncol Hematol, 2010

TABLE IV. Use of Hypomethylating Agents in Chronic Myelomonocytic Leukemia

References	Number of patients	Median age (years, range)	Phase of study	Treatment regimen	Response rates	Toxicity	Median survival (months)	Progression to acute myeloid leukemia
Aribi (2007) [59]	19	66 (44–82)	II	Decitabine 100 mg/m^2 per course in three different schedules, repeated every 4 weeks	CR: 58% HI: 11%	Myelosuppression associated complications: 8%	19	NR
Wijermans (2008) [65]	31	71 (53–81)	II	Decitabine 15 mg/m^2 over 4 hr IV three times per day on 3 consecutive days, with a total dose of 135 mg/m^2 per course, every 6 weeks	CR: 10% PR: 16% HI: 19%	Nausea, vomiting, pneumonia, mortality due to sepsis: 3%	15	NR
Costa (2010) [61]	38	70 (36–83)	II	Azacitidine 75 mg/m^2/day for 7 days or 100 mg/m^2/day for 5 days every 4 weeks	CR: 11% PR: 3% HI: 25%	Pneumonia, mortality due to sepsis: 3%	12	NR
Garcia-Manero (2011) [63]	41 (4 with CMML)	70 (31–91)	I	One cycle of subcutaneous azacitidine 75 mg/m^2 on the first 7 days of cycle 1, followed by oral azacitidine daily, 120–600 mg, on the first 7 days of each additional 28-day cycle	ORR: 35% in previously treated patients and 73% in previously untreated patients	diarrhea, nausea, vomiting,febrile neutropenia, fatigue	NR	NR
Braun (2011) [60]	39	71 (54–88)	II	Decitabine 20 mg/m^2 per day intravenously for 5 days every 28 days	CR: 10% PR: 20% HI: 8% ORR: 38%	Neutropenia and thrombocytopenia (36%), severe infection (20%)	18	NR
Thorpe (2012) [64]	10	66 (41–76)	II	Azacitidine 75 mg/m^2 for 7 days or azacitidine 100 mg/m^2 for 5 days every 28 days	CR: 20% HI: 40% ORR: 60%	Thrombocytopenia, pneumonia (20%)	29	NR
Ades (2013) [58]	76	70 (33–85)	II	Azacitidine 75 mg/m^2 for 5–7 days every 28 days	CR: 17% PR: 1% Marrow CR: 8% HI: 17% ORR: 43%	NR	29	31% after 1.2 years from azacitidine initiation
Wong (2013) [66]	11	65 (42–80)	II	Azacitidine 75 mg/m^2 for 7 days every 28 days	CR: 9% Marrow CR: 27% PR: 9% HI: 9% ORR: 55%	Local skin reactions (55%), nausea (36%), infection (73%)	17	18%
Fianchi (2013) [62]	31	69 (53–84)	II	Azacitidine 50–75 mg/m^2 for 7 days in 22 patients, and 100 mg *flat* dose for 5–7 days in nine patients	CR: 45% PR: 3% HI: 6% ORR: 54%	Grade 4 thrombocytopenia (6%), grade 4 anemia (6%)	37	16% after 12.7 months

CR, complete remission; PR, partial remission; HI, hematologic improvement; ORR, overall response rate; NR, not reported.

Tefferi et al *2013*

Azacitidine in CMML:
an Italian retrospective study

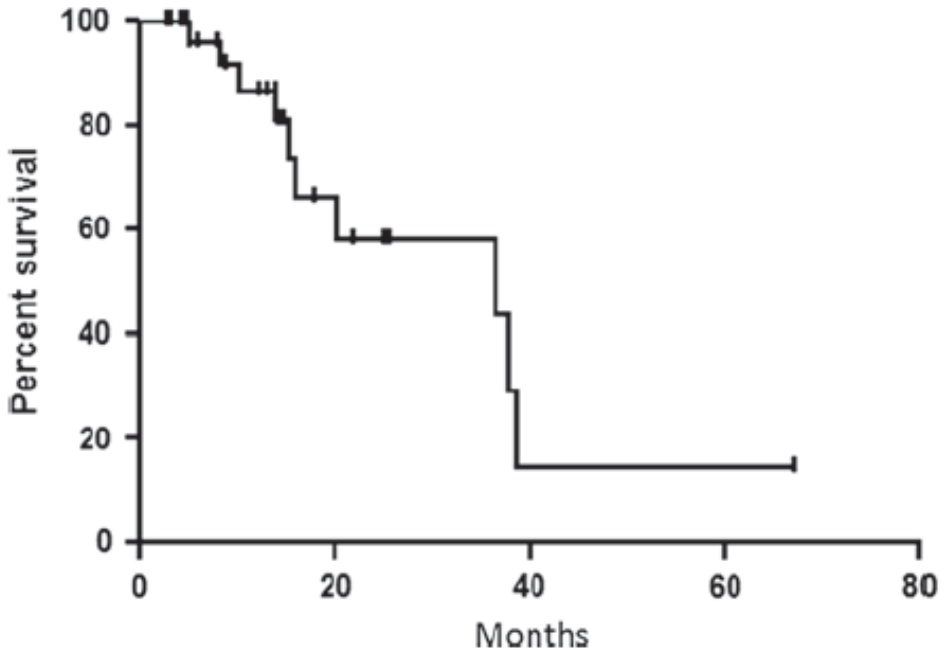
A retrospective study of 31 patients diagnosed with CMML and treated with azacitidine at nine Italian haematology centres (2005–2011)

Median OS
37 months

Median OS (months) in patients responding to azacitidine
vs. SD vs. PD
37 vs. 15 vs. 5 (p=0.07)

No differences stratifing for karyotype, PLT count, IPSS, CMML-1 vs CMML-2 and aza dose

Improved survival associated with low monocytes count (<10 x 10^9/L and PB blasts <5% at time of therapy start



The response rate was particularly high in this study. The authors suggest CMML may be very sensitive to azacitidine due high levels of methylation and high incidence of mutations in epigenetic regulator genes e.g. TET2, ASXL1 and EZH2

Fianchi L, et al. Leuk Lymphoma 2012

A phase II, open, multicenter study to evaluate the efficacy of low dose-Dacogen® (decitabine) in patients with chronic myelomonocytic leukemia

FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

Decitabine can be given in elderly high risk CMML patients, with acceptable safety profile.

Overall response rate at 6 mos (CR +PR+HI) of 50%.

Median duration of response is (10 ..)months

It is possible to discriminate decitabine responsive vs non responsive CMML patients prior therapy on the basis of DMR

CXCL4 and CXCL7 are overexpressed in non-responders and abrogates DAC's effect on primary cells. This may provide us new potential ways of therapeutic targeting

The Journal of Clinical Investigation RESEARCH ARTICLE

2015

Specific molecular signatures predict decitabine response in chronic myelomonocytic leukemia

Kristen Meldi,[1] Tingting Qin,[1] Francesca Buchi,[2] Nathalie Droin,[3] Jason Sotzen,[1] Jean-Baptiste Micol,[3,4] Dorothée Selimoglu-Buet,[3] Erico Masala,[2] Bernardino Allione,[5,6] Daniela Gioia,[6,7] Antonella Poloni,[6,8] Monia Lunghi,[6,9] Eric Solary,[3] Omar Abdel-Wahab,[4] Valeria Santini,[2,6] and Maria E. Figueroa[1]

STUDIO RANDOMIZZATO DI FASE III CON DECITABINA CON O SENZA IDROSSIUREA VS IDROSSIUREA DA SOLA IN PAZIENTI CON CMML

GFM-DAC-CMML

Obiettivo Primario

- Confrontare tra i due bracci l'EFS
- Gli eventi comprenderanno

  - Morte per qualsiasi causa

  - Trasformazione in LAM secondo i criteri WHO: >20% di blasti nel sangue periferico o ≥ 20% blasti midollari (e, per i blasti midollari, si tratta di un incremento ≥ 50%)
- - Progressione della mieloproliferazione definita come :
  - (i) incremento ≥ 50% delle dimensioni della milza (determinato tramite ecografia) o raddoppiamento dei WBC (nonostante la dose ottimale di HY o DAC, in assenza di infezioni concomitanti)
  - (ii) Manifestazione o persistenza dopo almeno 3 cicli di DAC o HY

Obiettivo Secondario

Confrontare tra i due bracci:

- Sopravvivenza totale
- Progressione in LAM
- Il numero di risposte totali e complete al ciclo 3 e 6
- Durata della risposta
- Tossicità (ematologica e non ematologica)
- Utilizzo delle risorse sanitarie
- Fattori prognostici di risposta e sopravvivenza con DAC e HY, usando in particolare:

- Gli score prognostici italo-spagnoli, tedeschi e francesi pubblicati

- Mutazioni somatiche

Azacitidine in patients with AML: real-world clinical experience – Italian named patient programme

Patient characteristics (n=82)

- Median age (range):
  - untreated: 77 (46–87) years
  - pretreated: 67 (29–81) years
- Type of AML
  - de-novo: 67%
  - secondary: 30%
- BM blasts
  - median (range):
    - untreated: 35 (20–80)
    - pretreated: 30 (20–90)
  - <30%: 46% (treated); 36% (untreated)
  - ≥30%: 54% (treated); 64% (untreated)
- Cytogenetic risk group*
  - intermediate: 54%
  - poor: 28%
  - N/A: 24%
- Prior therapy†
  - low-dose chemotherapy: 30%
  - high-dose chemotherapy: 70%

Azacitidine

Dose

Untreated patients
- **75mg/m²/day x 7: 66%**
- **100mg/day: 34%**
- **concomitant VPA: 6%**

Pretreated patients
- **75mg/m²/day x 7: 38%**
- **100mg/day: 62%**
- **concomitant VPA: 42%**

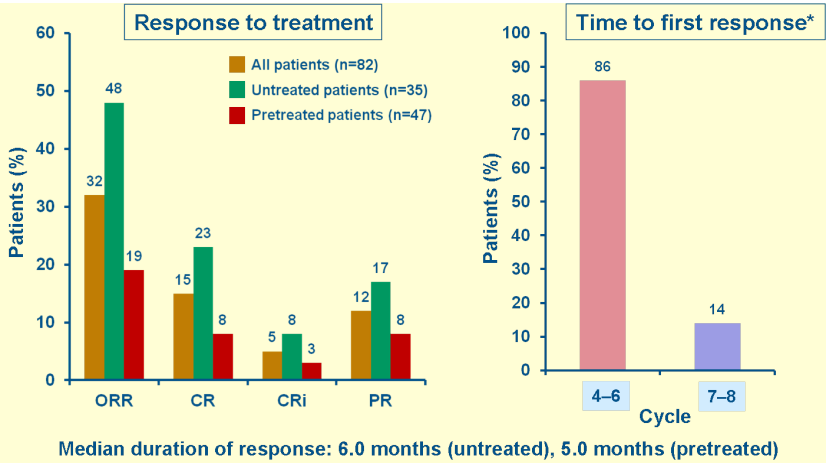
Endpoints

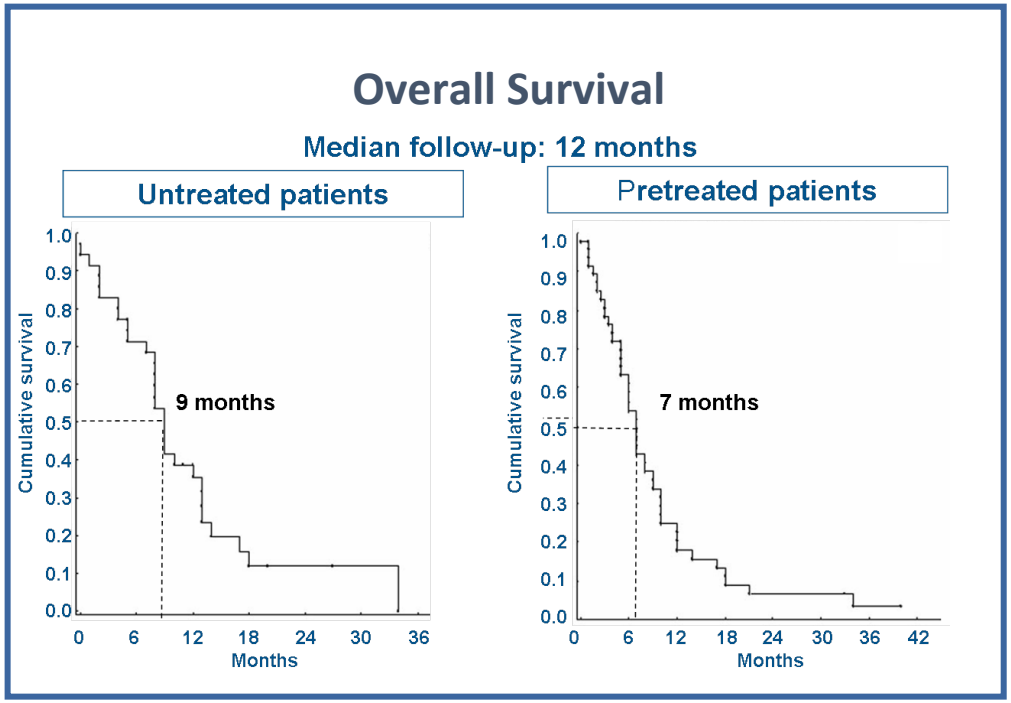
Primary
- **ORR†**

Secondary
- **Duration of response**
- **OS**
- **Safety**

Maurillo L, et al. Cancer 2012;118:1014–22

Azacitidine in patients with AML: real-world clinical experience – Italian named patient programme

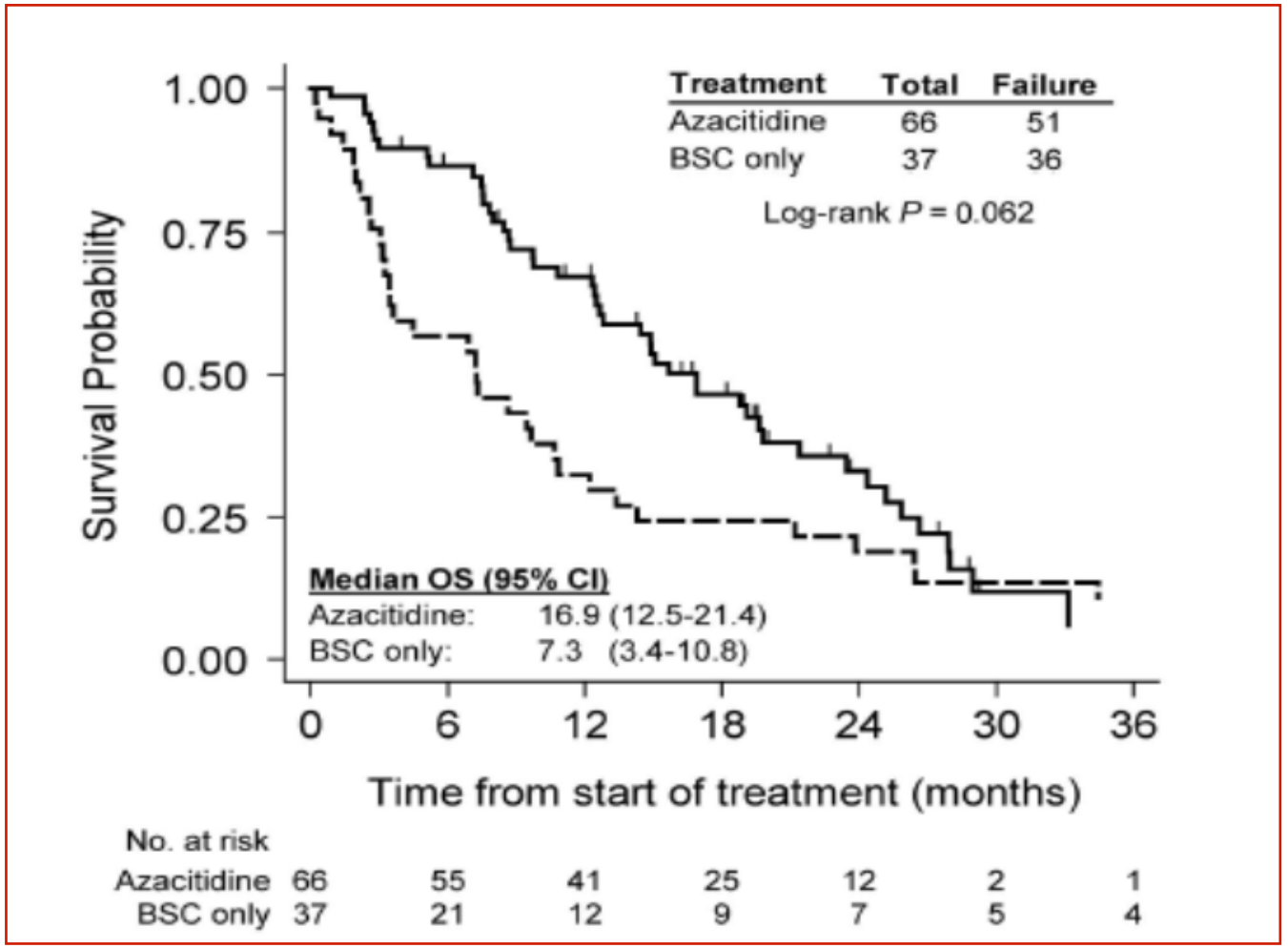




Median OS was longer in untreated patients compared with patients who had been pretreated prior to receiving azacitidine

Maurillo L, et al. Cancer 2012;118:1014–22

What happens in real life?
AZA treatment Dutch Experience



Dinmohamed et al, *Leukemia* 2015

Response to AZA is independent of p53 expression in HR MDS and secondary AML

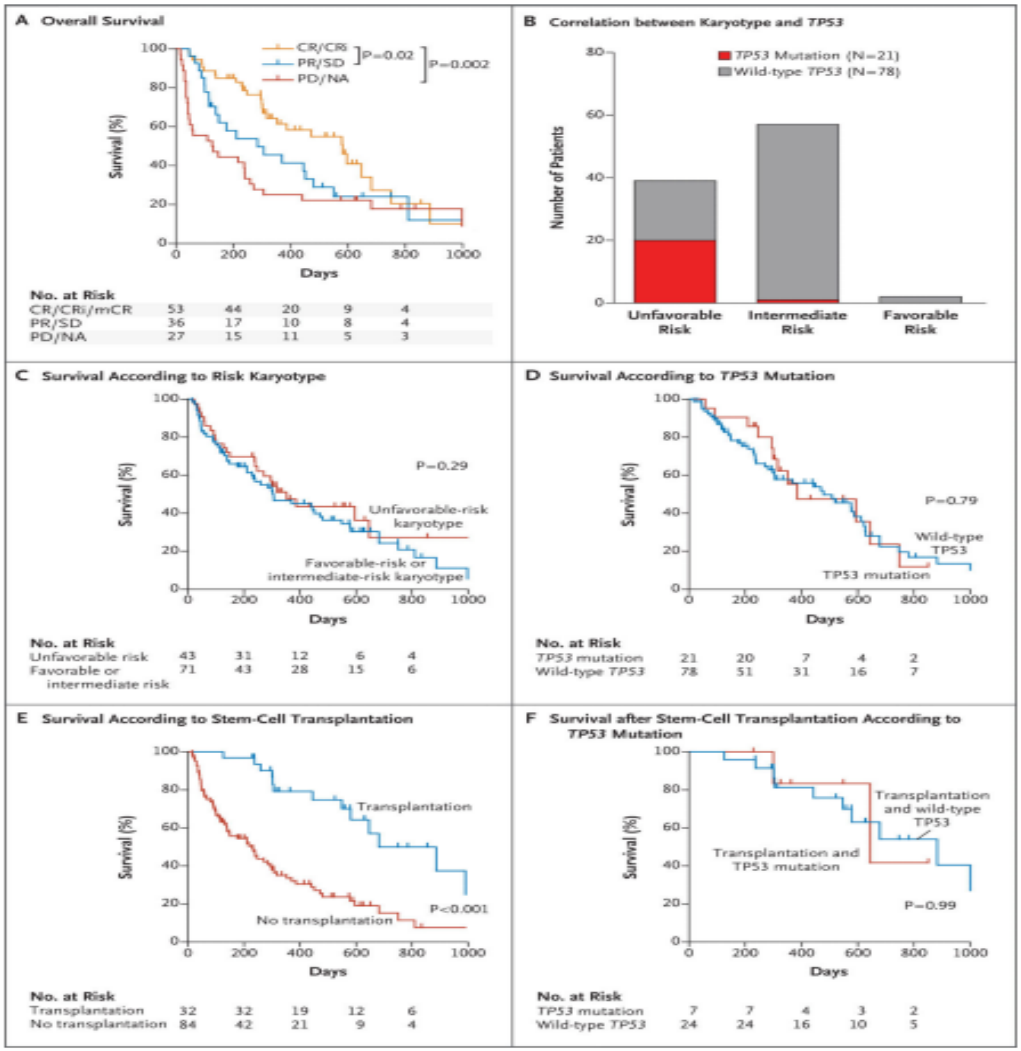
Table 2. Response to azacitidine.

N	p53 negative patients	p53 positive patients	P
5-Aza cycles Median (range)	4 (1-29)	5 (1-22)	0.926‡
All ORR (CR, PR, SD with HI) SD without HI	n=65 16 (25%) 23/32 (72%)	n=35 16 (46%) 9/32 (28%)	 0.033* 0.020*
MDS ORR (CR, PR, SD with HI)	n=29 4 (14%)	n=24 11 (46%)	 0.008*
sAML ORR (CR, PR, SD with HI)	n=30 11 (37%)	n=9 3 (33%)	
Very poor cytogenetics ORR (CR, PR, SD with HI) + abnormal Chr. 5 + monosomal KT	 3/9 (33%) 2/6 (33%) 1/4 (25%)	 7/21 (33%) 7/17 (41%) 5/14 (36%)	

For comparison between patients with and without TP53 mutations a Fisher's exact (*), χ^2 (+) or Mann-Whitney-U test (‡) was used. ORR: overall response rate; CR: complete remission; PR: partial remission; SD: stable disease; HI: hematologic improvement.

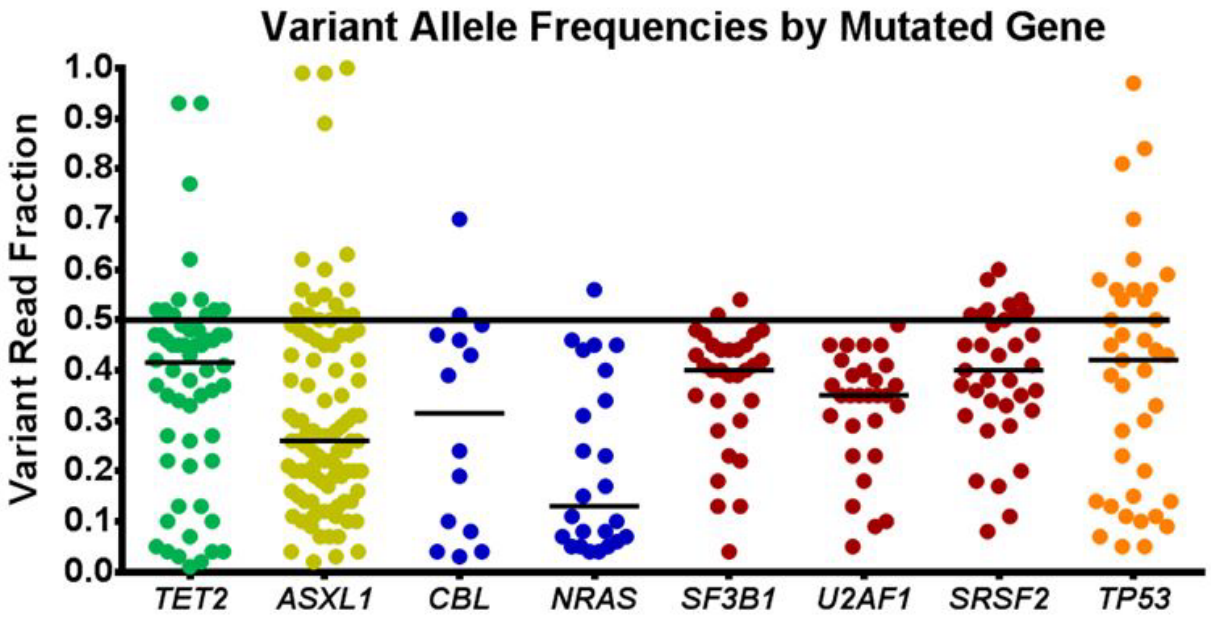
Muller-Thomas C et al, Haematologica 2014

Tp53 expression and Decitabine in AML and MDS



Welch et al, NEJM 2016

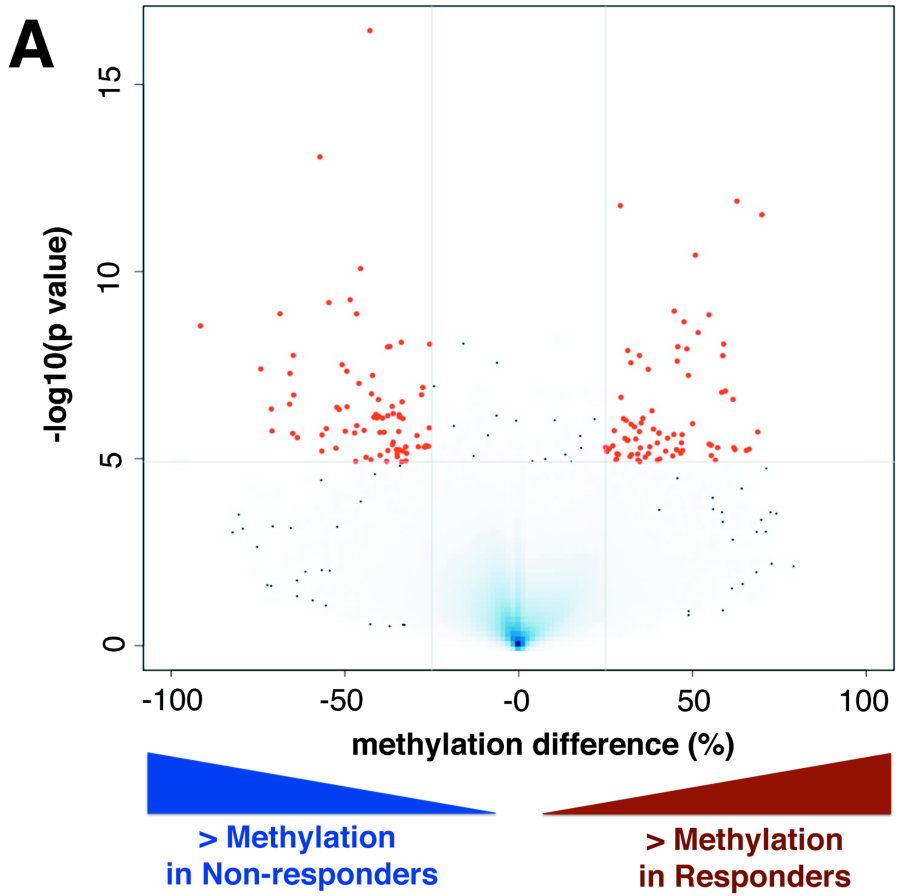
Hypomethylating Agents: Prediction of Response



Gene (n) *VAF ≥ 0.1*	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
TET2 **(50)**	**1.99** (1.05, 3.80)	**0.036**	**1.98** (1.02, 3.85)	**0.044**
TET2 **mut + *ASXL1* wt (23)**	**3.65** (1.38, 9.67)	**0.009**	**3.64** (1.35, 9.79)	**0.011**

Bejar et al, Blood 2014

Distinct DNA methylation profiles at diagnosis of CMML is associated with response to decitabine



Meldi, et al. JCI 2015

Most common adverse events with azacitidine

Table 2 Most common[1] adverse events (AEs) with azacitidine

Adverse event[2]	Percent of patients			
	AZA-001 (*N* = 175)		CALGB 9221 (*N* = 150)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Patients with at least 1 individual AE occurring in ≥ 20% of patients in the azacitidine group in AZA-001	97.7	80.0	100.0	92.7
Anemia	51.4	13.7	74.0	60.7
Neutropenia	65.7	61.1	34.0	24.0
Thrombocytopenia	69.7	58.3	68.7	56.0
Constipation	50.3	1.1	39.3	3.3
Diarrhea	21.7	0.6	40.0	3.3
Nausea	48.0	1.7	67.3	5.3
Vomiting	26.9	0	48.0	2.7
Fatigue	24.0	3.4	47.3	5.3
Injection-site erythema	42.9	0	33.3	0.7
Injection-site reaction	29.1	0.6	3.3	0
Pyrexia	30.3	4.6	51.3	2.0

[1]Greater than or equal to 20% of azacitidine-treated patients in AZA-001.
[2]Multiple reports of the same preferred term for a patient are counted only once.

Santini V, Eur J Haemat 2010

Median Duration of Common Adverse Events with AZA

	AZA-001 (*N* = 175)			CALGB 9221 (*n* = 150)		
Adverse event	Percent (%) of patients	Percent (%) of events resolved[2]	Median duration (d)	Percent (%) of patients	Percent (%) of events resolved[2]	Median duration (d)
Anemia	51.4	88.2	14	71.3	97.8	8
Neutropenia	65.7	88.3	16	34.0	98.4	9
Thrombocytopenia	69.7	86.5	15	68.0	96.0	8
Constipation	50.3	91.9	8	38.7	83.3	17
Diarrhea	21.7	95.8	3	36.0	93.5	8
Nausea	48.0	95.0	4	66.7	93.8	10
Vomiting	26.9	97.9	1	48.0	98.2	5
Fatigue	24.0	85.9	8	38.7	83.1	33
njection-site erythema	42.9	97.0	12	32.7	84.9	30
njection-site reaction	29.1	97.9	12	13.3	83.3	18
Pyrexia	30.3	91.9	5	51.3	93.0	7

[1]Greater than or equal to 20% of azacitidine-treated patients in AZA-001.
[2]Multiple reports of the same preferred term for a patient are counted, and percentages are based on the total number of events.

Santini V, Eur J Haemat 2010

Common adverse events with AZA by cycle

	Percent of patients by cycles								
	AZA-001					CALGB 9221			
System organ class preferred term[2]	Cycles 1–2 ($N = 175$)	Cycles 3–4 ($N = 147$)	Cycles 5–6 ($N = 130$)	Cycles 7–8 ($N = 107$)	Cycles 9–10 ($n = 89$)	Cycles 1–2 ($N = 150$)	Cycles 3–4 ($N = 122$)	Cycles 5–6 ($n = 83$)	Cycles 7–12[3] ($n = 66$)
Anemia	32.6	18.4	13.8	11.2	13.5	66.7	52.5	34.9	28.8
Neutropenia	50.3	31.3	27.7	18.7	20.2	26.7	24.6	21.7	22.7
Thrombocytopenia	54.3	29.9	25.4	19.6	21.3	58.0	44.3	30.1	40.9
Constipation	35.4	19.7	13.1	9.3	16.9	22.0	9.0	3.6	16.7
Diarrhea	12.0	7.5	3.8	4.7	4.5	21.3	13.9	10.8	10.6
Nausea	36.0	19.0	11.5	14.0	11.2	44.7	21.3	21.7	24.2
Vomiting	17.7	10.9	5.4	7.5	5.6	32.7	8.2	9.6	9.1
Fatigue	12.6	9.5	3.1	5.6	3.4	27.3	15.6	15.7	22.7
njection-site erythema	34.9	21.1	17.7	15.9	11.2	23.3	11.5	6.0	9.1
njection-site reaction	20.6	12.9	9.2	9.3	9.0	2.7	0	1.2	0
Pyrexia	16.0	6.1	3.8	5.6	6.7	24.7	21.3	14.5	25.8

[1]Greater than or equal to 20% of azacitidine-treated patients in AZA-001.
[2]Multiple reports of the same preferred term during a cycle are counted once.
[3]CALGB 9221 data were not reported in the same cycle groupings as AZA-001 after cycles 5–6.

Santini V, Eur J Haemat 2010

Selected Infection rates (Grade 3 or 4)

	Number of events (Rate per patient-year of exposure)			
	AZA-001[1]		CALGB 9221	
	Azacitidine $N = 114$	BSC $N = 102$	Azacitidine $N = 150$	BSC $N = 92$
Infections – total[2]	55(0.51)	24 (0.41)	29(0.21)	16 (0.37)
Bacteremia	1 (0.01)	0	0	0
Bronchitis	0	0	1 (0.01)	0
Cellulitis	2 (0.02)	3 (0.05)	1 (0.01)	1 (0.02)
Clostridium Difficile colitis	3 (0.03)	0	0	0
Lower respiratory tract infection	2 (0.02)	0	0	0
Neutropenic sepsis	3 (0.03)	0	0	0
Pneumonia	14(0.13)	8 (0.14)	7 (0.05)	4 (0.09)
Sepsis	6 (0.06)	3 (0.05)	2 (0.01)	4 (0.09)
Urinary tract infection	3 (0.03)	0	0	1 (0.02)

BSC, best supportive care.

[1]Includes patients preselected to BSC in AZA-001 who were then randomized to and received azacitidine ($n = 114$) or BSC ($n = 102$).
[2]Includes events not listed here.

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Selected bleeding event rates (Grade 3 or 4)

	Number of events (Rate per patient-year of exposure)			
	AZA-001[1]		CALGB 9221	
	Azacitidine *N* = 114	BSC *N* = 102	Azacitidine *N* = 150	BSC *N* = 92
Bleeding events – total[2]	37 (0.34)	27 (0.46)	20 (0.14)	7 (0.16)
Gastrointestina hemorrhage	1 (0.01)	1 (0.02)	0	0
Gingival bleeding	3 (0.03)	0	3 (0.02)	0
Hemorrhoidal bleeding	1 (0.01)	0	0	0
Melena	0	3 (0.05)	1 (0.01)	0
Mouth hemorrhage	2 (0.02)	1 (0.02)	1 (0.01)	0
Rectal hemorrhage	2 (0.02)	1 (0.02)	2 (0.01)	0
Cerebral hemorrhage	3 (0.03)	4 (0.07)	0	0
Hematuria	2 (0.02)	1 (0.02)	0	3 (0.07)
Epistaxis	10(0.09)	10 (0.17)	7 (0.05)	0

BSC, best supportive care.

[1]Includes patients preselected to BSC in AZA-001 who were then randomized to and received azacitidine ($n = 114$) or BSC ($n = 102$).
[2]Includes events not listed here.

Santini V, Eur J Haemat 2010

Common Side Effects of AZA and Recommendations for Management

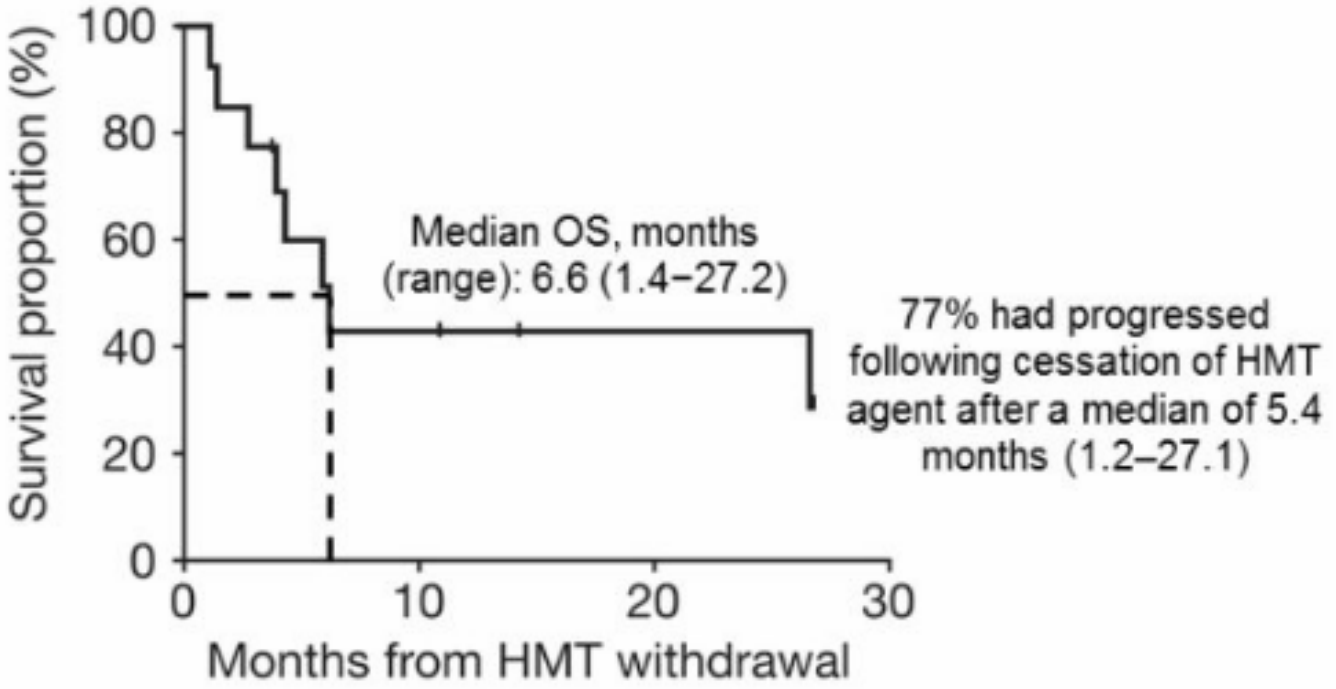
Adverse event	Monitoring	Prophylaxis	Therapy
Hematologic	CBC at regular intervals	Consider G-CSF if expected neutropenia exceeds 10 days	Delay next cycle until recovery of CBC Reduce dose in next cycle if blood values do not recover within 2 weeks of designated day 1 of next cycle Transfusion of RBC and platelets as required
Infection	Regular clinical examination Educate patient to seek medical care promptly if temp >38.5°C occurs	Consider G-CSF in following cycles Consider antibiotics (e.g., quinolones)	Antibiotics following guidelines for neutropenic fever
Nausea and emesis		Premedicate with antiemetics (metoclopramide, alizapride or 5-HT3 antagonist)	Escalate antiemetic regimen (5-HT3 antagonist, dexamethasone)
Diarrhea			I.V. fluids Loperamide
Constipation		Consider laxatives when using high dose 5-HT3 antagonists	Laxatives, stool softener
Injection site reaction	Clinical examination	Correct injection technique Rotation of injection sites	Symptomatic (evening primrose oil, cooling compresses, soothing lotion) Topical steroids

CBC complete blood count, *RBC* red blood cell, *G-CSF* granulocyte-colony stimulating factor

Santini V, Eur J Haemat 2010

The risk of terminating treatment prior to disease progression

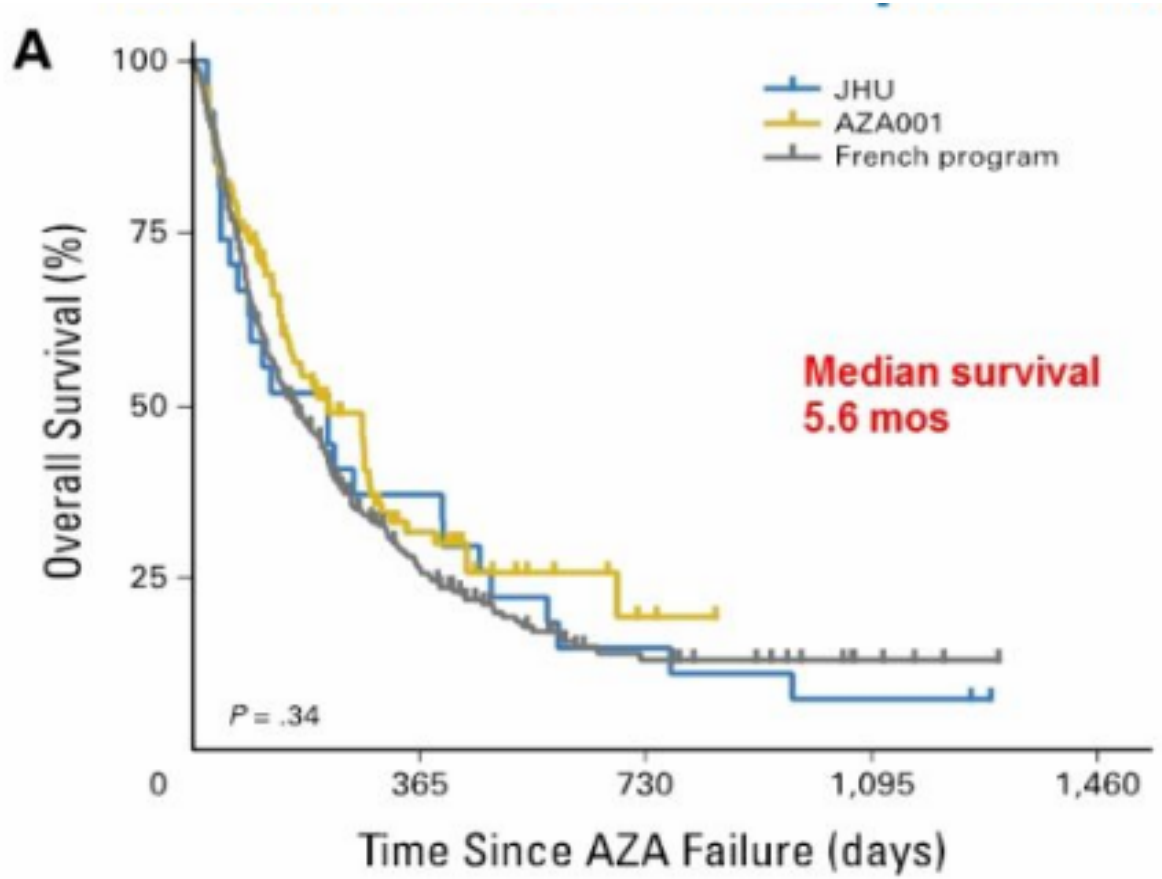
- Clinical outcomes in a series of 13 patients with MDS/CMML treated with HMT agents (azacitidine: n=12) who discontinued treatment while still in haematological remission



CMML: chronic myelomonocytic leukaemia
HMT: hypomethylating; OS: overall survival

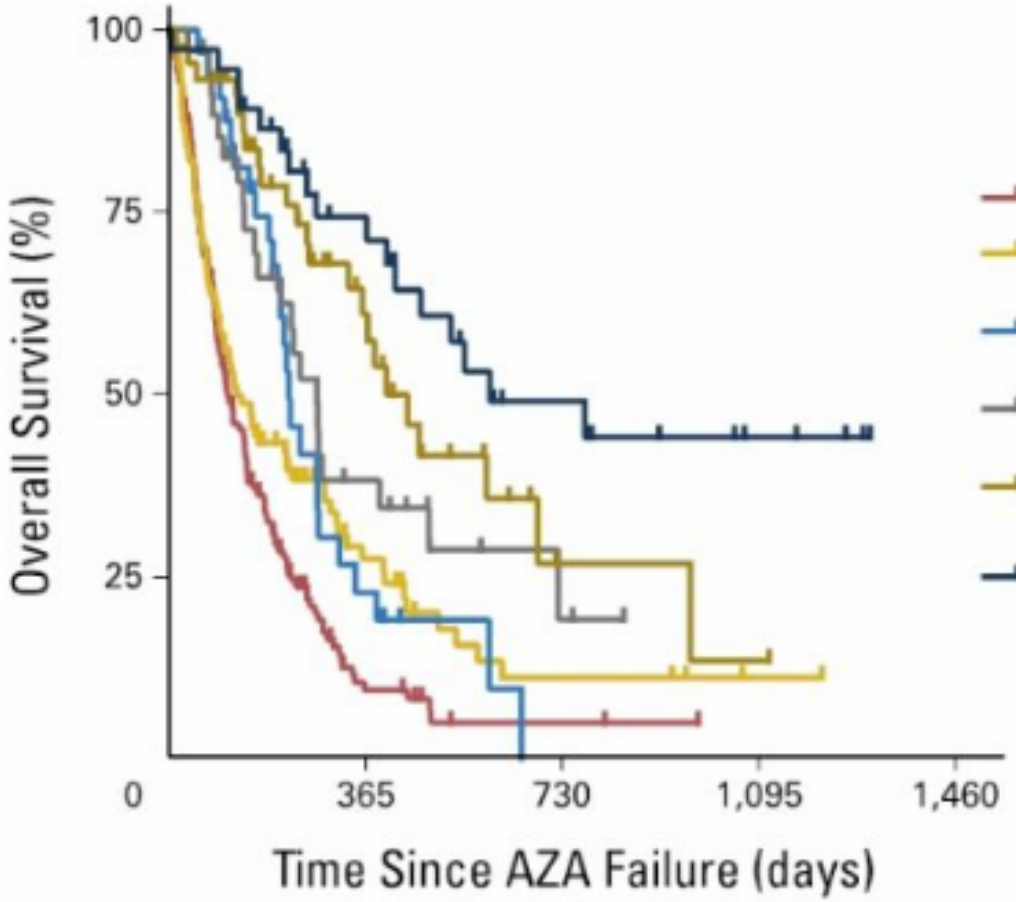
Voso MT, et al. Eur J Haematol 2013;90:345–8

Survival after AZA failure in MDS/AML patients



Prebet et al, JCO 29:3322 (2011)

Survival according to salvage therapy



Type of salvage	N	ORR	Median OS (months)
Unknown	165	NA	3.6
Best supportive care	122	NA	4.1
Low-dose chemotherapy	32	0/18	7.3
Intensive chemotherapy	35	3/22	8.9*
Investigational therapy	44	4/36	13.2*†
Allogeneic transplantation	37	13/19	19.5*†

Prebet et al, JCO 29:3322 (2011)

Grazie!!!!!!

FISM
FONDAZIONE
ITALIANA
SINDROMI
MIELODISPLASTICHE