L e complicanze infettive nelle MDS

Corrado Girmenia

UOSD Pronto Soccorso e Accettazione Ematologica,

AOU Policlinico Umberto I, Roma

Why infections are a challenging complication in MDS patients?

- Infections are a major cause of death in MDS patients
- Infections may represent an obstacle to adherence to MDS treatment schedule

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ORIGINAL ARTICLE

Causes of death in 2877 patients with myelodysplastic syndromes

Kathrin Nachtkamp[1] · Romina Stark[1] · Corinna Strupp[1] · Andrea Kündgen[1] · Aristoteles Giagounidis[2] · Carlo Aul[2] · Barbara Hildebrandt[3] · Rainer Haas[1] · Norbert Gattermann[1] · Ulrich Germing[1]

1969- 2014
Overall MDS population , 3792

→ Number of patients who died during the observation period, 2877

→ Patients with a clearly documented cause of death, 1665

→ 449 (27%) patients died as a result of infection

Table 1 Correlation of different patient- and disease-related parameters with causes of death in percentages

		AML	Infection	Bleeding	Cardiac insufficiency	Non-disease-related	Other disease-related	*P* value
Overall group		46.6 %	27.0 %	9.8 %	7.9 %	6.0 %	2.7 %	
WHO 2008 (*n* = 1665)	RCUD (*n* = 68)	33.8 %	23.5 %	10.3 %	10.3 %	14.7 %	7.4 %	<0.00005
	RARS (*n* = 89)	11.2 %	31.5 %	10.1 %	21.3 %	21.3 %	4.5 %	
	RCMD (*n* = 321)	40.5 %	31.2 %	9.0 %	6.9 %	9.0 %	3.4 %	
	RSCMD (*n* = 139)	31.7 %	36.7 %	10.8 %	11.5 %	5.8 %	3.6 %	
	5q− (*n* = 35)	48.6 %	22.9 %	0.0 %	14.3 %	11.4 %	2.9 %	
	RAEB I (*n* = 216)	43.5 %	31.5 %	9.3 %	6.0 %	5.6 %	4.2 %	
	RAEB II (*n* = 310)	55.5 %	22.6 %	11.0 %	6.1 %	2.3 %	2.6 %	
	CMML I (*n* = 151)	33.8 %	34.4 %	14.6 %	11.3 %	4.6 %	1.3 %	
	CMML II (*n* = 55)	54.5 %	20.0 %	16.4 %	7.3 %	1.8 %	0.0 %	
	RAEB-T (*n* = 254)	77.6 %	13.0 %	6.7 %	2.0 %	0.8 %	0.0 %	
	Unclassifiable (*n* = 5)	60.0 %	40.0 %	0.0 %	0.0 %	0.0 %	0.0 %	
	RARS-T (*n* = 22)	22.7 %	45.5 %	4.5 %	22.7 %	4.5 %	0.0 %	
IPSS (*n* = 740)	Low (*n* = 87)	44.8 %	29.9 %	5.7 %	9.2 %	5.7 %	4.6 %	<0.00005
	Int-1 (*n* = 245)	52.2 %	29.8 %	8.2 %	2.9 %	3.3 %	3.7 %	
	Int-2 (*n* = 189)	72.5 %	19.0 %	4.2 %	1.1 %	0.0 %	3.2 %	
	High (*n* = 219)	78.1 %	12.3 %	8.2 %	1.4 %	0.0 %	0.0 %	
IPSS-R (*n* = 660)	Very low (*n* = 30)	40.0 %	30.0 %	6.7 %	3.3 %	10.0 %	10.0 %	<0.00005
	Low (*n* = 134)	44.0 %	32.8 %	8.2 %	7.5 %	5.2 %	2.2 %	
	Intermediate (*n* = 176)	63.1 %	24.4 %	4.5 %	1.7 %	2.3 %	4.0 %	
	High (*n* = 144)	72.9 %	18.8 %	5.6 %	1.4 %	0 %	1.4 %	
	Very high (*n* = 176)	78.4 %	13.6 %	5.1 %	0.6 %	0 %	2.3 %	
WPSS (*n* = 459)	Very low	32.3 %	41.9 %	0.0 %	12.9 %	9.7 %	3.2 %	<0.00005
	Low	47.0 %	27.3 %	9.1 %	7.6 %	7.6 %	1.5 %	
	Intermediate	55.1 %	22.4 %	8.2 %	3.1 %	5.1 %	6.1 %	
	High	63.4 %	26.9 %	6.5 %	0.0 %	0.5 %	2.7 %	
	Very high	75.6 %	15.4 %	6.4 %	1.3 %	0.0 %	1.3 %	
Age (years) (*n* = 1665)	<80	50.6 %	26.3 %	9.2 %	6.4 %	4.8 %	2.7 %	<0.00005
	>80	23.9 %	30.8 %	13.0 %	16.6 %	13.0 %	2.8 %	
Gender (*n* = 1665)	Male	47.2 %	27.1 %	9.2 %	7.7 %	5.9 %	2.9 %	0.920
	Female	45.7 %	26.8 %	10.6 %	8.2 %	6..2 %	2.5 %	
Primary/therapy-related MDS (*n* = 1637)	pMDS	46.0 %	26.9 %	9.8 %	8.5 %	6.2 %	2.6 %	0.428
	tMDS	47.3 %	31.0 %	11.6 %	3.1 %	3.9 %	3.1 %	
Hb (g/dl) (*n* = 1605)	<7	41.3 %	29.4 %	14.7 %	6.9 %	6.0 %	1.8 %	0.141
	>7	46.5 %	26.9 %	9.3 %	8.4 %	6.0 %	2.9 %	
Platelets ($\times 10^6$/μl) (*n* = 1589)	<10	43.8 %	21.9 %	15.6 %	6.3 %	9.4 %	3.1 %	0.815
	>10	46.0 %	27.4 %	9.9 %	8.2 %	5.8 %	2.7 %	
ANC (/μl) (*n* = 1439)	<800	57.8 %	24.2 %	10.6 %	2.8 %	2.5 %	2.2 %	<0.00005
	>800	40.4 %	28.6 %	10.7 %	10.9 %	7.0 %	2.4 %	

Why infections are a challenging complication in MDS patients?

- Infections are a major cause of death in MDS patients
- Infections may represent an obstacle to adherence to MDS treatment schedule

Support Care Cancer (2015) 23:303–305
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LETTER TO THE EDITOR

Obstacles to adherence to azacitidine administration schedule in outpatient myelodysplastic syndrome and related disorders

Andrea Tendas · Maria Felicita Lissia · Daniela Piccioni · Liliana Tirimbelli · Laura Scaramucci · Marco Giovannini · Teresa Dentamaro · Alessio Perrotti · Paolo de Fabritiis · Pasquale Niscola

199 cycles in 21 patients: 56 (28%) delayed cycles

Table 1 Causal reasons of delayed administration of azacitidine

Reasons	Number of cycles (%)	Comments
Clinical complications	15 (27 %)	12/15 (80 %): infections
Center organizational problems	15 (27 %)	Public holidays
Hematological toxicity	11 (20 %)	10/11 (91 %): severe neutropenia
Disease evaluation	7 (12 %)	Usually after the sixth cycle and in case of suspected loss of response to azacitidine or disease progression
Personal and family patient'sproblems	8 (11 %)	In large part, inability of family members to take time off from their work to accompany the patient to the hospital for receiving the subcutaneous infusion
Total delayed cycles	56 (100 %)	Delayed cycles: 56 (31 %) of 178 cycles with evaluable intervals of administration

Table 2 Causal reasons of delayed administration of azacitidine in relation to the duration of delay

	Interval (days)	29–35		36–42		>42	
		n		*n*		*n*	
Tot		26		15		15	
			%		%		%
Clinical issue	Hematological toxicity	5	19.0	3	20.0	3	20.0
	Disease evaluation	1	4.0	4	27.0	2	13.0
	Complications	3	11.5	3	20.0	9	60.0
Organizational	Center	12	46.0	3	20.0	0	0.0
	Patient	5	19.5	2	13.0	1	7.0

How can we prevent infections from causing death or be an obstacle to adherence to treatment schedule?

- First: knowledge of the epidemiology, timing and risk of infections is required
- Second: indication, choice and timing of prevention strategies should be defined…. if possible.

Infection control in patients with myelodysplastic syndromes who are candidates for active treatment: Expert panel consensus-based recommendations

Corrado Girmenia[a,*], Anna Candoni[b], Mario Delia[c], Roberto Latagliata[a], Alfredo Molteni[d], Esther N. Oliva[e], Giuseppe A. Palumbo[f], Antonella Poloni[g], Prassede Salutari[h], Valeria Santini[i], Maria Teresa Voso[j], Pellegrino Musto[k]

BLOOD reviews
Blood Reviews 34 (2019) 16–25

Rate of grade 3 or higher infections from Phase II and III clinical trials in MDS patients treated according to the current strategies.

Author, year (reference)	Study treatment	Number and type of patients on study; mean age, years (range)	Type of grade ≥3 infections	
Fenaux P, 2009	AZA (1:1) vs. BSC	359 IR and HR MDS; 69 (38–88)	Febrile neutropenia: AZA 12.6%; BSC 6.9%. Pneumonia: AZA 10.3%; BSC 7.8%	HR
Kantarijan H, 2006	DEC (1:1) vs. BSC	170 IR and HR MDS; 70 (30–85)	Febrile neutropenia: DEC 23%; BSC 4%. Pneumonia: DEC 15%; BSC 9%. Overall infections: DEC 57%; BSC 52%	
Lübbert M, 2011	DEC (1:1) vs. BSC	233 IR and HR MDS; 70 (60–90)	Febrile neutropenia: DEC 25.4%; BSC 7.1%. Overall infections: DEC 57.9%; BSC 50%	
Garcia-Manero G, 2016	Rigosertib (2:1) vs. BSC	299 HR MDS (after failure of hypomethylating drugs); 74 (69–79)	Overall infections: rigosertib 12%; BSC 4%	
Sekeres MA, 2017	AZA vs. AZA+LENA vs. AZA + vorinostat	277 HR MDS and CMML; 70 (28–93)	Overall infections: AZA alone 8%; AZA+LENA 16%; AZA + vorinostat 11%	
Garcia-Manero G, 2017	AZA (1:1) vs. AZA + pracinostat	102 IR-2 and HR MDS; 70 (26–90)	Febrile neutropenia (any grade): AZA 20%; AZA + pracinostat 33%. Pneumonia (any grade): AZA 16%; AZA + pracinostat 18%	
Platzbecker U, 2015	Eltrombopag (2:1) vs. placebo	98 HR MDS; 73 (29–88)	Febrile neutropenia: eltrombopag 7%; placebo 21% Pneumonia: eltrombopag 16%; placebo 17% Sepsis: eltrombopag 13%; placebo 18%	
Santini V, 2016	LENA (2:1) vs. placebo	239 LR and IR MDS not 5q-; 71 (43-–87)	Infections: LENA 14.4%; placebo 3.8%	LR
List A, 2006	LENA	148 LR and IR MDS with 5q-; 71 (37–95)	Febrile neutropenia: 2% Pneumonia: 3%	
Fenaux P, 2011	LENA 10 mg or 5 mg (2:1) vs. placebo	205 LR and IR MDS not 5q-; 69 (36–86)	Febrile neutropenia: LENA 10 mg 1%; LENA 5 mg 3% Infections: LENA 10 mg 12%; LENA 5 mg 9%	
Oliva EN, 2017	Eltrombopag (2:1) vs. placebo	90 LR and IR MDS; 71 (29–91)	Febrile neutropenia: eltrombopag 7%; placebo 21% Pneumonia: eltrombopag 16%; placebo 21% Overall infections: eltrombopag 5%; placebo 9%	

The limits of clinical trials in describing the infectious risk in MDS patients

- Clinical trials vs real life (selection of patients)
- Generally, clinical trials are not designed to detail the different types and outcome of infection
- The use of «rate of infections per patient year» does not allow the proper description of the timing of infection (i.e. first 3 months vs subsequent period)
- It is not possible to show the impact of infections on the overall outcome
- It is difficult to hypothesize prevention strategies based on the clinical trials results

Infection control in patients with myelodysplastic syndromes who are candidates for active treatment: Expert panel consensus-based recommendations

Corrado Girmenia[a,*], Anna Candoni[b], Mario Delia[c], Roberto Latagliata[a], Alfredo Molteni[d], Esther N. Oliva[e], Giuseppe A. Palumbo[f], Antonella Poloni[g], Prassede Salutari[h], Valeria Santini[i], Maria Teresa Voso[j], Pellegrino Musto[k]

BLOOD reviews
Blood Reviews 34 (2019) 16–25

Most recent retrospective epidemiological studies on infections in MDS patients treated according to the current strategies.

Reference	Study endpoint	Patients on study	Infection complications
Ali AM, 2017	Infections during DEC 10 day/cycle treatment	85 pts AML (68%) and MDS 282 cycles	Incidence of infections: 96.3% in MDS and 77.5% in AML Microbiological documented infections in 44.8% Prevalence of bacterial infections (bacteremia and pneumonia) Viral infections 3.7%, fungal infections 1.2%
Schuck A, 2017	Impact of infections during AZA treatment	77 pts MDS 614 AZA cycles	81/614 AZA cycles (13%) with one or more infections Higher infections in the first 3 cycles Higher infections in non-responders vs. responders (P=0.002) Bacterial infections 88%, viral infections 5%, fungal infections 7% of infections
Trubiano JA, 2017	Incidence, etiology and timing of infections following AZA therapy for MDS	68 pts AML and MDS 884 AZA cycles	Infections in 25% of AZA cycles Higher infections in very high IPSS-R and in the first two AZA cycles Prevalence of bacterial infections Febrile neutropenia in 5.3% of AZA cycles, bacteremia 2%, invasive aspergillosis 0.3%
Pomares H, 2016	Invasive fungal infections in AML/MDS treated with AZA	121 pts AML (29%) and MDS 948 AZA cycles	Patients with febrile neutropenia 37% Fungal infections 1.6% (4.1% in pts with severe neutropenia)
Falantes JF, 2014	Patterns of infection in MDS and AML treated with AZA as salvage therapy	64 pts AML (33%) and MDS 523 AZA cycles	Patients with infections 31/64 (48%); infections in 14% of AZA courses Higher risk of infections and risk of fungal infections during the first 3 treatment cycles Pneumonia was the most common infection (35%)
Sullivan LR, 2013	Epidemiology and risk factors for infections requiring hospitalization in MDS	497 pts MDS	Incidence of IC 21% (103/497 pts); total of IC episodes 201 Prevalence of bacterial infections, 82% (bacteremia and pneumonia) of IC viral infections 8%, fungal infections 10% of IC Risk factors for IC: HR MDS, neutropenia, comorbidities
Merkel D, 2013	Incidence and predisposing risk factors for infections in AZA-treated pts	184 pts AML (15%) and MDS 928 AZA cycles	153/928 AZA cycles (16.5%) with one or more IC 75% of IC required hospitalization and 19.6% of IC were fatal Higher incidence in the first two cycles (26% and 23%) Poor cytogenetics, low PLT count and neutrophil count below 0.5×109/L recorded before first AZA cycle identified “prone to infections” patients (52.7% vs. 33.9%; 56.1% vs. 35%; 53.1% vs. 35.6%, respectively; P<0.05 for all comparisons).

Patterns of Infection in Patients With Myelodysplastic Syndromes and Acute Myeloid Leukemia Receiving Azacitidine as Salvage Therapy. Implications for Primary Antifungal Prophylaxis

Jose F. Falantes,[1] Cristina Calderón,[1] Francisco J. Márquez-Malaver,[1] Manuela Aguilar-Guisado,[2] Almudena Martín-Peña,[2] María L. Martino,[1] Isabel Montero,[1] Jose González,[1] Rocío Parody,[1] Jose A. Pérez-Simón,[1] Ildefonso Espigado[1]

Clinical Lymphoma, Myeloma & Leukemia, Vol. 14, No. 1, 80-6 © 2014

Table 1 Patient Characteristics

	Global Series (n = 64)	Prior IC (n = 18; 28.1%)	Frontline AZA (n = 46; 71.9%)	*P* Value[d]
Age, years, median (range)	68 (29-83)	66 (29-78)	68 (35-83)	.33
Number of AZA courses, n (median)	6 (1-50)	6 (2-16)	9 (2-50)	.08
WHO, n (%)	RARS: 2 (3.2) RCMD: 9 (14) CMML: 3 (4.7) RAEB-1: 3 (4.7) RAEB-2: 26 (40.6) AML: 21 (32.8)	MDS: 4 (22.2)[a] AML: 14 (77.8)	MDS: 39 (84.8)[b] AML: 7 (15.2)	<.001 <.001
IPSS, n (%)[c]				ns
Low Risk	3 (7)	0	3 (8.6)	
Int-1	10 (23.2)	1 (33.3)	8 (22.8)	
Int-2	11 (25.6)	1 (33.3)	10 (28.6)	
High Risk	19 (44.2)	1 (33.3)	14 (40)	

Figure 1 Incidence of Febrile Episodes in Each Course of Azacitidine

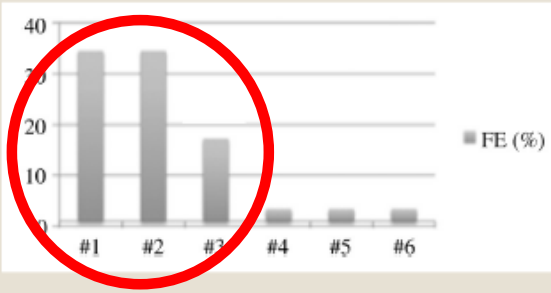
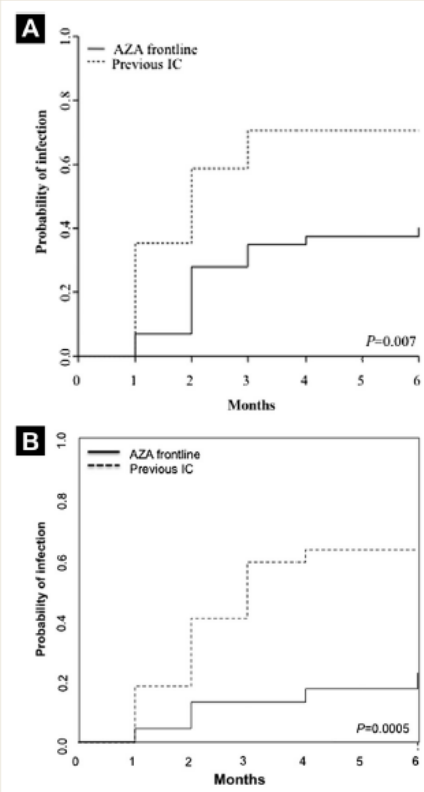


Figure 2 Cumulative Incidence Estimates From Competing Risks Data (Estimates at Different Time Points). (A) Patients Treated With Prior Intensive Chemotherapy vs. Patients Receiving Frontline Azacitidine Therapy; (B) Patients With Absolute Neutrophil Count > 0.5 × 10^9/L vs. Patients With Absolute Neutrophil Count > 0.5 × 10^9/L After 3 Courses of Azacitidine Therapy



Patterns of Infection in Patients With Myelodysplastic Syndromes and Acute Myeloid Leukemia Receiving Azacitidine as Salvage Therapy. Implications for Primary Antifungal Prophylaxis

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Table 5 Comparison Between Groups: Data on Microbiological Isolation and Outcome

	Global (n = 64)	Prior IC (n = 18)	AZA Frontline (n = 46)	*P* Value
FE per AZA course, n (%)	73/523 (13.95)	28/98 (18.7%)	45/425 (10.7%)	10^{-4} Risk difference: 18% OR: 3.36 (1.955-5.757)
Hospital admission, n (%)	26/64 (40.6%)	11/18 (61%)	15/46 (32.6%)	.04 Risk difference: 18% OR: 3.18 (1.025-10.41)
Hospital stay, d, median (range)	14 (4-80)	13 (4-80)	14 (5-57)	.9
Patients with microbiological isolation, n (%)	17/64 (26.6)	9/18 (5%)	8/46 (17.4%)	.01 Risk difference: 32% OR: 4.61 (1.378-16.07)
Type of isolation,[a] n	Bacterial: 6 Fungal: 4 Both: 4 Other: 1	Bacterial: 3 Fungal: 2 Both: 4 Other:	Bacterial: 3 Fungal: 2 Both: Other: 1	Fungal: .038 Risk difference: 22% OR: 4.9 (1.089-27.37)
Fungal isolation, n	*Aspergillus* spp: 6 *Candida* spp: 2	*Aspergillus* spp: 5 *Candida albicans*: 1	*Aspergillus* spp: 1 *Candida parapsilosis*: 1	.015 Risk difference: 22.4% OR: 12 (1.524-308.2) NNT=4
Cause of death, n (%)	Progression: 21 (58.4) Infection on AZA: 2 (5.5) Other: 14 (36.1)	Progression: 11 (79) Infection on AZA: 1 (7) Other: 3 (14)	Progression: 10 (46) Infection on AZA: 1 (4) Other: 11 (50)	.56

Abbreviations: AZA = azacitidine; FE = febrile episode; IC = intensive chemotherapy; OR = odds ratio; NNT = number needed to treat.
P values denote differences between the group that received previous IC and the group that received frontline AZA therapy for the corresponding parameter (Mid-I exact test and χ^2).
[a]5 of the cases were polymicrobial.

Based on the results of our study, primary antifungal prophylaxis should be recommended in patients receiving AZA therapy after previous IC, especially during the first courses of treatment, until hematopoiesis is restored. Considering the expected increase in the use of AZA in MDS and AML cases, not only in elderly patients but also in other clinical settings, randomized prospective studies are needed to better address this issue. In contrast, the risk for fungal infection was very low among patients receiving frontline AZA therapy. The latter group would not require antifungal prophylaxis.

Predicting infections in high-risk patients with myelodysplastic syndrome/acute myeloid leukemia treated with azacitidine: A retrospective multicenter study

Drorit Merkel,[1] Kalman Filanovsky,[2] Anat Gafter-Gvili,[3] Liat Vidal,[3] Ariel Aviv,[4] Moshe E. Gatt,[5] Itay Silbershatz,[6] Yair Herishanu,[7] Ariela Arad,[8] Tamar Tadmor,[9,10] Najib Dally,[11] Anatoly Nemets,[12] Ory Rouvio,[13] Aharon Ronson,[14] Katrin Herzog-Tzarfati,[15] Luiza Akria,[16] Andrei Braester,[16] Ilana Hellmann,[17] Shay Yeganeh,[18] Arnon Nagler,[1] Ronit Leiba,[19] Moshe Mittelman,[20] and Yishai Ofran[10,21]*

Am. J. Hematol. 88:130–134, 2013.

TABLE II. Univariate Analysis of Risk Factors for Infections in MDS Patients Treated with Azacitidine

Parameter	With infection	Without infection	*P*-value
Age			
<70	60 (19.0%)	256 (81.0%)	Ns
>70	93 (15.2%)	517 (84.8%)	
Sex			
Male	94 (15.5%)	511 (84.5%)	Ns
Female	59 (18.4%)	262 (81.6%)	
Cytogenetics			
Good	4 (12.5%)	28 (87.5%)	$P < 0.001$ (~)
Intermediate	78 (12.9%)	527 (87.1%)	
Poor	59 (24.4%)	183 (75.6%)	
Blasts			
0–5%	17 (12.1%)	123 (87.9%)	$P = 0.03$ (*)
6–10%	44 (21.3%)	163 (78.7%)	
11–20%	62 (14.8%)	356 (85.2%)	
21+%	30 (19.2%)	126 (80.8%)	
Transfusion dependency			
Yes	117 (18.7%)	508 (81.3%)	$P = 0.059$
No	19 (12.1%)	138 (87.9%)	
Azacitidine dose			
7 days	100 (18.0%)	456 (82%)	Ns
5 days	46 (15.2%)	257 (84.8%)	
Creatinine	1.057 ± 0.44	1.069 ± 0.44	Ns
Neutrophils			
<500 cells/μL	57 (27%)	154 (73%)	$P < 0.0001$
>500 cells/μL	95 (13.5%)	608 (86.5%)	
PLT			
<20,000 cells/μL	42 (29.2%)	102 (70.8%)	$P < 0.0001$
>20,000 cells/μL	111 (14.2%)	676 (85.8%)	
Hb			
<10	111 (20.4%)	434 (79.6%)	$P < 0.0001$
<10	42 (11.0%)	339 (89.0%)	

~Significant differences ($P < 0.0001$) between intermediate versus poor cytogenetics.

*Significant differences ($P = 0.03$) between 6 and 10% blasts versus 11–20% blasts.

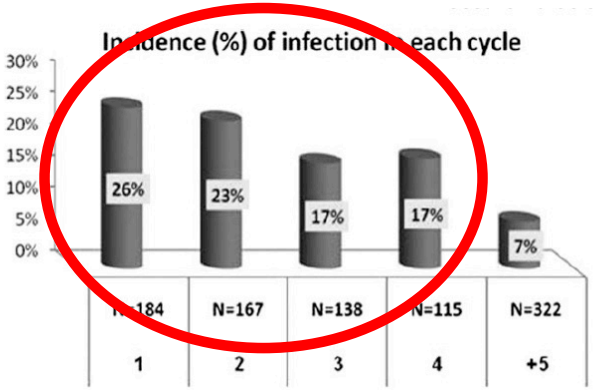

Figure 1. Incidence of infection events as a function of the sequential number of azacitidine cycle.

TABLE III. Multivariate Analysis of Risk Factors for Infections in MDS Patients Treated with Azacitidine

		95% C.I.		
	Odds ratio	Lower	Upper	Sig
PLT < 20,000	2.265	1.410	3.637	.001
Poor cytogenetics	1.770	1.171	2.674	.007
Hb < 10	1.755	1.101	2.798	.018

Out of the 124 cases which underwent a complete microbiology workup, bacterial, viral and fungal diseases were diagnosed in 73 (59%), 5 (4%), and 6 (4.8%) events respectively. Three of the five viral cases were diagnosed as H1N1.

LEUKEMIA & LYMPHOMA, 2017
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ORIGINAL ARTICLE: CLINICAL

Incidence, etiology and timing of infections following azacitidine therapy for myelodysplastic syndromes

Jason A. Trubiano[a,b], Michael Dickinson[c], Karin A. Thursky[a,b,d], Timothy Spelman[b], John F. Seymour[b,c], Monica A. Slavin[a,b,d] and Leon J. Worth[a,b]

[a]Department of Infectious Diseases, Peter MacCallum Cancer Centre, East Melbourne, Australia; [b]Department of Medicine, University of Melbourne, Melbourne, Australia; [c]Department of Haematology, Peter [illegible] Australia; [d]Victorian Infectious Diseases Service, Royal Melbourne Hospital at the P

884 AZA cycles in 68 patients

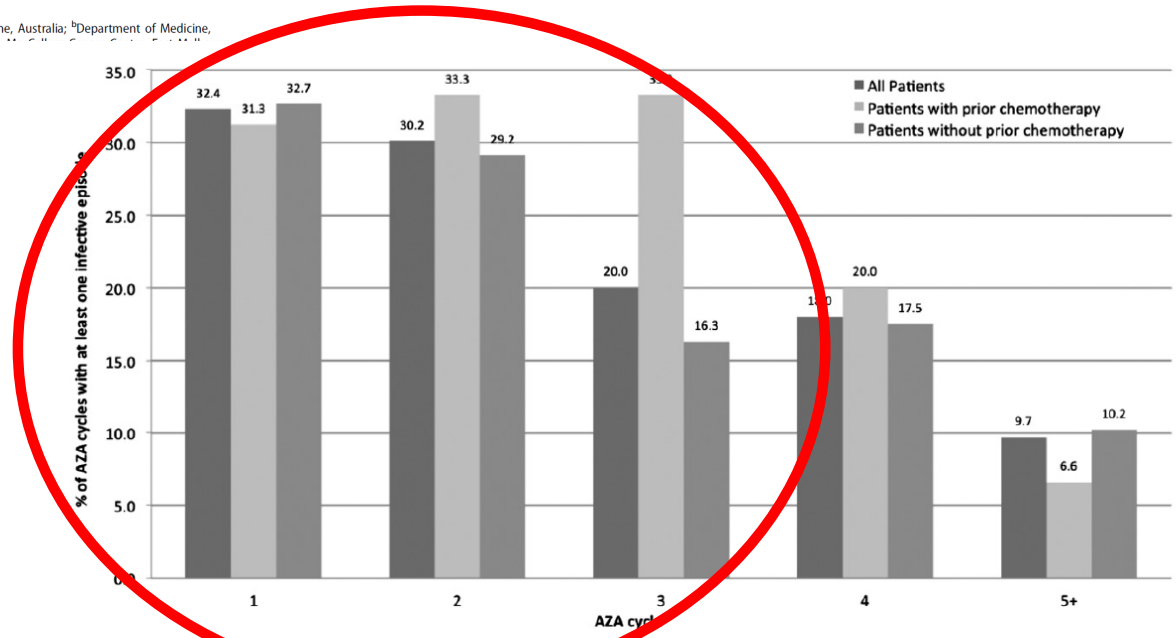

Figure 1. Proportion of azacitidine cycles* complicated by ≥1 infection episode. AZA: azacitidine. *The total number of AZA cycles ($n = 884$) with at least one infection event was 14.03% (124/884). #The total number of AZA cycles administered for each cycle number are: (i) AZA cycle 1, 68; (ii) AZA cycle 2, 63; (iii) AZA cycle 3, 55; (iv) AZA cycle 4, 50; (v) AZA cycle 5+, 648.

Febrile neutropenia complicated 5.3% of AZA cycles, pneumonia 3.2%, upper respiratory tract infections 2.9%, skin and soft tissue infections 2.4%, bloodstream infections 1.8%.

69% of febrile neutropenia episodes, 63% of pneumonia episodes, 68% of skin and soft tissue infections, 63% of bloodstream infections, and 36% of urinary tract infections occurred in the first five AZA cycles. Five of six IFD cases occurred in cycle 1 or 2 of AZA therapy.

LEUKEMIA & LYMPHOMA, 2017
VOL. 58, NO. 10, 2379–2386
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ORIGINAL ARTICLE: CLINICAL

Incidence, etiology and timing of infections following azacitidine therapy for myelodysplastic syndromes

Jason A. Trubiano[a,b], Michael Dickinson[c], Karin A. Thursky[a,b,d], Timothy Spelman[b], John F. Seymour[b,c], Monica A. Slavin[a,b,d] and Leon J. Worth[a,b]

[a]Department of Infectious Diseases, Peter MacCallum Cancer Centre, East Melbourne, Australia; [b]Department of Medicine, University of Melbourne, Melbourne, Australia; [c]Department of Haematology, Peter MacCallum Cancer Centre, East Melbourne, Australia; [d]Victorian Infectious Diseases Service, Royal Melbourne Hospital at the Peter Doherty Institute, Melbourne, Australia

884 AZA cycles in 68 patients

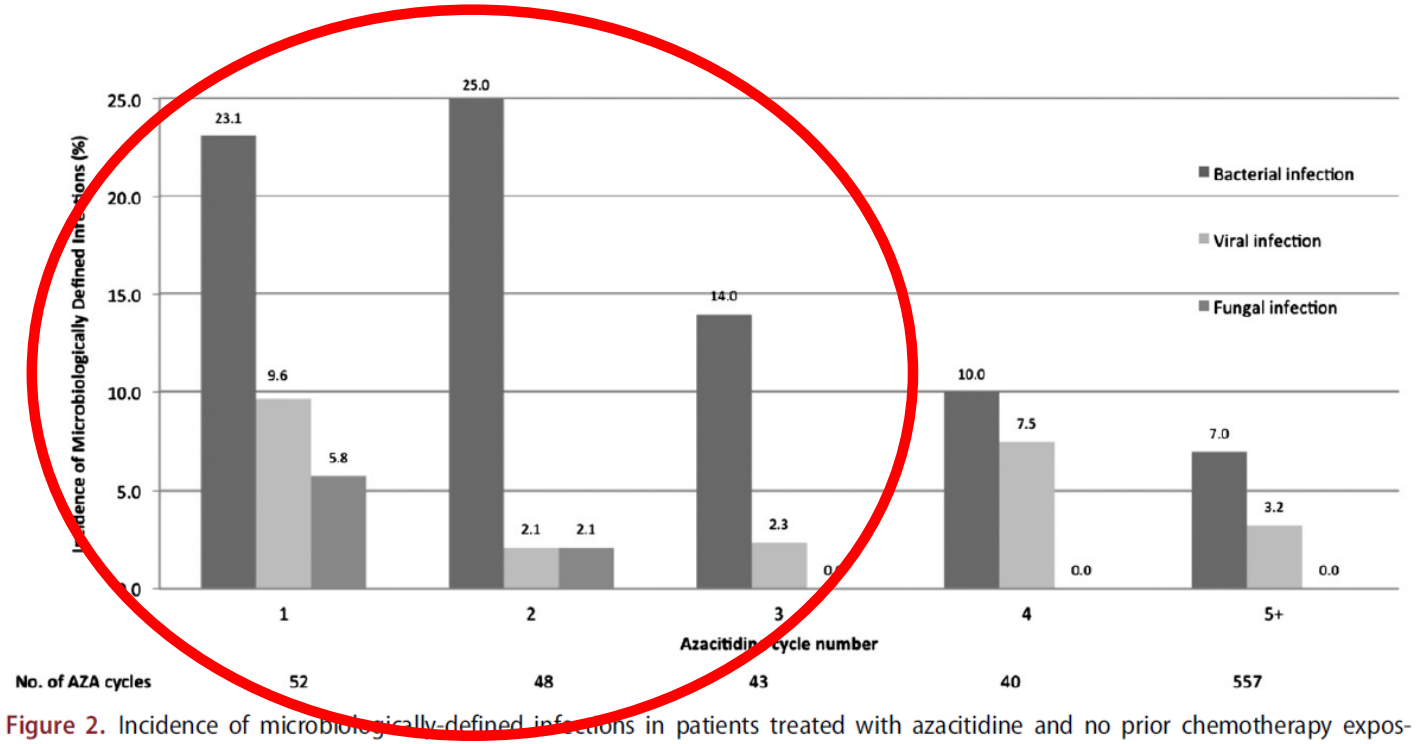

Figure 2. Incidence of microbiologically-defined infections in patients treated with azacitidine and no prior chemotherapy exposure. AZA: azacitidine.

All fungal infections documented in the first 2 cycles

Pulmonary infections in patients with myelodysplastic syndromes receiving frontline azacytidine treatment

Hematological Oncology. 2020;38:189–196.

Roberto Latagliata[1] | Pasquale Niscola[2] | Luana Fianchi[3] | Maria Antonietta Aloe Spiriti[4] | Luca Maurillo[5] | Ida Carmosino[1] | Laura Cesini[1] | Chiara Sarlo[6] | Annalina Piccioni[7] | Alessia Campagna[4] | Maria Lucia De Luca[1] | Daniela De Benedittis[1] | Marco Mancini[1] | Massimo Breccia[1] | Marianna Criscuolo[3] | Francesco Buccisano[5] | Maria Teresa Voso[5] | Giuseppe Avvisati[6] | Agostino Tafuri[4] | Paolo De Fabritiis[2] | Robin Foà[1] | Corrado Girmenia[1]

Retrospective, multicenter study (7 centers in Rome) including 234 MDS patients treated with AZA. The total number of AZA cycles was 2886 (median 8 cycles per patient). There were 111 episodes of PI (3.8% of AZA cycles) in 81 patients (34.6%).

TABLE 2 Classification of 111 pulmonary infection episodes according to results of the microbiological and radiological diagnostic work-up

Classification of Pulmonary Infection	Number of Cases (%)
Pulmonary infection of unknown origin	71 (64.0)
Pulmonary invasive fungal disease	27 (24.3)
Proven	0
Probable aspergillosis[a]	13
Possible	13
Pneumocystis jiroveci pneumonia	1
Bacterial pulmonary infection	11 (9.9)
Streptococcus pneumoniae	4
Klebsiella pneumoniae	2
Escherichia coli	2
Pseudomonas aeruginosa	1
Staphylococcus spp	2
Influenza pulmonary infection	2 (1.8)

[a]Mainly based on the results of the chest CT scan and the galactomannan

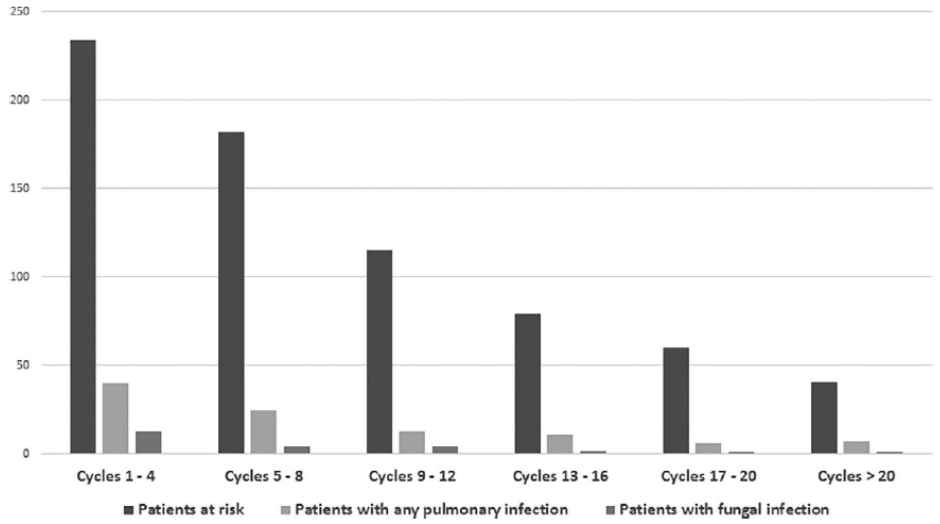

FIGURE 1 Number of patients with all pulmonary infections and fungal pulmonary infections according to azacytidine (AZA) cycles

PIs
5.1% of cycles 1-4
3.2% of cycles >4

P-IFD
32.5% of early PIs
21% of late PIs

Pulmonary infections in patients with myelodysplastic syndromes receiving frontline azacytidine treatment

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Cumulative survival according to the development of pulmonary infection along the entire AZA treatment (A) and during the first 4 AZA cycles (B). Only 85 episodes of pulmonary infection unrelated to acute leukemia progression were considered.

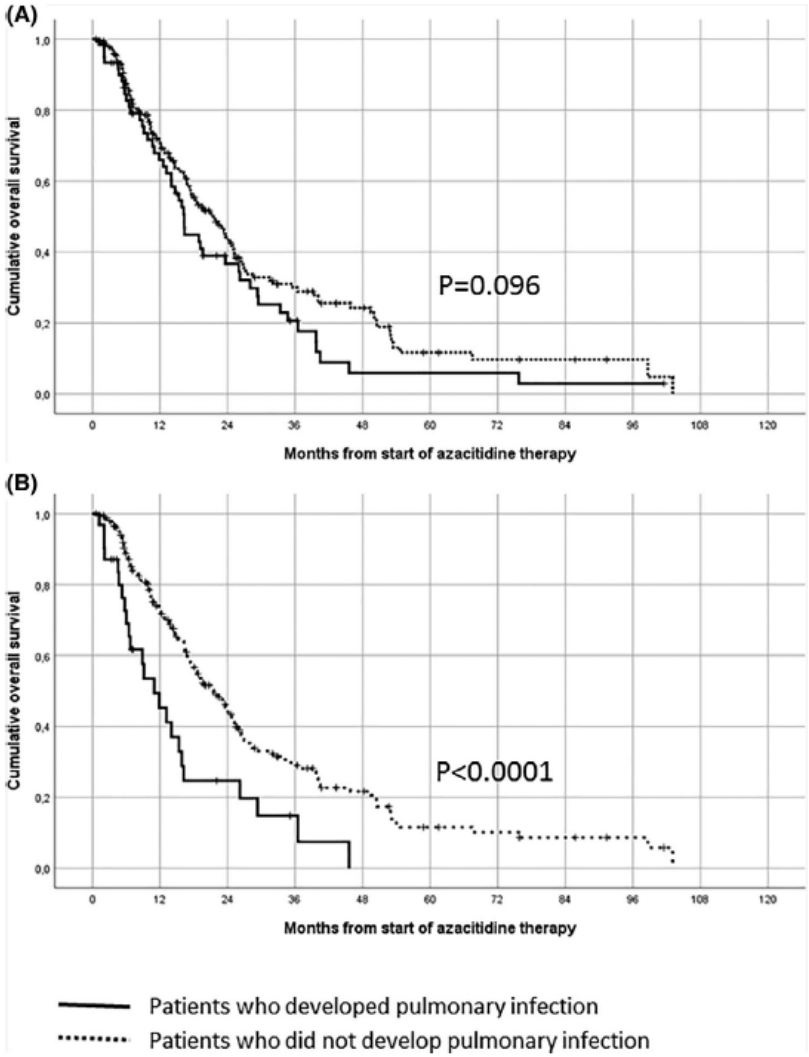

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TABLE 3 Probability of death at 2 years from the start of AZA therapy

		Univariate		Multivariate	
	OS, %	OR (95% CI)	*P*	OR (95% CI)	*P*
Male vs Female	43 vs 39	0.87 (0.62-1.21)	.41		
Age, <70 y vs ≥70 y	45 vs 37	0.83 (0.62-1.21)	.24		
Underlying chronic obstructive pulmonary disease, no vs yes	43 vs 43	0.98 (0.60-1.13)	.93		
Underlying diabetes requiring pharmacological therapy, no vs yes	42 vs 53	1.22 (0.67-2.20)	.52		
Level of hemoglobin at the start of AZA therapy, <10 g/dL vs ≥10 g/dL	35 vs 55	1.89 (1.32-2.70)	<.0001	1.76 (1.22-2.53)	.003
PMN number at the start of AZA therapy, <1.0 vs ≥1.0 × 10^9/L	50 vs 31	0.70 (0.51-0.95)	.023		
Bone marrow blast cells at the start of AZA therapy, ≤10% vs >10%	44 vs 39	0.75 (0.58-.0.96)	.035		
PAL unrelated PI documented during the first 4 mo of AZA therapy, yes vs no	25 vs 44	2.16 (1.39-3.36)	<.0001	2.13 (1.37-3.33)	.001

Abbreviations: AZA, azacytidine; OR, odds ratio; OS, overall survival; PAL, progressed to acute leukemia.

Infection control in patients with myelodysplastic syndromes who are candidates for active treatment: Expert panel consensus-based recommendations

Corrado Girmenia[a,*], Anna Candoni[b], Mario Delia[c], Roberto Latagliata[a], Alfredo Molteni[d], Esther N. Oliva[e], Giuseppe A. Palumbo[f], Antonella Poloni[g], Prassede Salutari[h], Valeria Santini[i], Maria Teresa Voso[j], Pellegrino Musto[k]

BLOOD reviews
Blood Reviews 34 (2019) 16–25

Risk factors of infectious complications in MDS patients: summary of available literature data.

Risk factors	Comments
Age	In most of studies there was **no clear association** between age and infectious risk. [23, 26, 41]
Comorbidities	Comorbidities had **variable and no clear influence** in the rate of infections [23, 41].
Neutrophil count	Absolute neutrophil counts before each azacitidine cycle were found to be **risk factors** in the univariate analysis [26]. In another study there was no relationship between neutrophil counts lower than 0.5×10^9/L and probability of infectious complications [25]. Severe neutropenia was associated with a **higher incidence of proven/probable invasive fungal diseases (IFDs)** in MDS patients receiving azacitidine.[24]
Hemoglobin levels	**Low hemoglobin levels** (<10 g/dL) was predictive of the risk of infection during the first two cycles of therapy at multivariate analysis [26]. This correlation **was not observed** in another study [41].
Platelet counts	**Low platelet counts** ($<20\times10^9$/L) was predictive of the risk of infection during the first two cycles of azacitidine therapy at multivariate analysis in a study [26], conversely in another real-world experience in MDS patients treated with azacitidine, **higher platelet level** was the only factor associated with an increased incidence of febrile events [41].
Blast percentage, cytogenetic risk and International Prognostic Scoring System Revised (IPSS-R)	Marrow blast percentage before each azacitidine cycle was found to be risk factor in the univariate analysis, but not in the multivariate model [26]. Poor cytogenetics was predictive of the risk of infection during the first two cycles of therapy at multivariate analysis [26]. **A very high IPSS-R** has been identified as an independent risk factor for infections in azacitidine-treated patients, with a relevant attributable mortality, in a study [4], while IPSS or IPSS-R had no influence in the rate of infections in another experience [23].
Hypomethylating agents treatment	**Response**: response to azacitidine impacted on the probability of infections in one study [23], while no correlation was observed in another experience [41]. **Dosage**: a higher risk of infectious complications was observed in patients treated with azacitidine 75 mg/m^2 for 7 days, than in those receiving 5 days of therapy [39,40]. This association was not observed in other experiences [23,26] The rate of infections in decitabine-treated patients did not decrease when reducing the decitabine dose.[46] **Cycles**: the rate of infectious events was higher in the **first 3 azacytidine cycles** and tended to decline with sequential cycles .[7,23,25,26,41,42]

Infection in MDS patients: evidence of literature

- Frequent and severe complication mainly in HR MDS
- Pulmonary infections occur in about 30% of patients and represent an independent factor in the probability of survival
- Crucial problem in the first HMA cycles

Infection control guidelines in MDS?

Infections in myelodysplastic syndromes

Andréa Toma,[1] Pierre Fenaux,[2] François Dreyfus,[3] and Catherine Cordonnier[1,4]

[1]Department of Hematology, Assistance Publique-Hôpitaux de Paris (APHP), Henri Mondor University Hospital, Créteil; [2]Department of Hematology, Avicenne Hospital, APHP, Paris, Paris 13 University; [3]Department of Hematology, Cochin Hospital, APHP, Paris, and Paris 6 University; and [4]Université Paris-Est Créteil Val de Marne, Créteil, France

haematologica | 2012; 97(10)

Comments on the current practices for prevention and management of infectious complications in myelodysplastic syndromes

As infection has rarely been an end point in therapeutic trials in MDS, it is impossible to propose evidence-based guidelines for the prevention and treatment of infection in these patients. However, a few recommendations can be made.

Antibacterial prophylaxis

Whether antibacterial prophylaxis may benefit patients with MDS receiving myelosuppressive treatment (mainly hypomethylating agents or chemotherapy) has not been established.

Antifungal prophylaxis

This is because, unlike in AML or allogeneic HCT recipients, this incidence in MDS patients is lower than the rate that is usually considered to be that justifying primary prophylaxis (typically at least 5%).[174] Furthermore, MDS patients may have prolonged neutropenia, requiring prolonged prophylactic triazoles, a situation which has been associated with the risk of acquired resistance to those drugs.[175,176] Thus, antifungal prophylaxis with triazoles cannot currently be recommended fo MDS patients receiving hypomethylating agents outside controlled trials.

Two prospective randomized studies, one using GM-CSF[165] and one using G-CSF,[166] were performed around two decades ago in neutropenic MDS patients. The study, using G-CSF doses ranging from 0.5 to 10 μg/kg/d in high-risk patients, did not show any difference in the rate of infections or in overall survival between the 2 treatment arms.[166] However, the overall survival of the subgroup of refractory anemia with an excess of blasts had a shorter survival in the G-CSF group when compared to the controls. This study was never published as a full paper. In the study with GM-CSF, the dose of 3 μg/kg/d of GM-CSF was compared to supportive care and was shown to decrease the rate of infections from 33% in the supportive care group to 15% in the treated group. However, no benefit in survival or in risk of AML transformation was observed.[165]

Therefore, no clear recommendation can be made for the use of G- or GM-CSF as routine infection prophylaxis in MDS patients with neutropenia who are not receiving myelosuppressive treatment.[154,170,171] Likewise, in patients receiving myelosuppressive treatment, no indication for G- or GM-CSF has been clearly established, especially in higher-risk patients in whom these agents could potentially increase the risk of AML progression.

Iron chelation

Whether iron chelation can reduce the risk of infection is still not known.

BLOOD RESEARCH VOLUME 48 · NUMBER 2 June 2013 REVIEW ARTICLE

Use of azacitidine for myelodysplastic syndromes: controversial issues and practical recommendations

Yoo-Jin Kim[1], Jun Ho Jang[2], Jae-Yong Kwak[3], Je-Hwan Lee[4], Hyeoung-Joon Kim[5]

Recommendation

Effective management of adverse events resulting from treatment with azacitidine may help to prolong treatment duration and exposure of patients to therapeutically effective doses. The expert panel recommends careful and regular monitoring for adverse events, particularly within the first 2 to 3 cycles in patients treated with azacitidine. Full blood counts should be conducted every week during the first 2 cycles and thereafter every 2 weeks or at the discretion of the treating physician. Patients should be reminded to report symptoms of fever or any signs or symptoms of bleeding as soon as possible. Management of patients with cytope-

Dose intensity is crucial in the first 3 cycles particularly in higher risk patients!!!

Dose reductions or delays may decrease exposure of patients to therapeutically effective levels of drug. As such, dose modifications are not recommended in the early treatment phase (first 3 cycles) in patients with more advanced disease (i.e., a high blast percentage or a complex karyotype).

SUPPORTIVE CARE[r]

- Pre-transplant
  - Transplant and non-transplant patients should receive support.
  - Transfusion products should be irradiated with 25 Gy or per institution standard.
  - Patients with ≥5% marrow blasts who are candidates for reduced-intensity conditioning (RIC) are encouraged to receive "debulking" therapy with HMA or induction chemotherapy. Transplantation should be carried out as long as patients are responding; it should not be delayed until the response is lost.
- Clinical monitoring
  - Psychosocial support (See NCCN Guidelines for Survivorship)
  - Quality-of-life assessment
  - Transfusions[qq]:
    - ◊ RBC transfusions (CMV-safe) are recommended for symptomatic anemia, and platelet transfusions are recommended for thrombocytopenic bleeding. However, they should not be used routinely in patients with thrombocytopenia in the absence of bleeding unless platelet count <10,000/mcL. Irradiated products are suggested for transplant candidates.
  - Antibiotics are recommended for bacterial infections, but no routine prophylaxis is recommended except in patients with recurrent infections.
- Aminocaproic acid or other antifibrinolytic agents may be considered for bleeding refractory to platelet transfusions or profound thrombocytopenia.
- Iron chelation:
  - If >20 to 30 RBC transfusions have been received, consider daily chelation with deferoxamine subcutaneously or deferasirox orally to decrease iron overload, particularly for patients who have lower-risk MDS or who are potential transplant candidates (LOW/INT-1). For patients with serum ferritin levels >2500 ng/mL, aim to decrease ferritin levels to <1000 ng/mL.[rr] (See Discussion). Patients with low creatinine clearance (<40 mL/min) should not be treated with deferasirox or deferoxamine.

PREVENTION OF FUNGAL INFECTIONS

See Antifungal Agents (FEV-B) for dosing, spectrum, and specific comments/cautions

Overall Infection Risk in Patients with Cancer[a]	Disease/Therapy Examples	Antifungal Prophylaxis See Antipneumocystis Prophylaxis (INF-6)	Duration
Intermediate to High	ALL	Consider: • Fluconazole[g] or an echinocandin[h] • Amphotericin B products[i] (category 2B)	Typically until resolution of neutropenia
	MDS (neutropenic)	Consider: • Posaconazole[g] (category 1) • Voriconazole,[g] fluconazole,[g] an echinocandin,[h] or amphotericin B products[i] (all category 2B)	
	AML (neutropenic)		
	Autologous HCT with mucositis[f]	Consider: • Fluconazole[g] or an echinocandin[h] (both category 1)	
	Autologous HCT without mucositis	Consider no prophylaxis (category 2B)	N/A
	Allogeneic HCT (neutropenic)	Consider: • Fluconazole[g] or an echinocandin[h] (both category 1) • Voriconazole,[g] posaconazole,[g] or amphotericin B products[i] (all category 2B)	Continue during neutropenia[j]
	Significant GVHD receiving immunosuppressive therapy	Consider: • Posaconazole[g] (category 1) • Voriconazole,[g] echinocandin, or amphotericin B products[i] (all category 2B)	Until resolution of significant GVHD

GENERAL RECOMMENDATIONS FOR VACCINATION IN PATIENTS WITH CANCER[ee,ff]

General comments

- Live vaccines should NOT be administered during chemotherapy or periods of significant immunosuppression, such as treatment of GVHD.
- The safety of vaccines in patients receiving immunostimulatory drugs is unclear. Some emerging data suggest vaccines (ie, influenza) can be given safely.
- All household members should be up-to-date with vaccines.

Influenza vaccination

- Patients with hematologic or solid tumor malignancies should receive inactivated or recombinant influenza vaccine annually.[gg]

Pneumococcal vaccination

- The pneumococcal conjugate vaccine (PCV13) should be administered to newly diagnosed adults with cancer who are pneumococcal vaccine-naïve, followed by the polysaccharide pneumococcal vaccine (PPSV23) at least 8 weeks later. Subsequent doses of PPSV23 should follow current PPSV23 recommendations for adults at high risk. For patients who have previously received PPSV23, the PCV13 dose should be given at least 1 year after the last PPSV23 dose. For those who require additional doses of PPSV23, the first such dose should be given no sooner than 8 weeks after the PCV13 dose.
- Pneumococcal antibody responses to some serotypes in PCV7 were decreased following co-administration of the meningococcal conjugate vaccine, the meningococcal conjugate vaccine MenACWY-D, and PCV-7. Therefore, PCV7 should not be given with MenACWY-D but can be given with MenACWY-CRM.

Meningococcal vaccination

- The addition of serogroup B meningococcal vaccination has been recommended for patients at increased risk for meningococcal disease. Patients at increased risk for meningococcal disease should receive quadrivalent MenACWY vaccine series and monovalent meningococcal serogroup B vaccine series. At-risk patients include those with persistent complement component deficiencies, those taking a complement C5 inhibitor (eg, eculizumab, ravulizumab), or those with anatomic or function asplenia. MenACWY vaccine is given in 2 doses ≥8 weeks apart; Serogroup B vaccine is available in a 2- or 3-dose series, depending on the vaccine formulation used.

Human papillomavirus (HPV) vaccination

- The recombinant 3-dose HPV vaccine should be offered to patients of both sexes up to 26 years of age and may be considered in patients up to 45 years of age.

Travel vaccines

- ID consult for travel vaccines is recommended.

[ee] Vaccination should be deferred in patients who are unlikely to respond (eg, patients who received anti–B-cell antibodies within 6 months, induction and consolidation chemotherapy for acute leukemia).
[ff] For prevention of infection in cancer survivors, including vaccination recommendations, see the NCCN Guidelines for Survivorship.
[gg] Age-appropriate vaccines are recommended. High-dose flu vaccine is recommended for patients >65 years of age.

Differences and Temporal Changes in Risk of Invasive Pneumococcal Disease in Adults with Hematological Malignancies: Results from a Nationwide 16-Year Cohort Study

Clinical Infectious Diseases® 2021;72(3):463–71

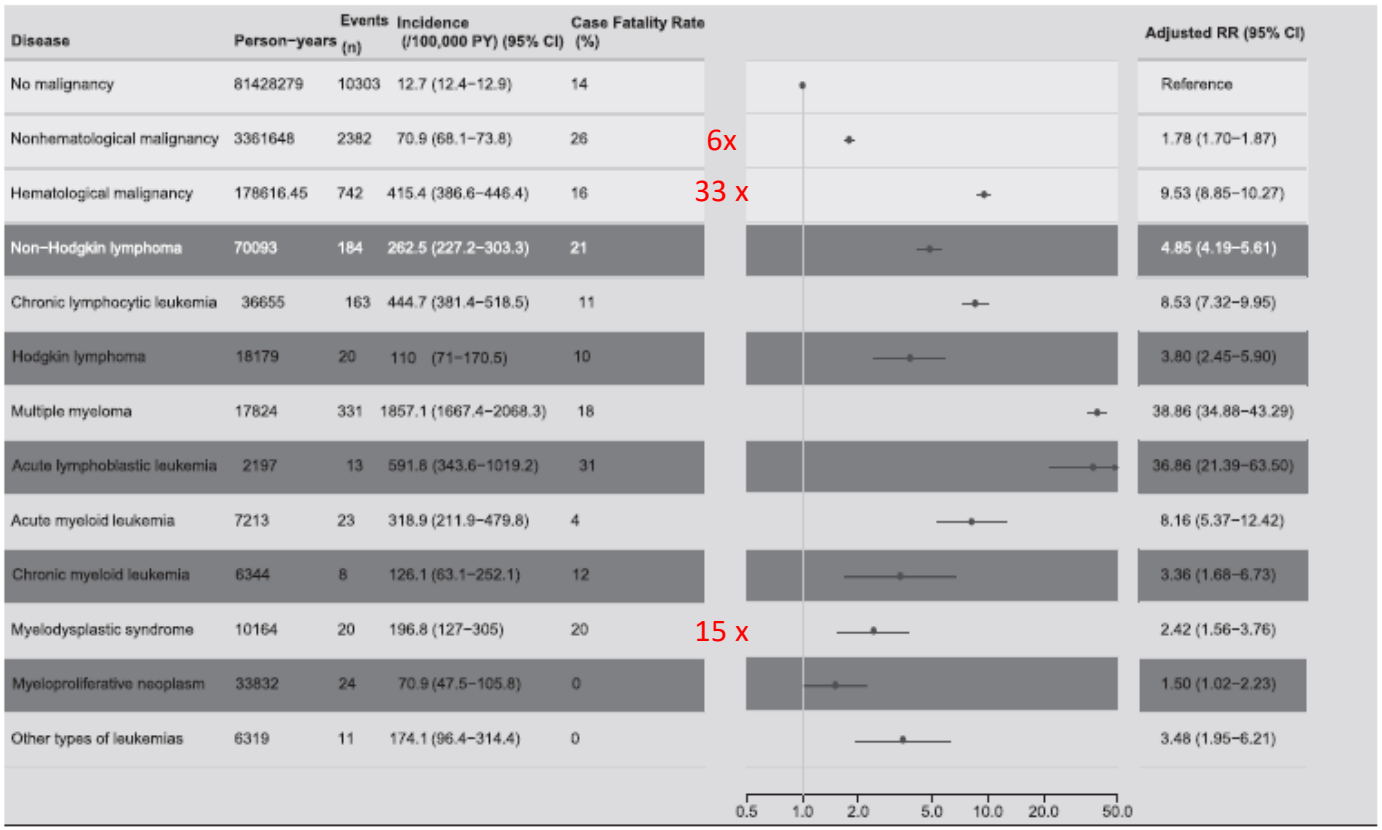
Michael Asger Andersen,[1,2] Carsten Utoft Niemann,[1] Klaus Rostgaard,[2] Tine Dalby,[3] Rasmus Sørrig,[1] Daniel M. Weinberger,[4] Henrik Hjalgrim,[1,2] and Zitta Barrella Harboe[3,5]

[1]Department of Hematology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [2]Department of Epidemiology Research, Statens Serum Institut, Copenhagen, Denmark, of Bacteria, Parasites and Fungi, Statens Serum Institut, Copenhagen, Denmark, [4]Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, Connec and [5]Department of Pulmonary and Infectious Diseases, Hospital of Nordsjælland, University of Copenhagen, Copenhagen, Denmark

Patients with hematological malignancies (HM) are among those with the highest risk of IPD, with incidences ranging between 13–50 times higher when compared with the background population, and with HM patients accounting for up to 10% of all IPD episodes in adults. We explored temporal changes in the risk of IPD and associated mortality in adults with HM, compared to the risk in patients with non-Hematological cancers and cancer-free individuals during 16 years in Denmark.

Table 1. Incidence and Case Fatality Rates of Invasive Pneumococcal Diseases in Patients With and Without Hematological Malignancies, Denmark 2000–2016

Disease	Person-years	Events (n)	Incidence (/100,000 PY) (95% CI)	Case Fatality Rate (%)	Adjusted RR (95% CI)
No malignancy	81428279	10303	12.7 (12.4–12.9)	14	Reference
Nonhematological malignancy	3361648	2382	70.9 (68.1–73.8)	26	1.78 (1.70–1.87)
Hematological malignancy	178616.45	742	415.4 (386.6–446.4)	16	9.53 (8.85–10.27)
Non–Hodgkin lymphoma	70093	184	262.5 (227.2–303.3)	21	4.85 (4.19–5.61)
Chronic lymphocytic leukemia	36655	163	444.7 (381.4–518.5)	11	8.53 (7.32–9.95)
Hodgkin lymphoma	18179	20	110 (71–170.5)	10	3.80 (2.45–5.90)
Multiple myeloma	17824	331	1857.1 (1667.4–2068.3)	18	38.86 (34.88–43.29)
Acute lymphoblastic leukemia	2197	13	591.8 (343.6–1019.2)	31	36.86 (21.39–63.50)
Acute myeloid leukemia	7213	23	318.9 (211.9–479.8)	4	8.16 (5.37–12.42)
Chronic myeloid leukemia	6344	8	126.1 (63.1–252.1)	12	3.36 (1.68–6.73)
Myelodysplastic syndrome	10164	20	196.8 (127–305)	20	2.42 (1.56–3.76)
Myeloproliferative neoplasm	33832	24	70.9 (47.5–105.8)	0	1.50 (1.02–2.23)
Other types of leukemias	6319	11	174.1 (96.4–314.4)	0	3.48 (1.95–6.21)



PY, number of events, crude incidence rates, and case-fatality rates are shown for all groups. RR for IPD in individuals with a hematological malignancy are adjusted for age, gender, calendar year, morbidity, and type of malignancy. Persons with more than one malignancy count multiple times for person years, events, and incidences.
Abbreviations: CI, confidence interval; IPD, invasive pneumococcal disease; PY, person years; RR, rate ratio.

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Michael Asger Andersen,[1,2] Carsten Utoft Niemann,[1] Klaus Rostgaard,[2] Tine Dalby,[3] Rasmus Sørrig,[1] Daniel M. Weinberger,[4] Henrik Hjalgrim,[1,2] and Zitta Barrella Harboe[3,5]

[1]Department of Hematology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [2]Department of Epidemiology Research, Statens Serum Institut, Copenhagen, Denmark, [3]Department of Bacteria, Parasites and Fungi, Statens Serum Institut, Copenhagen, Denmark, [4]Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, Connecticut, USA, and [5]Department of Pulmonary and Infectious Diseases, Hospital of Nordsjælland, University of Copenhagen, Copenhagen, Denmark

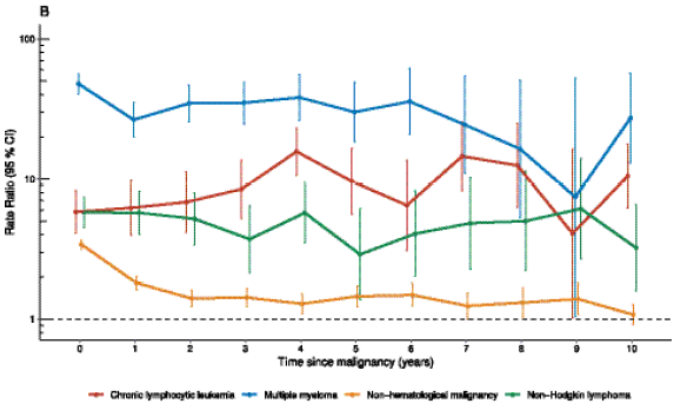


Figure 3. Time to invasive pneumococcal disease since time of diagnosis of malignancy. *A*, Individuals with any nonhematological malignancy. *B*, Individuals with and without hematological malignancies. RR estimates are adjusted for age, gender, calendar year, comorbidity, and type of malignancy. The y-axis shows the RR, and the x-axis shows the time since malignancy, with 0 being the year of diagnosis. Abbreviations: CI, confidence interval; CLL, chronic lymphocytic leukemia; IPD, invasive pneumococcal disease; RR, rate ratio.

Clinical Infectious Diseases® 2021;72(3):463–71

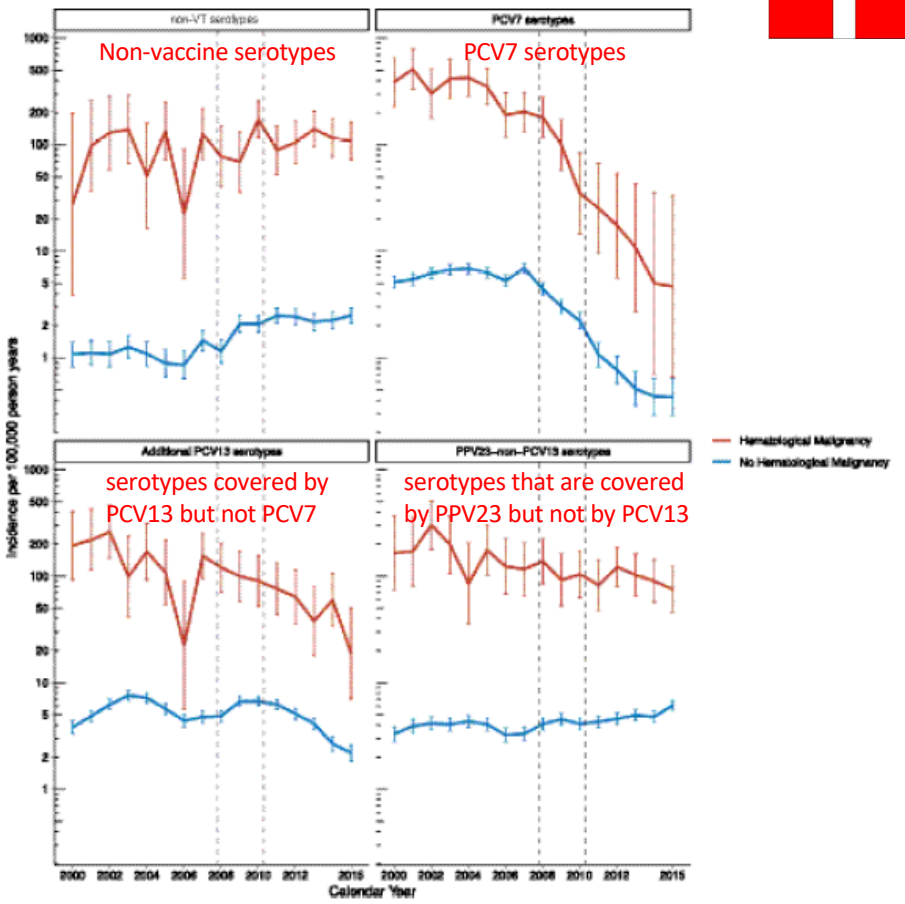


Figure 2. Incidence rates of invasive pneumococcal disease in the Danish population for individuals with and without a hematological malignancy according to serotypes included in pneumococcal vaccines. The vaccine groups were PCV7 (PCV7 serotypes), additional PCV13 serotypes (serotypes covered by PCV13 but not PCV7), PPV23 non-PCV13 serotypes (serotypes that are covered by PPV23 but not by PCV13), and non-VT (non-VT, defined as all serotypes that are not covered by PCV7, PCV13, or PPV23). Abbreviations: PCV7, 7-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; PPV23, 23-valent pneumococcal polysaccharide vaccine; VT, vaccine serotype.

- The risk of IPD in patients with HM was up to 39 times higher when compared to the background population and was highest for multiple myeloma, acute lymphoblastic leukemia, and chronic lymphocytic leukemia.
- Unlike other malignancies, the increased IPD risk did not wane with the time since HM diagnosis.
- We found a vaccination uptake of only ≤2% in patients with HM and ≤1% for those with other types of malignancies.

Use of Recombinant Zoster Vaccine in Immunocompromised Adults Aged ≥19 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022

MMWR / January 21, 2022 / Vol. 71 / No. 3

Tara C. Anderson, DVM, PhD[1]; Nina B. Masters, PhD[1,2]; Angela Guo, MPH, MBA[1]; Leah Shepersky, MPH[1]; Andrew J. Leidner, PhD[3]; Grace M. Lee, MD[4]; Camille N. Kotton, MD[5]; Kathleen L. Dooling, MD[1]

Summary

What is already known about this topic?

Immunocompromised persons experience a higher incidence of herpes zoster and related complications. On July 23, 2021, the Food and Drug Administration expanded the indication for use of recombinant zoster vaccine (RZV) to include immunodeficient or immunosuppressed adults.

What is added by this report?

On October 20, 2021, the Advisory Committee on Immunization Practices recommended 2 RZV doses for prevention of herpes zoster and related complications in immunodeficient or immunosuppressed adults aged ≥19 years.

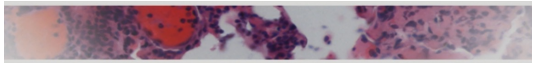
What are the implications for public health practice?

RZV is the first herpes zoster vaccine approved for use in immunocompromised persons. With moderate to high vaccine efficacy and an acceptable safety profile, RZV has the potential to prevent considerable herpes zoster incidence and related complications.

Dosing schedule. Two RZV doses are necessary, regardless of previous history of HZ or previous receipt of HZ vaccine live. The second RZV dose should typically be given 2–6 months after the first; for persons who are or will be immunodeficient or immunosuppressed and who would benefit from a shorter vaccination schedule, **the second dose can be administered 1–2 months after the first** (*2*). If the second RZV dose is given sooner than 4 weeks after the first, a valid second dose should be repeated at least 4 weeks after the dose given too early. The vaccine series does not need to be restarted if more than 6 months have elapsed since the first dose.

Timing of vaccination. When possible, patients should be vaccinated **before becoming immunosuppressed**. Otherwise, **providers should consider timing vaccination** when the immune response is likely to be most robust (i.e., during periods of lower immunosuppression and stable disease). RZV may be administered to patients who previously received varicella vaccine. RZV is not a live virus vaccine; therefore, RZV may be administered while patients are taking antiviral medications.

Is COVID-19 vaccination effective in MDS and AML patients?



Responses to SARS-CoV-2 Vaccines in Patients with Myelodysplastic Syndrome and Acute Myeloid Leukemia

Akriti Jain, Ning Dong, Somedeb Ball, Elaine Tan, Junmin Whiting, Rami Komrokji, Kendra Sweet, Onyee Chan, David Sallman, Eric Padron, Andrew Kuykendall, Anna Giuliano, Jeffrey E. Lancet

Patient Characteristics	n	D1	After dose 1 (D29)	P value	After dose 2 (D57)	P value
Overall	46	0 (0%)	32 (69.6%)		44(95.7%)	
Prior lines of therapy						
None, n (%)	2	0 (0%)	2 (100%)	1.000	2 (100%)	1.000
First line, n (%)	25	0 (0%)	17 (68%)		24 (96%)	
Subsequent line, n (%)	19	0 (0%)	13 (68.4%)		18 (94.7%)	
On active therapy at the time of vaccination						
Yes, n (%)	15	0 (0%)	14 (93.3%)	0.018	14 (93.3%)	1.000
No, n (%)	31	0 (0%)	18 (58.1%)		30 (96.8%)	
ALC						
ALC ≤1 x10^9/L	12	0 (0%)	9 (75%)	0.729	12 (100%)	1.000
ALC >1 x10^9/L	34	0 (0%)	23 (67.6%)		32 (94.1%)	
ANC						
ANC ≤1 x10^9/L	6	0 (0%)	6 (100%)	0.157	6 (100%)	1.000
ANC >1 x10^9/L	40	0 (0%)	26 (65%)		38 (95%)	
Therapy within 3 months prior to vaccination						
None/Observation	31	0 (0%)	18 (58.1%)	0.181	30 (96.8%)	0.191
Hypomethylating agent	6	0 (0%)	6 (100%)		6 (100%)	
ESAs	2	0 (0%)	2 (100%)		1 (50%)	
IMIDs	1	0 (0%)	1 (100%)		1 (100%)	
Targeted therapy	8	0 (0%)	5 (83.3%)		6 (100%)	

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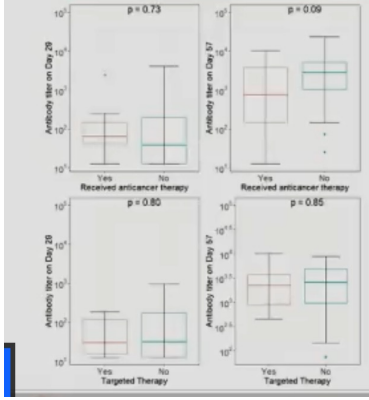
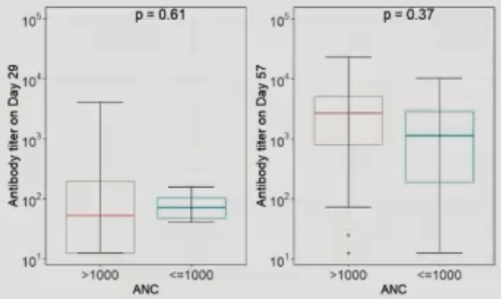
Responses Based on Therapy



- Therapy, including targeted therapies, prior to vaccination did not affect antibody levels following 1st or 2nd dose.

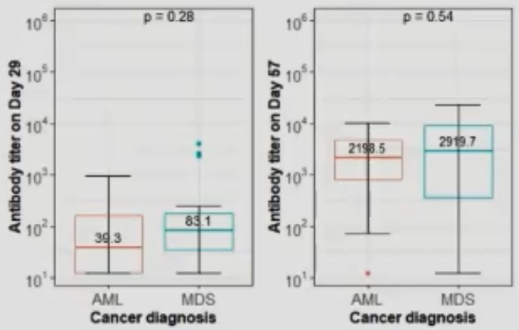
Responses Based on ANC

- No difference in antibody levels following 1st or 2nd dose based on ANC



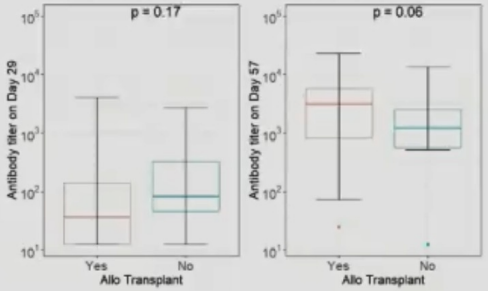
Antibody Levels:

- Antibody levels were significantly higher after the 2nd vaccine dose than after 1st dose (mean 3806.5 vs 315, p<0.0001).
- This difference was observed across the different variables and patient subsets.

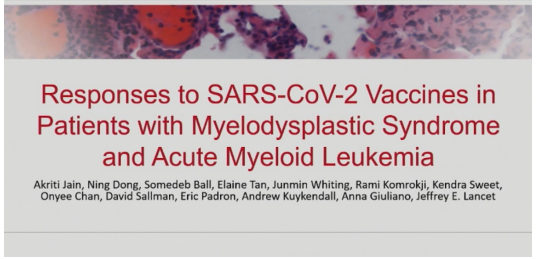


Responses Based on Transplant History

- No significant difference in antibody levels following 1st or 2nd dose based on transplant history



Is COVID-19 vaccination effective in MDS and AML patients?



Conclusions:

- In this observational study, the vast majority of patients with AML and MDS converted to seropositivity after two doses of the vaccine.
- Most clinical and laboratory variables (including neutropenia and lymphopenia) did not affect the seropositivity rate.
- However, majority of the patients in our study were in remission and not on active treatment. Hence, we do not know what the response rates might be in patients who are on active treatment. Further studies are needed for AML, MDS patients with active disease.

- Antibody titer levels increased dramatically following the 2nd vaccine dose, indicating the potential utility of serial vaccination in poorly-responsive patients.
- While these findings should be substantiated in a larger and more diverse cohort, mRNA-1273 SARS-CoV-2 vaccine appears to induce a strong humoral response in a population of patients with AML and MDS.

Infection control in patients with myelodysplastic syndromes who are candidates for active treatment: Expert panel consensus-based recommendations

Corrado Girmenia[a,*], Anna Candoni[b], Mario Delia[c], Roberto Latagliata[a], Alfredo Molteni[d], Esther N. Oliva[e], Giuseppe A. Palumbo[f], Antonella Poloni[g], Prassede Salutari[h], Valeria Santini[i], Maria Teresa Voso[j], Pellegrino Musto[k]

BLOOD reviews
Blood Reviews 34 (2019) 16–25

Prevention of infection in MDS patients

	LR supportive care	LR Lenalidomide	IR-HR HMA
S.pneumoniae vaccination	YES at onset of disease	YES at onset of disease	YES at onset of disease
Influenza vaccination	YES annually	YES annually	YES annually
Herpes zoster vaccination	YES at onset of disease	YES at onset of disease	YES at onset of disease
COVID-19 vaccination	YES	YES	YES
Antibacterial prophylaxis	NO	NO	Consider in the first months
Mould-active antif. prophylaxis	NO	NO	Consider in the first months
Anti-herpetic prophylaxis	NO	NO	NO
Chronic HBV inf. (HBsAg +, HBV-DNA +)	As in immunocompetent	Tenofovir, entecavir	Tenofovir, entecavir
Resolved HBV inf. (Anti HBc-Ag +)	As in immunocompetent	Monitoring of seroreversion and/or viremic rebound	Monitoring of seroreversion and/or viremic rebound