Fungal infections

Corrado Girmenia

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Infections in Patients With Aplastic Anemia

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Seminars in Hematology, Vol 46, No 3, July 2009, pp 269–276

Table 3. Important Common Pathogens Complicating Severe Aplastic Anemia

Fungal	Bacteria	Viruses	Helminths
Aspergillus spp.	*Staphylococcus* spp.	Hepatitides A, B, C	*Strongyloides stercoralis*
Zygomycetes	*Stenotrophomonas maltophilia*	Herpes simplex virus	
(*Rhizopus* spp., *Mucor* spp.	*Pseudomonas aeruginosa*	Varicella zoster virus	
Cunninghamella bertholletiae)	Enterobacteriaciae	Cytomegalovirus	
Candida spp.	(*E coli*)	Influenza A, B	
Fusarium spp.	*Klebsiella* spp.	Respiratory syncytial virus	
	Bacillus cereus	Parainfluenza virus	

- Epidemiology
- Diagnostic approach
- Prevention strategies

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How I treat acquired aplastic anemia

Andrea Bacigalupo

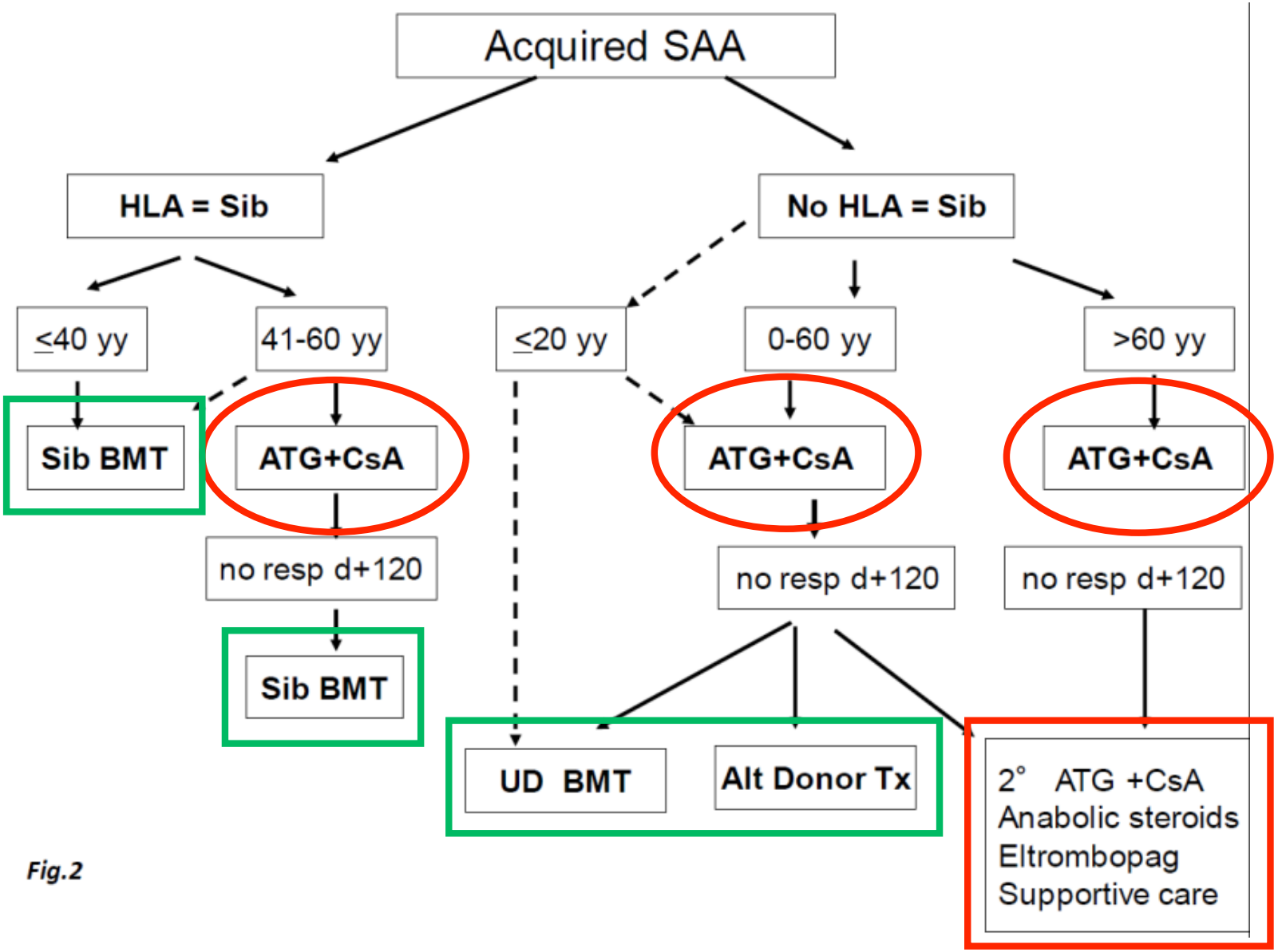

Fig.2

Monitoring of IFDs in AA patients

- Surveillance-driven approach:
  - Galactomannan (2 x w)
  - Nasal swabs (filamentous fungi)
  - CT scan if clinically indicated
- Clinically-driven approach
  - No galactomannan surveillance
  - Intensification if clinically indicated (persistent fever, pulmonary infiltrates, sinonasal infect.)
    - CT scan
    - Galactomannan, 3 consecutive days
    - Cultures as indicated
- Diversification of the strategy according to local resources
  - First IST
  - Second IST
  - Allogeneic SCT, matched sibling vs mismatched/unrelated

Bone Marrow Transplantation (2013) **48,** 168–173

www.nature.com/bmt

REVIEW

Supportive care in severe and very severe aplastic anemia

B Höchsmann[1], A Moicean[2], A Risitano[3], P Ljungman[4] and H Schrezenmeier[1] for the EBMT Working Party on Aplastic Anemia

Severe AA patients with prolonged periods of severe neutropenia have a high mortality due to mold especially aspergillus infections.[2,6,7] Therefore, prophylactic antifungals are often used, but there are no uniform recommendations and no study showing clinical benefit in AA patients.

In our opinion, prophylactic antifungals should be used in general for patients with very severe AA.[26] Voriconazole or posaconazole appear to be more effective than fluconazole, as they have activity against *Aspergillus* and also some other mold species. Antifungal prophylaxis should also be considered during the first months after antithymocyte globulin (ATG) therapy and after SCT as long as neutropenia and/or lymphopenia is present. There are no general recommendations for prophylaxis against *Pneumocystis jirovecii* pneumonia (PJP).[9] In transplanted patients, PJP-prophylaxis is routinely given. For patients after immunosuppressive therapy with ATG, the usage of antiviral and PJP-prophylaxis depends on the individual center, but many use such prophylaxis until T-cell recovery.

Guidelines for the diagnosis and management of adult aplastic anaemia

British Journal of Haematology, 2016, **172,** 187–207

Sally B. Killick, Writing Group Chair[1] Nick Bown,[2] Jamie Cavenagh,[3] Inderjeet Dokal,[4] Theodora Foukaneli,[5] Anita Hill,[6] Peter Hillmen,[6] Robin Ireland,[7] Austin Kulasekararaj,[7] Ghulam Mufti,[7] John A. Snowden,[8] Sujith Samarasinghe,[9] Anna Wood, BCSH Task Force Member[10] and Judith C. W. Marsh[7] on behalf of the British Society for Standards in Haematology

A mould (aspergillus) active azole, preferably itraconazole or posaconazole, should be used as prophylaxis. In the UK, prophylaxis against *Pneumocystis jirovecii* is not routinely given.

- **Aplastic anaemia patients who are severely neutropenic should be given prophylactic antibiotics and antifungal therapy according to local policies. Grade 2B**
- **Aplastic anaemia patients receiving immunosuppressive therapy (IST) should also receive prophylactic anti-viral agents, although routine prophylaxis against *Pneumocystis jirovecii* is not necessary. Grade 2C**

Granulocyte transfusions may be potentially life saving in severe sepsis, such as invasive fungal disease, particularly for patients due to proceed to HSCT (Quillen *et al*, 2009).

Hematology 2013

Management of the refractory aplastic anemia patient: what are the options?

Judith C. W. Marsh[1,2] and Austin G. Kulasekararaj[1,2]

What is the best prophylaxis for SAA?

Prophylaxis for SAA is a controversial issue and practice varies widely due to the lack of prospective studies. Many centers use prophylactic antibiotics and antifungals in SAA to help prevent gram-negative infections and invasive fungal infections, but other centers choose not to use antifungal prophylaxis and instead commence systemic antifungals early with febrile neutropenic episodes. Antiviral prophylaxis with acyclovir or valacyclovir should be used during and after ATG therapy. During ATG therapy, subclinical reactivation of CMV and EBV is common but self-limiting, and therefore does not require antiviral treatment. EBV posttransplantation lymphoproliferative disorder has only very rarely been reported after ATG, most often after rabbit ATG. It is not our practice to give *Pneumocystis* prophylaxis with ATG, but this is done routinely in some centers in the United States. Nebulized pentamidine is an appropriate drug for prophylaxis because cotrimoxazole is myelosuppressive.

Blood Cells, Molecules and Diseases 55 (2015) 40–47

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Diagnosis and management of acquired aplastic anemia in childhood. Guidelines from the Marrow Failure Study Group of the Pediatric Haemato-Oncology Italian Association (AIEOP)

Angelica Barone [a,1], Annunziata Lucarelli [b,1], Daniela Onofrillo [c,1], Federico Verzegnassi [d,1], Sonia Bonanomi [e], Simone Cesaro [f], Francesca Fioredda [g], Anna Paola Iori [h], Saverio Ladogana [i], Anna Locasciulli [j], Daniela Longoni [e], Marina Lanciotti [g], Alessandra Macaluso [k], Rosalba Mandaglio [l], Nicoletta Marra [m], Baldo Martire [n], Matteo Maruzzi [i], Giuseppe Menna [m], Lucia Dora Notarangelo [o], Giovanni Palazzi [p], Marta Pillon [q], Ugo Ramenghi [r], Giovanna Russo [s], Johanna Svahn [g], Fabio Timeus [t], Fabio Tucci [u], Chiara Cugno [v], Marco Zecca [v], Piero Farruggia [k,2], Carlo Dufour [g,*,2], Paola Saracco [r,2]

7.3. Anti-infection treatment

There are no controlled studies on safety and efficacy of anti-microbial agents in treatment and prophylaxis of pediatric patients with AA. Most data come from meta-analyses and controlled trials conducted in adult oncology patients with febrile neutropenia.

7.3.1. Prophylaxis

Antibiotic prophylaxis may be considered in patients with neutrophils of <200/mmc, between day 30 and day 90 after IST start (*Level of evidence EO*; *Strength of consensus 7.3*; *level of consensus C*). Anti-fungal prophylaxis may be considered in subjects with neutrophil persistently <200/mmc (*Level of evidence EO*; *Strength of consensus 7.1*; *level of consensus C*). Prophylaxis for anti-*Pneumocystis jiroveci* is indicated with oral cotrimoxazole or with pentamidine by aerosol if lymphocyte values are low ($CD4^+ < 400$/mmc or total lymphocytes < 1000/mmc) (*Level of evidence EO*; *Strength of consensus 8.7*; *level of consensus B*). Anti-viral prophylaxis may be taken in account in patients with severe lymphopenia after ATG (*Level of evidence EO*; *Strength of consensus 7.1*; *level of consensus C*).

Antifungal prophylaxis in patients with Aplastic Anemia

	Mould active antifungal prophylaxis			PJP prophylaxis	
	sAA - IST	vsAA - IST	AA - HSCT	AA -IST	AA-HSCT
EBMT WP-AA	?	YES +++	YES +++	?	YES+++
BSSH	NO	YES ++	/	NO	/
AIEOP	NO	YES +	/	YES +++	/

Epidemiology of IFDs in AA populations

- Several case reports
- Few case series
- No prospective study
- No specific data on infections in clinical trials

Haematologica 1999; 84:114-118 original paper

Fusarium infections in patients with severe aplastic anemia: review and implications for management

CORRADO GIRMENIA, ANNA PAOLA IORI, FEDERICA BOECKLIN, ANTONELLA TOROSANTUCCI,* PAOLA CHIANI,* PAOLO DE FABRITIIS, FABRIZIO TAGLIETTI, ANTONIO CASSONE,* PIETRO MARTINO

*Dipartimento di Biotecnologie Cellulari ed Ematologia, University "La Sapienza", and *Department of Bacteriology and Medical Mycology, Istituto Superiore di Sanità, Rome, Italy*

Table 1. Summary of published cases of invasive fusarium infections in patients with aplastic anemia.

Ref.	Sex/age	Previous therapy for SAA	Documented sites of infection	Organism isolated	Treatment	Outcome
2*	F/34	CSA	Lung, heart, liver, spleen, kidney,gut	*Fusarium sp*	AmB	Died
2*	M/29	CSA, PDN, ALG	Paranasal sinus, skin	*Fusarium sp*	AmB, G-CSF	Survived
8	F/66	Androgens, PDN	Esophagus, liver, spleen, cecum	*F. oxysporum*	no	Died
9	M/46	BMT	Skin, lungs, spleen, kidneys, testes, lymph nodes	*F. solani*	AmB, ketoconazole	Died
10	M/50	No	Skin, lung	*Fusarium sp*	AmB, miconazole	Died
11*	M/43	ALG	Nail, skin, blood	*F. solani*	AmB	Died
12	F/15	Unreported	Paranasal sinus, skin	*Fusarium sp*	no	Died
13	M/49	BMT	Skin, lungs, kidneys, esophagus, heart	*F. oxysporum*	AmB, itraconazole	Died
14	F/40	ALG	Sinonasal infection	*F. chlamydosporum*	AmB, itraconazole, surgical excision	Survived
Present case*	F/3	CSA, ALG, G-CSF, PDN	Skin, lungs	*Fusarium sp*	Liposomal AmB, WBC transfusions from G-CSF stimulated donors	Died

*ALG = antilymphocyte globulin, CSA = cyclosporin-A, PDN = prednisone, AmB = amphotericin B. * observed at the Dipartimento di Biotecnologie Cellulari ed Ematologia, University "La Sapienza", Rome, Italy.*

From 1999 to 2016 only 3 further case-reports of invasive fusariosis in aplastic anemia

Infections in Patients with Aplastic Anemia

Cancer 2003;98:86–93.

Experience at a Tertiary Care Cancer Center

Harrys A. Torres, M.D.[1]
Gerald P. Bodey, M.D.[1]
Kenneth V. I. Rolston, M.D.[1]
Hagop M. Kantarjian, M.D.[2]
Issam I. Raad, M.D.[1]
Dimitrios P. Kontoyiannis, M.D., Sc.D.[1]

Retrospective, period 1994-2000,
52 patients,
42 (81%) with infectious episodes

TABLE 2
Sites of 56 Microbiologically Documented Infections in Patients with Aplastic Anemia

	No. by causative agent (%)				
Site of infection	Bacteria	Fungi	Virus	Polymicrobial	Total
Bloodstream	14	0	0	7	21 (38)
Upper respiratory tract	1	1	2	2	6 (11)
Pulmonary	3	3	1	2	9 (16)
Soft tissue	4	0	2	2	8 (14)
Genitourinary	3	0	1	0	4 (7)
Gastrointestinal	4	0	1	0	5 (9)
Disseminated	2	0	1	0	3 (5)
Total[a]	31 (55)	4 (7)	8 (14)	13 (23)	56 (100)

[a] Percentages may not total 100 due to rounding.

TABLE 4
Characteristics of Infectious Episodes in Patients with Aplastic Anemia Based on the Presence of Neutropenia[a]

Characteristic	Neutropenia (ANC < 500)	Nonneutropenia (ANC ≥ 500)	*P* value
No. of IEs	43	57	—
Prior use of high-dose adrenal corticosteroids[b] (%)	14/18 (78)	13/14 (93)	NS
No. of severe IEs[c] (%)	34/43 (79)	17/54 (31)	<0.01
Type of pathogen (%)			
Bacterial	16/25 (64)	13/16 (81)	NS
Fungal	9/25 (36)	0/16 (0)	<0.01
Viral	7/25 (28)	3/16 (19)	NS
No. of deaths due to infection	5/42 (12)	0/56 (0)	0.01

ANC: absolute neutrophil count; IEs: infectious episodes; NS: not significant.
[a] Data refer to the number and percentage of 100 episodes for which information about ANC was available.
[b] Refers to > 600 mg of equivalent of prednisone.
[c] Based on the presence of sepsis at the onset of IE.

12 deaths,
5 infection-related death, 4 due to fungi

Infections in Patients with Aplastic Anemia

Cancer 2003;98:86–93.

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TABLE 5
Reported Causes of Death in Patients with Aplastic Anemia

Characteristic	Scott et al., 1959[16]	Vincent and deGruchy, 1967[17]	Twomey et al., 1973[18]	Doney et al., 1981[19]	Marmont et al., 1983[4]	Weinberger et al., 1992[3]	Storb et al., 1994[20]	Current study	Total
No. of patients studied	39	43	22	19	42	150	39	42	396
No. of deaths (%)[a]									
Total	22 (56)	27 (63)	12 (55)	11 (58)	16 (38)	58 (39)	3 (8)	12 (29)	161 (41)
Due to infection	7 (32)	18 (42)	8 (36)	7 (37)	11 (26)	36 (62)	3 (100)	5 (56)[b]	95 (59)
Cause of death									
Bacteria	1	15	8	4	8	13	0	0	49
Fungi	1	0	0	2	1	14	2	0	20
Viruses	0	0	0	0	2	0	0	0	2
Multiple microbes	5	3	0	1	0	9	1	4[c]	23

Rate of IFDs: 5-10% of patients

EUROPEAN JOURNAL OF Haematology

European Journal of Haematology 88 (526–534)

ORIGINAL ARTICLE

Epidemiology of infections in children with acquired aplastic anaemia: a retrospective multicenter study in Italy

Paola Quarello[1], Paola Saracco[2], Mareva Giacchino[1], Desirèe Caselli[3], Ilaria Caviglia[4], Daniela Longoni[5], Stefania Varotto[6], Ippolita Rana[7], Angela Amendola[8], Aldo Misuraca[9], Maria Licciardello[10], Paolo Paolucci[11], Saverio Ladogana[12], Elisa Rivetti[2], Carlo Dufour[4], Elio Castagnola[4]

Retrospective, 1996-2007,
78 patients:
6 nsAA, 34 SAA, 38 vsAA
111 IE in 42 (54%) patients

Table 2 Aetiologies and localisations of documented infections in children with aplastic anaemia

		Day 0–120 from IST		Day >120 from IST	
Diagnosis	Clinical picture	Aetiology	Number of episodes	Aetiology	Number of episodes
MDI	Bacteremia	*S. aureus*	3	*Coagulase negative staphylococci*	4
		Streptococcus viridans	3	*S. aureus*	3
		K. pneumoniae	1	*Corynebacterium* spp	2
		E. colacae	1	*Alpha-haemolyticus Streptococcus*	1
		E. coli	1	*K. pneumoniae*	1
				E. cloacae	1
				B. cepacia	1
				Proteus spp	1
	Skin and soft tissues[1]	*Streptococcus* spp	1	*Coagulase negative staphylococci*	1
		P. aeruginosa	1		
	Urinary tract	*E. coli*	1	*E. coli*	2
				Morganella sp	1
	Pneumonia	–	–	*Aspergillus* sp	2
	Sinusitis	*Mucor ramosissimus*	1	–	–
CDI	Pneumonia[2]	–	5	–	6
	Skin and soft tissue[1]	–	3	–	2
	Stomatitis/pharyngitis	–	7	–	3
	Varicella	–	–	–	1

MDI, microbiologically documented infection; CDI, clinically documented infection.
[1]Including three cases of CVC exit site/tunnel infections (2 MDI, 1 CDI), [2]two cases evaluated as possible invasive fungal disease, 1 as reactivation of latent tuberculosis (all within day 120).

IFD occurred in 3/72 (4.2%) pts with sAA and vsAA before d 120, and in 2/69 (2.9%) after d 120

Decreased Infection-Related Mortality and Improved Survival in Severe Aplastic Anemia in the Past Two Decades

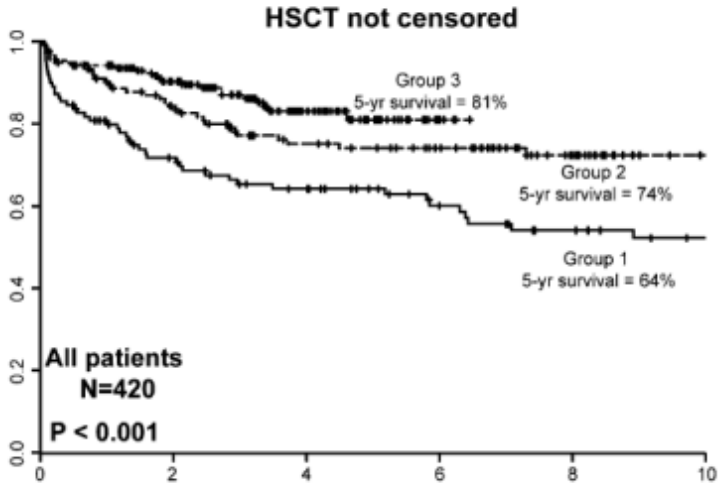
Jessica M. Valdez,[1,2,a] Phillip Scheinberg,[3,a] Olga Nunez,[3] Colin O. Wu,[4] Neal S. Young,[3] and Thomas J. Walsh[2,5]

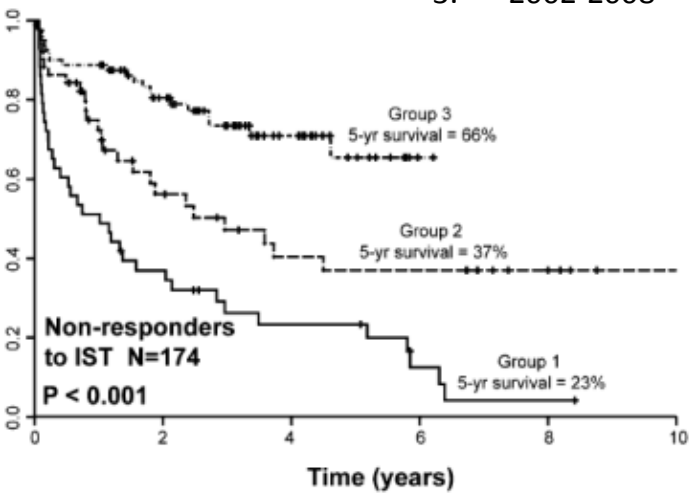
[1]Howard Hughes Medical Institute, National Institutes of Health Research Scholars Program, [2]Pediatric Oncology Branch, National Cancer Institute, and [3]Hematology Branch [4]Office of Biostatistics Research, National Heart, Lung and Blood Institute, Bethesda, Maryland; and [5]Transplantation-Oncology Infectious Diseases Program, Weill Cornell Medical College of Cornell University, and New York Presbyterian Hospital, New York, New York

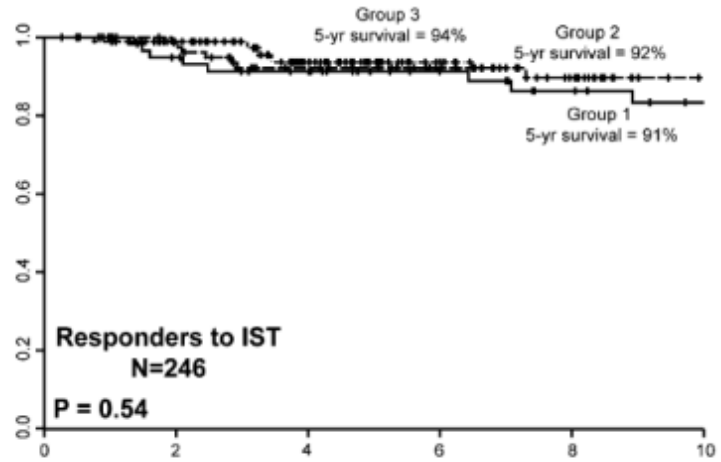
Clinical Infectious Diseases 2011;52(6):726–735

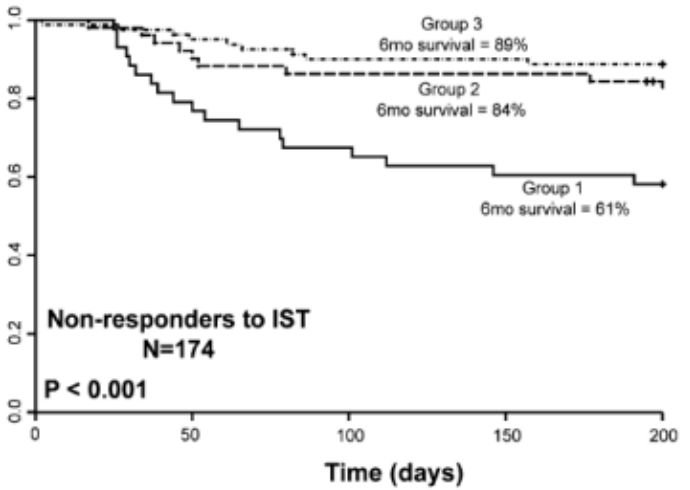
Unresponsive to initial IST at 6 months

1. 89-96
2. 96-2002
3. 2002-2008









Infection-related mortality decreased from 37% in group 1 to 11% in group 3, p<.001

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Table 5. Multivariate Logistic Regression Analysis of the Probability of Death within 1 Year for Patients Unresponsive to Initial Immunosuppressive Therapy

Risk factor	Effect of covariate and risk of death[a]				Effect of antifungal therapy[b]			
Baseline risk	Coefficient (β)	SD	OR	*P*	Coefficient (β)	SD	OR	*P*
Age	0.033	0.012	1.034	.004	0.064	0.024	1.066	.007
ANC <200 cells/μL	2.056	0.633	7.818	.001	2.623	1.234	13.777	.034
ARC	0.114	0.234	1.120	.627	…	…	…	…
ALC	-.297	0.399	0.743	.457	…	…	…	…
Platelet count	-.096	0.267	0.908	.719	…	…	…	…
Bacteremia only	0.919	0.542	2.508	.090	…	…	…	…
Fungal infection	2.751	0.665	15.666	<.001	…	…	…	…
Voriconazole	…	…	…	…	-2.550	0.967	0.078	.008

NOTE. The bacteremia-only group did not include patients with a concomitant fungal infection. Fungal groups were those who had a fungal isolate identified in blood, secretions, and/or tissue (seeTable 4). The amphotericin B group does not include liposomal formulations. Voriconazole refers to any voriconazole-containing regimen. Natural log-transformed counts log(ANC+1), log(ARC+1), log(ALC+1), and log(platelet+1) were used to reduce the skewness of these variables. ALC, absolute lymphocyte count; ANC, absolute neutrophil count; ARC, absolute reticulocyte count; OR, odds ratio; SD, standard deviation.

[a] Includes age, ANC, ARC, ALC, Platelet count, bacteremia-only infection, and fungal infection.

[b] After fungal infection was found to be an independent variable predicting probability of death, a separate analysis was performed to assess the effect of voriconazole vs amphotericin B as a predictor of death (includes age, ANC, and antifungal therapy defined by 0 if amphotericin B was used and 1 if a voriconazole-containing regimen was used). There were insufficient numbers of patients receiving echinocandins to be included in this analysis. Covariates not statistically significant in the first analysis were not included in the antifungal analysis.

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Table 4. Infections and Causes of Death in Patients with Severe Aplastic Anemia

Variable	Total(*n*=174)	Group 1(*n*=43)	Group 2(*n*=51)	Group 3(*n*=80)
Infection				
Pneumonia				
Bacterial[a]	6 (3)	3 (7)	2 (4)	1 (1)
Fungal[b]	18 (10)	13 (30)	3 (6)	2 (3)
Viral	0 (0)	0 (0)	0 (0)	0 (0)
Sinusitis				
Bacterial[c]	4 (2)	0 (0)	0 (0)	4 (5)
Fungal[d]	12 (7)	7 (16)	1 (2)	4 (5)
Mucocutaneous HSV	20 (11)	0 (0)	13 (25)	7 (9)
Viral respiratory infections[e]	6 (3)	0 (0)	3 (6)	3 (4)
GI parasitic infections[f]	18 (10)	6 (14)	8 (16)	4 (5)
Pulmonary tuberculosis	2 (1)	2 (5)	0 (0)	0 (0)
Ecthyma				
Bacterial[g]	1 (1)	1 (2)	0 (0)	0 (0)
Fungal[h]	1 (1)	1 (2)	0 (0)	0 (0)
Meningitis[i]	2 (1)	0 (0)	0 (0)	2 (3)
Total deaths	84 (48)	37 (86)	25 (49)	22 (28)
Infection-related deaths[j]	39 (22)	16 (37)	14 (27)	9 (11)
Fungal[j]	17 (10)	8 (19)	7 (14)	2 (3)
Sepsis	16 (9)	4 (9)	6 (12)	6 (8)
Pneumonia	6 (3)	4 (9)	1 (2)	1 (1)
Hemorrhage	6 (3)	1 (2)	2 (4)	3 (4)
MDS/leukemia	6 (3)	1 (2)	2 (4)	3 (4)
HSCT	16 (9)	5 (12)	4 (8)	7 (9)

The frequency of IFDs decreased from 49% in group 1 to 8% in group 3, p<.001
Aspergillus species most common fungal pathogens

High-dose cyclophosphamide for severe aplastic anemia: long-term follow-up

BLOOD, 18 MARCH 2010 • VOLUME 115, NUMBER 11

Robert A. Brodsky,[1,2] Allen R. Chen,[2] Donna Dorr,[1] Ephraim J. Fuchs,[2] Carol Ann Huff,[2] Leo Luznik,[2] B. Douglas Smith,[2] William H. Matsui,[2] Steven N. Goodman,[2] Richard F. Ambinder,[2] and Richard J. Jones[2]

[1]Division of Hematology, Department of Medicine and [2]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Johns Hopkins University School of Medicine, Baltimore, MD

Table 2. Causes of death in treatment-naive cohort

Age, y	Sex	Severity	Survival after high-dose cyclophosphamide, mo	Cause of death
45	Male	VSAA	5	Presumed fungal sepsis
47	Female	VSAA	5	Bronchiolitis obliterans with organizing pneumonia
16	Female	VSAA	8	Respiratory distress syndrome after unrelated BMT
8	Female	SAA	18	Presumed fungal sepsis
52	Female	VSAA	2	Presumed fungal sepsis

There were 8 (18.2%) cases of severe fungal infections in the 44 treatment-naive patients, all within the first 3 months; 3 of these patients died, whereas the remaining 5 recovered. The cumulative incidence of developing such an infection, considering the one death that occurred at 2 months, was 21%. In contrast, 10 (43.5%) of the 23 refractory patients acquired a severe fungal infection after high-dose cyclophosphamide; 5 of these patients died and 5 recovered (Table 3). Nine of the 10 fungal infections occurred within the first 2 months, as did one death, corresponding to a 2-month cumulative incidence for fungal infection of 39%. However, one fungal infection occurred at 34 months, 2 months after treatment for a relapse, making the 34-month cumulative incidence 49%.

Table 3. Cause of death in patients with refractory SAA

Age, y	Sex	Severity	Survival after high-dose cyclophosphamide, mo	Cause of death
35	Female	VSAA	9	Presumed fungal sepsis
19	Male	VSAA	1	Presumed fungal sepsis
58	Female	SAA	46	GVHD after unrelated BMT
38	Female	SAA	36	Presumed fungal sepsis
27	Male	SAA	63	Cerebral hemorrhage
12	Female	VSAA	2	Bacterial sepsis
56	Female	VSAA	2	Presumed fungal sepsis
56	Male	VSAA	2	Bacterial sepsis

Fluconazole prophylaxis

Risk of IFDs during IST in AA patients

- Initial IST (ATG-CsA)
  - Few data
  - Presumably low (AIEOP, 4% in children)
- Unresponsive to initial IST (ATG-CsA)
  - Few data
  - 8% in adults (NIH, NCI)
  - IFDs, significantly associated with survival (OR 15.7)
- Other IST options (i.e. cyclophosphamide)
  - Very high infectious risk

Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America

Alison G. Freifeld,[1] Eric J. Bow,[9] Kent A. Sepkowitz,[2] Michael J. Boeckh,[4] James I. Ito,[5] Craig A. Mullen,[3] Issam I. Raad,[6] Kenneth V. Rolston,[6] Jo-Anne H. Young,[7] and John R. Wingard[8]

Clin Infect Dis 2011;52;4:e56-e93

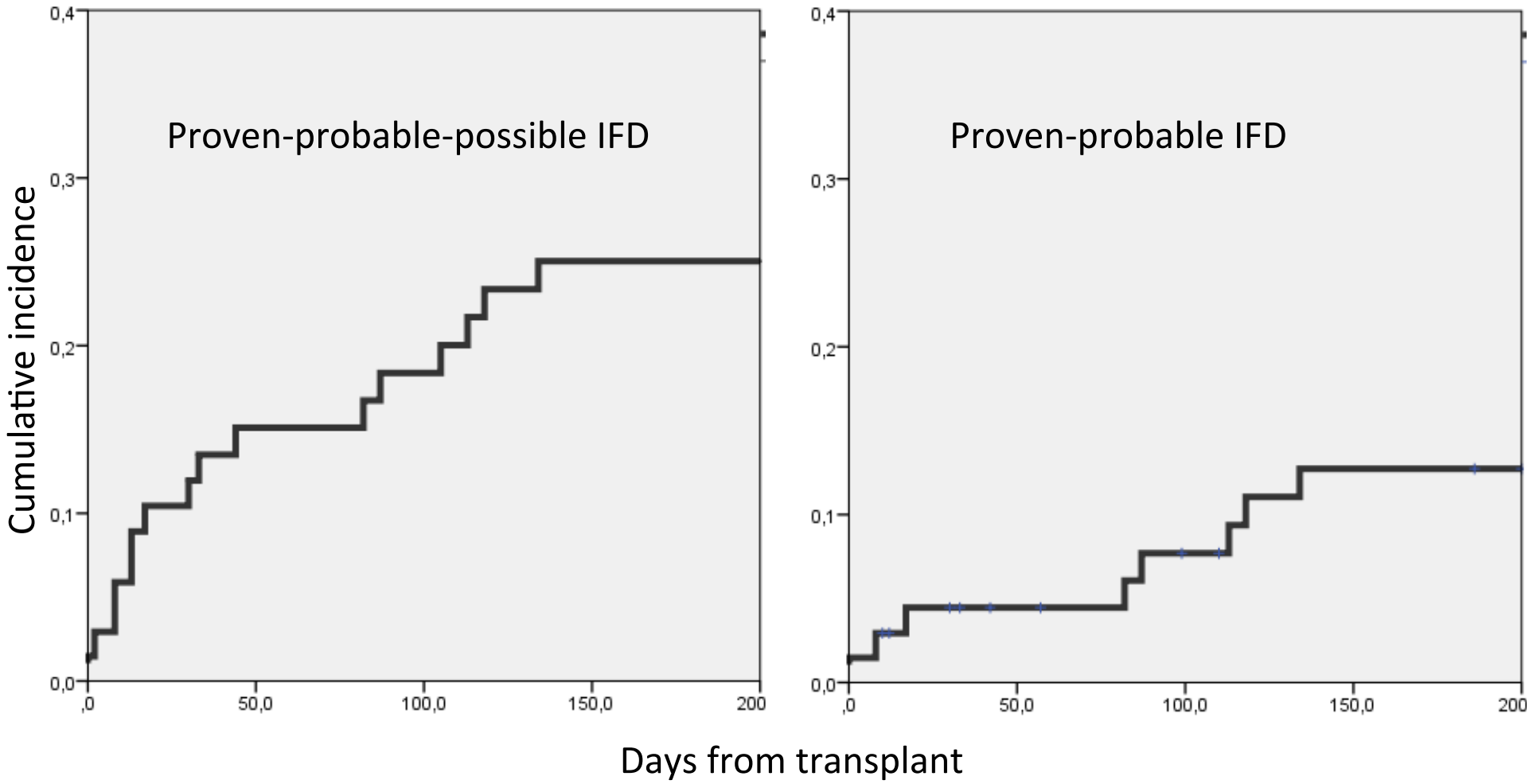
IDSA Guidelines

Primary antifungal prophylaxis in neutropenic patients

- Prophylaxis against Candida is recommended in AL and allo-SCT(AI)
  - fluco, itra, vori, posa, mica , caspo are all acceptable alternatives
- Prophylaxis against Aspergillus with posaconazole is recommended in AML/MDS patients.
- Prophylaxis against Aspergillus in SCT patients during engraftment has not been shown to be efficacious, however, a mould active agent is recommended in:
  - SCT patients with anticipated prolonged neutropenic period (2 weeks) (CIII)
  - prolonged period of neutropenia immediately prior to SCT (CIII)

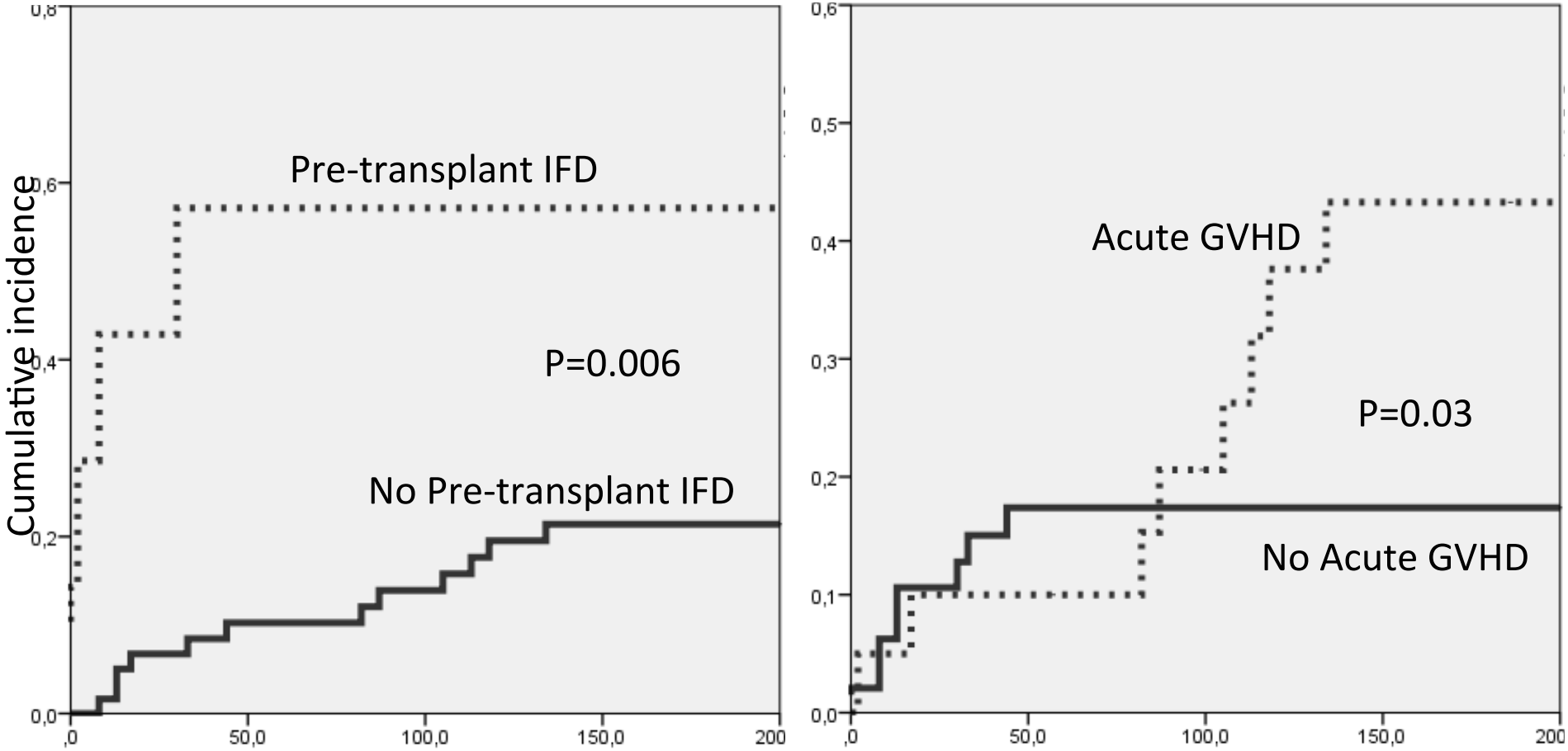
Proven, probable and possible IFDs in 68 aplastic anemia patients submitted to allogeneic HSCT.

Data from the prospective 2008-2010 GITMO study



Proven-probable Aspergillosis, 8 cases; proven invasive candidiasis, 1 case; possible pulmonary IFD, 8 cases
8 cases pre engraftment, 9 cases after engraftment

Proven, probable and possible IFDs in 68 aplastic anemia patients submitted to allogeneic HSCT.
Data from the prospective 2008-2010 GITMO study



Multivariate analysis:

- IFD pre transplant, no vs yes: OR 0.054 (95% CI 0.01-0.25), p<0.0001
- Sem cell source, bone marrov vs periph: OR 0.33 (95% CI 0.11-0.99), p=0.048
- Condit. Regimen, myeloabl vs non-myeloabl: OR 4.7 (95% CI 1.46-15.12), p=0.01
- Acute GVHD, 0-I vs II-IV:OR 0.10 (95% CI 0.03-0.38), p=0.001
- No significant impact of age, type of donor, antifungal prophylaxis, TBI

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doi:10.1182/blood-2016-08-693481

How I treat acquired aplastic anemia

Andrea Bacigalupo

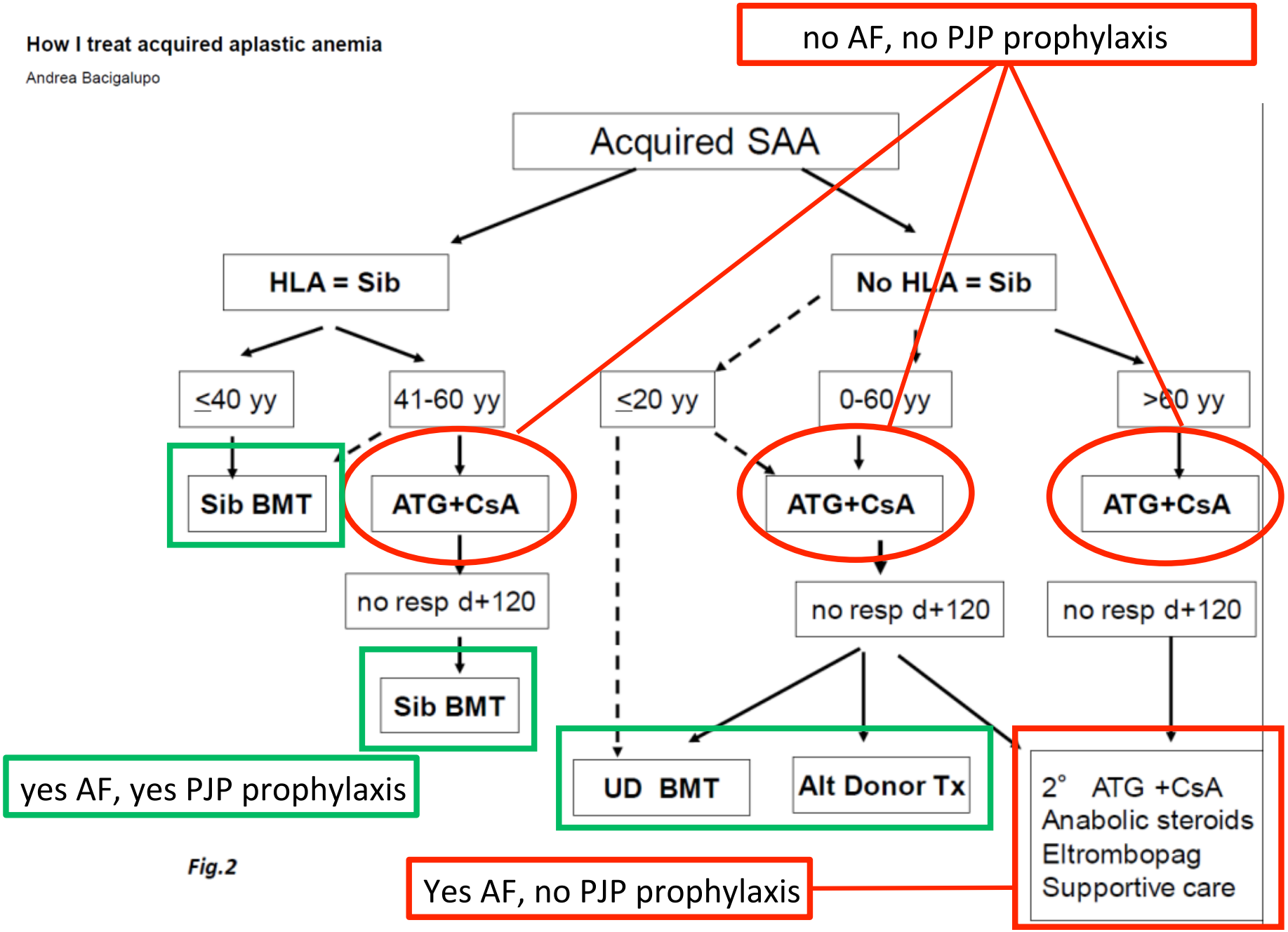

Fig.2