



Empirische Therapie bei febriler Neutropenie

Helmut Ostermann

31.3.2015





- Mantle cell lymphoma St IV with BM involvement
- MIPI Score 8, High risk, median survival 37 months
- 3 x R-DHAP Induction: VGPR
- Cyclofosfamide Mobilisation



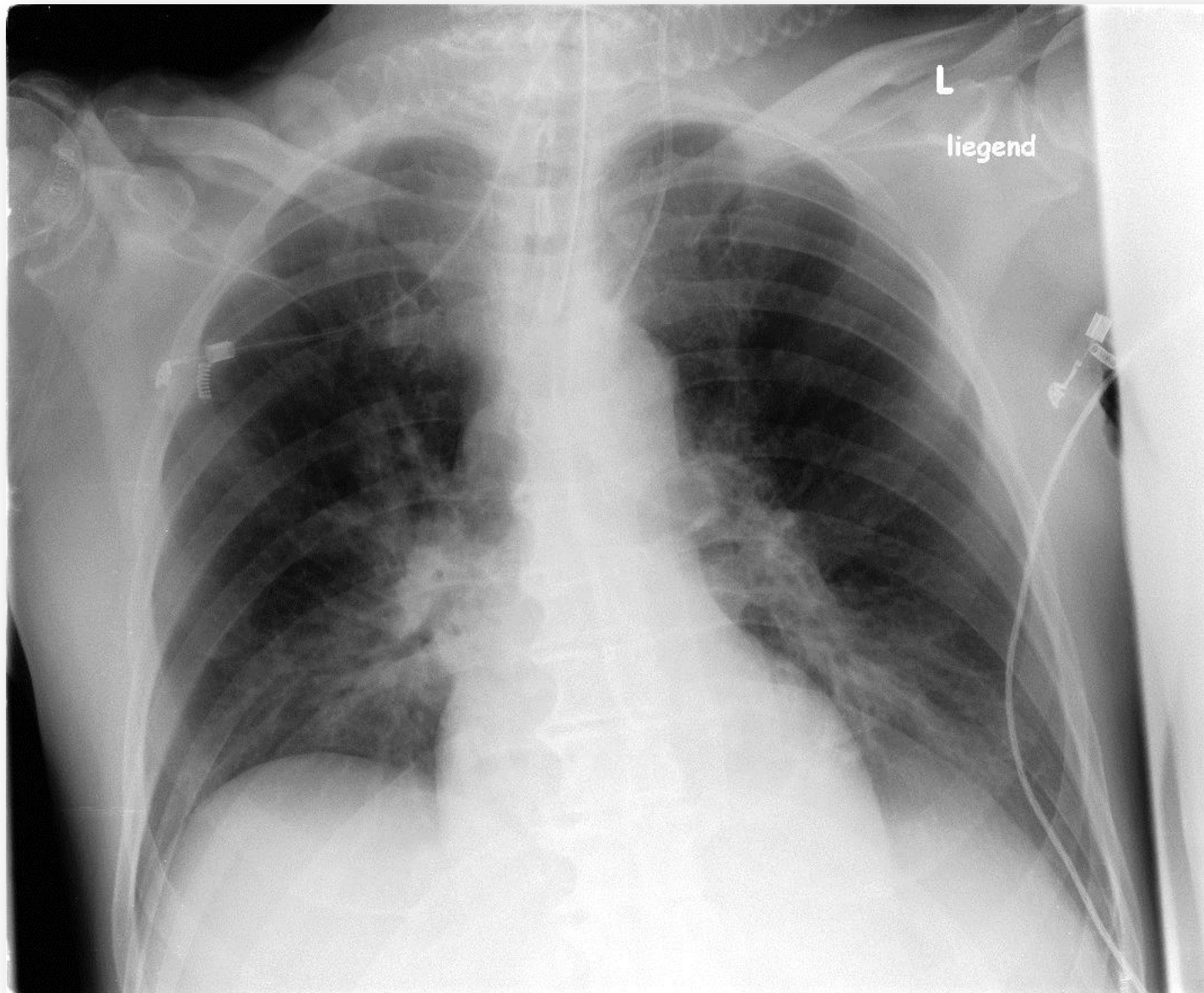
- Highdose BEAM
- Day 4 after PBSCT 25.1.2013
 - Leukocytes: 20/ul
 - Fever
 - Hypotension
 - ICU
- Treatment:
 - Piperacillin – Tazobactam
 - Amikacin
 - Intubation, CVVH, Catecholamines
- Death 27.1.2013 4:30

Case Report M.B. 69 Years

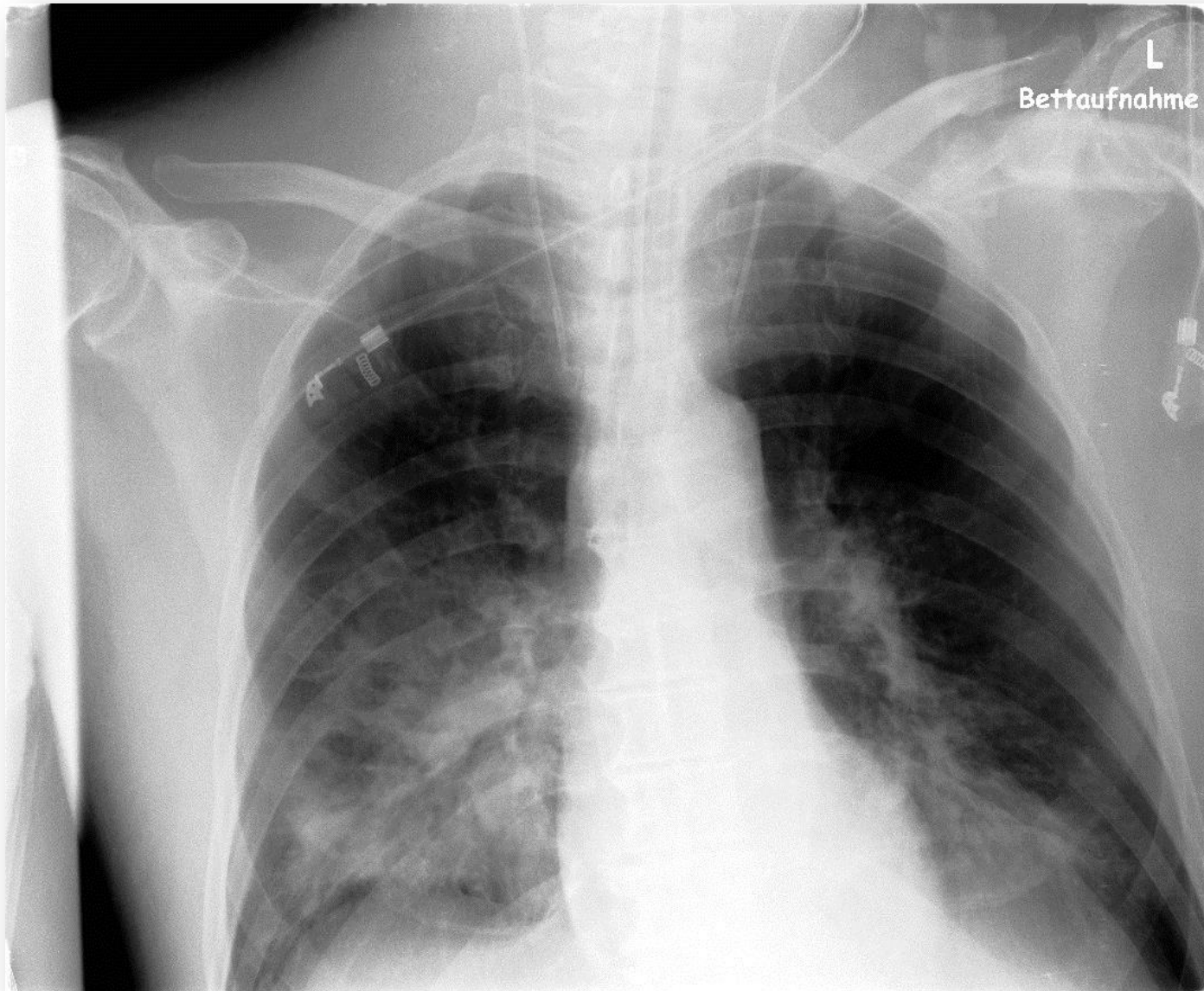


	25.1. 5:15	25.1 23:30	26.1. 6:00	26.1. 23:00
CRP	11	28	36	43
IL-6	58638	139000	171000	191000
Lactate	3,7	5,6	8,9	13,8
LDH	293	249	363	4561
PTT	35	44	60	88

Case Report M.B. 69 Years, 25.1.



Case Report M.B. 69 Years; 26.1.





- Microbiology

- 25.1. Blood cultures negative
- 25.1. BAL: Candida
- 21.1. Stool: ESBL

- **Septic Shock in Granulocytopenia**

- Fieber oft einziges Symptom der Infektion in Granulozytopenie
- Hohes Risiko – langwierige Diagnostik nicht möglich
- Empirische Therapie notwendig

Management of fever of unknown origin in adult, neutropenic patients—Guideline of the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Medical Oncology (DGHO)

--Manuscript Draft--

Authors: Werner J. Heinz¹, Dieter Buchheidt², Maximilian Christopeit³, Florian Weissinger⁴,
Hermann Einsele¹, Rolf Mahlberg⁵, Helmuth Ostermann⁶, Xaver Schiel⁷, Janne J.
Vehreschild^{8,9}, Georg Maschmeyer¹⁰, Oliver A. Cornely^{8,9,11}, Meinolf Karthaus¹², Silke
Neumann¹³, Olaf Penack¹⁴, Markus Ruhnke¹⁵, Michael Sandherr¹⁶, Hartmut Link¹⁷

■ Hochrisiko

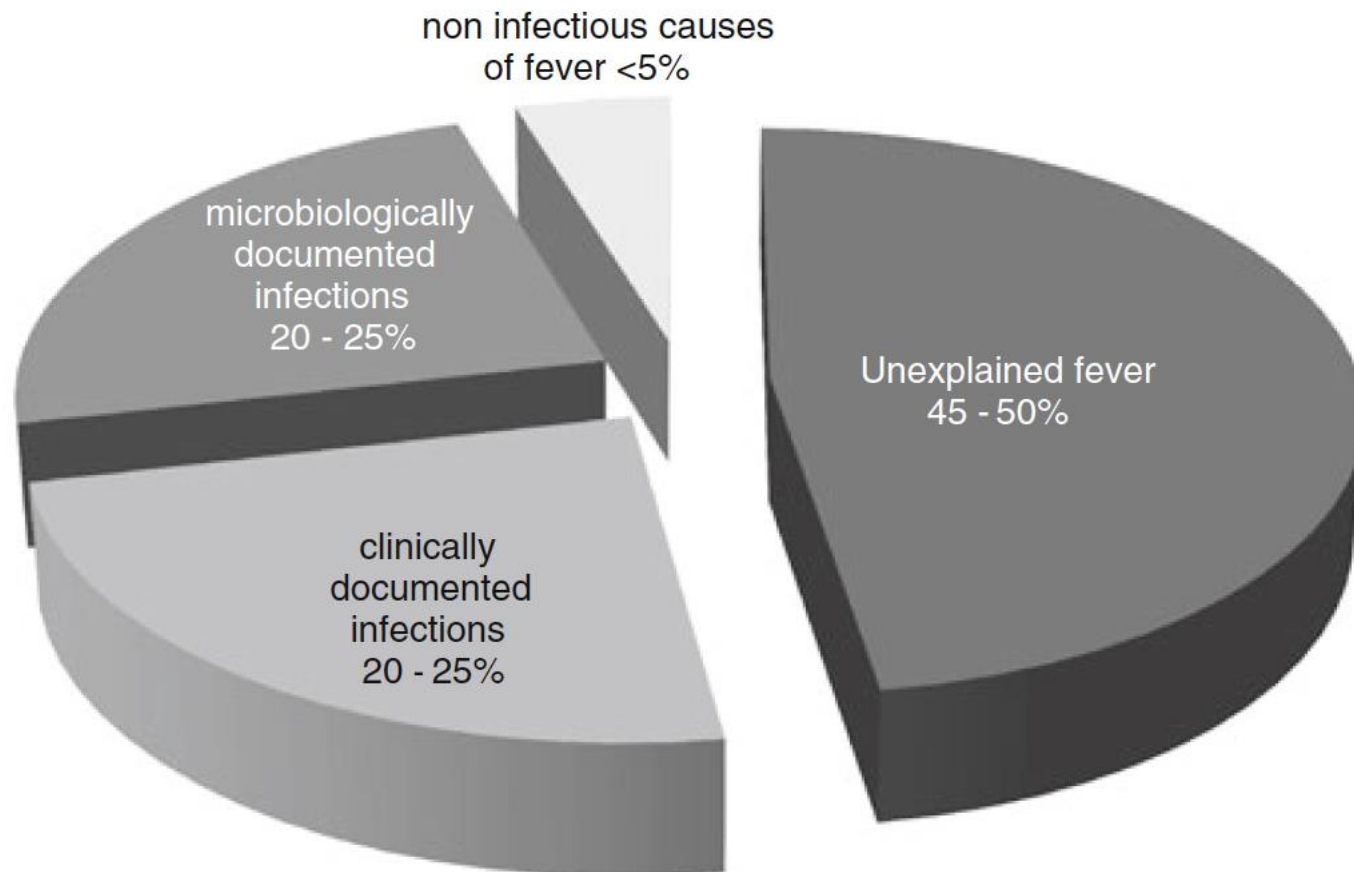
- > 7 Tage Granulozytoenie
- < 100 Granulozyten / μ l
- +/- signifikante Komorbiditäten

■ Niedrigrisiko

- < 7 Tage Granulozytopenie
- keine/wenige Komorbiditäten



- Bei erstmaligem Fieber
 - Körperlicher Untersuchungsbefund
 - Blutkulturen
 - Labor (Niere, Gerinnung, Laktat)
 - CT





ELSEVIER

Seminars in
NUCLEAR
MEDICINE

The Use of FDG-PET/CT in Patients With Febrile Neutropenia

Fidel J. Vos, MD, PhD,^{*,‡} Chantal P. Bleeker-Rovers, MD, PhD,^{*,‡} and Wim J.G. Oyen, MD, PhD^{†,‡}

PET CT in diagnosing infection in febrile neutropenia

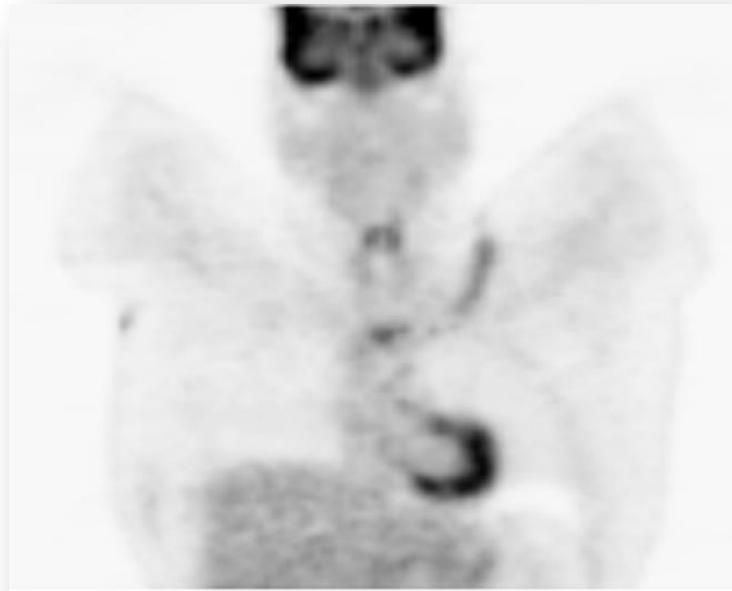


References	FDG-PET or FDG-PET/CT	Design	Aim	No. of Patients
Miceli et al ²¹	FDG-PET/CT	Retrospective case series, selected patients with septic thrombophlebitis	Detection of septic thrombophlebitis	9
Mahfouz et al ³⁵	FDG-PET	Retrospective cohort, selected patients with pathologic extraskkeletal FDG uptake	Detection of infectious foci	248 (27 neutropenic)
Chamilos et al ^{38*} (nonneutropenic)	FDG-PET/CT	Retrospective case series, selected patients with IFI	Detection of IFI	16
Xu et al ⁴³	FDG-PET/CT	Prospective case series, selected patients with IFI	Guiding treatment in IFI	3
Hot et al ⁴⁴	FDG-PET/CT	Prospective case series, selected patients with IFI	Detection of IFI	30
Vos et al ³⁴	FDG-PET/CT	Prospective cohort, subsequent patients with febrile neutropenia	Febrile neutropenia, detection source of fever	28
Guy et al ³⁶	FDG-PET/CT	Prospective cohort, subsequent patients with febrile neutropenia	Febrile neutropenia, detection source of fever, and effect on treatment	20
Koh et al ³⁷	FDG-PET/CT	Retrospective case-control study. Subsequent patients with febrile neutropenia	Febrile neutropenia, detection source of fever, and effect on treatment	37 vs 76

PET in diagnosing Infection in febrile neutropenia



PET in diagnosing Infection in febrile neutropenia

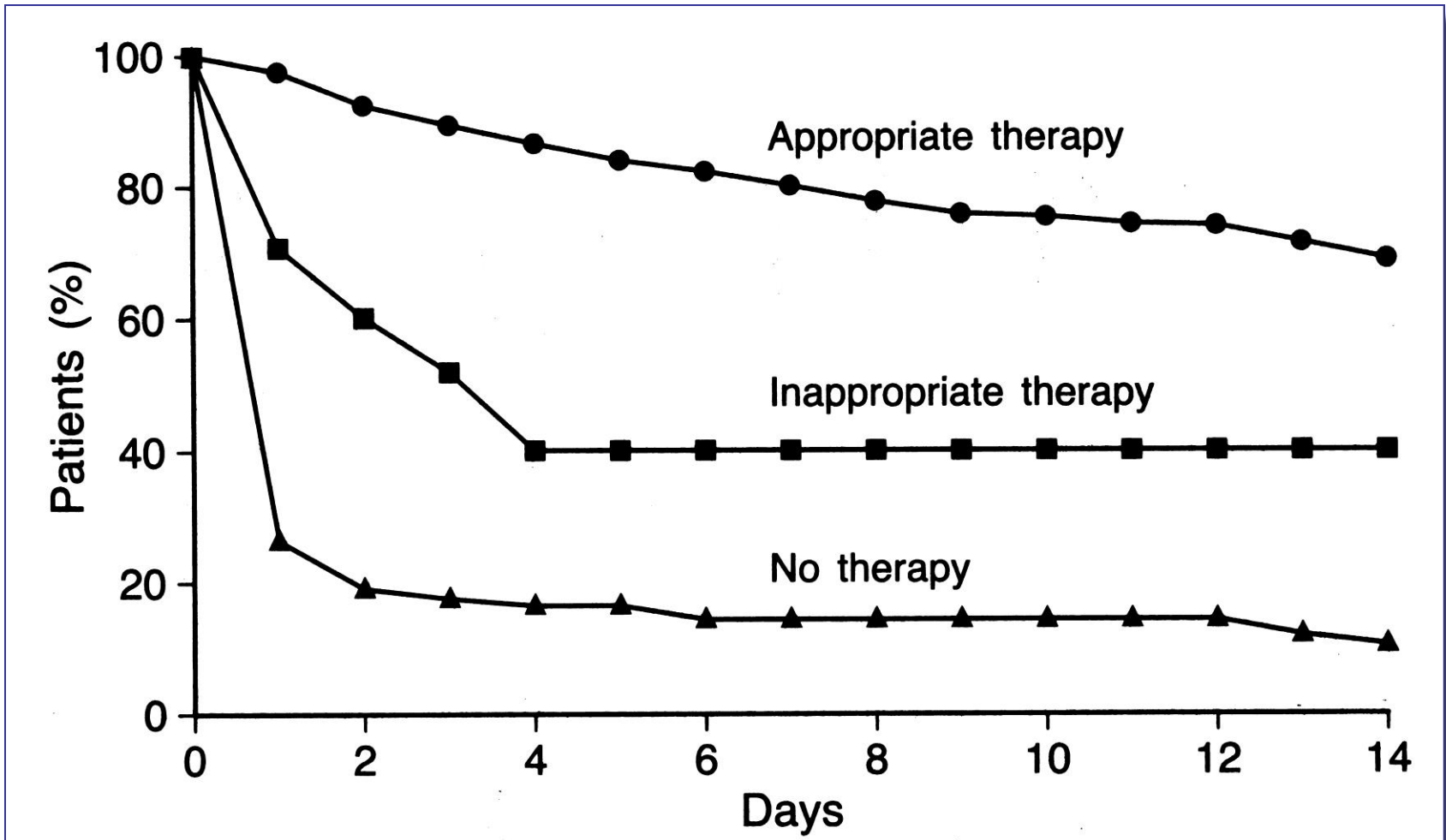


FUO - Therapie



Initiale Antibiotikatherapie E.coli Bakteriämie

Bodey et al, Am J Med 1972, 81:85



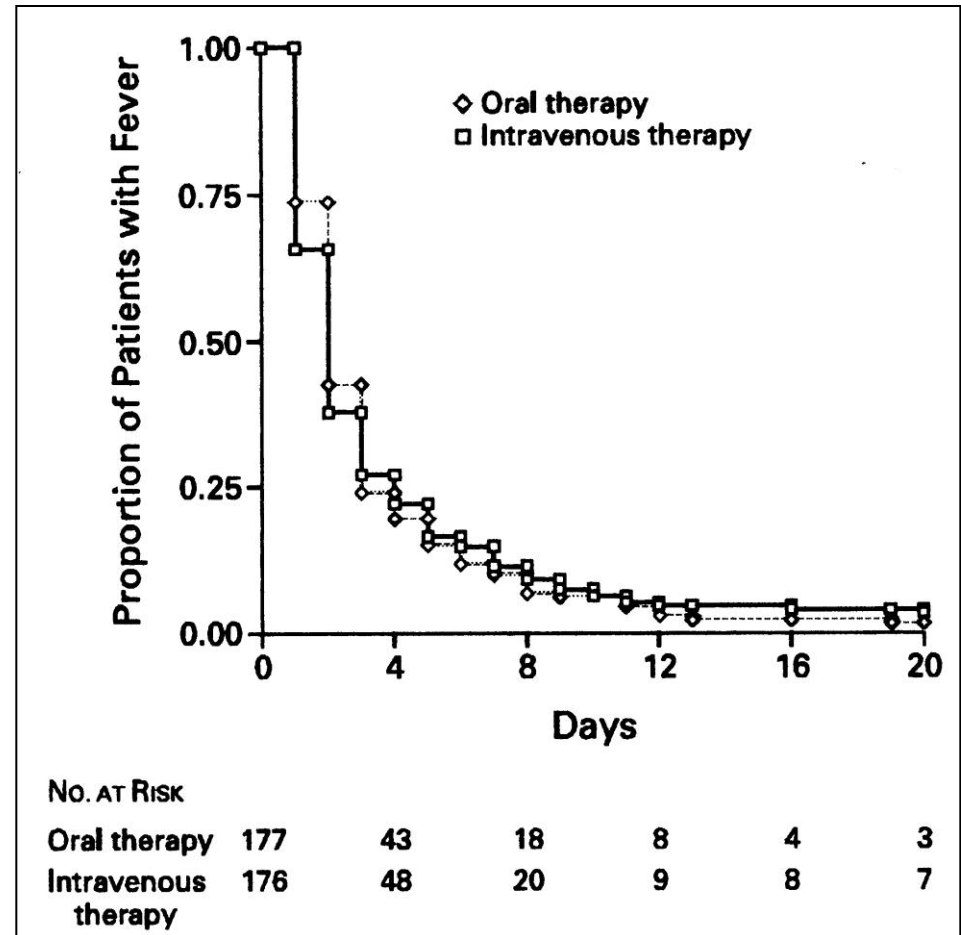
- Empirische, kalkulierte Therapie
- Risikoadaptiert
- ? Schematisiertes Umsetzen der Initialtherapie ?
- ? Dauer der Therapie ?
- ? Deeskalation bei Entfieberung in Neutropenie ?

Oral vs i.v. Antibiose bei Niedrigrisikopatienten

Kern et al NEJM 1999, 341:312



- Ciprofloxacin oral + Amoxicillin-Clavulansäure vs Ceftazidim i.v.
- Neutropenie < 10 Tage
- Keine Komorbidität
- 312 Patienten
- Erfolg in 86% vs 84%



In addition, the following assessments (Table 2) are recommended in order to identify situations in which outpatient management of neutropenic fever is possible (**BIII**):

Duration of neutropenia	<u>to</u> be expected for a maximum of 7 days overall
General	No signs of CNS infection, severe pneumonia or catheter infection
	No signs of sepsis or shock
	None of the following: associated organ failure, pronounced abdominal pain ($\pm$ diarrhea), intravenous supportive therapy, dehydration, recurrent vomiting, necessity of permanent or close monitoring (e.g. metabolic <u>decompensation</u> , <u>hypercalcemia</u>)
	No new ECG abnormalities requiring treatment
	No new severe organ impairment



Oral antibiotics	No <u>fluoroquinolone</u> prophylaxis or therapy within the last 7 days
	Oral medication feasible
	Compliance with oral medication to be expected
Outpatient management	Medical care ensured (different options):
	Patient does not live alone; Patient/co-inhabitants have a telephone; Patient can reach clinic skilled at treatment of neutropenic patients within 1 hour
	Patient is conscious, knows, and understands the risks

Risk groups		
	Standard risk $\leq 7d$	High risk ($> 7d$)
1. Line (AI)	Outpatient therapy possible*: 1. <u>amoxicillin/clavulanate</u> + ciprofloxacin 2. <u>amoxicillin/clavulanate</u> + levofloxacin Hospitalization (<u>i.v.</u>) indicated* 3. <u>ceftazidime</u>, cefepime 4. <u>piperacillin/tacobactam</u>, 5. 3rd / 4th generation cephalosporin + aminoglycoside	1. <u>piperacillin/tazobactam</u> 2. <u>ceftazidime</u>, cefepime 3. <u>imipenem</u>, <u>meropenem</u>,
2. line § - instability $\geq 72-96$ h (AII)	• <u>imipenem</u>, • <u>meropenem</u>, after 1,2,3 also • <u>piperacillin/tacobactam</u>	• after 1,2: <u>imipenem</u>, <u>meropenem</u> • after 3: <u>addition of glycopeptide or aminoglycoside</u>

<u>further options (CIII)</u>	Increased risk for gram positive infections[#]: + <u>glycopeptide</u> or linezolid Increased risk for antibiotic resistant gram negative bacteria: + <u>aminoglycoside</u>	
<u>antifungal therapy</u>		<u>empirical</u> (expected neutropenia > 9 days) <u>preemptive</u>

Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia (Review)

Paul M, Dickstein Y, Schlesinger A, Grozinsky-Glasberg S, Soares-Weiser K, Leibovici L



**THE COCHRANE
COLLABORATION®**

Monotherapy vs Combination



Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Beta-lactam-aminoglycoside combination therapy	Beta-lactam monotherapy			
All cause mortality	Study population		RR 0.87 (0.75 to 1.02)	7186 (44 studies)	⊕⊕⊕⊕ high
	83 per 1000	72 per 1000 (62 to 85)			
Any nephrotoxicity - Ag dosing regimen (Copy)	Study population		RR 0.45 (0.35 to 0.57)	6608 (39 studies)	⊕⊕⊕⊕ high
	57 per 1000	26 per 1000 (20 to 33)			



	Level	Evidence
<u>cAmB</u>	E	I
ABLC	D	I
ABCD	D	I
<u>L-AmB</u>	A	I
Caspofungin	A	I
Itraconazole <u>i.v.</u>	B	I
Micafungin	C	II
Voriconazole	B	I

- Duration of antimicrobial treatment
 - At least 7 days if persistent neutropenic (BIII)
 - At least 2 days after recovery of neutrophils (BIII)



Infection (2012) 40:613–619
DOI 10.1007/s15010-012-0269-y

CLINICAL AND EPIDEMIOLOGICAL STUDY

Intestinal colonisation and blood stream infections due to vancomycin-resistant enterococci (VRE) and extended-spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBLE) in patients with haematological and oncological malignancies

B. J. Liss · J. J. Vehreschild · O. A. Cornely ·
M. Hallek · G. Fätkenheuer · H. Wisplinghoff ·
H. Seifert · M. J. G. T. Vehreschild



- 513 Patients, 1012 inpatient stays
- Stool culture within 72 hours
- Blood cultures in febrile neutropenia

- 1805 stool samples
- 2677 Blood cultures

- Empiric treatment of febrile neutropenia
 - Ceftriaxone / Gentamycin
 - Piperacillin / Tazobactam

 - In case of colonization
 - VRE Linezolid
 - ESBL Meropenem

ESBL // VRE in Haem Onc



- 17.7% ESBL colonised
- 9.9% VRE colonised

Blood Stream Infections



- 6 / 90 ESBL colonised
- 2 / 423 not ESBL colonised
- 1 / 51 VRE colonised
- 0 / 462 not VRE colonised



Support Care Cancer

DOI 10.1007/s00520-014-2582-8

ORIGINAL ARTICLE

Risk factors for piperacillin/tazobactam-resistant Gram-negative infection in hematology/oncology patients with febrile neutropenia

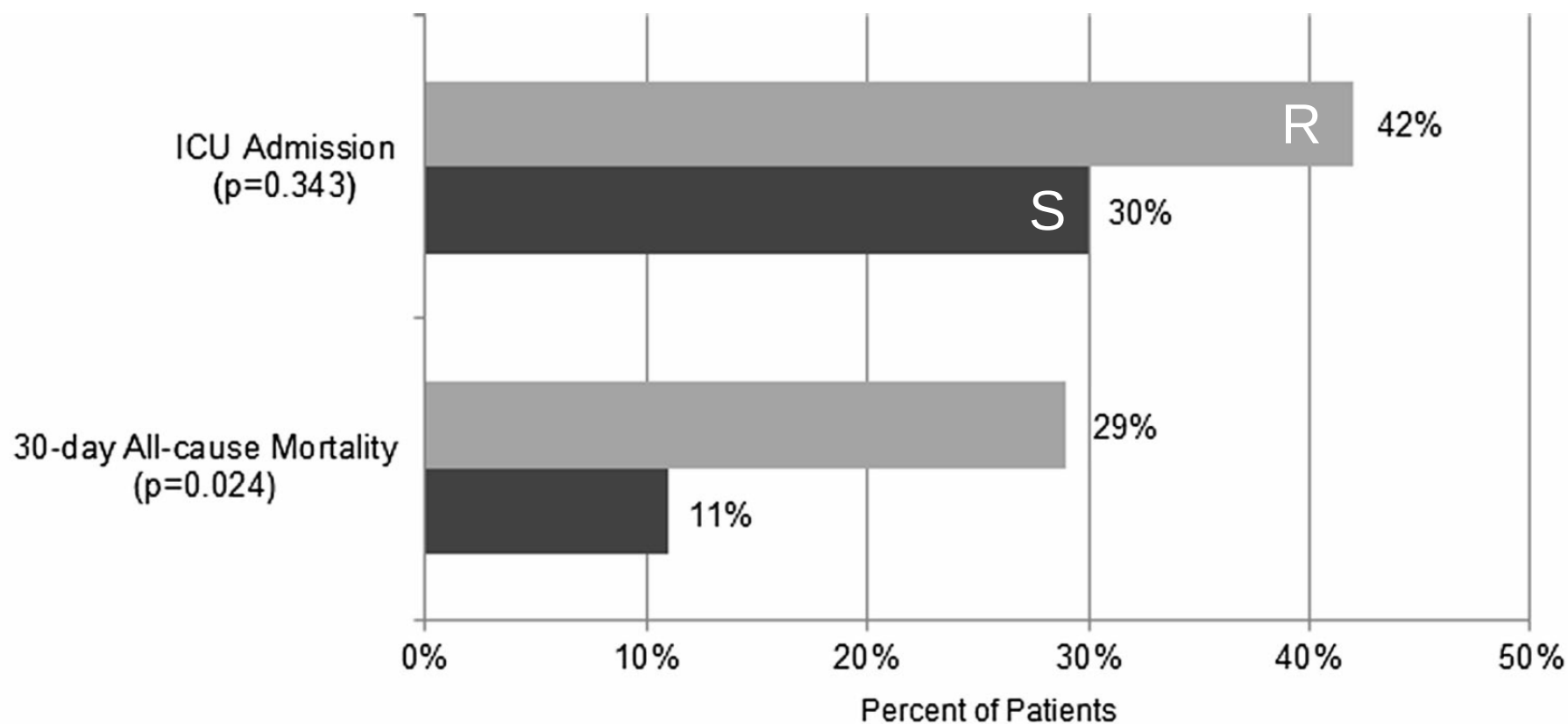
**Bernard L. Marini • Shannon M. Hough •
Kevin S. Gregg • Haya Abu-Seir • Jerod L. Nagel**



- Retrospective Study
- 847 patients
- 171 episodes GNR
 - 147 Pip-Tazo sensitive
 - 24 Pip-Tazo resistant

	PTZ-S (<i>n</i> =147)	PTZ-R (<i>n</i> =24)	<i>P</i> value
History of PTZ-R	4 (3 %)	2 (8 %)	0.199
<u>Antibiotic use, previous 90 days</u>			
Antibiotic therapy >14 days	50 (34 %)	16 (67 %)	0.003
Number of antibiotic courses	1 (0–7)	2 (0–4)	0.005
Number of antibiotics	2 (0–10)	3 (0–8)	0.006
Specific antibiotics, previous 90 days			
PTZ	52 (35 %)	17 (71 %)	0.002
Cefepime	21 (14 %)	6 (25 %)	0.224
Other penicillin	30 (20 %)	4 (17 %)	0.789
Other cephalosporin	28 (19 %)	6 (25 %)	0.581
Aztreonam	7 (5 %)	1 (4 %)	>0.999
Carbapenem	6 (4 %)	1 (4 %)	>0.999
Fluoroquinolone	44 (30 %)	9 (38 %)	0.480
Aminoglycoside	16 (11 %)	3 (13 %)	0.734
Sulfamethoxazole/trimethoprim	13 (9 %)	2 (8 %)	>0.999
Vancomycin	55 (37 %)	13 (54 %)	0.176
Other	50 (34 %)	11 (46 %)	0.358
<u>LOS prior to culture</u>	4 (0–63)	13 (0–22)	0.002

Pip-Tazo resistant GNR in febrile neutropenia



Antimicrobial-resistant Gram-negative bacteria in febrile neutropenic patients with cancer: current epidemiology and clinical impact

Enrico M. Trecarichi and Mario Tumbarello

Table 1. Prevalence of bacterial pathogens in children and adults with haematological malignancies: a systematic review of the literature																
Reference	Country	Period	Setting	Patients' age	Neutro-penia, %	Total bacterial isolates	Source of bacterial isolates	BSI, n (%)	Gram-Negative, n (%)	<i>Escherichia coli</i> , n (%) ^a	<i>Klebsiella pneumoniae</i> , n (%) ^a	<i>Enterobacter</i> spp., n (%) ^a	<i>Pseudo-monas aeruginosa</i> , n (%) ^a	<i>Acineto-bacter</i> spp., n (%) ^a	<i>Stenotro-phomonas maltophilia</i> , n (%) ^a	Others, n (%) ^a
Al-Tonbary <i>et al.</i> 2011 [6]	Egypt	2007–2008	Haematology and oncology	Children	NR	221	Clinical samples	95 (42.9)	70 (31.7)	34 (48.6)	11 (15.7)	0	25 (35.7)	0	0	0
Aslan <i>et al.</i> 2012 [7]	Turkey	2007–2010	Haematology and oncology	Children	100	171	BSI	171 (100)	43 (25.1)	13 (30.2)	9 (20.9)	0	3 (7)	0	3 (7)	7 (16.3)
Baskaran <i>et al.</i> 2007 [8]	Malaysia	2004–2005	Haematology	Adults	100	73	BSI	73 (100)	44 (60.3)	16 (36.2)	11 (25.7)	5 (11.2)	4 (9)	2 (4.5)	1 (2.2)	4 (9)
Cattaneo C <i>et al.</i> 2010 [9]	Italy	2004–2007	Haematology	Adults	NR	333	Clinical samples	NR	182 (54.7)	90 (24.4)	NR	NR	39 (21.4)	4 (2.2)	10 (5.5)	39 (21.4)
Chen <i>et al.</i> 2010 [10]	Taiwan	2002–2006	Haematology	Adults	100	801	BSI	801 (100)	516 (64.4)	103 (19.9)	86 (16.7)	38 (7.3)	47 (9.1)	54 (10.5)	48 (9.4)	140 (27.1)
Chong Y <i>et al.</i> 2010 [11]	Japan	2006–2008	Haematology	All	100	135	BSI	142 (100)	68 (50.4)	26 (38.2)	13 (19.1)	5 (7.4)	21 (30.9)	NR	NR	3 (4.4)
El-Mahallawy <i>et al.</i> 2011 [12]	Egypt	2006	Haematology and oncology	Children	100	239	BSI	239 (100)	59 (24.7)	9 (15.2)	6 (10.2)	2 (3.4)	13 (22.1)	20 (33.9)	1 (1.7)	8 (13.5)
Ghosh <i>et al.</i> 2012 [13]	India	2008–2010	Haematology	All	100	79	Clinical samples	NR	44 (55.7)	11 (25)	10 (22.7)	0	12 (27.3)	10 (22.7)	0	1 (2.3)
Gudiol <i>et al.</i> 2013 [14 [■]]	Spain	2006–2010	Haematology	Adults	100	277	BSI	277 (100)	154 (55.6)	71 (46.1)	31 (20.2)	12 (7.8)	32 (20.8)	2 (1.3)	2 (1.3)	1 (0.6)
Lv <i>et al.</i> 2013 [15]	China	2010	Haematology	Children	NR	78	BSI	79 (100)	34 (43.6)	12 (35.3)	12 (35.3)	0	5 (14.7)	0	0	5 (14.7)
Huang <i>et al.</i> 2011 [16]	Taiwan	2003–2005	Haematology and oncology	Adults	57.8	588	BSI	588 (100)	435 (73.9)	109 (25.1)	85 (19.5)	43 (9.9)	68 (15.6)	60 (13.8)	NR	NR
Irfan <i>et al.</i> 2008 [17]	Pakistan	2001–2006	Haematology and oncology	All	100	805	BSI	805 (100)	352 (43.7)	129 (36.6)	41 (11.6)	30 (8.5)	34 (9.7)	52 (14.8)	7 (2)	58 (16.5)
Kjellander <i>et al.</i> 2012 [18]	Sweden	2002–2008	Haematology	Adults	100	794	BSI	794 (100)	372 (46.9)	141 (37.9)	78 (20.9)	43 (11.6)	42 (11.3)	1 (0.3)	6 (1.6)	58 (15.6)
Kumar <i>et al.</i> 2010 [19]	India	NR	Haematology and oncology	All	NR	935	Clinical samples	484 (51.8)	626 (66.9)	106 (16.9)	99 (15.8)	29 (4.6)	245 (39.1)	93 (14.9)	NR	54 (8.7)
Mebis <i>et al.</i> 2010 [20]	Belgium	1994–2008	Haematology	Adults	100	3624	Skin, stool, blood, and urine	NR	1696 (46.8)	910 (53.6)	NR	NR	140 (15.4)	NR	NR	NR
Miedema <i>et al.</i> 2013 [21]	Netherlands and Switzerland	2004–2011	Haematology	Children	100	248	BSI	248 (100)	68 (27.4)	25 (10.1)	10 (4.1)	NR	12 (17.6)	NR	NR	NR
Prabhash <i>et al.</i> 2010 [22]	India	2007	Haematology and oncology	All	NR	484	BSI	484 (100)	330 (68.2)	53 (16.1)	35 (10.7)	11 (3.3)	147 (44.5)	56 (16.9)	NR	28 (8.5)
Ram <i>et al.</i> 2012 [23]	Israel	2007–2011	Haematology	Adults	59	179	Clinical samples	134 (74.8)	120 (67.1)	49 (40.9)	18 (15)	7 (5.8)	19 (15.8)	3 (2.5)	7 (5.8)	18 (14.2)
Samosis <i>et al.</i> 2013 [24]	Greece	2007–2011	Haematology and oncology	All	39.4	108	BSI	108 (100)	71 (65.8)	19 (26.8)	18 (25.3)	2 (2.8)	19 (26.8)	3 (4.2)	NR	10 (14.1)
Schelenz <i>et al.</i> 2013 [25 [■]]	United Kingdom	1997–2010	Haematology and oncology	Adults	NR	872	BSI	872 (100)	324 (37.2)	101 (31.2)	43 (13.3)	NR	56 (17.3)	14 (4.3)	53 (16.3)	14 (4.4)
Swati <i>et al.</i> 2010 [26]	India	2006	Haematology	All	100	62	Clinical samples	41 (60.3)	47 (75.8)	10 (21.2)	21 (44.6)	1 (2.2)	5 (10.6)	8 (17.1)	0	2 (4.3)
Tumbarello <i>et al.</i> 2009 [27]	Italy	2000–2005	Haematology	Adults	62.2	241	BSI	241 (100)	98 (40.7)	42 (42.8)	9 (9.2)	5 (5.1)	31 (31.5)	4 (4.1)	2 (2.1)	3 (3.1)
Cattaneo <i>et al.</i> 2008 [28]	Italy	2004–2005	Haematology	Adults	59.2	147	Clinical samples	64.9	80 (54.4)	38 (47.5)	NR	NR	13 (16.2)	2 (2.5)	4 (5)	23 (28.8)
Poon <i>et al.</i> 2012 [29]	Singapore	2008–2010	Haematology	Adults	100	157	BSI	157 (100)	82 (52.3)	37 (45.1)	27 (32.9)	NR	11 (13.4)	1 (1.2)	NR	6 (7.4)

Reference	Country	Period	Setting	Patients' age	Neutro- penia, %	Total bacterial isolates	Source of bacterial isolates	BSI, n (%)	Gram- Negative, n (%)	<i>Escherichia coli</i> , n (%) ^a	<i>Klebsiella pneumo- niae</i> , n (%) ^a	<i>Entero- bacter spp.</i> , n (%) ^a	<i>Pseudo- monas aeruginosa</i> , n (%) ^a	<i>Acineto- bacter spp.</i> , n (%) ^a	<i>Stenotro- phomonas maltophilia</i> , n (%) ^a	Others, n (%) ^a
Al-Tonbary <i>et al.</i> 2011 [6]	Egypt	2007–2008	Haematology and oncology	Children	NR	221	Clinical samples	95 (42.9)	70 (31.7)	34 (48.6)	11 (15.7)	0	25 (35.7)	0	0	0
Aslan <i>et al.</i> 2012 [7]	Turkey	2007–2010	Haematology and oncology	Children	100	171	BSI	171 (100)	43 (25.1)	13 (30.2)	9 (20.9)	0	3 (7)	0	3 (7)	7 (16.3)
Baskaran <i>et al.</i> 2007 [8]	Malaysia	2004–2005	Haematology	Adults	100	73	BSI	73 (100)	44 (60.3)	16 (36.2)	11 (25.7)	5 (11.2)	4 (9)	2 (4.5)	1 (2.2)	4 (9)
Cattaneo C <i>et al.</i> 2010 [9]	Italy	2004–2007	Haematology	Adults	NR	333	Clinical samples	NR	182 (54.7)	90 (24.4)	NR	NR	39 (21.4)	4 (2.2)	10 (5.5)	39 (21.4)
Chen <i>et al.</i> 2010 [10]	Taiwan	2002–2006	Haematology	Adults	100	801	BSI	801 (100)	516 (64.4)	103 (19.9)	86 (16.7)	38 (7.3)	47 (9.1)	54 (10.5)	48 (9.4)	140 (27.1)
Chong Y <i>et al.</i> 2010 [11]	Japan	2006–2008	Haematology	All	100	135	BSI	142 (100)	68 (50.4)	26 (38.2)	13 (19.1)	5 (7.4)	21 (30.9)	NR	NR	3 (4.4)
El-Mahallawy <i>et al.</i> 2011 [12]	Egypt	2006	Gramnegative bacteria 51.3% E.Coli 32.1% Pseudomonas 20.1% Klebsiella 19.5% Acinetobacter 8.2% Enterobacter spp. 4.7% Stenotrophomonas 3.7%								2	2 (3.4)	13 (22.1)	20 (33.9)	1 (1.7)	8 (13.5)
Ghosh <i>et al.</i> 2012 [13]	India	2008–2010									7	0	12 (27.3)	10 (22.7)	0	1 (2.3)
Gudiol <i>et al.</i> 2013 [14 ^a]	Spain	2006–2010									2	12 (7.8)	32 (20.8)	2 (1.3)	2 (1.3)	1 (0.6)
Lv <i>et al.</i> 2013 [15]	China	2010									3	0	5 (14.7)	0	0	5 (14.7)
Huang <i>et al.</i> 2011 [16]	Taiwan	2003–2005									5	43 (9.9)	68 (15.6)	60 (13.8)	NR	NR
Irfan <i>et al.</i> 2008 [17]	Pakistan	2001–2006									5	30 (8.5)	34 (9.7)	52 (14.8)	7 (2)	58 (16.5)
Kjellander <i>et al.</i> 2012 [18]	Sweden	2002–2006									9	43 (11.6)	42 (11.3)	1 (0.3)	6 (1.6)	58 (15.6)
Kumar <i>et al.</i> 2010 [19]	India	NR									3	29 (4.6)	245 (39.1)	93 (14.9)	NR	54 (8.7)
Mebis <i>et al.</i> 2010 [20]	Belgium	1994–2006										NR	140 (15.4)	NR	NR	NR
Miedema <i>et al.</i> 2013 [21]	Netherlands and Switzerland	2004–2011										NR	12 (17.6)	NR	NR	NR
Prabhash <i>et al.</i> 2010 [22]	India	2007	Haematology and oncology	All	NR	484	BSI	484 (100)	330 (68.2)	53 (16.1)	35 (10.7)	11 (3.3)	147 (44.5)	56 (16.9)	NR	28 (8.5)
Ram <i>et al.</i> 2012 [23]	Israel	2007–2011	Haematology	Adults	59	179	Clinical samples	134 (74.8)	120 (67.1)	49 (40.9)	18 (15)	7 (5.8)	19 (15.8)	3 (2.5)	7 (5.8)	18 (14.2)
Samosis <i>et al.</i> 2013 [24]	Greece	2007–2011	Haematology and oncology	All	39.4	108	BSI	108 (100)	71 (65.8)	19 (26.8)	18 (25.3)	2 (2.8)	19 (26.8)	3 (4.2)	NR	10 (14.1)
Schelenz <i>et al.</i> 2013 [25 ^a]	United Kingdom	1997–2010	Haematology and oncology	Adults	NR	872	BSI	872 (100)	324 (37.2)	101 (31.2)	43 (13.3)	NR	56 (17.3)	14 (4.3)	53 (16.3)	14 (4.4)
Swati <i>et al.</i> 2010 [26]	India	2006	Haematology	All	100	62	Clinical samples	41 (60.3)	47 (75.8)	10 (21.2)	21 (44.6)	1 (2.2)	5 (10.6)	8 (17.1)	0	2 (4.3)
Tumbarello <i>et al.</i> 2009 [27]	Italy	2000–2005	Haematology	Adults	62.2	241	BSI	241 (100)	98 (40.7)	42 (42.8)	9 (9.2)	5 (5.1)	31 (31.5)	4 (4.1)	2 (2.1)	3 (3.1)
Cattaneo <i>et al.</i> 2008 [28]	Italy	2004–2005	Haematology	Adults	59.2	147	Clinical samples	64.9	80 (54.4)	38 (47.5)	NR	NR	13 (16.2)	2 (2.5)	4 (5)	23 (28.8)
Poon <i>et al.</i> 2012 [29]	Singapore	2008–2010	Haematology	Adults	100	157	BSI	157 (100)	82 (52.3)	37 (45.1)	27 (32.9)	NR	11 (13.4)	1 (1.2)	NR	6 (7.4)

In vitro Sensitivities in febrile Neutropenia



Reference	Country	Period	Setting	Patients' age	Neutropenia, %	Source of bacterial isolates	BSI, %	Number of isolates, n	Cefepime, %	Ceftazidime, %	Imipenem, %	Meropenem, %	Piperacillin/tazobactam, %	Quinolones, %	Amikacin, %	Gentamicin, %
<i>Escherichia coli</i>																
Aslan <i>et al.</i> 2012 [7]	Turkey	2007–2010	Oncology	Children	100	BSI	100	13	100	15.4	100	100	100	66.7	7.7	69.2
Baskaran <i>et al.</i> 2007 [8]	Malaysia	2004–2005	Haematology	Adults	100	BSI	100	16	87.5	87.5	100	100	100	37.5	93.8	75
Chen <i>et al.</i> 2010 [10]	Taiwan	2002–2006	Haematology	Adults	100	BSI	100	103	90	NR	100	NR	92	50	99	NR
Chong Y <i>et al.</i> 2010 [11]	Japan	2006–2008	Haematology	All	100	BSI	100	26	53.8	NR	NR	NR	NR	NR	NR	NR
Ghosh I <i>et al.</i> 2012 [13]	India	2008–2010	Haematology	All	100	Clinical samples	0	11	NR	NR	90.9	90.9	NR	NR	NR	NR
LV <i>et al.</i> 2013 [15]	China	2010	Haematology	Children	NR	BSI	100	12	NR	25	100	100	100	66.6	91.7	16.7
Kjellander <i>et al.</i> 2012 [18]	Sweden	2002–2008	Haematology	Adults	100	BSI	100	141	NR	97.9	100	NR	90.8	84	NR	98.6
Kumar P <i>et al.</i> 2010 [19]	India	NR	Haematology and oncology	All	NR	Clinical samples	51.8	106	18.8	20.8	94.7	92.3	43.4	14.9	71.5	47.4
Prabhash <i>et al.</i> 2010 [22]	India	2007	Haematology and oncology	All	NR	BSI	100	53	NR	22.6	NR	91.5	49.1	20.8	60.4	NR
Trecarichi <i>et al.</i> 2009 [31]	Italy	2000–2007	Haematology	Adults	67.7	BSI	100	62	58.1	58.1	100	100	87.1	37.1	98.4	77.4
<i>Klebsiella pneumoniae</i>																
Aslan <i>et al.</i> 2012 [7]	Turkey	2007–2010	Oncology	Children	100	BSI	100	9	55.6	33.3	100	100	42.9	42.9	55.6	33.3
Baskaran <i>et al.</i> 2007 [8]	Malaysia	2004–2005	Haematology	Adults	100	BSI	100	11	90.9	90.9	100	100	81.8	81.8	100	100
Chen <i>et al.</i> 2010 [10]	Taiwan	2002–2006	Haematology	Adults	100	BSI	100	86	97	NR	100	NR	88	80	99	NR
Chong <i>et al.</i> 2010 [11]	Japan	2006–2008	Haematology	All	100	BSI	100	13	84.6	NR	NR	NR	NR	NR	NR	NR
Ghosh <i>et al.</i> 2012 [13]	India	2008–2010	Haematology	All	100	Clinical samples	0	10	NR	NR	10	10	NR	NR	NR	NR
LV <i>et al.</i> 2013 [15]	China	2010	Haematology	Children	NR	BSI	100	12	NR	50	100	100	100	83.3	100	50
Kjellander <i>et al.</i> 2012 [18]	Sweden	2002–2008	Haematology	Adults	100	BSI	100	78	NR	98.7	100	NR	91	98.7	NR	100
Kumar <i>et al.</i> 2010 [19]	India	NR	Haematology and oncology	All	NR	Clinical samples	51.8	99	8.1	26.8	100	100	38.8	36.1	67.5	49.9
Swati <i>et al.</i> 2010 [26]	India	2006	Haematology	All	90.1	Clinical samples	38.1	21	76.1	NR	100	100	95.2	28.5	85.7	19
Prabhash <i>et al.</i> 2010 [22]	India	2007	Haematology and oncology	All	NR	BSI	100	35	NR	28.6	NR	100	37.1	37.1	54.3	NR

In vitro Sensitivities in febrile Neutropenia



Reference	Country	Period	Setting	Patients' age	Neutropenia, %	Source of bacterial isolates	BSI, %	Number of isolates, n	Cefepime, %	Ceftazidime, %	Imipenem, %	Meropenem, %	Piperacillin/tazobactam, %	Quinolones, %	Amikacin, %	Gentamicin, %
<i>Escherichia coli</i>																
Aslan <i>et al.</i> 2012 [7]	Turkey	2007–2010	Oncology	Children	100	BSI	100	13	100	15.4	100	100	100	66.7	7.7	69.2
Baskaran <i>et al.</i> 2007 [8]	Malaysia	2004–2005	Haematology	Adults	100	BSI	100	16	87.5	87.5	100	100	100	37.5	93.8	75
Chen <i>et al.</i> 2010 [10]	Taiwan	2002–2006	Haematology	Adults	100	BSI	100	103	90	NR	100	NR	92	50	99	NR
Chong Y <i>et al.</i> 2010 [11]	Japan	2006–2008	Haematology	All	100	BSI	100	26	53.8	NR	NR	NR	NR	NR	NR	NR
Ghosh I <i>et al.</i> 2012 [13]	India	2008–2010	Haematology	All	100	Clinical samples	0	11	NR	NR	90.9	90.9	NR	NR	NR	NR
LV <i>et al.</i> 2013 [15]	China	2010	Haematology	Children	NR	BSI	100	12	NR	25	100	100	100	66.6	91.7	16.7
Kjellander <i>et al.</i> 2012 [18]	Sweden	2002–2008	Haematology	Adults	100	BSI	100	141	NR	97.9	100	NR	90.8	84	NR	98.6
Kumar P <i>et al.</i> 2010 [19]	India	NR	Haematology and oncology	All	NR	Clinical samples	51.8	106	18.8	20.8	94.7	92.3	43.4	14.9	71.5	47.4
Prabhash <i>et al.</i> 2010 [22]	India	2007	Haematology and oncology	All	NR	BSI	100	53	NR	22.6	NR	91.5	49.1	20.8	60.4	NR
Trecarichi <i>et al.</i> 2009 [31]	Italy	2000–2007	Haematology	Adults	67.7	BSI	100	62	58.1	58.1	100	100	87.1	37.1	98.4	77.4
<i>Klebsiella pneumoniae</i>																
Aslan <i>et al.</i> 2012 [7]	Turkey	2007–2010	Oncology	Children	100	BSI	100	9	55.6	33.3	100	100	42.9	42.9	55.6	33.3
Baskaran <i>et al.</i> 2007 [8]	Malaysia	2004–2005	Haematology	Adults	100	BSI	100	11	90.9	90.9	100	100	81.8	81.8	100	100
Chen <i>et al.</i> 2010 [10]	Taiwan	2002–2006	Haematology	Adults	100	BSI	100	86	97	NR	100	NR	88	80	99	NR
Chong <i>et al.</i> 2010 [11]	Japan	2006–2008	Haematology	All	100	BSI	100	13	84.6	NR	NR	NR	NR	NR	NR	NR
Ghosh <i>et al.</i> 2012 [13]	India	2008–2010	Haematology	All	100	Clinical samples	0	10	NR	NR	10	10	NR	NR	NR	NR
LV <i>et al.</i> 2013 [15]	China	2010	Haematology	Children	NR	BSI	100	12	NR	50	100	100	100	83.3	100	50
Kjellander <i>et al.</i> 2012 [18]	Sweden	2002–2008	Haematology	Adults	100	BSI	100	78	NR	98.7	100	NR	91	98.7	NR	100
Kumar <i>et al.</i> 2010 [19]	India	NR	Haematology and oncology	All	NR	Clinical samples	51.8	99	8.1	26.8	100	100	38.8	36.1	67.5	49.9
Swati <i>et al.</i> 2010 [26]	India	2006	Haematology	All	90.1	Clinical samples	38.1	21	76.1	NR	100	100	95.2	28.5	85.7	19
Prabhash <i>et al.</i> 2010 [22]	India	2007	Haematology and oncology	All	NR	BSI	100	35	NR	28.6	NR	100	37.1	37.1	54.3	NR

E. Coli in vitro sensitivities (%)



Drug	Mean	Min	Max
Carbapenem	97	90.9	100
Piperacillin-Tazobactam	95 (India: 43.4; 49.1)	87.1	100
Cefepime	68.1	18.8	100
Ceftazidim	46.7	15.4	94.7
Amikacin	74.6	7.7	99
Gentamycin	64.1	16.7	98.6
Fluoroquinolones	47.2	14.9	66.7



Drug	Mean	Min	Max
Carbapenem	98	90	100
Piperacillin-Tazobactam	71.8	37.1	100
Cefepime	68.7	8.1	90.9
Ceftazidim	54.7	28.6	98.7
Amikacin	80.3	54.3	100
Gentamycin	58.7	19	100
Fluoroquinolones	61.1	28.5	98.7

Pseudomonas aeruginosa in vitro sensitivities (%)



Drug	Mean	Min	Max
Imipenem	71.4	24	100
Meropenem	50.1		
Piperacillin-Tazobactam	78.3	61.6	100
Cefepime	53.6	34	100
Ceftazidim	62.3	30	100
Amikacin	61.8	11	100
Gentamycin	78.3	34.9	100
Fluoroquinolones	51.6	18	94



- 6 studies, mean sensitivities
- Imipenem 61.8%
- Meropenem 48.0%
- Piperacillin-Tazobactam 53.3%
- Ceftazidime 64.1%
- Cefepime 42.6%
- Amikacin 52.6%
- Fluoroquinolones 58.1%



- Diagnostik und Therapieeinleitung parallel
- In der Regel Monotherapie
- Lokale Resistenzlage Resistenzlage beachten
- Reevaluation nach 72 – 120 h
- Offene Fragen
 - Antibiotikaprophylaxe?
 - CT bei Fieber?
 - Screening für MDR?