

FEBRİL NÖTROPENİ : 2009' DA NELER OLDU?

Dr Alpay AZAP

Ankara Üniversitesi Tıp Fakültesi

İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD



- ❖ Infectious Diseases Working Party of EBMT
- ❖ Infectious Diseases Group of EORTC
- ❖ Supportive Care Group of the European LeukemiaNet
- ❖ Immunocompromised Host Society





- Eylül 2005 Fransa
- 24 ülkeden 59 uzman

1. Nötropenik Hastalarda Florokinolon Profilaksisi
2. FEN Tedavisinde Aminoglikozit Kullanımı
3. FEN Tedavisinde Glikopeptid ve Diğer Anti G(+) ajanlar
4. Ampirik Antifungal Tedavi
5. Antifungal Profilaksi
6. Antifungal Tedavi (aspergillozis ve candidiazis)



2nd
European
Conference on
Infections in
Leukemia

Eylül 2007

24 ülkeden 53 uzman

- ECIL 1'de yer alan 3 başlık yenilendi
ampirik AF tedavi, AF profilaksi ve AF tedavi
- Herpes Virus İnfeksiyonlarına Yaklaşım
HSV, VZV, CMV, HHV6, HHV7, EBV
- Diğer Viral İnfeksiyonlara Yaklaşım
Solunum Virusları, Influenza, Parainfluenza, Polyoma



- Eylül 2009 Fransa
- 19 Ülkeden 59 uzman

- ECIL 1 ve 2’de yer alan 4 başlık yenilendi
ampirik AF tedavi, AF profilaksi ve AF tedavi
Herpes Virus İnfeksiyonlarına Yaklaşım
- Zigomikoz
- İnvaziv mantar infeksiyonlarında non-invaziv yöntemler

Fever and neutropenia: the early years

Gerald P. Bodey*

*Department of Infectious Diseases, Infection Control and Employee Health, The University of Texas,
M. D. Anderson Cancer Center, 1515 Holcombe Boulevard (Unit 402), Houston, TX 77030, USA*

The importance of neutropenia as a predisposing factor for infection in patients with haematological malignancies was not clearly appreciated until effective therapeutic agents became available. This led to the important advance of administering antibiotics promptly to neutropenic patients when they developed fever, before a diagnosis was established. Although some antibiotics available in the 1960s had activity against many pathogens *in vitro*, they were ineffective against infections in neutropenic patients. The development of methods to administer white blood cell transfusions along with antibiotics was beneficial to some patients. The development of new antibiotics was of critical importance, such as methicillin for treatment of *Staphylococcus aureus* and carbenicillin for *Pseudomonas aeruginosa*. Prevention of infection was attempted, using isolation rooms, air filtration and prophylactic antibiotics. All of these early efforts laid the foundations for the many important current investigations.

2009'da Yayınlanan Makaleler

- **Anahtar kelimeler:** Ateş, Febril nötropeni,
Profilaksi, İnfeksiyon,
Viral infeksiyon, İmmünsupresyon,
Malignite Fungal infeksiyon

1453 İngilizce makaleye ulaşıldı

159 makale hematoloji-onkoloji hastalarında infeksiyonların önlenmesi, tanısı ve tedavisi ile ilgiliydi.

159 makalenin (27'si pediatrik yaş grubunda) konu dağılımı

- **30 makale:** bakteriyel infeksiyonların tedavisi
- **13 makale:** bakteriyel infeksiyonların önlenmesi (antibiyotikler ve granülosit koloni stimüle edici faktörler)
- **24 makale:** hematoloji-onkoloji hastalarında febril nütropeni gelişmesine ve seyrine etki eden faktörler ve erken tanı yöntemleri
- **22 makale:** invaziv fungal infeksiyonların tedavisi
- **7 makale:** invaziv fungal infeksiyonların tanısı
- **13 makale:** invaziv fungal infeksiyonların profilaksisi
- **17 makale:** viral infeksiyonların tanı, tedavi ve önlenmesi
- **6 makale:** infeksiyonların ekonomik yükleri ve maliyet

Dosya ve Klasör Görevleri

- Yeni klasör oluştur
- Bu klasörü Web'de yayımla
- Bu klasörü paylaş

Diğer Yerler

- ALPAY 1 (F:)
- Belgelerim
- Paylaşılan Belgeler
- Bilgisayarı
- Ağ Bağlantıları

Ayrıntılar

fen 2010
Dosya Klasörü
Değiştirilme Tarihi: 2010-02-08, 14:54

m 1 burk	m 53 abx vs gcsf in prfx	m 105 fen risk factors	m 157 HHV 6 ensefalt
m 2 crp	m 54 mka for ifi	m 106 fen ekonomik maliyeti	m 158 bk. virus kit
m 3 pmnl tf	m 55 meme ca fen riski	m 107 intermittan vs daly amfoB	m 159 altuzamb cmv prfx
m 4 vre	m 56 risk asmint fen ped rev	m 108 mgmint of fen rev	
m 5 resp vir	m 57 acilde fen tdvsi hemg	m 109 imp underdosing	
m 6 cost of hosp	m 58 kns msa ica genleri	m 110 bakt ve mantar tanı ticari PCR	
m 7 oral vs IV	m 59 yeni af ajanlar rev	m 111 tiflts rev	
m 8 aft cand rev	m 60 tiflit ped	m 112 caspo in ped	
m 9 risk deg ped	m 61 fen tdv prot	m 113 sk. AREA OVER NOT CURVE	
m 10 aft cand rev	m 62 tzp tdv ped	m 114 vs cro ak ped	
m 11 pct predict ped	m 63 abx vs gcsf	m 115 idame in low risk fen	
m 12 aft vor	m 64 granit b. ped	m 116 bakteremi tanısında PCR	
m 13 inf in anl	m 65 liposomal amfoB rev	m 117 farklı mem dozu	
m 14 meme sk HL da fen	m 66 tek doz genta ped	m 118 protein C ped	
m 15 bakteremi predict crp ped	m 67 fen ped rev	m 119 populabon pk of itra	
m 16 HINI ve fen	m 68 ampik. vs preempt ifi tdv cordonnier	m 120 tiflit rev	
m 17 pct ped	m 69 imp as emprk 1stline	m 121 fen ped rev	
m 18 akc cada fen cost	m 70 crp vs endobel growth fac	m 122 karbrpm erken kesilebilir	
m 19 diagn in ifi	m 71 sefepim dozu	m 123 pct crp fen ped	
m 20 risk belleleme pct crp	m 72 fep ve ak tdv	m 124 h ficolin level predict fen	
m 21 prevention of fen	m 73 caspo amfo comb cost	m 125 anc cip vs cro ak ped	
m 22 impact of prevent fen memeca	m 74 cazın viridans etkisi	m 126 caz prfx vs lev prfx	
m 23 mgmint of chem ind fen solidtm	m 75 tzp caz vs caz atm comb ped	m 127 prfx ekonomik mi	
m 24 prfx ab for fen	m 76 invcandida tanı mannan	m 128 ekınokandiner rev	
m 25 acil serv predict	m 77 viridans strep mem rez	m 129 CT guided lung biopsy	
m 26 din drivdiagn ifi	m 78 empirik vs preempt ifi tdv	m 130 breakthrh ifi	
m 27 vori vs itra ifi prfx	m 79 antibakt modifikasyon rev	m 131 imp vs tzp mnoterp ped turk	
m 28 vori serum düz prfx	m 80 monoterapi	m 132 vori prfx: zygomycoz	
m 29 vori as prfx agent	m 81 mantar biyolojisi jac	m 133 vori caspo prfx inseat	
m 30 cytolin lev predict fen turk	m 82 ifi tdv tarihcesi	m 134 impct of prfx on cand spp	
m 31 citrullin mukoizt fen	m 83 ifi prfx jac	m 135 non-myeoloablatif kit inf	
m 32 ifi risk in lypthprolifds	m 84 fen tdv tarihcesi jac	m 136 ifi prevent wellfitt mask	
m 33 okit ve sepsis	m 85 ifi tari tdv jac	m 137 fungal pnömori yeni tdv	
m 34 cost efectiv vori vs ampho	m 86 mukoizt jac	m 138 posa prfx	
m 35 daptomisn pk pd in fen	m 87 farklı ates ölç yerleri hemg	m 139 prfx of ifi alman rehberi	
m 36 periodontit tdv fen	m 88 ayaktan tdv moks	m 140 ifi prfx ped turk	
m 37 imp dozu 3g olmak	m 89 combi vs monoterapi	m 141 prfx against asp	
m 38 NHL fen risk	m 90 ciltten ates ölç	m 142 hhv 6 ve kit	
m 39 ab prfx	m 91 caspo ped ifi tdv	m 143 adenovirus tdv edilmeli	
m 40 gcsf ve fen	m 92 fende CRP ped	m 144 pp65 vs pcr in CMV	
m 41 PCR ile preempt IA	m 93 itra efıc safety	m 145 influ vaccin kit	
m 42 AF tdv rev	m 94 emesis predict bakteremi ped	m 146 resp virus in kit	
m 43 IL8 predict fen	m 95 korhexil kateter akıt	m 147 impact of donor CMV status	
m 44 fosfomisın in fen	m 96 diagn of lung infiltrates	m 148 hepatit B kit	
m 45 IFI erken tanı PCR	m 97 prevent fen GCSF	m 149 foscarnet preemptif tdv	
m 46 meme ca pegGCSF fen	m 98 tzp vs fep ped turk	m 150 prfx: IVIG for cmv	
m 47 pk pd caspo ped	m 99 mgmint of bacteremia rev	m 151 cmv status donr recip	
m 48 ates olctnede yeni yontem	m 100 prevent treat of ifi rev	m 152 cmv reakt effector CD4	
m 49 biapenem in fen	m 101 prevent fen GCSF rev	m 153 grb ve grA levls predict CMV GVHD	
m 50 myelobüctdv predict fen	m 102 filgastrin vs peg filgastrim	m 154 krnk aktif EBV hst	
m 51 CT based preempt tx ifi	m 103 fen in anl mds rev	m 155 ECIL 2 hsv vzv ebv	
m 52 valgnc cmv preemp akıt	m 104 fende yenikler rev	m 156 hepatit B react ped	

Tür: Metin Belgesi
Değiştirilme Tarihi: 2010-02-08 21:58
Boyut: 1,97 KB

H-ficolin serum concentration and susceptibility to fever and neutropenia in paediatric cancer patients

European Journal of Haematology 83 (251–257)

ORIGINAL ARTICLE

Serum vascular endothelial growth factor in adult haematological patients with neutropenic fever: a comparison with C-reactive protein

Sari Hämäläinen¹, Auni Juutilainen^{1,2}, Irma Matinlauri³, Taru Kuittinen¹, Esko Ruokonen⁴, Irma Koivula¹, Esa Jantunen^{1,2}

¹Department of Medicine, Kuopio University Hospital, Kuopio, Finland; ²Institute of Clinical Medicine/Internal Medicine, University of Kuopio,

ELSEVIER

journal homepage: www.ejconline.com

The predictive value of interleukin-8 (IL-8) in hospitalised patients with fever and chemotherapy-induced neutropenia

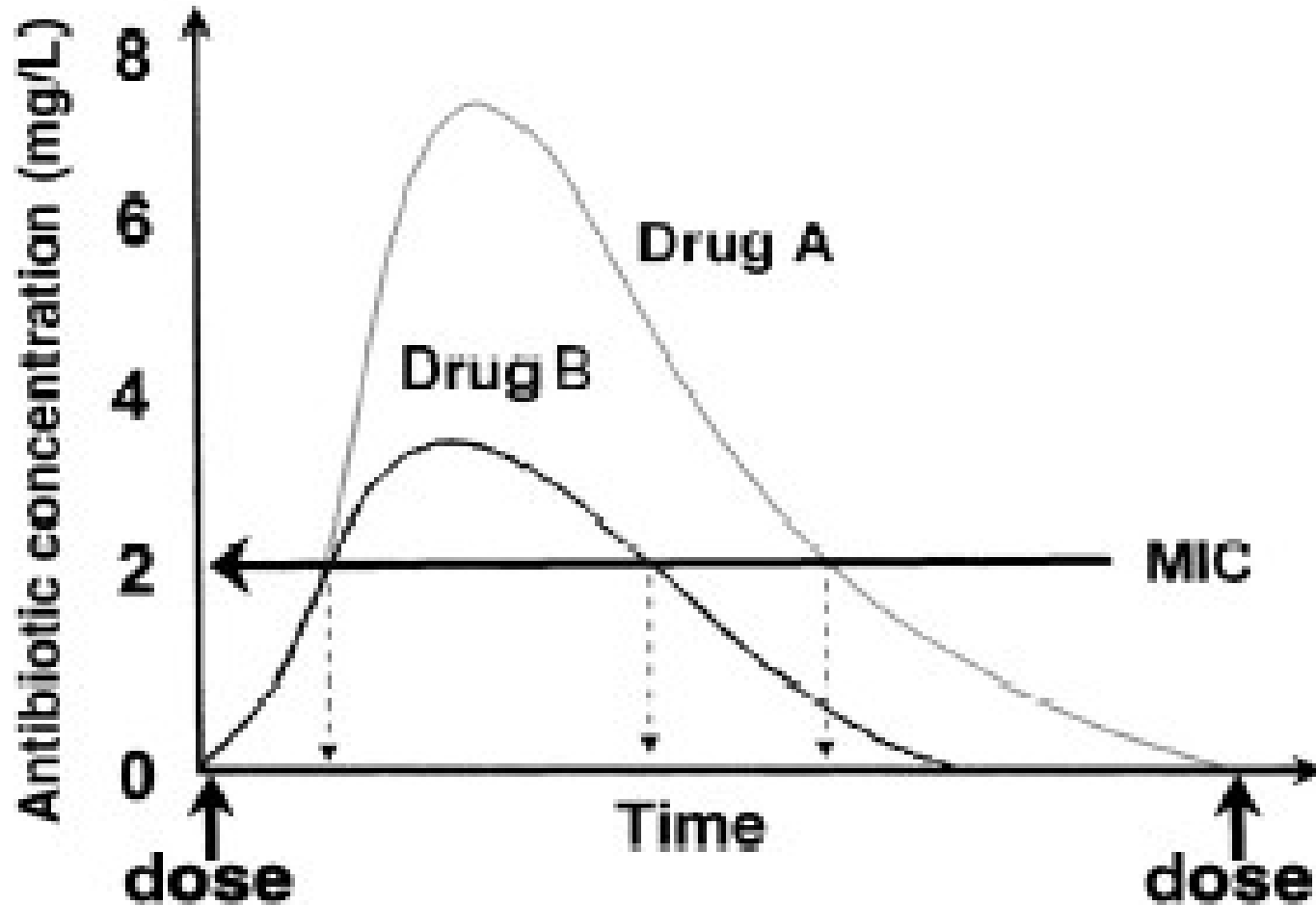
Yvonne H. Tromp, Simon M.G.J. Daenen, Wim J. Sluiter, Edo Vellenga*

Reassessment of Recommended Imipenem Doses in Febrile Neutropenic Patients with Hematological Malignancies[∇]

F. Lamoth,^{1†} T. Buclin,^{2†} C. Csajka,² A. Pascual,¹ T. Calandra,¹ and O. Marchetti^{1*}

Infectious Diseases Service¹ and Division of Clinical Pharmacology and Toxicology,² Department of Medicine, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Lausanne, Switzerland

Antimicrob Agents Chemother 2009;53:785-7



Reassessment of Recommended Imipenem Doses in Febrile Neutropenic Patients with Hematological Malignancies[∇]

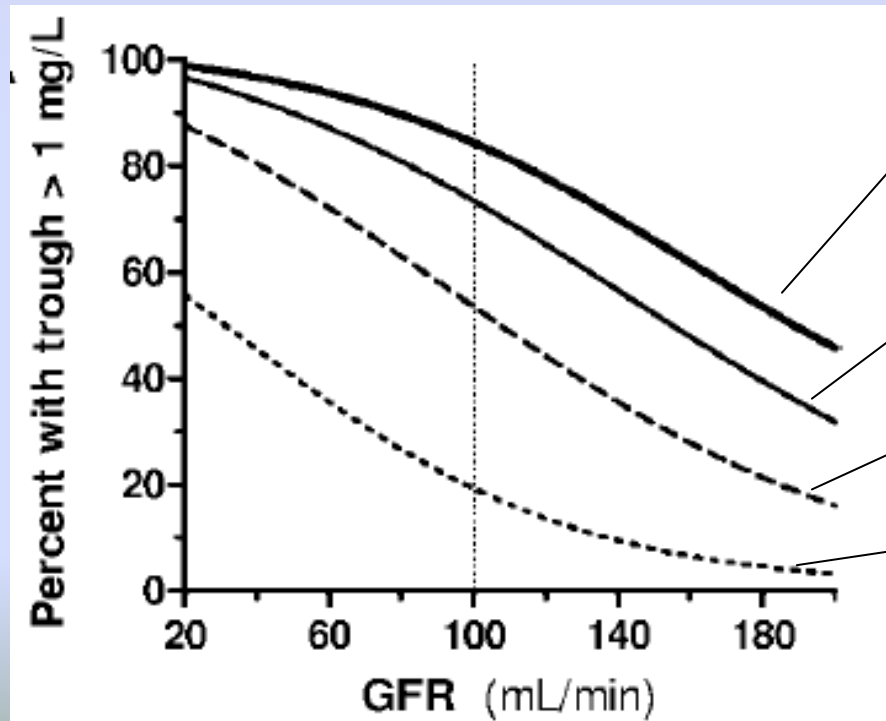
F. Lamoth,^{1†} T. Buclin,^{2†} C. Csajka,² A. Pascual,¹ T. Calandra,¹ and O. Marchetti^{1*}

Infectious Diseases Service¹ and Division of Clinical Pharmacology and Toxicology,² Department of Medicine, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Lausanne, Switzerland

Antimicrob Agents Chemother 2009;53:785-7

57 hastadan, 159 ölçüm (86 plato, 73 tepe düzeyi)

Hedef: Tüm doz aralığı boyunca İPM düzeyi > 1mg/L(MİK₉₀) olması



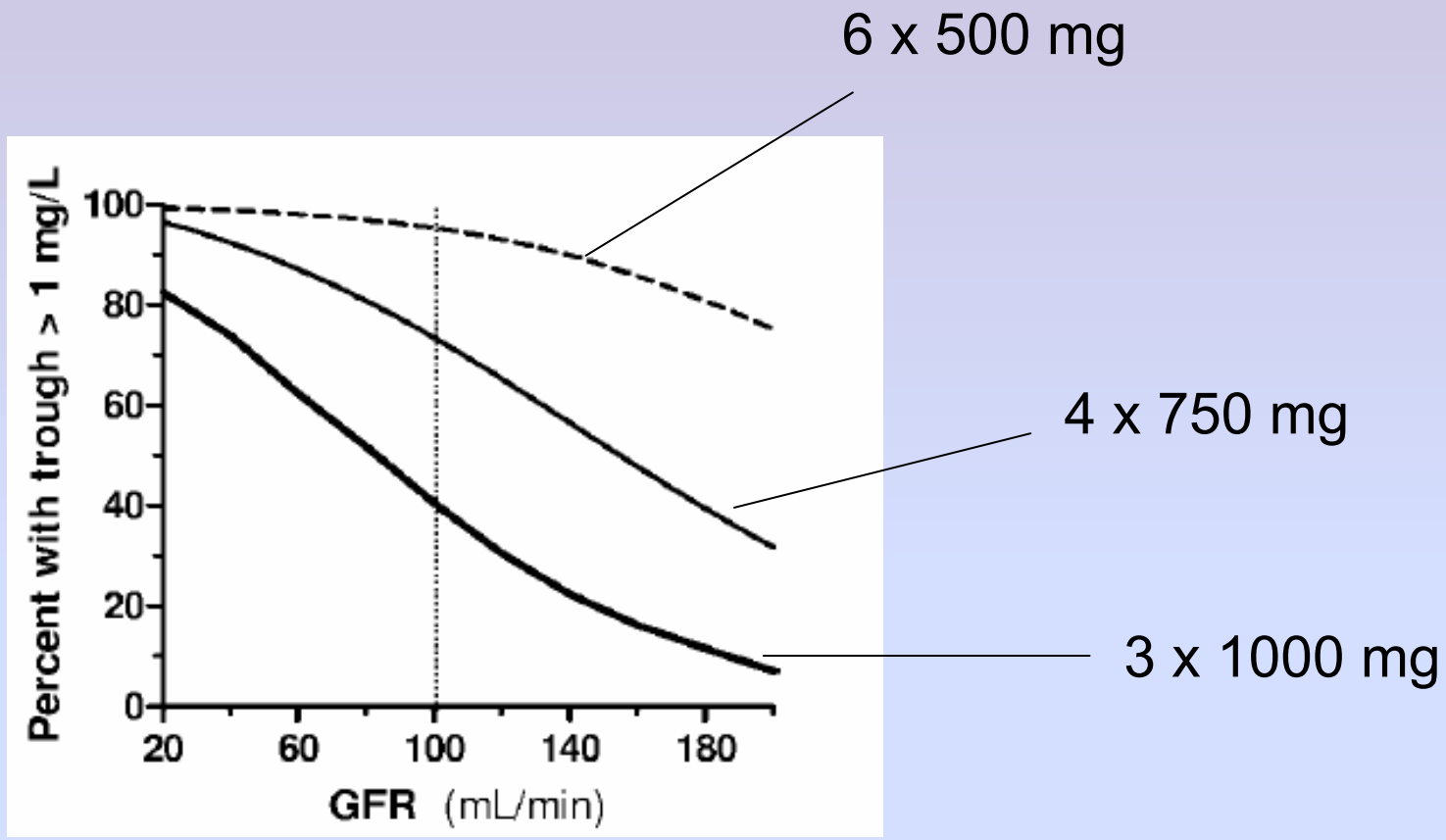
4 x 1000 mg

4 x 750 mg

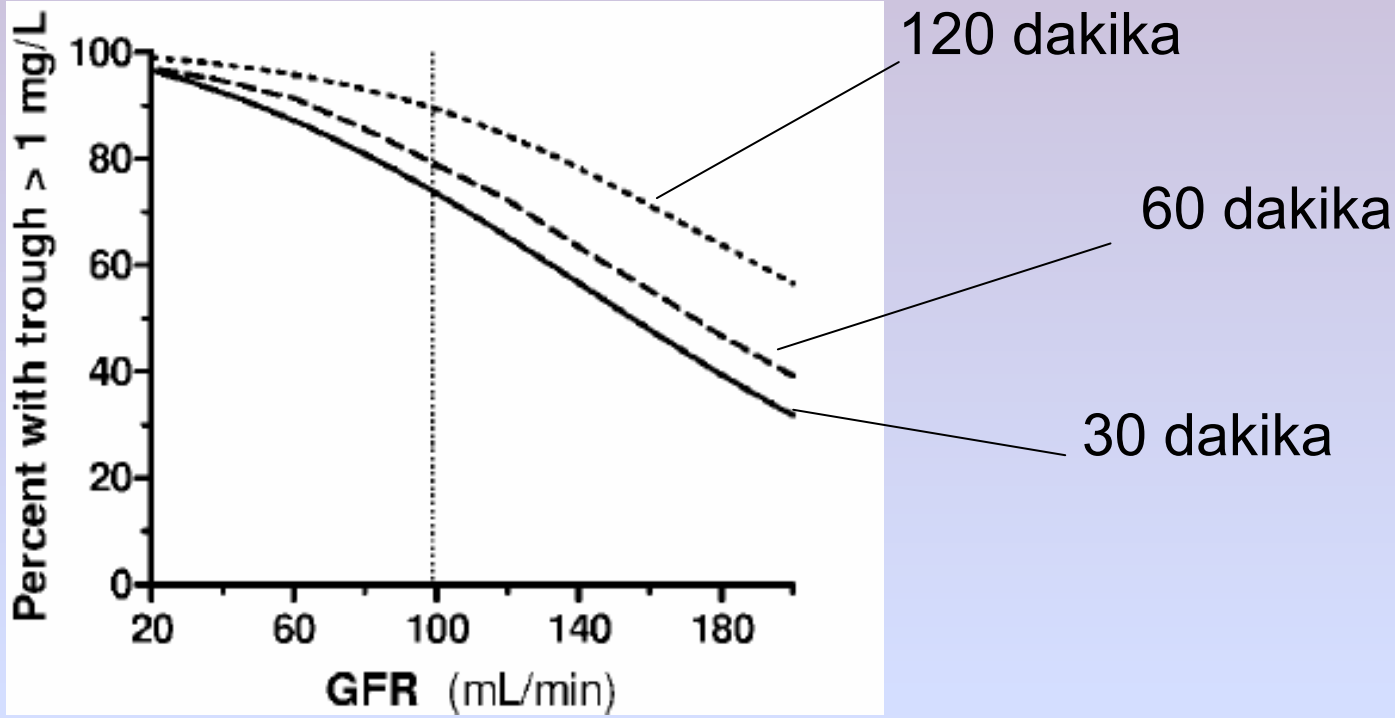
4 x 500 mg

4 x 250 mg

30 dakika infüzyon



30 dakika infüzyon



4 x 750 mg, farklı infüzyon süreleri

SONUÇ:

2 g/gün doz olguların %53'ünde,

3 g/gün doz %90'ında hedefi tutturur.

4x500 mg yerine 6x500 mg veya 4 x 750 mg (2 s infüzyon)

Imipenem underdosing as a cause of persistent neutropenic fever?

Frédéric Lamoth¹, Thierry Buclin², Andres Pascual¹,
Thierry Calandra¹ and Oscar Marchetti^{1*}

Ateşi ≥ 3 gün süren 29 nötropenik hasta (%79 AL, ortanca yaş: 58)

14 (%48) MDİ, 9 (%31) KDİ, 6 (%21) NBA

16 Hastada persistan ateşin nedeni bulunmuş.

13 Hastada persistan ateşin nedeni belli değil

8'inde imipenem serum plato düzeyleri düşük (<1 mg/L)

3'ünde sebep düzey düşüklüğü

5'inde sebep kesin değil (başka faktörler var)

Imipenem dosing schedule	Imipenem trough blood concentration ^a	Assessment of response to imipenem therapy at time of obtention of trough concentrations: duration of fever/clinical course	Modification of imipenem dosing schedule	Days to resolution of fever after imipenem dose adjustment
0.5 g qid	1 mg/L	3 days/persistent fever and enterocolitis	increase infusion time from 30 to 120 min	1
0.5 g qid	<0.25 mg/L	4 days/persistent fever	100% increase: 1 g qid	3
0.5 g tid	0.7 mg/L	6 days/persistent fever	33% increase: 0.5 g qid	1

Sonuç:

Persistan ateşi olan hastaların bir kısmında olası neden imipenem serum düzey düşüklüğü

Ateşi devam eden hastalarda 3-5 günde düzey ölçülebilir.

Three-day treatment with imipenem for unexplained fever during prolonged neutropaenia in haematology patients receiving fluoroquinolone and fluconazole prophylaxis: A prospective observational safety study

Lennert Slobbe^a, Loes van der Waal^a, Lydia R. Jongman^a, Pieterella J. Lugtenburg^b, Bart J.A. Rijnders^{a,c,*}

^aDepartment of Internal Medicine, Division of Infectious Diseases, 's Gravendijkwal 230, Erasmus MC, Rotterdam, The Netherlands

^bDepartment of Internal Medicine, Division of Haematology, Erasmus MC, Rotterdam, The Netherlands

^cDepartment of Medical Microbiology, Erasmus MC, Rotterdam, The Netherlands

>10 gün nütropeni beklenen,
yoğun tedavi alan akut lösemi ve allojeneik HKHN alıcıları
Retrospektif çalışma

Profilaksi: Siprofloksasin 2 x 500 mg + flukonazol 1 x 400 mg
+ oral kolistin 4 x 200 mg (ilk 10 gün)
+ penisilin (5. günden 15. güne, mukozit + ise)
+ rektal ve vajinal sürüntü takibi (FQRGNAB) 2/hafta

Table 1 – Characteristics of 166 haematologic patients with prolonged neutropaenia.

Characteristic	Value
Age, mean years (range)	53.9 (19–80)
Male sex	98 (59.0)
<i>Underlying haematologic disorder</i>	
AML/MDS ^a (137 neutropaenic periods)	64 (38.6)
Multiple myeloma (47 neutropaenic periods)	47 (28.3)
Non-Hodgkin lymphoma (64 neutropaenic periods)	36 (21.7)
Acute lymphatic leukaemia (16 neutropaenic periods)	8 (4.8)
Other ^b (12 neutropaenic periods)	11 (6.6)
<i>Co-morbidity</i>	
Cardiovascular	42 (25.3)
Respiratory	7 (4.2)
Other ^c	5 (3.0)

Data presented are numbers (%) of patients unless otherwise indicated.

a AML/MDS, acute myeloid leukaemia/myelodysplastic syndrome.

b Other, Hodgkin lymphoma ($n = 6$), chronic myeloid leukaemia ($n = 3$), aplastic anaemia ($n = 2$).

c Other, autoimmune disorders requiring regular immunosuppressive therapy ($n = 3$), ulcerative colitis ($n = 1$), HIV ($n = 1$).

Table 2 – Main characteristics of the neutropaenic periods (n = 276).

Characteristic	Value
<i>Haematological treatment course (%)</i>	
High-dose chemotherapy	182 (65.9)
Autologous stem cell transplantation	86 (31.2)
Allogeneic stem cell transplantation	8 (2.9)
<i>Mean days of neutropaenic period (SD^b)</i>	
All neutropaenic periods	20.5 (11.5)
AML/MDS ^c (remission and consolidation, n = 127)	28.2 (11.3)
MM ^d , autologous stem cell transplantation (n = 47)	12.7 (4.0)
Non-Hodgkin lymphoma (n = 64)	14.6 (6.7)
Acute lymphatic leukaemia (n = 16)	18.3 (11.7)
Allogeneic stem cell transplantation (n = 8)	11.9 (1.7)
<i>Neutropaenic periods classified according to febrile episodes</i>	
Neutropaenia without fever	74
Neutropaenia with 1 febrile episode	113
Neutropaenia with 2 febrile episodes	57
Neutropaenia with >2 febrile episodes	32

Data presented are numbers of neutropaenic periods.

a Neutropaenic, neutrophil count $<0.5 \times 10^9/l$.

b SD, standard deviation.

c AML/MDS, acute myeloid leukaemia/myelodysplastic syndrome.

d MM, multiple myeloma.

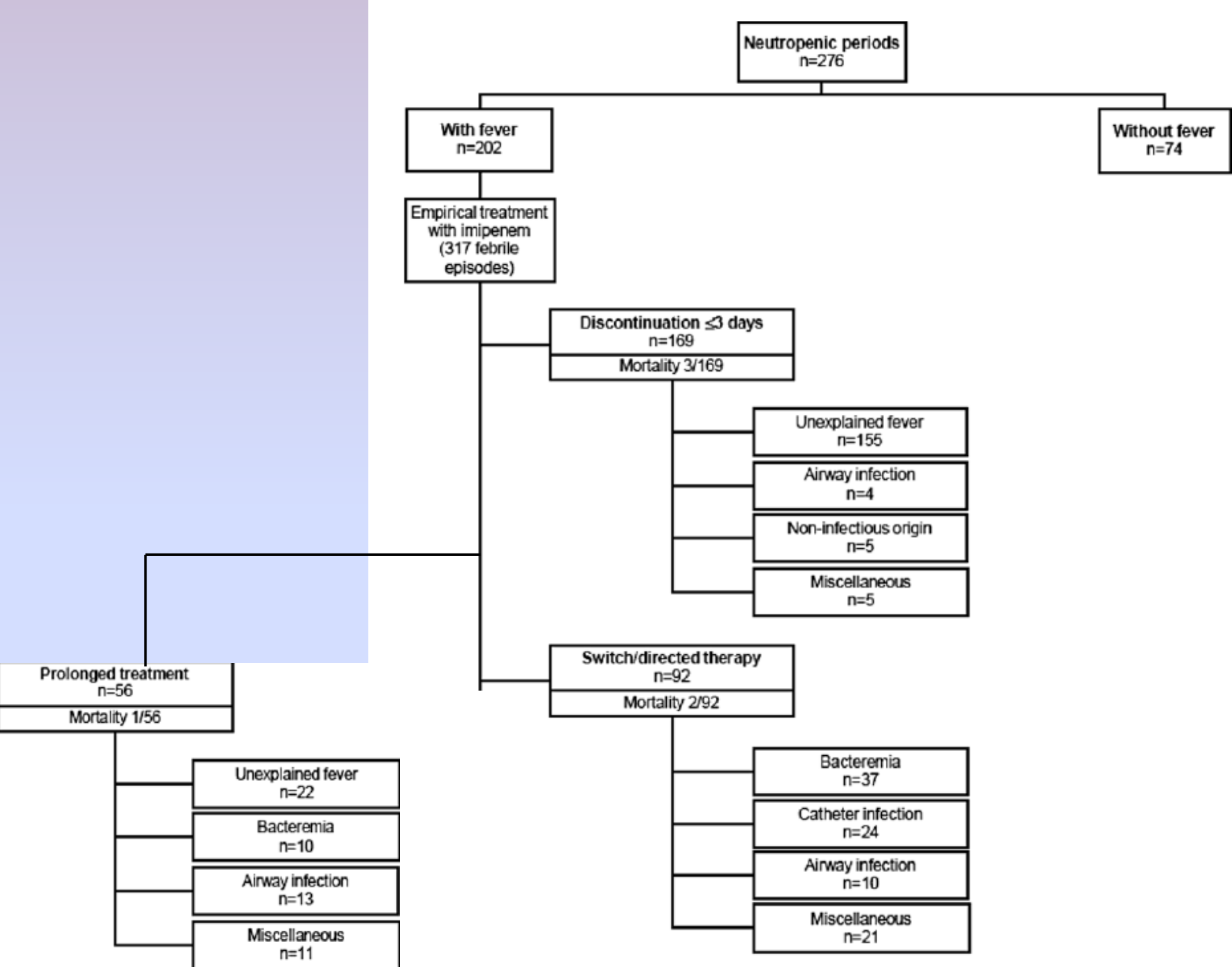


Table 3 – Data on fatal outcome of 6 patients.

Infectious cause	Underlying disease	Cause of death	Days after start of neutropaenia ^f
Yes	AML/MDS	Proven/probable aspergillosis jaw and lung	36
Yes	AML/MDS	Refractory AML, typhlitis and possible IPA	48
No	AML/MDS ^b	ARDS ^d no infectious origin	41 ^a
No	AML/MDS	Reanimation after EMD ^e no autopsy	15
No	AML/MDS	Progressive AML	28
No	HL ^c	Cardiogenic shock due to left ventricular dysfunction induced by myositis	16 ^a

a Patients already recovered from neutropaenia.

b AML/MDS, acute myeloid leukaemia/myelodysplastic syndrome.

c HL, Hodgkin lymphoma.

d ARDS, acute respiratory distress syndrome.

e EMD, electromechanic dissociation.

f Neutropaenia, neutrophil count $<0.5 \times 10^9/l$.

Mortalite: 6/166 (%3.6)

SONUÇ:

Siprofloksasin ve flukonazol profilaksisi altında FEN gelişen hastalarda

Klinik ve/veya mikrobiyolojik odak tespit edilemediği takdirde;

ateş düşmese de geniş spektrumlu antibiyotik 3. gün sonunda kesilebilir.

doi:10.1016/j.ijantimicag.2008.10.007

Fosfomycin in paediatric cancer patients: a feasible alternative to glycopeptides?

Sir,

Int J Antimicrob Agents. 2009 Apr;33(4):389.

- 1 ocak 2004-30 Nisan 2006, 57 pediyatrik (medyan yaş 7.1) hasta,
- Standart tedavi PIP-TAZ + 100 fosfomisin kullanılan atak
- %34'ünde başlangıç tedavide %66 72. saatte fosfomisin eklenmiş
- Medyan kullanım süresi 5 gün (1-10 gün)
- 150 mg/kg/gün dozda
- Teikoplanin kullanımını %90 azalmış, kaybedilen hasta yok.

Sonuç:

Fosfomisin ampirik glikopeptid kullanımına iyi bir alternatif olabilir.

Index to Predict Invasive Mold Infection in High-Risk Neutropenic Patients Based on the Area Over the Neutrophil Curve

Rodrigo D. Portugal, Marcia Garnica, and Marcio Nucci

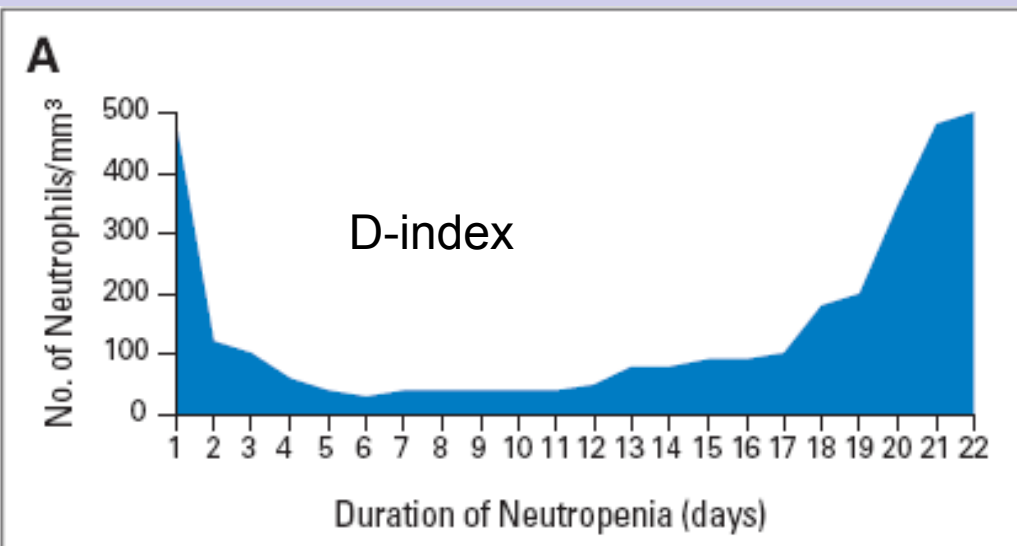
From the University Hospital, Hematology Service, Universidade Federal do Rio de Janeiro, Cidade Universitaria, Rio de Janeiro, Brazil.

A B S T R A C T

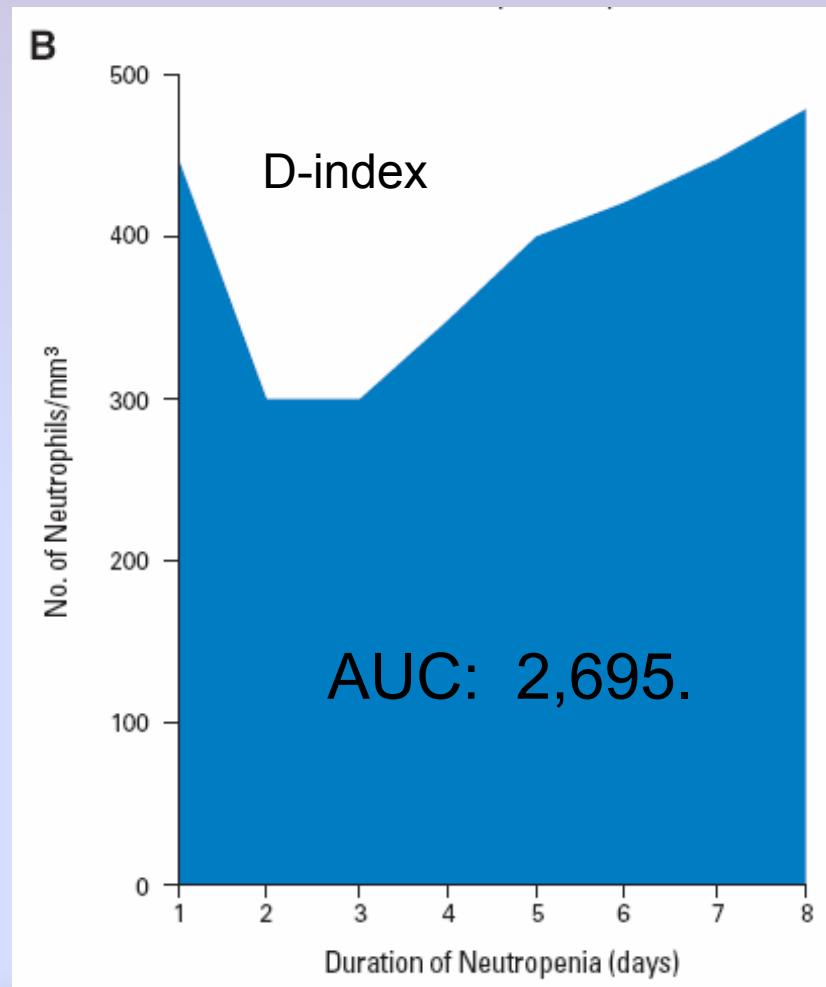
Purpose

AML remisyon indüksiyon tedavisi alan;
11 IFI gelişen, 33 IFI gelişmeyen hastada günlük nötrofil sayılarından
“D-indeks” ve “c-D-indeks” hesaplanmış

Mantar infeksiyonu gelişimi nötropeni süresi ve derinliği ile ilişkili



AUC: 2,697.



Parameters Used for the Creation of the D-Index

The observed AUC (A_o) is obtained by the trapezium rule,

$$A_o = \sum_{i=2}^n (t_i - t_{i-1}) \frac{N_{i-1} + N_i}{2}$$

$$A_o = [1/2 (450 + 300)] + [1/2 (300 + 300)] \\ + [1/2 (300 + 400) \times 2] + [1/2 (400 + 480) \times 3]$$

$$A_o = 375 + 300 + 700 + 1,320 = 2,695 \text{ days} \cdot \text{neutrophils}/\mu\text{L}.$$

The A_e , considering 7 days of neutropenia, is:

$$A_e = 7 \times 500 = 3,500 \text{ days} \cdot \text{neutrophils}/\mu\text{L}.$$

Finally, the D-index is the difference $A_e - A_o = 805 \text{ days} \cdot \text{neutrophils}/\mu\text{L}$.

Table 2. Predictive Values of the D-Index (cutoff = 6,200) and c-D-Index (cutoff = 5,800) According to the Prevalence of IMI

Prevalence of IMI (%)	%			
	D-Index		c-D-Index	
	PPV	NPV	PPV	NPV
5	11	100	10	99
10	21	100	19	98
15	30	100	28	97

Abbreviations: c-D-index, cumulative D-index; IMI, invasive mold infection; PPV, positive predictive value; NPV, negative predictive value.

SONUÇ

D-indeks ve c-D-indeks:

Hesaplaması kolay

Negatif prediktif değeri çok yüksek

Galaktomannan ve beta-glukanla birlikte kullanılabilir
preemptif tedaviyi yönlendirmede kullanımı?

A prospective, randomised study on the use of well-fitting masks for prevention of invasive aspergillosis in high-risk patients

G. Maschmeyer^{1*}, S. Neuburger², L. Fritz¹, A. Böhme³, O. Penack⁴, R. Schwerdtfeger⁵, D. Buchheidt⁶ & W.-D. Ludwig⁷ on behalf of the Infectious Diseases Working Party (AGIHO) of the German Society of Haematology and Oncology

¹Department of Haematology and Oncology, Ernst-von-Bergmann Clinic, Potsdam; ²Department of Haematology and Oncology, Charité University Medical School, Campus Virchow-Klinikum, Berlin; ³Department of Internal Medicine II, Johann-Wolfgang-Goethe-University Medical Centre, Frankfurt am Main; ⁴Department of Hematology and Oncology, Charité University Medical School, Campus Benjamin Franklin, Berlin; ⁵Center for Bone Marrow and Stem Cell Transplantation, Charité University Medical School, Campus Benjamin Franklin, Berlin; ⁶Department of Hematology and Oncology, Charité University Medical School, Campus Benjamin Franklin, Berlin; ⁷Department of Hematology and Oncology, Charité University Medical School, Campus Benjamin Franklin, Berlin

Annals of Oncology 20: 1560–1564, 2009

Prospektif, randomize, çok merkezli çalışma

Akut lösemi indüksiyon tedavisi veya allojeneik HKHN,

HEPA ve/veya LAF oda, oral polyene, flukonazol

+/-

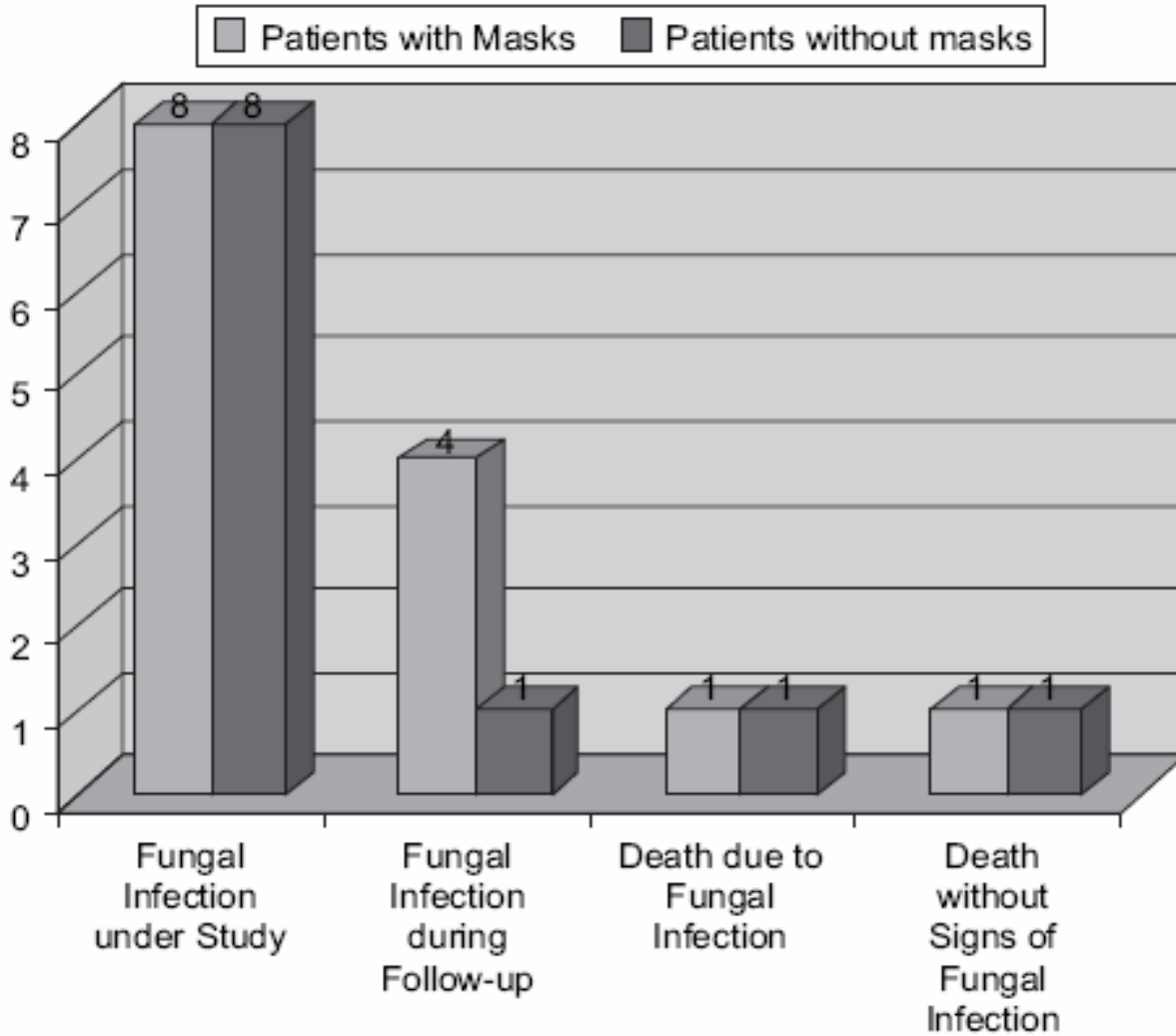
Oda dışına çıkarken FFP2 maskesi

Hedef:192 hasta (α hata:0.05, β hata:0.20, insidans:%25, %50 azalma)

Maske kolu: 41 hasta

Kontrol kolu: 39 hasta alıřma sonlandırılmıř.

- Nötropeni süresi (medyan) : 21.2 gün (4-85)
- Oda dıřına ıkma (medyan): 7 kez (0-40)
- Maske hakkında görüş:
katlanılabilir: %65, rahatsız:%26, katlanılmaz:%9
- Maskeler günlük deęiřtirilmiř.
- Bir merkez (26 hasta) inřaat bildirmiř.



Sonuç: FFP2 maske ile takip İA riskini azaltmıyor.
NEDEN???

© 1999 Randy Glasbergen.
www.glasbergen.com



Türkçesi : <http://desteksiz.ada.net.tr>

"Seçenekleri yeniden dinlemek için 49a basınız....
Neden aradığınızı unuttuysanız 50ye basınız..."

Teşekkürler....