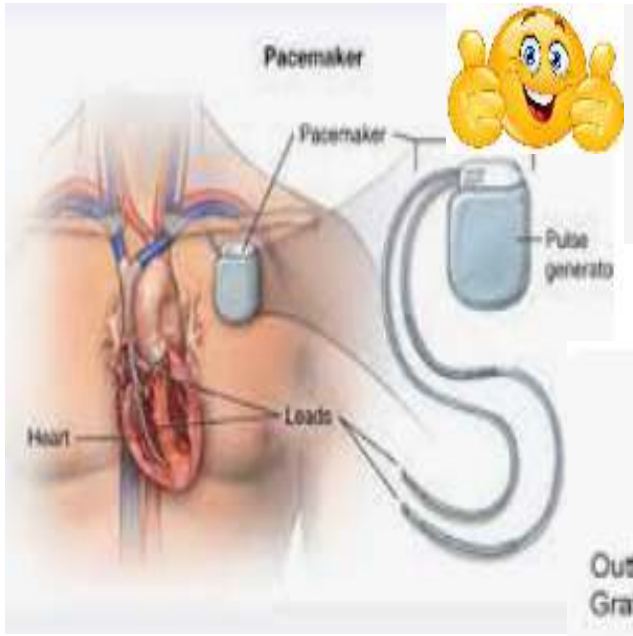
Solid Organ Nakli Alıcılarında Dirençli Bakteriyel Enfeksiyonların Yönetimi

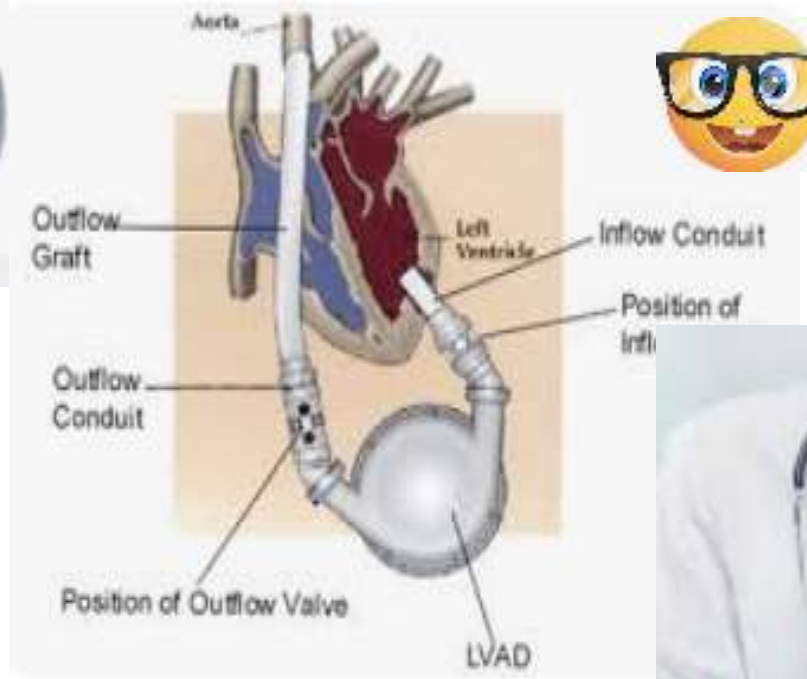
Dr. Nuran SARI

Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD.

BAŞKENT ÜNİVERSİTESİ

50 y, E


Pacemaker
Pacemaker
Pulse generato
Heart
Leads


Aorta
Outflow Graft
Left Ventricle
Inflow Conduit
Position of Infl
Outflow Conduit
Position of Outflow Valve
LVAD

Sorun!

- Bakteriyemi
- Donör kaynaklı enfeksiyonlar
- LVAD enfeksiyonları
- **SOTr enfeksiyonları**
- İnfektif endokardit
- Dirençli bakteriyel enfeksiyonlar

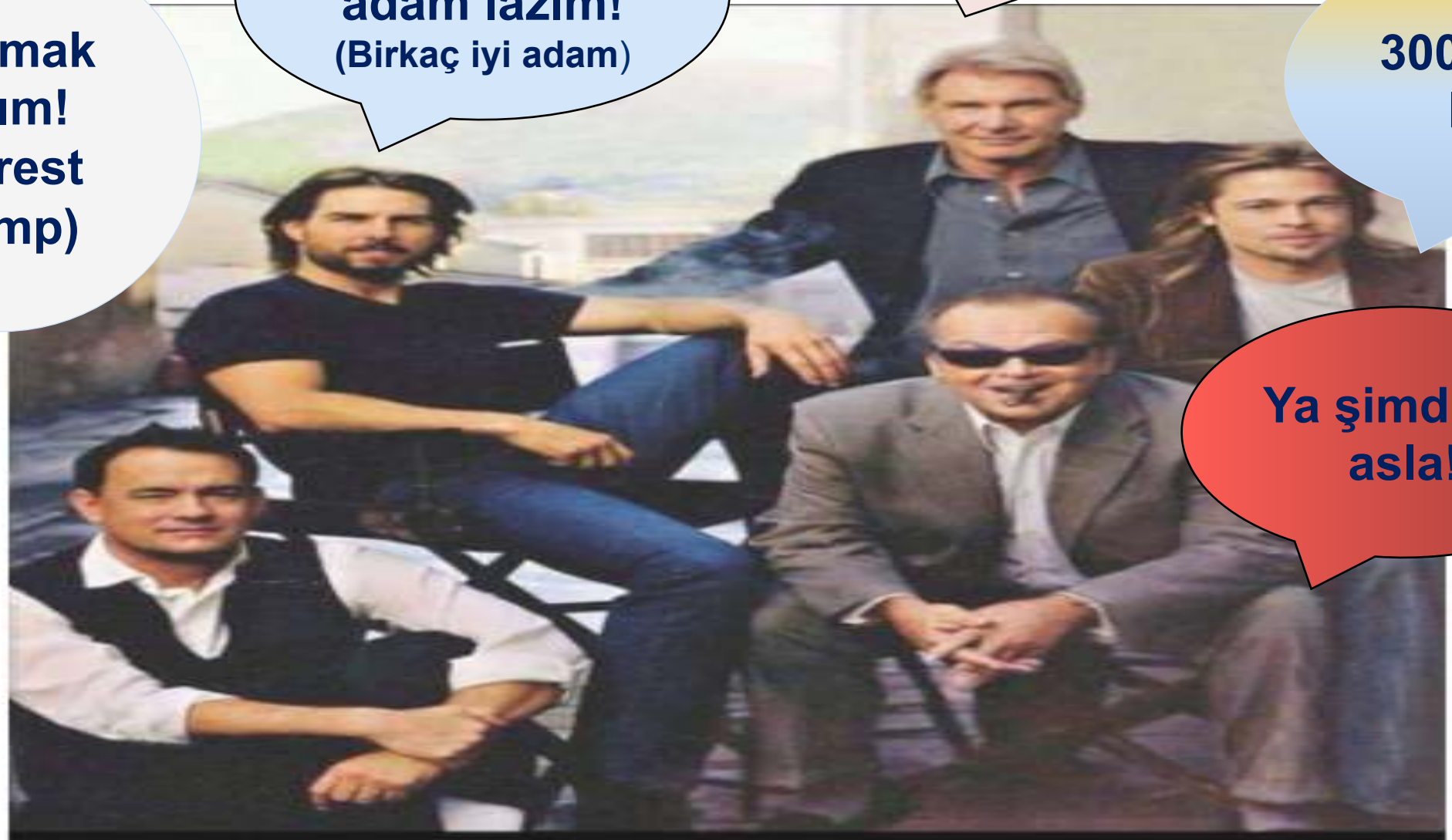
Ne yapmak lazım !!!

Kaçmak lazım!
(Kaçak)

Birçok iyi adam lazım!
(Birkaç iyi adam)

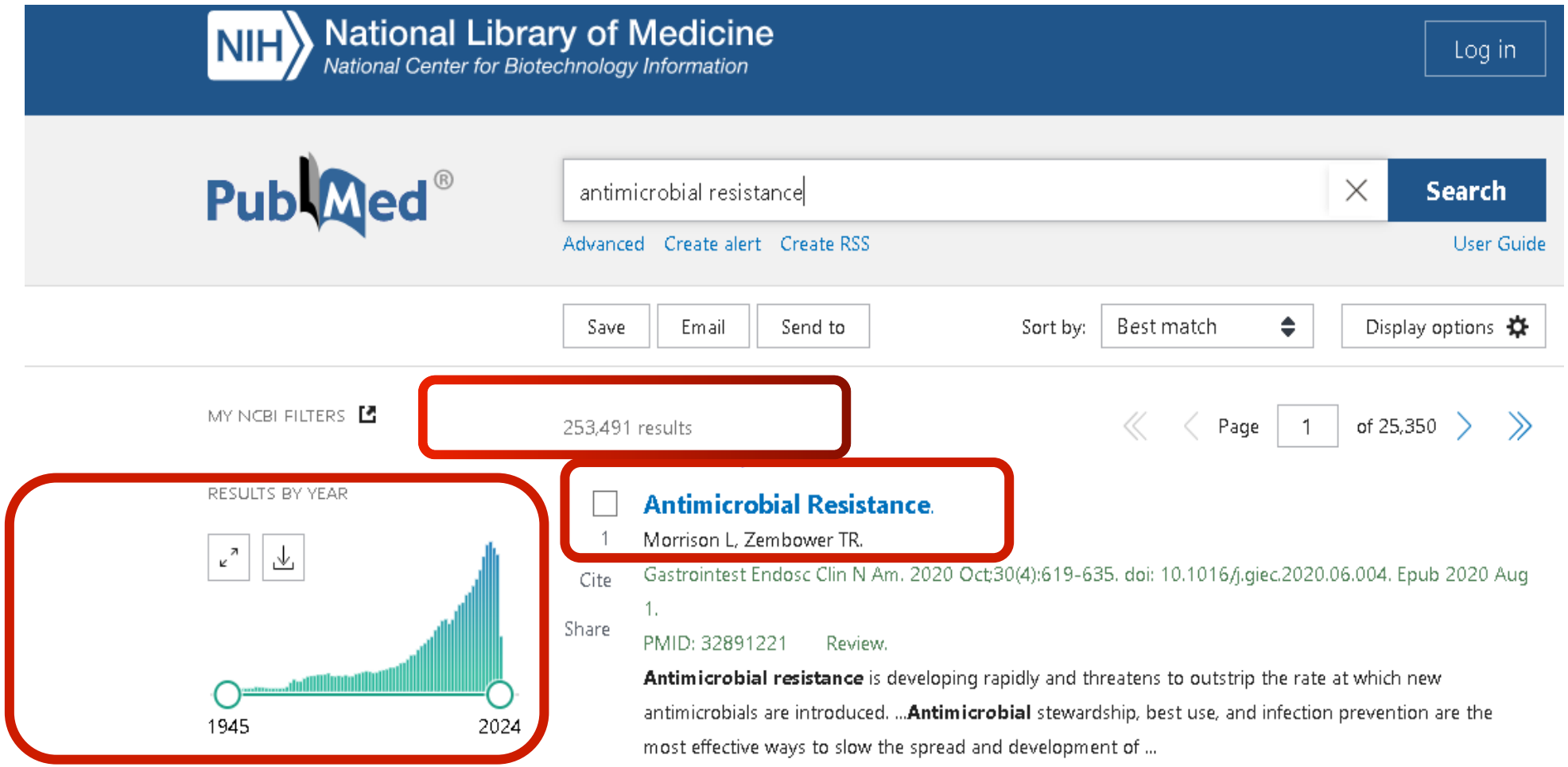
Koşmak lazım!
(Forest Gump)

300 Spartalı lazım!

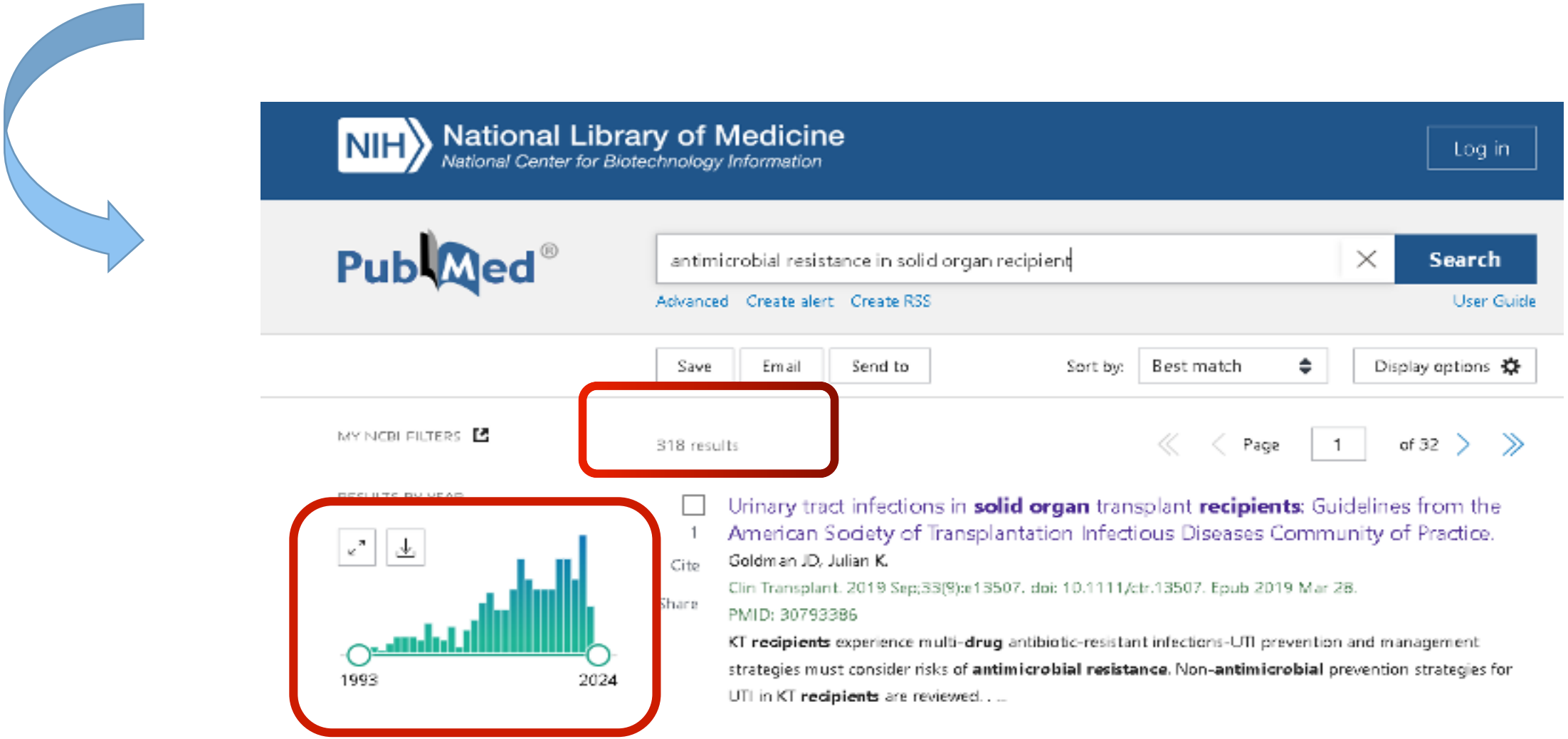


Ya şimdi, ya asla!

Antimikrobiyal Direnç

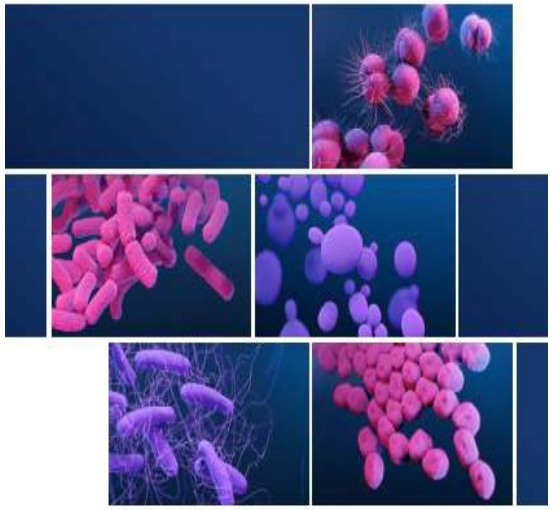


Solid Organ Nakil Alıcılarında Antimikrobiyal Direnç



ANTIBIOTIC RESISTANCE THREATS
IN THE UNITED STATES

2019



Acil Tehtidler

- Carbapenem-resistant *Acinetobacter*
- *Candida auris* (*C. auris*)
- *Clostridioides difficile* (*C. difficile*)
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant *Neisseria gonorrhoeae* (*N. gonorrhoeae*)

Ciddi tehtidler

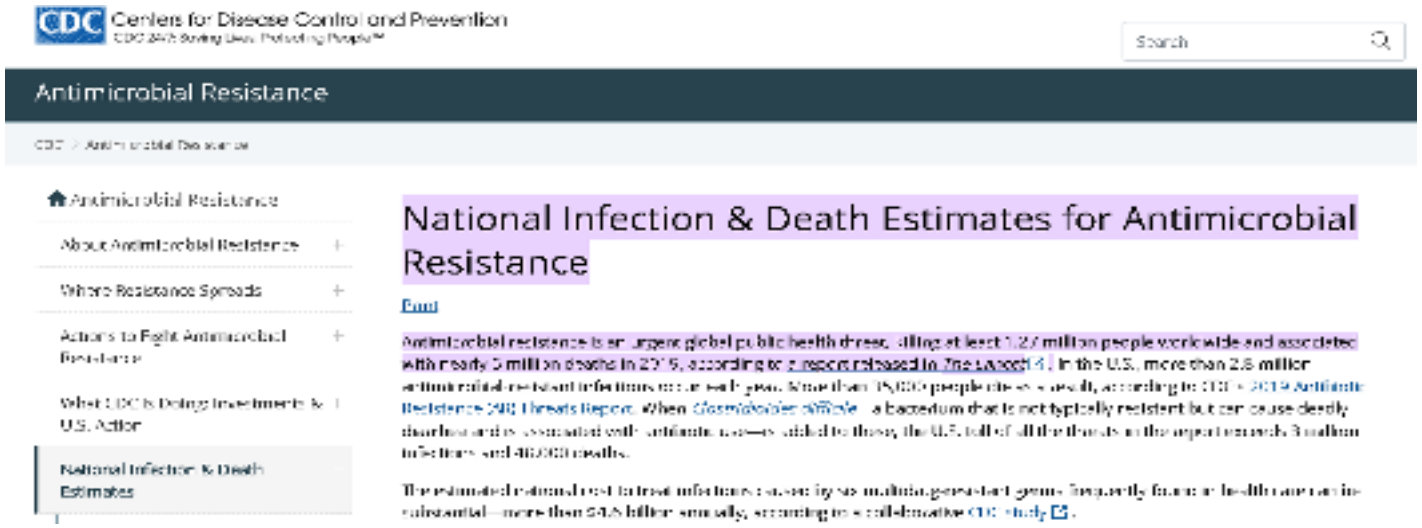
- Drug-resistant *Campylobacter*
- Drug-resistant *Candida*
- Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae
- Vancomycin-resistant *Enterococci* (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa* (*P. aeruginosa*)
- Drug-resistant nontyphoidal *Salmonella*
- Drug-resistant *Salmonella* serotype Typhi
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Drug-resistant *Streptococcus pneumoniae* (*S. pneumoniae*)
- Drug-resistant Tuberculosis (TB)

Diğer tehtidler

- Erythromycin-resistant group A *Streptococcus*
- Clindamycin-resistant group B *Streptococcus*

İzlem listesi

- Azole-resistant *Aspergillus fumigatus* (*A. fumigatus*)
- Drug-resistant *Mycoplasma genitalium* (*M. genitalium*)
- Drug-resistant *Bordetella pertussis* (*B. pertussis*)



2019 –AMR global halk sağlığı sorunu!!!

- Her yıl >2.8 milyon dirençli infeksiyon
- 1.27 milyon ölüm
- 5 milyon ilişkili ölümler
- 4.6 milyar $

World Health Organization

Preventing Antimicrobial Resistance Together

HANDLE ANTIMICROBIALS WITH CARE

Antibiotics
Antivirals
Antifungals
Antiparasitics

- **AMR- İnsan, hayvan, bitki, çevre-tek sağlık –bütün sektörleri ilgilendiriyor**
- **2050 - Antimikrobiyal direnç**
  - 10 milyon ölüm (yıl)
  -100 milyar $

✓ **Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR)**

✓2012 yılında

✓ 30 Avrupa birliği, 26 diğer

- ***Enterococcus faecium***
- ***Staphylococcus aureus***
- ✓***Klebsiella pneumoniae***
- ✓***Acinetobacter spp.***
- ✓***Pseudomonas aeruginosa***
- ✓ ***Escherichia coli***
- ***Streptococcus pneumoniae***

Antimicrobial resistance surveillance in Europe

2023

BOS, Kan izolatları

Bacterial species	Antimicrobial group/agent or specific resistance mechanism	Antimicrobial agent(s)
E. coli	Aminopenicillins	Ampicillin or amoxicillin
	Third-generation cephalosporins	Cefotaxime, ceftriaxone or ceftazidime
	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin, levofloxacin or ofloxacin
	Aminoglycosides	Gentamicin or tobramycin
K. pneumoniae	Third-generation cephalosporins	Cefotaxime, ceftriaxone or ceftazidime
	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin, levofloxacin or ofloxacin
	Aminoglycosides	Gentamicin or tobramycin
P. aeruginosa	Piperacillin-tazobactam	Piperacillin-tazobactam
	Ceftazidime	Ceftazidime
	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Aminoglycosides	Tobramycin
Acinetobacter spp.	Carbapenems	Imipenem or meropenem
	Fluoroquinolones	Ciprofloxacin or levofloxacin
	Aminoglycosides	Gentamicin or tobramycin
S. aureus	MRSA	Cefoxitin or oxacillin[a]
	Fluoroquinolones	Ciprofloxacin, levofloxacin or ofloxacin[b]
	Rifampicin	Rifampicin
S. pneumoniae	Penicillins	Penicillin or oxacillin[c]
	Third-generation cephalosporins	Cefotaxime or ceftriaxone
	Fluoroquinolones	Levofloxacin or moxifloxacin[d]
	Macrolides	Azithromycin, clarithromycin or erythromycin
E. faecalis	High-level aminoglycoside resistance	Gentamicin
E. faecium	Aminopenicillins	Ampicillin or amoxicillin
	High-level aminoglycoside resistance	Gentamicin
	Vancomycin	Vancomycin

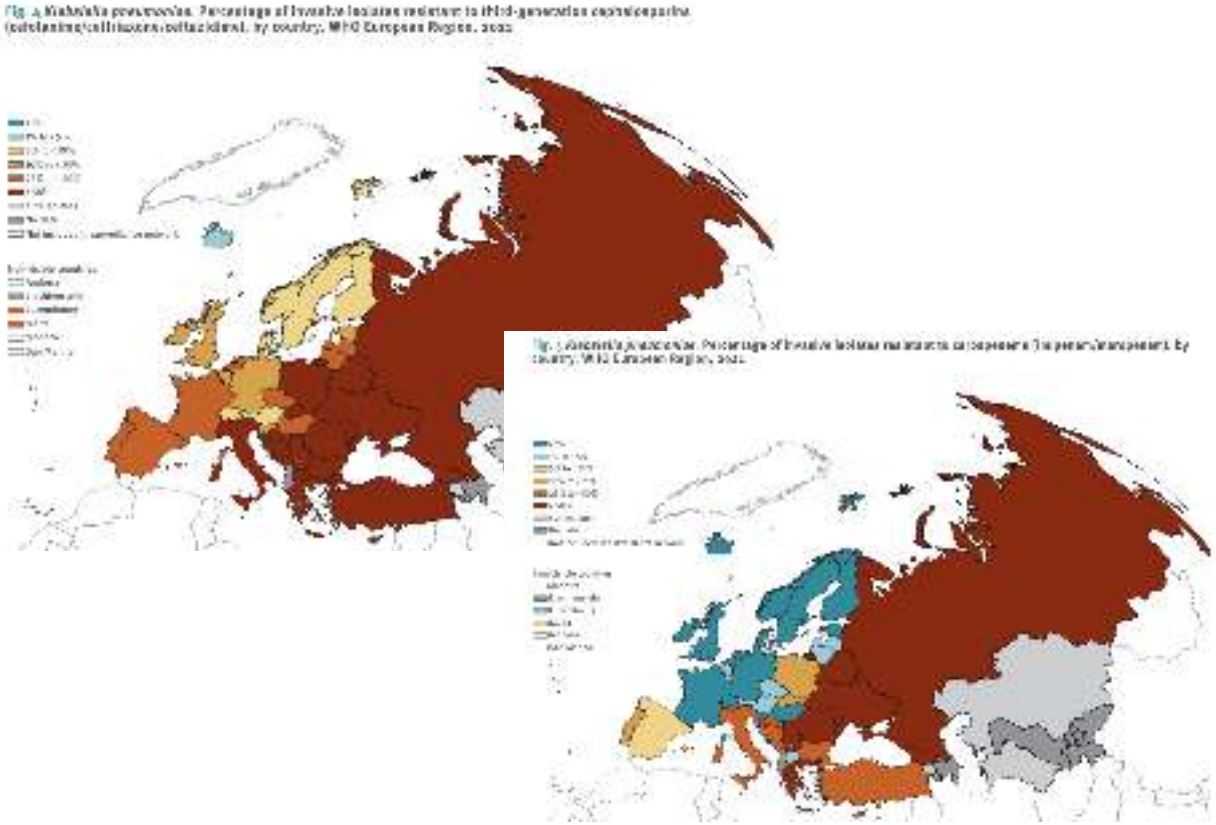


Fig. 7 *Acinetobacter* species. Percentage of invasive isolates with resistance to carbapenems (imipenem/meropenem), by country, WHO European Region, 2023

Türkiye SHİE Etken Dağılımı-2022

ULUSAL
SAĞLIK HİZMETİ İLİŞKİLİ
ENFEKSİYONLAR SÜRVEYANS AĞI
(USHİESA)
ETKEN DAĞILIMI ve ANTİBİYOTİK
DİRENÇ RAPORU 2022

Mikroorganizmalar	Tüm Enfeksiyonlar		Pnömoni		VİP		VİO		ÜSE		Kİ-İYE		KDE		SKİ-KDE		CAE	
	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%	Sayı	%
Tüm mikroorganizmalar	54030	100.0	2786	100.0	8558	100.0	1746	100.0	1608	100.0	7191	100.0	7825	100.0	16824	100.0	3338	100.0
Gram pozitif koklar	6678	12.4	117	4.2	222	2.6	53	3.0	133	8.3	564	7.8	1563	20.0	2753	16.4	706	21.2
S. aureus	1658	3.1	91	3.3	164	1.9	40	2.3	9	0.6	35	0.5	440	5.6	449	2.7	266	8.0
Koagülaz negatif stafilokoklar	1678	3.1	8	0.3	14	0.2	4	0.2	2	0.1	9	0.1	339	4.3	920	5.5	209	6.3
Enterococcus spp	3167	5.9	8	0.3	20	0.2	4	0.2	121	7.5	512	7.1	739	9.4	1345	8.0	215	6.4
Streptococcus spp	131	0.2	10	0.4	19	0.2	4	0.2	1	0.1	5	0.1	30	0.4	25	0.1	14	0.4
Diğer gram (+) koklar	44	0.1	0	0.0	5	0.1	1	0.1	0	0.0	3	0.0	15	0.2	14	0.1	2	0.1
Gram (-) koklar	2	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.0	1	0.0	0	0.0
Gram (+) basiller	148	0.3	23	0.8	40	0.5	4	0.2	0	0.0	1	0.0	11	0.1	30	0.2	20	0.6
Enterobacterales	16951	31.4	895	32.1	2319	27.1	461	26.4	845	52.5	3472	48.3	2058	26.3	4340	25.8	1225	36.7
Citrobacter spp	86	0.2	7	0.3	7	0.1	2	0.1	5	0.3	11	0.2	14	0.2	17	0.1	15	0.4
Enterobacter spp	1025	1.9	63	2.3	130	1.5	15	0.9	38	2.4	186	2.6	123	1.6	254	1.5	120	3.6
Escherichia coli	3197	5.9	103	3.7	186	2.2	33	1.9	313	19.5	1004	14.0	404	5.2	457	2.7	445	13.3
Klebsiella spp	11259	20.8	668	24.0	1820	21.3	378	21.6	445	27.7	2013	28.0	1341	17.1	3195	19.0	536	16.1
Proteus spp	596	1.1	24	0.9	85	1.0	18	1.0	29	1.8	167	2.3	40	0.5	129	0.8	46	1.4
Serratia spp	548	1.0	28	1.0	68	0.8	11	0.6	10	0.6	26	0.4	112	1.4	226	1.3	30	0.9
Diğer Enterobacterales'ler	240	0.4	2	0.1	23	0.3	4	0.2	5	0.3	65	0.9	24	0.3	62	0.4	33	1.0
Non-fermantatif gram (-) bakteriler	27521	50.9	1699	61.0	5894	68.9	1218	69.8	626	38.9	3061	42.6	3524	45.0	7642	45.4	1346	40.3
Acinetobacter spp	12793	23.7	809	29.0	2968	34.7	694	39.7	263	16.4	1086	15.1	1705	21.8	3623	21.5	535	16.0
Pseudomonas spp	13785	25.5	809	29.0	2656	31.0	494	28.3	358	22.3	1954	27.2	1692	21.6	3696	22.0	791	23.7
Stenotrophomonas spp	683	1.3	58	2.1	193	2.3	24	1.4	4	0.2	12	0.2	82	1.0	251	1.5	13	0.4
Burkholderia spp	93	0.2	1	0.0	15	0.2	4	0.2	1	0.1	3	0.0	16	0.2	41	0.2	3	0.1
Haemophilus spp	20	0.0	11	0.4	5	0.1	0	0.0	0	0.0	0	0.0	1	0.0	1	0.0	0	0.0
Diğer non-fermantatif gram negatif basiller	147	0.3	11	0.4	57	0.7	2	0.1	0	0.0	6	0.1	28	0.4	30	0.2	4	0.1

ULUSAL
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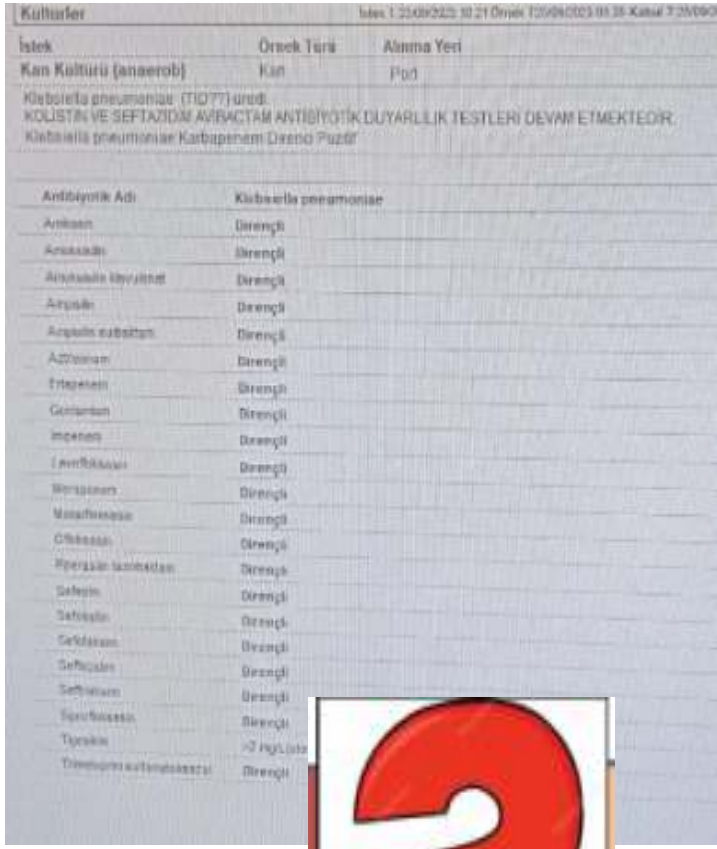
ETKEN DAĞILIMI ve ANTİBİYOTİK
DİRENÇ RAPORU 2022

Klebsiella pneumoniae SHİ KDİ Direnç Dağılımı

Antibiyotik	Mukozal bariyer hasarlı-laboratuvar tarafından doğrulanmış kan dolaşımı enfeksiyonu			Laboratuar tarafından doğrulanmış kan dolaşımı enfeksiyonu			Santral kateter ilişkili kan dolaşımı enfeksiyonu			Toplam		
	Dirençli	Toplam	Dirençli %	Dirençli	Toplam	Dirençli %	Dirençli	Toplam	Dirençli %	Dirençli	Toplam	Dirençli %
Amikasin	21	49	**42.9**	434	1073	**40.4**	1266	2690	**47.1**	1721	3812	**45.1**
Amoksisilin-klavulanat	36	44	**81.8**	694	891	**77.9**	1906	2169	**87.9**	2636	3104	**84.9**
Gentamisin	14	37	**37.8**	480	988	**48.6**	1246	2418	**51.5**	1740	3443	**50.5**
İmipenem	25	37	**67.6**	384	763	**50.3**	1244	1949	**63.8**	1653	2749	**60.1**
Kolistin	6	17	**35.3**	152	488	**31.1**	556	1450	**38.3**	714	1955	**36.5**
Levofloksasin	15	16	**93.8**	337	472	**71.4**	1061	1278	**83.0**	1413	1766	**80.0**
Meropenem	29	44	**65.9**	544	1030	**52.8**	1773	2637	**67.2**	2346	3711	**63.2**
Netilmisin	1	1	**100.0**	19	22	**86.4**	66	75	**88.0**	86	98	**87.8**
Piperasilin-tazobaktam	33	45	**73.3**	797	1070	**74.5**	2167	2591	**83.6**	2997	3706	**80.9**
Sefepim	35	41	**85.4**	792	967	**81.9**	2165	2438	**88.8**	2992	3446	**86.8**
Sefoksitin	7	9	**77.8**	276	390	**70.8**	771	1007	**76.6**	1054	1406	**75.0**
Sefotaksim	6	9	**66.7**	126	167	**75.4**	350	414	**84.5**	482	590	**81.7**
Seftazidim	32	38	**84.2**	866	1063	**81.5**	2301	2613	**88.1**	3199	3714	**86.1**
Seftriakson	34	42	**81.0**	731	899	**81.3**	1905	2159	**88.2**	2670	3100	**86.1**
Siprofloksasin	40	44	**90.9**	710	1020	**69.6**	2027	2536	**79.9**	2777	3600	**77.1**
Tobramisin	2	2	**100.0**	84	105	**80.0**	244	301	**81.1**	330	408	**80.9**

Dirençli infeksiyonlar !

Yeni antibiyotik !

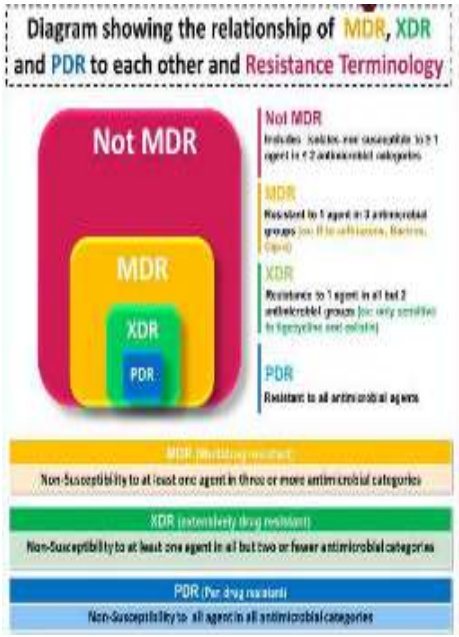


- **Kombinasyon/monoterapi !**
- **Yüksek doz !**
- **Uzamış infüzyon!**

Yanıt!!!

Direnç Tanımları

- **Çok ilaç dirençli-ÇİD (Multidrug−resistant MDR)**
  - ✓ ≥ 3 antibiyotik sınıfında en az birer ajana dirençli
- **Genişlemiş dirençli (Extensively drug resistant-XDR)**
  - ✓ ≤2 antibiyotik sınıfında birer ajan dışındakilere direnç
- **Tam ilaç dirençli-TİD (Pandrug−resistant (PDR)**
  - ✓ Tüm lisanslı antibiyotiklere



> Clin Microbiol Infect. 2012 Mar;18(3):268-81. doi: 10.1111/j.1469-0691.2011.03570.x. Epub 2011 Jul 27.

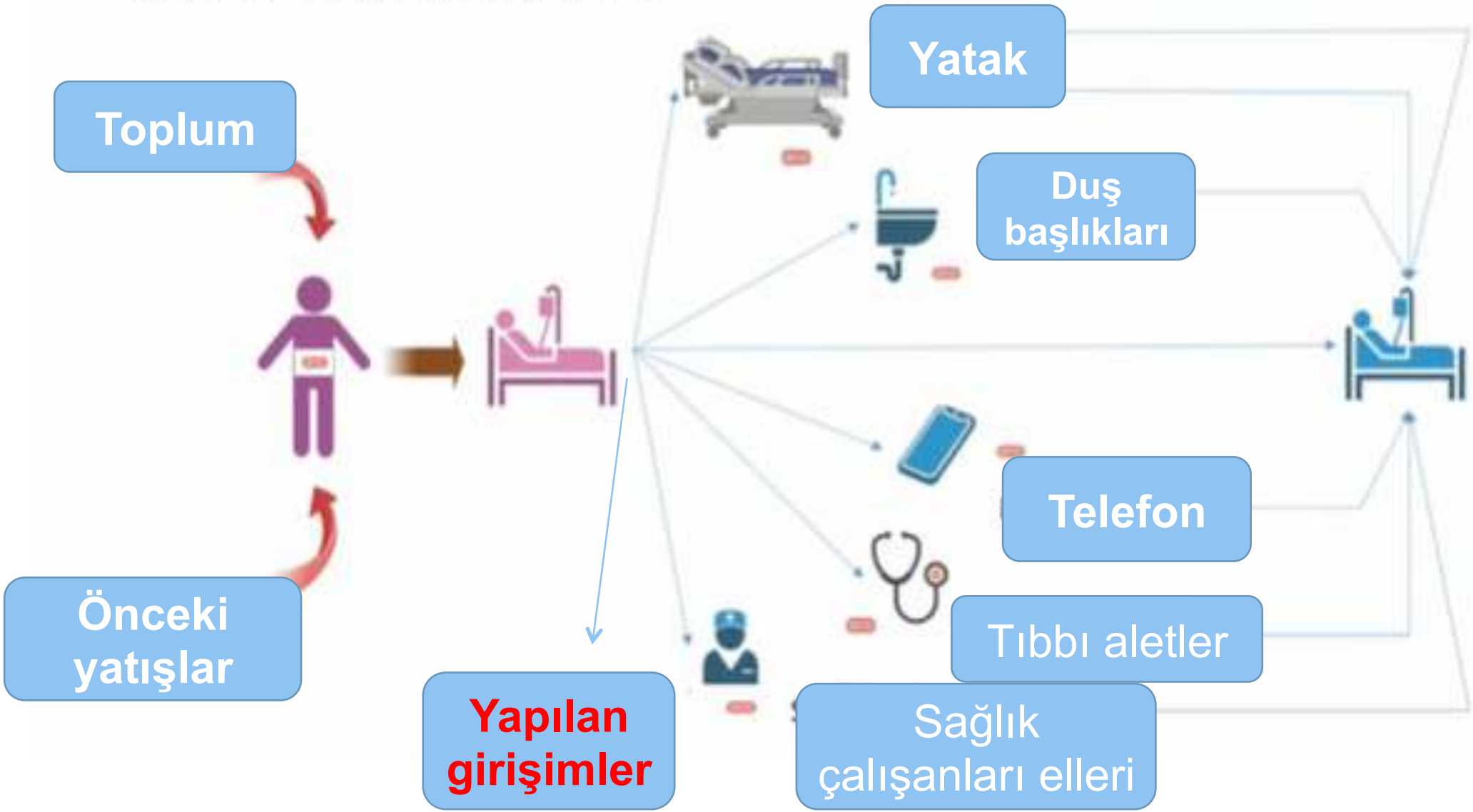
Multidrug−resistant, extensively drug−resistant and pandrug−resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance

A-P Magiorakos [1], A Srinivasan, R B Carey, Y Carmeli, M E Falagas, C G Giske, S Harbarth, J F Hindler, G Kahlmeter, B Olsson-Liljequist, D L Paterson, L B Rice, J Stelling, M J Struelens, A Vatopoulos, J T Weber, D L Monnet

Difficult to treat resitance (DTR)

- **Tüm beta-laktamlar (karbapenemler dahil)**
- **BLİ kombinasyonlar**
- **Florokinolonlar**

Dirençli Bakterilerin Nozokomiyal Bulaş Yolları



Organ Nakli Sonrası Enfeksiyon Zaman Çizelgesi

	0-30 gün	30-180 gün	180 gün ve sonrası
Patojen	Cerrahi komplikasyonlar, nozokomiyal infeksiyonlar, pretransplant kolonizasyonlar, donor-kaynaklı infeksiyonlar, fırsatçı infeksiyon riski düşük	İyatrojenik immunsüpresyon etkisi, yüksek fırsatçı infeksiyon riski	Toplum kaynaklı patojenler, ımmussüpresif tedavi yoğunluğu, rejeksiyon durumu hayat boyu fırsatçı infeksiyon sıklığı
Bakteri	Gram-negatif ve pozitif bakteriler (çoklu ilaç dirençli suşlar dahil) Clostridioides difficile, pretransplant kolonizasyon (Burkholderia cepacia)	Nokardiya, tüberküloz, tüberküloz dışı mikobakteri, nozokomiyal gram-negatif/pozitif bakteri	Streptokoklar, Legionella, Listeria,nozokomiyal bakteriler, hospitalizasyonda bakteriyel fırstaçı infeksyonlar riski çözülmez
Mantar	Kandida, Aspegillus kistik fibroz dışında yaygın değildir	Küfler (Aspergillus, mukormikoz), *Kandida*, *Pneumocystis* daha az yaygın	Kriptokok, enfdemik mikozlar, invazif küf infefksiyonları, Profilaksi almıyorsa *Pneumocystis*, toksoplazmozis
Virüs	Solunum virüsleri, herpesvirüsler rutin antiviral profilaksi iel günümüzde yaygın değildir	Herpesvirüsler (CMV), BK virüs, solunum virüsleri	Kronik viral infeksiyonların reaktivasyonu, EBV, solunum virüsleri, norovirüs, JC virüs
DİĞer	Donör kaynaklı bakteri/mantar/virüs	Profilaksi rejimi ve endemik patojenler (leishmanasis, Chagas hastalığı, gastrointestinal parazitler	T hücre baskılayıcı tedaviler, rejeksiyon tedavileri fırsatçı infeksiyon riskini artırır.

*Fishman JA. Infection in Organ Transplantation.American Journal of Transplantation 2017
*Singh N, Haidar G, Limaye PA. Infections in solid organ recipients. In: Bennett JE, Dolin R. 2020:

Nakil tipine göre en sık saptanan mikroorganizmalar

Organ nakil tipi	CAİ sıklığı (%)	CAİ en sık yol açan patojenler	CAI sebep olan ikincil patojenler
Böbrek	3-11	S. *aureus,* KNS, Enterokok,	Gram-negatif mo. Candida spp.
Pankreas/ Böbrek	9-45	*S.aureus*, KNS, Enterokok,	Gram-negatif mo. (E. *coli, Klebsiella spp.*)
Karaciğer	10-37	Gram-negatif mo. (Enterobacteriacea, Acinetobacter, pseudomonas) *S.aureus*, KNS, Enterokok, *Candida spp.*	
Barsak/ multiviseral	14-53	Sıklıkla polimikrobiyal Gram-negatif mo. *(Pseudomonas,E.coli, Klebsiella spp.)* *Candida spp.*, Anaerop. Enterokok	*S.aureus*, KNS,
Kalp	4-19	KNS MRSA Enterokok	Gram-negatif mo. *(Enterobacteraceae,Pseudomonas, Stenotrophophomonas.)*, Candida spp.
Akciğer	5-19	*Pseudomonas spp.* E. *coli,* *Klebsiella spp.* *Candida spp.* *S.aureus,* Enterokok, KNS *Burcholderia spp.*	*Stenotrophophomonas* *Aspergillus*

Anesi AJ: Perioperative Antibiotic Prophylaxis to Prevent Surgical Site Infections in Solid Organ Transplantation. Transplantation 2018

Antimikrobiyal direnç sorunu

- **Antimikrobiyal direncin artması ;**
  - **İnfeksiyonların kontrol edilememesi ve salgınlar,**
  - **Etkin tedavinin sağlanamaması,**
  - **Kombinasyon, çoklu antibiyotik tedavileri ---yan etkiler,**
  - **Çoklu girişimler,**
  - **Uzayan yatış süreleri,**
  - **Mortalite ve morbidite ,**
  - **Maliyetlerdeki artışlar,**

MDR Gram Negatif İnfeksiyonların Yönetimi

Journal of Antimicrobial Chemotherapy

Treatment of infections caused by multidrug-resistant Gram-negative bacteria: report of the British Society for Antimicrobial Chemotherapy/ Healthcare Infection Society/British Infection Association

ScienceDirect

Review Article

Guidelines for the diagnosis, treatment, prevention and control of infections caused by carbapenem-resistant gram-negative bacil

SPECIAL ISSUE-TRANSPLANT INFECTIOUS DISEASES

Multidrug-resistant Gram-negative bacterial infections in so organ transplant recipients—Guidelines from the American Society of Transplantation Infectious Diseases Community c Practice

Stephanie M. Pouch | Gopi Patel | on behalf of the AST Infectious Diseases Community of Practice

Abstract

These updated guidelines from the Infectious Diseases Community of Practice of the American Society of Transplantation review the diagnosis, prevention, and management of infections due to multidrug-resistant (MDR) Gram-negative bacilli in the pre- and post-transplant period. MDR Gram-negative bacilli, including carbapenem-resistant Enterobacteriaceae, MDR Pseudomonas aeruginosa, and carbapenem-resistant Acinetobacter baumannii, remain a threat to successful organ transplantation. Clinicians now have access to at least five novel agents with activity against some

IMMUNOCOMPROMISED HOSTS INVITED ARTICLE

The Global Challenge of Carbapenem-Resistant Enterobacteriaceae in Transplant Recipients and Patients

Clinical Microbiology and Infection

CMI CLINICAL

Clinical Infectious Diseases

IDSA GUIDELINES

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Infectious Diseases Society of America 2023 Guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections

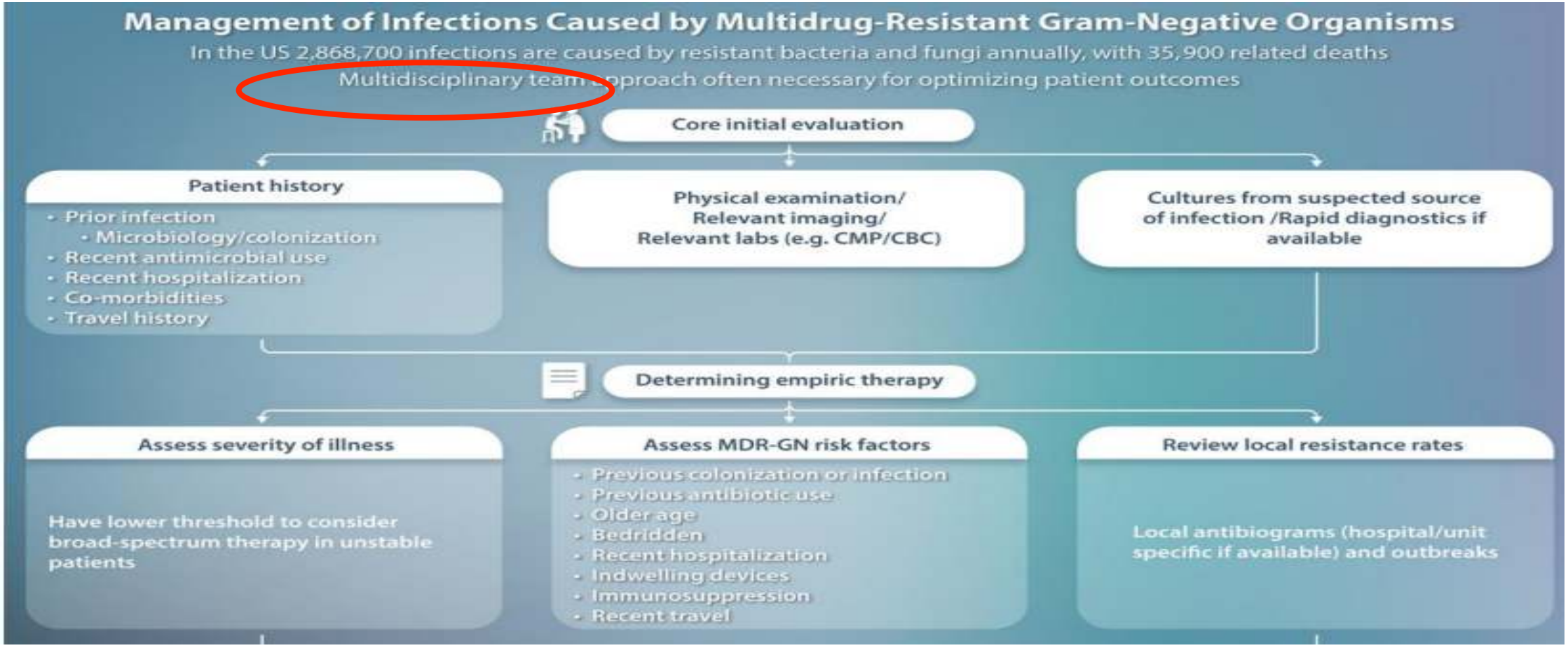
Pranita D. Tamma, Samuel L. Aitken, Robert A. Bonomo, Amy J. Mathers, David van Duin, and Cornelius J. Clancy

Background. The Infectious Diseases Society of America is committed to providing up-to-date guidance on the treatment of antimicrobial-resistant infections. This guidance document focuses on infections caused by extended-spectrum β-lactamase-producing Enterobacterales, AmpC β-lactamase-producing Enterobacterales, carbapenem-resistant Enterobacterales, *Pseudomonas aeruginosa* with difficult-to-treat resistance, carbapenem-resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia*. This updated document replaces previous versions of the guidance document.

Methods. A panel of 6 infectious diseases specialists with expertise in managing antimicrobial-resistant infections formulated questions about the treatment of infections caused by extended-spectrum β-lactamase-producing Enterobacterales, AmpC β-lactamase-producing Enterobacterales, carbapenem-resistant Enterobacterales, *Pseudomonas aeruginosa* with difficult-to-treat resistance, carbapenem-resistant *Acinetobacter baumannii*, and *S. maltophilia*. Because of differences in the epidemiology of resistance and availability of specific anti-infectives internationally, this document focuses on the treatment of infections in the United States.

Results. Preferred and alternative suggested treatment approaches are provided with accompanying rationales, assuming the causative organism has been identified and antibiotic susceptibility results are known. Approaches to empiric treatment, transitioning to oral therapy, duration of therapy, and other management considerations are also discussed briefly. Suggested approaches apply for both adult and pediatric populations, although suggested antibiotic dosages are provided only for adults.

MDR Gram Negatif İnfeksiyonların Yönetimi



Clinical Infectious Diseases
STATE OF THE ART REVIEW

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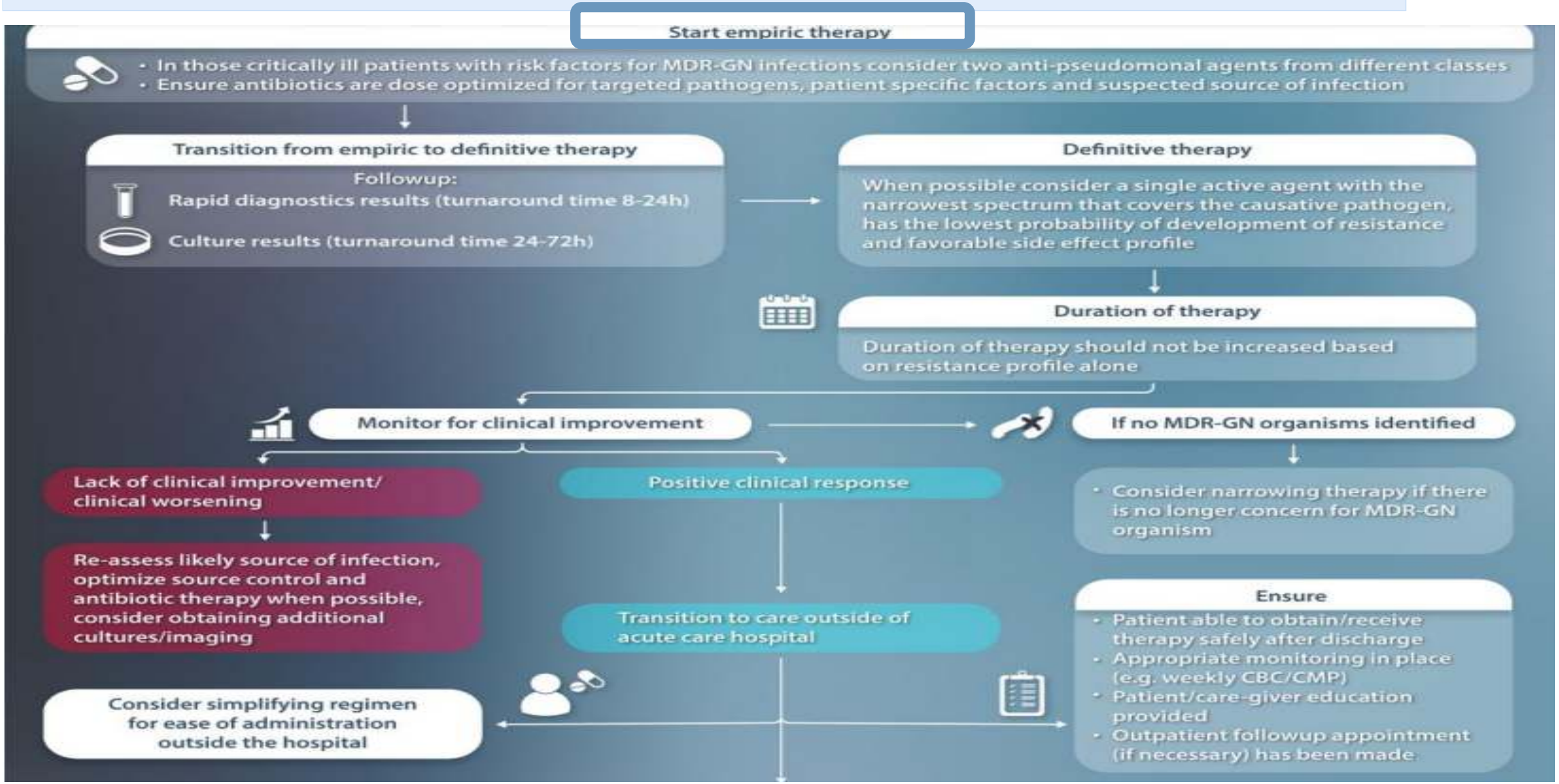
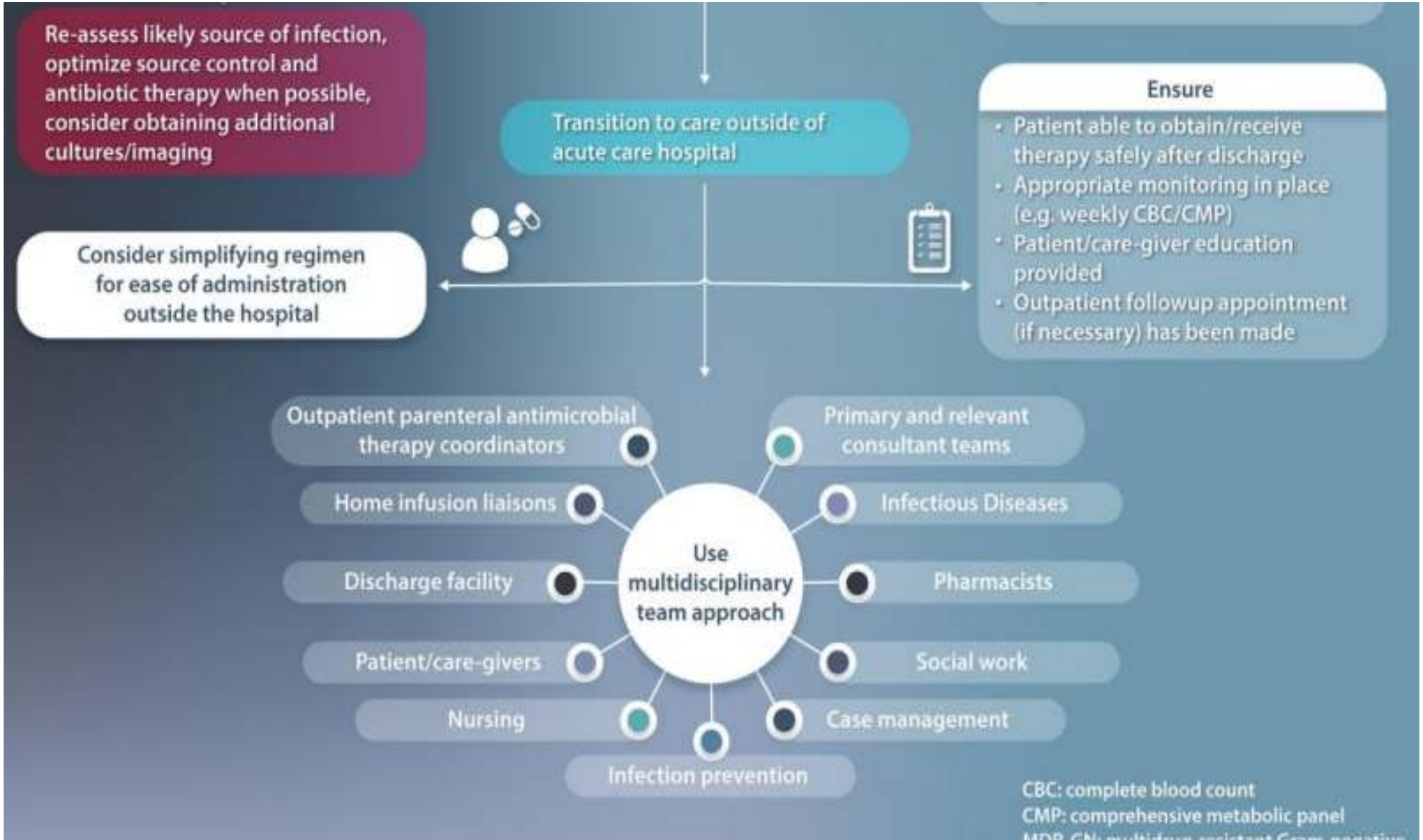
State of the Management of Infections Caused by Multidrug-Resistant Gram-Negative Organisms

2023

MDR Gram Negatif İnfeksiyonların Yönetimi



MDR Gram Negatif İnfeksiyonların Yönetimi



Clinical Microbiology and Infection 28 (2022) 521–547

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Guidelines

European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine)

- **Enterobacterales (3GCephRE),**
- **CR Enterobacterales (CRE),**
- **CR P. aeruginosa (CRPA)**
- **CR A. baumannii(CRAB)**

* **RKÇ/ Gözlemsel çalışmalar/GRADE**

* **Monoterapi/kombinasyon karşılaştırmaları**

Karbapenem Dirençli GNB invitro aktif antibiyotikler

	CRAB	ESBLs	CRPA non-MBL	CRE non-CP	CRE-KPC	CRE-OXA-48	CRE-MBL
New antibiotics							
Ceftolozane-tazobactam	No	Yes	Yes	No	No	No	No
Ceftazidime-avibactam	No	Yes	Yes	+/–	Yes	Yes	No
Meropenem-vaborbactam	No	Yes	No	+/–	Yes	No	No
Imipenem-cilastatin/ relebactam	No	Yes	Yes	+/–	Yes	No	No
Plazomicin	No	Yes	+/–	Yes	Yes	Yes	+/–
Eravacycline	Yes	Yes	No	Yes	Yes	Yes	Yes
Cefiderocol	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Old antibiotics							
Polymyxins	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Aminoglycosides	+/–	+/–	+/–	+/–	+/–	+/–	+/–
Fosfomycin iv	No	Yes	+/–	+/–	+/–	+/–	+/–
Aztreonam	No	No	+/–	No	No	No	+/–
Tigecycline	Yes	Yes	No	Yes	Yes	Yes	Yes
Temocillin	No	Yes	No	No	+/–	No	No

3. Kuşak SP. Dirençli Enterobacterales

-Kan dolaşımı infeksiyonları (KDİ), ciddi enfeksiyonlar- İmipenem, meropenem
-Septik şok yoksa- Ertapenem
-Düşük risk-ciddi olmayan enfeksiyonlar- Piperasilin-tazobaktam, amoksisilin/klavulanik asit, kinolon, cotrimaksazol (kİYE)
-kİYE-Septik şok yoksa -aminoglikozid, IV fosfomisin

*Tigesiklin, sefepim önerilmez
* Sefoperazon-sulbaktam, ampisilin-sulbaktam-yeterli kanıt yok

Karbapenem Dirençli Enterobacterales

-Ciddi enfeksiyonlar,
Meropenem-vaporbaktam veya seftazidim-avibaktam,
-MBL, tüm antibiyotiklere direnç,
Sefiderokol, Meropenem-vaporbaktam ve seftazidim-avibaktam
-kİYE-Septik şok yoksa- invitro etkili ise Aminoglikozid, plazomisin (tigesiklin yerine)

-Tigesiklin-KDİ/HKP/VİP önerilmez,
*Gerekliyse pnömonide yüksek doz verilir

-İmipenem-relebaktam, fosfomisin monoterapisi yeterli kanıt yok

Karbapenem Dirençli Enterobacterales' de Kombinasyon Tedavisi

-CAZ-AVİ, Mem-Vaporbactam, Sefiderokol duyarlı ise- kombinasyon önerilmez

-MBL, yeni ab direnç- Aztreonam+ CAZ/AVİ

-Ciddi infeksiyonlar, yalnızca polimiksin, aminoglikozid, tigesiklin, fosfomisin duyarlı yeni BL/BLİ erişilemiyorsa birden fazla ilaçla tedavi

- MIC<= 8 olmadıkça meropenemli kombinasyonlardan kaçın, yeni BL-BLI kullanılamıyorsa yüksek doz, uzamış infüzyon, kombinasyonda
- Ciddi olmayan hastada, iyi klinik, kaynak kontrolü , bireyselleştirilmiş monoterapiye geçiş

Karbapenem dirençli *Pseudomonas aeruginosa*

-CRPA – DTR-ciddi enf. invitro duyarlı ise Ceftolozane-tazobaktam
(yeni BLBLI CAZ-AVİ, sefiderokol, mem-vaporbaktam yeterli kanıt yok)

-Ciddi infeksiyonlarda Polimiksin, aminoglikozid, fosfomisin, iki invitro etkili ilaç

-Ciddi olmayan, düşük riskli hastada monoterapi

Karbapenem dirençli *Acinetobacter baumanii*

-HAP/VAP Sulbaktam duyarlı ise –Ampisilin-sulbaktam
-Sulbaktam dirençli ise polimiksin, yüksek doz tigesiklin,
-Yüksek riskli hastalarda iki aktif antibiyotik ile kombinasyon- polimiksin, aminoglikozid, tigesiklin, sulbaktam,
-MIC≤ 8 mg/L meropenem yüksek doz, uzamış infüzyon + Kombinasyonda

Journal of Microbiology, Immunology and Infection 55 (2022) 359–386

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Review Article

Recommendations and guidelines for the treatment of infections due to multidrug resistant organisms☆

Cheng Len Sy [a,1], Pao-Yu Chen [b,1], Chun-Wen Cheng [c,1], Ling-Ju Huang [d,x,1], Ching-Hsun Wang [e,1], Tu-Hsuan Chang [f], Yi-Chin Chang [g], Chia-Jung Chang [h], Ing-Moi Hii [i], Yu-Lung Hsu [j], Ya-Li Hu [k], Pi-Lien Hung [l], Chen-Yen Kuo [m], Pei-Chin Lin [n,o], Po-Yen Liu [p], Ching-Lung Lo [q], Shih-Hao Lo [r], Pei-Ju Ting [s], Chien-Fang Tseng [h], Hsiao-Wei Wang [t], Ching-Hsiang Yang [l], Susan Shin-Jung Lee [a,u,*], Yao-Shen Chen [a,u], Yung-Ching Liu [v], Fu-Der Wang [w]

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- CRAB
- DTR-Pa
- CRE
- Optimal tedavi- tedavi süreleri

Karbapenem Dirençli Enterobacterales Tedavisi

Table 3 Recommended treatment options for carbapenem-resistant Enterobacterales (CRE).

Bloodstream infections	Ceftazidime/avibactam 2.5 g IV q8h (2D) Meropenem/vaborbactam[a] 4 g IV q8h (2C) Imipenem/cilastatin/relebactam[a] 1.25 g IV q6h (2C) Polymyxin based combinations[b]: Colistin[c] 5 mg CBA/kg IV loading dose, then 2.5 mg CBA × (1.5 × CrCl + 30) IV q12 h + Tigecycline 100 mg IV loading dose, then 50 mg IV q12 h (2D) or Meropenem[b] 1 g IV q8h by extended infusion (2D)	7–14 days[d]
Complicated urinary tract infections	Ceftazidime/avibactam 2.5 g IV q8h (2D) Meropenem/vaborbactam[a] 4 g IV q8h (2C) Imipenem/cilastatin/relebactam[a] 1.25 g IV q6h (2C) Aminoglycosides: Gentamicin 5–7 mg/kg/day IV QD (2D) or Amikacin dose 15 mg/kg/day IV QD (2D) or Plazomicin[a] 15 mg/kg IV q12h (2D)	5–7 days[d]
Complicated intra-abdominal infections	Ceftazidime/avibactam 2.5 g q8h + metronidazole 500 mg q6h (2D) Imipenem/cilastatin/relebactam[a] 1.25 g IV q6h (2C) Tigecycline 100 mg IV loading dose, then 50 mg IV q12 h (2D)[e] Eravacycline[a] 1 mg/kg IV q12hr (2D) Polymyxin based combinations[b] Colistin[c] 5 mg CBA/kg IV loading dose, then 2.5 mg CBA × (1.5 × CrCl + 30) IV q12 h + Tigecycline 100 mg IV loading dose, then 50 mg IV q12 h (2D) or Meropenem[b] 1 g IV q8h by extended infusion (2D)	5–7 days[d]

[a] Imipenem/cilastatin/relebactam, meropenem/vaborbactam, plazomicin and eravacycline have not been approved by the Taiwan Food and Drug Administration (Jan 2022).
[b] Choice of combination antimicrobial therapy based on susceptibility test is recommended. Extended-infusion of meropenem for 3 h is suggested if meropenem MIC is ≤ 8 mg/L.
[c] One MIU colistin methanesulfonate = 33 mg colistin base activity.
[d] Definite treatment duration should be individualized according to infection sites, source control, the underlying comorbidities and the initial response to therapy.
[e] Combinations of tigecycline with polymyxin or meropenem is suggested in clinically unstable patients.
Abbreviations: CBA: colistin base activity, CrCl: creatinine clearance, g: grams, IV: intravenous, kg: kilograms, L:liters, mg: milligrams, MIU: million international units, q6h: every 6 h, q8h: every 8 h, q12 h: every 12 h, qd: every 24 h.
Recommendations: 1: strong recommendations; 2: weak recommendations.
Level of Evidence: A/High, B/Moderate, C/Low, D/Very low.

Karbapenem dirençli *P. aeruginosa* tedavisi

Table 2 Recommended treatment options for infections due to carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) and difficult-to-treat *P. aeruginosa* (DTR-PA).

Clinical Syndrome	Recommended treatment	Duration
Any clinical syndrome due to CRPA susceptible to other antimicrobial agents	Piperacillin[a] 3—4 g IV q6h (2D) Piperacillin/tazobactam[a] 3.375—4.5 g IV q6h (2D) Ceftazidime[a] 2 g IV q8h (2D) Cefepime[a] 2 g IV q8-12 h (2D) Cefpirome[a] 2 g IV q12 h (2D) Ciprofloxacin 400 mg IV q8h (2D) Levofloxacin 750 mg IV qd (2D) Amikacin[b] 15 mg/kg IV qd (2D)	5—14 days[c]
Any clinical syndrome due to DTR-PA	Colistin[d] monotherapy or combination therapy (2C) Ceftolozane/tazobactam[e,f] 1.5—3 g IV q8h (2C) Ceftazidime/avibactam[e] 2.5 g IV q8h (2C) Imipenem/cilastatin/relebactam[e,g] 1.25 g IV q6h (2C)	5—14 days[c]

[a] Anti-pseudomonal penicillins or cephalosporins combined with aminoglycosides may be considered when the antimicrobial susceptibility testing results are interpreted as susceptible.

[b] Aminoglycoside monotherapy is only indicated for urinary tract infections.

[c] The suggested treatment duration is 5—10 days for complicated urinary tract infection and complicated intra-abdominal infection. A treatment course of 10—14 days is suggested for hospital-acquired or ventilator-associated pneumonia and bloodstream infection. Definitive treatment durations should be individualized according to infection sites, source control, the underlying comorbidities and the initial response to therapy.

[d] Colistin dose: 5 mg CBA/kg IV loading dose, then 2.5 mg CBA × (1.5 × CrCl + 30) IV q12 h. One MIU colistin methanesulfonate = 33 mg colistin base activity.

[e] β-Lactam/β-lactamase inhibitors may be considered when the antimicrobial susceptibility testing results are interpreted as susceptible.

[f] Ceftolozane/tazobactam 3 g (2 g ceftolozane/1 g tazobactam), infused intravenously for 1 h every 8 h, is indicated for hospital-acquired pneumonia or ventilator-associated pneumonia.

[g] Imipenem/cilastatin/relebactam has not been approved by the Taiwan Food and Drug Administration (Jan 2022).

Abbreviations: CBA:colistin base activity, CrCl: creatinine clearance, g: grams, IV: intravenous, kg: kilograms, mg: milligrams, MIU: million international units, q6h: every 6 h, q8h: every 8 h, q12 h: every 12 h, qd: every 24 h.

Recommendations: 1: strong recommendations; 2: weak recommendations.

Level of Evidence: A/High, B/Moderate, C/Low, D/Very low.

Karbapenem dirençli *A. baummanii* tedavisi

Table 1 Recommended treatment options for infections due to carbapenem-resistant *Acinetobacter baumannii*.

Clinical syndrome	Recommended Treatment	Alternative Treatment	Duration
Pneumonia	Colistin[a] 5 mg CBA/kg IV loading dose, then 2.5 mg CBA × (1.5 × CrCl + 30) IV q12 h +/-Imipenem/cilastatin[b] 500 mg IV q6h (2D) or Meropenem[b] 2 g IV q8h (2D) + Adjunctive colistin inhalation[a] 1.25–15 MIU/day IH in 2–3 divided doses (2D)	Sulbactam 6–9 g/day IV in 3 or 4 divided doses (2D)[c] Colistin[a] 5 mg CBA/kg IV loading dose, then 2.5 mg CBA × (1.5 × CrCl + 30) IV q12 h + Tigecycline[d,e] 100 mg IV loading dose, then 50 mg IV q12 h + Sulbactam 6–9 g/day IV in 3 or 4 divided doses (2D)[c]	at least 7 days
Bloodstream infections	Colistin[a] 5 mg CBA/kg IV loading dose, then 2.5 mg CBA × (1.5 × CrCl + 30) IV q12 h +/-Imipenem/cilastatin[b] 500 mg IV q6h (2D) or Meropenem[b] 2 g IV q8h (2D)	Colistin[a] 5 mg CBA/kg IV loading dose, then 2.5 mg CBA × (1.5 × CrCl + 30) IV q12 h + Tigecycline[d] 100 mg IV loading dose, then 50 mg IV q12 h (2D)[c] or Sulbactam 6–9 g/day IV in 3–4 divided doses (2D)[c]	10–14 days

[a] One MIU colistin methanesulfonate = 33 mg colistin base activity. For dosage of inhaled colistin please refer to "Recommendations and guidelines for the treatment of pneumonia in Taiwan". J Microbiol Immunol Infect 2019; 52: 172-99.
[b] Carbapenem: has *in vitro* synergistic benefit if carbapenem MIC ≤32 mg/L. Infusion time suggested to be > 3 h for each dose.
[c] No significant statistical difference on clinical outcomes between the alternative regimens.
[d] Tigecycline combination can be considered if tigecycline MIC ≤2 mg/L.
[e] Tigecycline monotherapy is not recommended for the treatment of pneumonia.

Abbreviations: CBA:colistin base activity, CrCl: creatinine clearance, g: grams, IV: intravenous, IH: inhalation, kg: kilograms, mg: milligrams, MIU: million international units, q6h: every 6 h, q8h: every 8 h, q12 h: every 12 h.
Grade of Recommendations: 1: strong recommendations; 2: weak recommendations.
Level of Evidence: A/High, B/Moderate, C/Low, D/Very low.

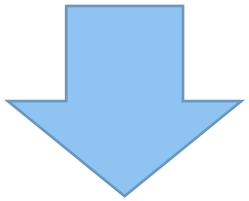
Solid Organ Nakli Hastalarında MDR-GNB Tedavisi

SPECIAL ISSUE-TRANSPLANT INFECTIOUS DISEASES

Clinical TRANSPLANTATION WILEY

Multidrug-resistant Gram-negative bacterial infections in solid organ transplant recipients—Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice

Stephanie M. Pouch[1] | Gopi Patel[2] | on behalf of the AST Infectious Diseases Community of Practice



- ✓ CR *Enterobacteriaceae,*
- ✓ MDR *Pseudomonas aeruginosa,*
- ✓ CR *Acinetobacter baumanni*
- ✓ *Stenotrophomanas maltophilia*

Enterobacteriaceae tedavisi

Organism	Recommendation	Grade
All	Source control should be aggressively pursued	Strong, moderate
	Early Transplant Infectious Disease consultation	Strong, moderate
ESBL-producing Enterobacteriaceae	Carbapenems	Strong, high
Carbapenem-resistant Enterobacteriaceae	Systemic infections:	
	Preferred regimens:	Strong, moderate
	• Ceftazidime/avibactam	Strong, low
	• Meropenem/vaborbactam	Strong, low
	• Ceftazidime/avibactam plus aztreonam for metallo-β-lactamase-producing CRE	
	Alternative regimens:	Strong, moderate
	• Individualized combination regimen with two or more of the following:	Strong, low
	o High-dose, continuous, or extended-infusion carbapenem	
	o Colistin or polymyxin B	
	o Tigecycline	
	• Dual-carbapenem therapy (ertapenem plus doripenem or meropenem)	
	Uncomplicated UTI:	
	• Oral fosfomycin (if susceptible and with follow-up)	Strong, moderate
	• Intravenous aminoglycosides including plazomicin (if susceptible)	Strong, low

Pseudomonas aeruginosa tedavisi

MDR and XDR *Pseudomonas aeruginosa*	Preferred regimens:	
	• High-dose continuous or extended-infusion antipseudomonal β-lactam	Strong, moderate
	• Ceftolozane/tazobactam	Strong, moderate
	• Ceftazidime/avibactam	Strong, moderate
	Alternative regimens:	Strong, moderate
	• Individualized combination regimen with two of the following: o High-dose continuous or extended-infusion antipseudomonal β-lactam o Aminoglycoside o Colistin or polymyxin B o Ciprofloxacin or levofloxacin	
	• Adjunctive aerosolized colistin or tobramycin for pneumonia	Weak, low
PDR *Pseudomonas aeruginosa*	Individualized combination regimen with three of the following:	
	• High-dose continuous or extended-infusion antipseudomonal β-lactam	Strong, moderate
	• Colistin or polymyxin B	
	• Aminoglycosides	
	• Adjunctive aerosolized colistin or tobramycin for pneumonia	Weak, low

CR. Acinetobacter baumanii

Preferred regimen:	
• Combination therapy with a carbapenem plus colistin or polymyxin B	Strong, moderate
Alternate regimens:	
Monotherapy with:	Strong, moderate
• Ampicillin/sulbactam if susceptible[a] (sulbactam dose ≥9 g daily, dose adjusted for creatinine clearance)	Weak, low
• Minocycline	

MDR Stenotrophomanas maltophilia

Preferred regimen:	
• High-dose SXT (15 mg/kg/d trimethoprim, dose adjusted for creatinine clearance)	Strong, moderate
Alternatives (combination therapy if SXT-resistant recommended):	
• Ceftazidime	Strong, low
• Minocycline	Strong, low
• Levofloxacin	Strong, low
• Ceftazidime/avibactam plus aztreonam	Weak, low

Risk factors for infections caused by carbapenem-resistant Enterobacterales: an international matched case-control-control study (EURECA)

www.thelancet.com Vol 57 March, 2023

Önceki CRE ile kolonizasyon, enfeksiyon riskini 6.9 kat artırıyor !

Clinical Microbiology and Infection 25 (2019) 807–817

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Guidelines

ESCMID-EUCIC clinical guidelines on decolonization of multidrug-resistant Gram-negative bacteria carriers

E. Tacconelli [1, 2, *], F. Mazzaferri [2], A.M. de Smet [3], D. Bragantini [2], P. Eggimann [4], B.D. Huttner [5, 6], E.J. Kuijper [7], J.-C. Lucet [8, 9], N.T. Mutters [10, 11], M. Sanguinetti [12], M.J. Schwaber [13, 14], M. Souli [15, 16], J. Torre-Cisneros [17], J.R. Price [18], J. Rodríguez-Baño [19]

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- **Dekolonizasyon önerilmiyor**

- **Hastanede kalış süresi**
- **Mortaliteye etkisiz**

Current Infectious Disease Reports (2022) 24:63–75
https://doi.org/10.1007/s11908-022-00778-1

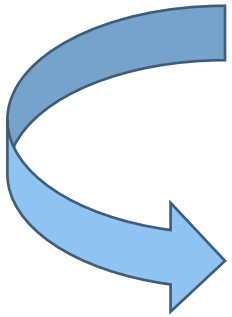
ANTIMICROBIAL DEVELOPMENT AND DRUG RESISTANCE (KC CLAEYS AND J SMITH, SECTION EDITORS)

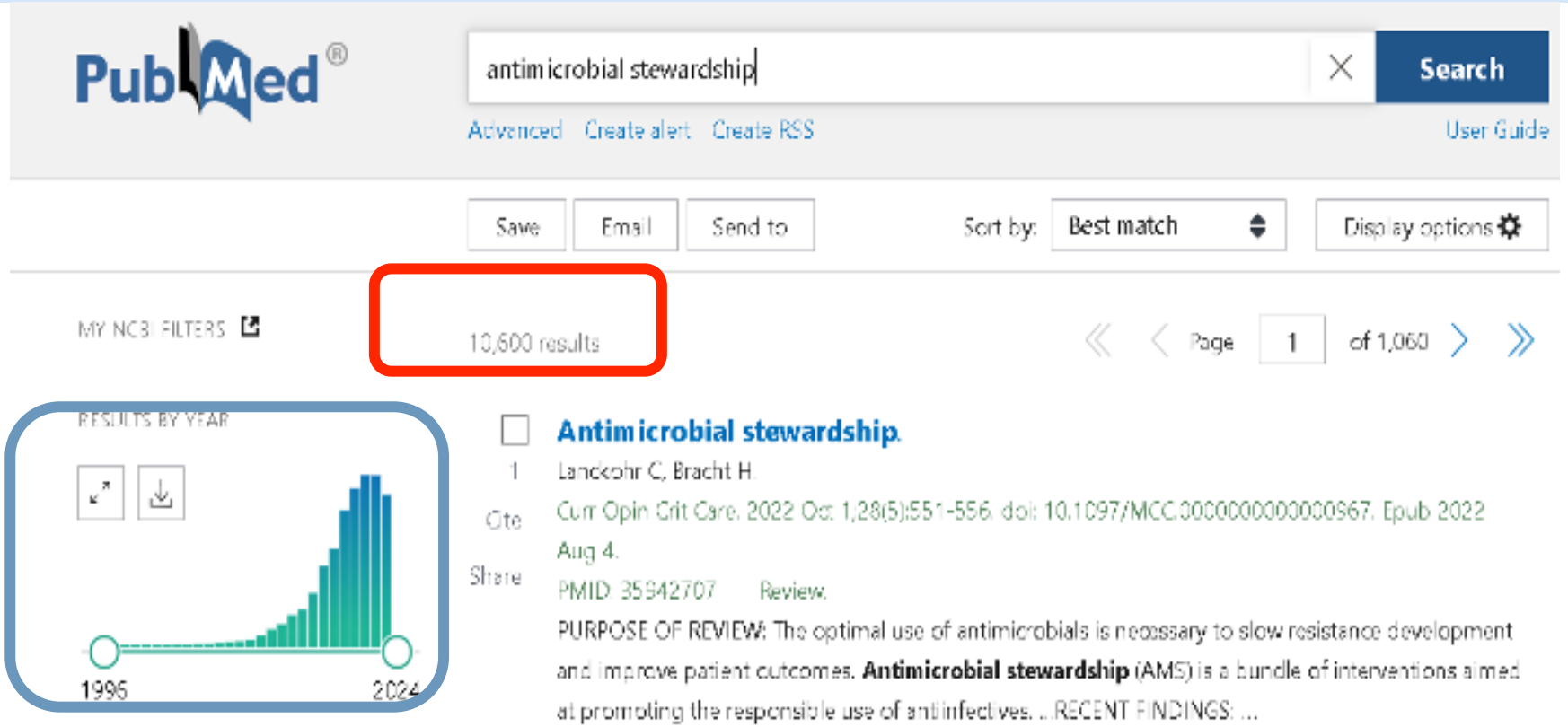
Challenges of Antimicrobial Resistance and Stewardship in Solid Organ Transplant Patients

Miranda So[1,2] · Laura Walti[1]

- Etkili antimikrobiyaller olmadan hastalar güvenli bir şekilde nakil ameliyatı geçiremez!
- İmmunsüpresif tedavi sürdürülemez!
- AMY yapılmalı

Antimikrobiyal Yönetim





Solid organ nakil alıcılarında antimikrobiyal yönetim

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Antimicrobial stewardship in solid organ transplant recipient

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Page 1 of 8

RESULTS BY YEAR

1

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Brazilian perspective: **antimicrobial stewardship** in **solid organ transplant**.

Porto APM, Tavares BM, de Assis DB, Mendes ET, Girão ES, Perdigão Neto LV, Falcão MAP, de Oliveira MS, Freire MP, Guimaraes T, Arantes T, Levin AS, Costa SF.

Transpl Infect Dis. 2022 Oct;24(5):e13874. doi: 10.1111/tid.13874.

PMID: 36254511 Review.

BACKGROUND: The incidence of multidrug resistant organisms (MDROs) infections among **solid organ transplant** (SOT) patients is very high in Brazil. METHODS: This review will discuss **antimicrobial** use and resistance in SOT in Brazil, highlighting the main ...

> Transpl Infect Dis. 2022 Oct;24(5):e13852. doi: 10.1111/tid.13852.

Importance of antimicrobial stewardship in solid organ transplant recipients: An ESCMID perspective

Petros Ioannou [1], Stamatis Karakonstantis [1], Jeroen Schouten [2], Tomislav Kostyanev [3 4], Esmita Charani [5], Vera Vlahovic-Palcevski [6], Diamantis P Kofteridis [1];
Supported by the ESCMID Study Group for Antimicrobial Stewardship - ESGAP [1]

- **Antimikrobiyaller, enfeksiyöz komplikasyon, morbidite/mortalite**
- **Direnç sorunu – AMY önemli**
- **SOTr antimikrobiyallerin uygun başlatılmalı/ sonlandırılmalı,**
- **Yan etki takibi/doz optimizasyonu (FK/ FD)/ terapötik düzey**
- **IV–oral, bakteri, mantar, virüs**

- **En uygun doz/uygulama yolu/en kısa süre/kaynak kontrolü**
- **Biyobelirteçler/yeni moleküler hızlı tanı testler**
- **Antimikrobiyal reçeteleme rasyonel/ optimize/hedefe yönelik tedavi**
- **Yerel reçetelemede AMY uyulması**
- **AMY aktif dahil olunmalı**
- **Denetim-geri bildirim**

Solid Organ Nakil Hastalarında Perioperatif Profilaksi

Organ nakil tipi	IDSA/ASHP/SIS /SHEAkılavuzları	Alternatif yaklaşım	Intraoperatif tekrar dozu	Postoperatif doz	Penisilin allerjisi	Postoperatif süre
Böbrek	Tek 1.kuşak sefalosporin (örn, sefazolin)	Sefazolin 2 gr IV	4 saatde bir	Sefazolin 2 gr 8 saatte bir	Vankomisin veya Klindamisin 900 IV + gentamisin 5mg/kg IV	≤ 24 saat
Pankreas/ Pankreas-böbrek	Tek 1. kuşak sefalosporin (örn, sefazolin)	Ampisilin-sulbaktam 3 gr IV + flukonazol 400 mg IV	2 saatte bir (flukonazol ek doz yok)	Ampisilin-sulbaktam 1.5 gr 6 saatte bir	Vankomisin veya Klindamisin 900 IV + gentamisin 5mg/kg IV ve flukonazol 400 mg IV	Antibakteriyel ≤ 48 saat Antifungal x1 doz
Karaciğer	3. kuşak sefalosporin + ampisilin veya Tek piperasilin-tazobaktam	Ampisilin-sulbaktam 3 gr IV +/- flukonazol 400 mg IVx1	2 saatte bir (flukonazol ek doz yok)	Ampisilin-sulbaktam 1.5 gr 6 saatte bir	Levofloksasin 750 mgIV+ vankomisin +/- flukonazol 400 mg IVx1	Antibakteriyel ≤ 24 saat Antifungal x1 doz
Kalp Öncesinde ventrikül destek cihazlı	Tek 1.kuşak sefalosporin (örn, sefazolin)	Vankomisin + Seftriakson 1 gr IV veya Sefepim 2 gr IV	4 saatde bir	Vankomisin başına kg/GFH Seftriakson 1gr 24 saatte bir Sefepim 2 gr 8 saatte bir	Vankomisin + Levofloksasin 750 mg IV 24 saatte bir	≤ 48 saat
Öncesinde ventrikül destek cihazsız	Tek 1.kuşak sefalosporin (örn, sefazolin)	Vankomisin + Sefazolin	4 saatde bir	Sefazolin 1 gr 6 saatte bir Vankomisin başına kg/GFH	Vankomisin + Levofloksasin 750 mg IV 24 saatte bir	≤ 48 saat
Akciğer	Tek 1.kuşak sefalosporin (örn, sefazolin)	Vankomisin+ Seftriakson 1 gr IV veya Sefepim 2 gr IV	4 saatde bir	Vankomisin başına kg/GFH Sefepim 2 gr 8 saatte bir	Vankomisin + Levofloksasin 750 mg IV 24 saatte bir	≤ 72 saat

Perioperative Antibiotic Prophylaxis to Prevent Surgical Site Infections in Solid Organ Transplantation

Anesi, Judith A. MD[1]; Blumberg, Emily A. MD[1]; Abbo, Lilian M. MD[2]

Author Information

Transplantation 102(1):p 21-34, January 2018. | DOI: 10.1097/TP.0000000000001948

Prevention of infection and optimizing vaccination in the solid organ transplant candidate and recipient

Ryu, HaYoung[a]; Narayanan, Navaneeth[b,c]; Bhatt, Pinki J.[b,c]

Author Information

Current Opinion in Organ Transplantation 26(4):p 445-455, August 2021. | DOI: 10.1097/MOT.0000000000000902

Transplantasyon öncesi tarama

Test	Candidate	Deceased donor	Living donor
Viral			
HIV			
HIV antibody/antigen (fourth generation HIV screening test)	x	x	x
HIV nucleic acid amplification testing (NAT)		x[b]	x[b]
Cytomegalovirus (CMV) IgG antibody	x	x	x
Hepatitis B virus (HBV)			
HBV surface antigen (HBsAg)	x	x	x
HBV core antibody (HBcAb-IgM and IgG, or total core antibody)	x	x	x
HBV surface antibody (HBsAb)	x		
HBV NAT		x[b]	x[b]
Hepatitis C virus (HCV)			
HCV antibody	x	x	x
HCV NAT	x[c]	x	x
Epstein--Barr virus (EBV) antibody (EBV VCA IgG, IgM)	x	x	x
West Nile virus serology or NAT (seasonal)			x
Parasitic			
Toxoplasma IgG antibody	x	x	x
Strongyloides IgG (if from endemic areas)	x	x	x
Trypanosoma cruzi serology (if from endemic areas)	x	x	x
Fungal			
Coccidioides serology (if from endemic areas)	x	x	x
Bacterial			
Syphilis (any of the following)	x	x	x
Fluorescent treponema antibody absorption (FTA-ABS)			
T. pallidum particle agglutination (TPPA)			
T. pallidum enzyme immunoassay (TP-EIA)			
Rapid plasma reagin (RPR)			
Venereal Disease Research Laboratory (VDRL)			
Tuberculosis (any of the following)	x		x
Purified protein derivative (PPD)			
Interferon gamma release assay (IGRA)			
Urine culture		x	
Blood culture		x	

Transplantasyon sonrası profilaksi

Transplanted organ	Organism	Risk factors	Prophylactic agent	Duration
Kidney	*Pneumocystis*	All patients	TMP-SMX[a]	6 months
	Candida	Candiduria	Fluconazole	7–14 days
Pancreas/intestine	*Pneumocystis*	All patients	TMP-SMX	6 months
	Candida	All patients	Fluconazole/Echinocandin	2–4 weeks (4 weeks for small bowel transplant)
Liver	*Pneumocystis*	MELD score >30, ATG, CMV disease, second transplant	TMP-SMX	6 months
	Candida	Antibiotic use >5 days, ICU stay >5 days, yeast colonization, re-transplantation or need for second abdominal surgery, high transfusion requirement, choledochojejunostomy, pancreatitis, posttransplant hemodialysis	Fluconazole/Echinocandin	2–4 weeks
Heart	*Pneumocystis*	All patients	TMP-SMX	12 months or lifelong[b]
	Candida	None		
Lung	*Pneumocystis*	All patients	TMP-SMX	Lifelong
	Aspergillus	All patients, especially if these risk factors are present: pretransplant or posttransplant *Aspergillus* colonization, single-lung transplant, positive intraoperative culture in cystic fibrosis patient	Aerosolized amphotericin B, or voriconazole	4–6 week or lifelong
	Candida	None		

Adapted from Husain *et al.*[15•], Aslam and Rotstein [16•] and Hand [13]. ATG, antithymocyte globulin; CMV, cytomegalovirus; MELD, model for end-stage liver disease; TMP-SMX, trimethoprim-sulfamethoxazole.

[a]TMP-SMX is preferred. However, atovaquone may be used as an alternative for patients also at risk of toxoplasmosis.

[b]Lifelong duration dependent on toxoplasma serostatus.

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Ryu, HeYoung[a]; Narayanan, Navaneeth[b,c]; Bhatt, Pinki J.[b,c]

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Current Opinion in Organ Transplantation 26(4):p 445-455, August 2021. | DOI: 10.1097/MOT.0000000000000903

Nakil sonrası viral profilaksi

Kidney	D+/R−	High	6-month vGCV (preferred), IV GCV or vACV
	R+	Intermediate	3-month vGCV (preferred), IV GCV or vACV
Pancreas and kidney/pancreas	D+/R−	High	3--6-month vGCV (preferred) or IV GCV
	R+	Intermediate	3-month vGCV (preferred) or IV GCV
Liver	D+/R−	High	3–6-month vGCV[b] or IV GCV
	R+	Intermediate	3-month vGCV or IV GCV
Heart	D+/R−	High	3–6-month vGCV (preferred) or IV GCV
	R+	Intermediate	3-month vGCV (preferred) or IV GCV
Lung, heart--lung	D+/R−	High	At least 6–12-month vGCV or IV GCV
	R+	Intermediate	6–12-month vGCV or IV GCV
Intestinal	D+/R−	High	6-month vGCV or IV GCV
	R+	High	3-month vGCV or IV GCV
Composite tissue allograft	D+/R−	High	6-month vGCV or IV GCV
	R+	High	3-month vGCV or IV GCV
All	D−/R−	Low	Monitor for clinical symptoms; consider antiviral prophylaxis against other herpes infections

Adapted with permission from Razonable and Humar [18]. vGCV, valganciclovir; IV GCV, intravenous ganciclovir; vACV, valacyclovir; TMP-SMX, trimethoprim-sulfamethoxazole.

[a]Alternate therapy, such as preemptive therapy can be considered in kidney (D+/R−, R+), pancreas and kidney/pancreas (D+/R−, R+), liver (D+/R−, R+), and heart (D+/R−, R+). Preemptive therapy is not recommended for lung and heart--lung recipients and is less preferred for intestinal and composite tissue allograft recipients.

[b]Valganciclovir use in liver recipients is not US FDA-approved because of high rate of tissue-invasive disease; however, experts still recommend its use for CMV prophylaxis in liver recipients.

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Solid organ nakil alıcılarında aşılama

Vaccine	Inactivated (i)/Live-attenuated (LA)	Pretransplant		Posttransplant	
		Pediatric	Adult	Pediatric	Adult
Influenza	LA[a]	Yes/Yes	Yes/Yes	Yes/No	Yes/No
Hepatitis A[b]	I	Yes[j]	Yes[j]	Yes[j]	Yes[j]
Hepatitis B	I	Yes[j]	Yes[j]	Yes[j]	Yes[j]
Pertussis	I	Yes	Yes[m]	Yes	Yes[m]
Diphtheria	I	Yes	Yes[m]	Yes	Yes[m]
Tetanus	I	Yes[j]	Yes	Yes[j]	Yes
Inactivated polio vaccine	I	Yes	Yes	Yes	Yes
Haemophilus influenza type B[c]	I	Yes[j]	Yes[j]	Yes[j]	Yes[j]
Streptococcus pneumoniae					
Protein-conjugated	I	Yes	Yes	Yes	Yes
Polysaccharide	I	Yes	Yes	Yes	Yes
Neisseria meningitides[d]					
Serogroups ACYW	I	Yes	Yes	Yes	Yes
Serogroup B[e]	I	Yes	Yes	Yes	Yes
Human papillomavirus	I	Yes	Yes	Yes	Yes
Rabies[f]	I	Yes[j]	Yes[j]	Yes[j]	Yes[j]
Varicella					
Live-attenuated[g] (Varivax)	LA	Yes[j]	Yes[j]	No[n]	No[n]
Subunit (Shingrix)	I	-	Yes	-	Yes
Rotavirus	LA	Yes	-	No	-
Measles/mumps/rubella (MMR)	LA	Yes[j]	Yes[j]	No[n]	No[n]
BCG[h]	LA	Yes	Yes	No	No
Smallpox[k]	LA	No	No	No	No
Anthrax	I	No	No	No	No

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Alıcı Kolonizasyon/Enfeksiyon

- ✓ Perioperatif antibiyotik rejimi bilinen alıcının kolonizanların kapsanmalı !
- ✓ Alıcı aktif bir enfeksiyon nedeniyle tedavi görüyorsa, bu tedaviye ameliyathanede ve ameliyat sonrası başlangıçta planlandığı gibi devam edilmelidir !

Review > Transpl Infect Dis. 2022 Oct;24(5):e13957. doi: 10.1111/tid.13957.

Machine learning, antimicrobial stewardship, and solid organ transplantation: Is this the future?

Yousra Kherabi [1], Jonathan Messika [2], Nathan Peiffer-Smadja [1 3]

Makine öğrenmesi

- ✓ **SOTr bulaşıcı komplikasyonların tahminini**
- ✓ **Bulaşıcı hastalıkların tanı ve tedavisi**
- ✓ **Antimikrobiyal direncin bireysel tahmini**
- ✓ **Immünsüpresif ilaçlarla etkileşim**
- ✓ **uygun antimikrobiyal doz seçimi**

- **SOT'da MÖ için büyük klinik veritabanlarının geliştirilmesi zor**
- **Literatür az**

Ülkemizden

flora

DERLEME/REVIEW

FLORA 2024;29(1):1-24 • doi: 10.5578/flora.2024011051

Dirençli Gram-Negatif Bakteri İnfeksiyonlarının Yönetiminde Sık Karşılaşılan Sorunlar ve Çözüm Önerileri: Klinik Pratiğe Yönelik Uzman Görüşü

Common Problems and Solutions in the Management of Resistant Gram-Negative Bacterial Infections: Expert Opinion on Clinical Practice

Şua SÜMER[1], Özlem KURT AZAP[2], Gökhan AYGÜN[3], Halis AKALIN[4], Murat AKOVA[5], İftihar KÖKSAL[6]

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Makale atfı: *Sümer Ş, Kurt Azap Ö, Aygün G, Akalın H, Akova M, Köksal İ. Dirençli gram-negatif bakteri infeksiyonlarının yönetiminde sık karşılaşılan sorunlar ve çözüm önerileri: Klinik pratiğe yönelik uzman görüşü. FLORA 2024;29(1):1-24.*

KLİMİK TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI DERNEĞİ

Bilimle Sağlıkla 37.YIL

Dirençli Gram Negatif Çomak İnfeksiyonları Tanı ve Tedavi Rehberi
Mayıs 2023-Aralık 2024
40 panelist

> Exp Clin Transplant. 2024 Jan;22(Suppl 1):153-159. doi: 10.6002/ect.MESOT2023.O38.

An Emerging Issue: Carbapenem-Resistant Enterobacteriaceae in Solid-Organ Transplantation

Tuğba Yanık Yalçın [1], Nuran Sarı, Çağla Sarıkaş, Çiğdem Erol, Özlem Azap, Hande Arslan, Mehmet Haberal

Affiliations + expand

PMID: 38385389 DOI: 10.6002/ect.MESOT2023.O38

Free article

Sonuç olarak

-Hastalığın doğru tanısı (kolonizasyon-kontaminasyon ayrımı)

-Ciddi enfeksiyonlarda kombinasyon, yüksek doz, uzamış infüzyon

-En düşük MİK olan tercih, de-eskalasyon, ardışık/oral tedavi,

-Hasta bazlı karar

-Multidisipliner Antimikrobiyal yönetim (AMY)

-Lokal sürveyans verileri

-Tanı ve tedavi kılavuzları

-Donor ve alıcı tarama sonuçları takibi

-Preop bağışıklama,

-Uygun preop-postoperatif profilaksi,

-İnfeksiyon/ odak kontrolü

Atina Akademisi, Sokrates Ödülü
16 Nisan 2024

TEŞEKKÜRLER