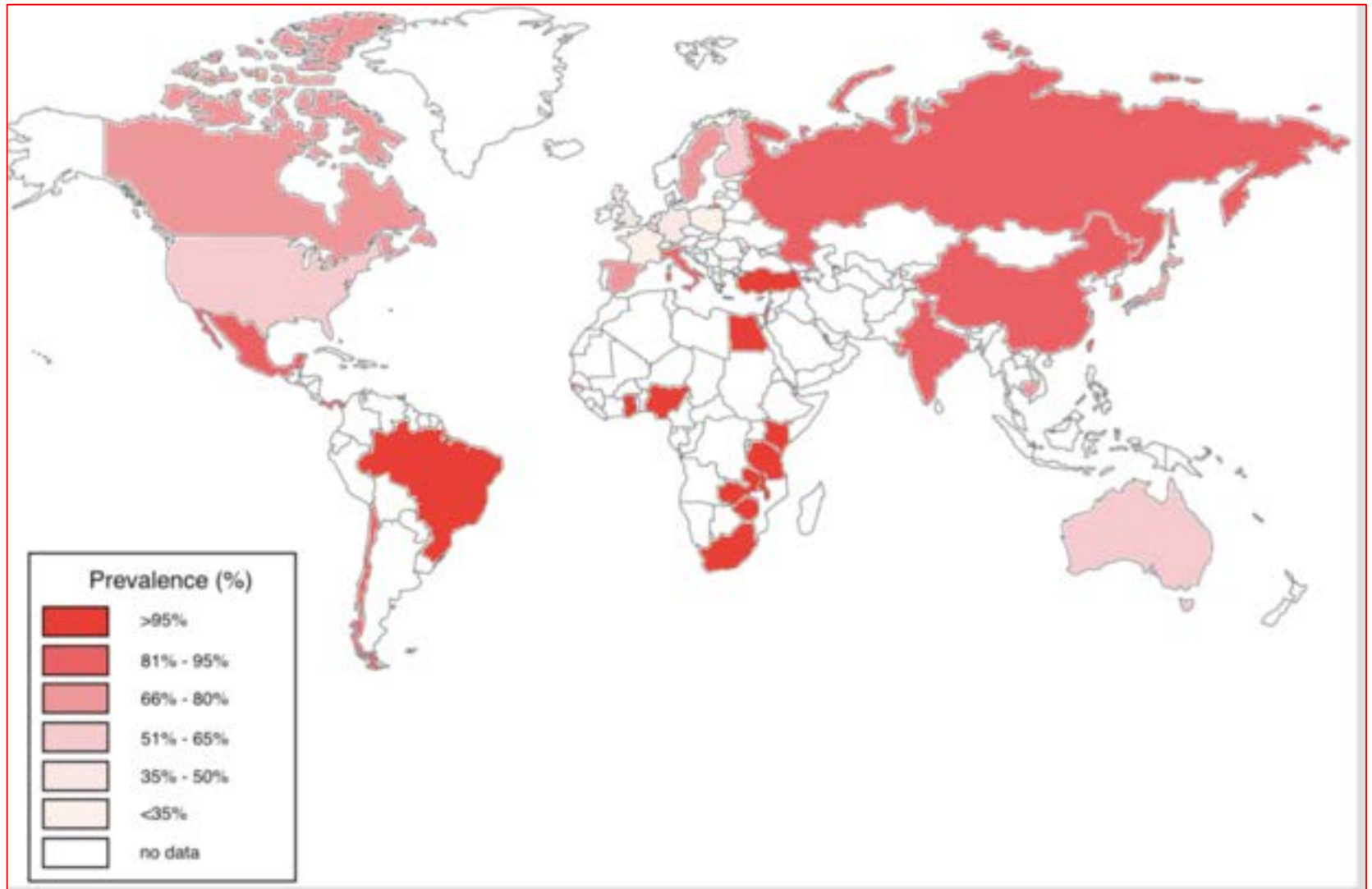


ALLO-HKHN SONRASI CMV
ENFEKSİYONU :

HÜCRESEL TEDAVİ Mİ,
İLAÇ TEDAVİSİ Mİ?

Dr.Sinem Civriz Bozdağ

CMV seroprevelansı yüksektir..



Early cytomegalovirus reactivation remains associated with increased transplant-related mortality in the current era: a CIBMTR analysis

Pierre Teira,^{1,*} Minoo Battiwalla,^{2,*} Muthalagu Ramanathan,^{3,*} A. John Barrett,^{2,*} Kwang Woo Ahn,^{4,5} Min Chen,⁴ Jaime S. Green,⁶ Ayman Saad,⁷ Joseph H. Antin,⁸ Bipin N. Savani,⁹ Hillard M. Lazarus,¹⁰ Matthew Seftel,¹¹ Wael Saber,⁴ David Marks,¹² Mahmoud Aljurf,¹³ Maxim Norkin,¹⁴ John R. Wingard,¹⁴ Caroline A. Lindemans,¹⁵ Michael Boeckh,¹⁶ Marcie L. Riches,¹⁷ and Jeffery J. Auletta¹⁸

Key Points

- Cytomegalovirus after bone marrow transplantation remains associated with lower survival but not prevention of leukemia relapse.

Single-center studies have reported an association between early (before day 100) cytomegalovirus (CMV) reactivation and decreased incidence of relapse for acute myeloid leukemia (AML) following allogeneic hematopoietic cell transplantation. To substantiate these preliminary findings, the Center for International Blood and Marrow Transplant Research (CIBMTR) Database was interrogated to analyze the impact of CMV reactivation on hematologic disease relapse in the current era. Data from 9469 patients transplanted with bone marrow or peripheral blood between 2003 and 2010 were analyzed according to 4 disease categories: AML (n = 5310); acute lymphoblastic leukemia (ALL, n = 1883); chronic

myeloid leukemia (CML, n = 1079); and myelodysplastic syndrome (MDS, n = 1197). Median time to initial CMV reactivation was 41 days (range, 1-362 days). CMV reactivation had no preventive effect on hematologic disease relapse irrespective of diagnosis. Moreover, CMV reactivation was associated with higher nonrelapse mortality [relative risk [RR] among disease categories ranged from 1.61 to 1.95 and P values from .0002 to <.0001; 95% confidence interval [CI], 1.14-2.61). As a result, CMV reactivation was associated with lower overall survival for AML (RR = 1.27; 95% CI, 1.17-1.38; P<.0001), ALL (RR = 1.46; 95% CI, 1.25-1.71; P<.0001), CML (RR = 1.49; 95% CI, 1.19-1.88; P = .0005), and MDS (RR = 1.31; 95% CI, 1.09-1.57; P = .003). In conclusion, CMV reactivation continues to remain a risk factor for poor posttransplant outcomes and does not seem to confer protection against hematologic disease relapse. (*Blood*. 2016;127(20):2427-2438)

CMV infeksiyonu

- CMV izolasyonu ya da viral protein/nükleik asitin vücutta herhangi bir sıvı veya dokuda saptanması

-prim CMV infeksiyonu

saptanması

-rekür CMV infeksiyonu

doküman en az 4

haftadır virus saptanmayan birinde tekrar infeksiyon saptanması

**APKHN sonrası CMV
infeksiyonu %30-50**

Endojen;latent reaktivasyon

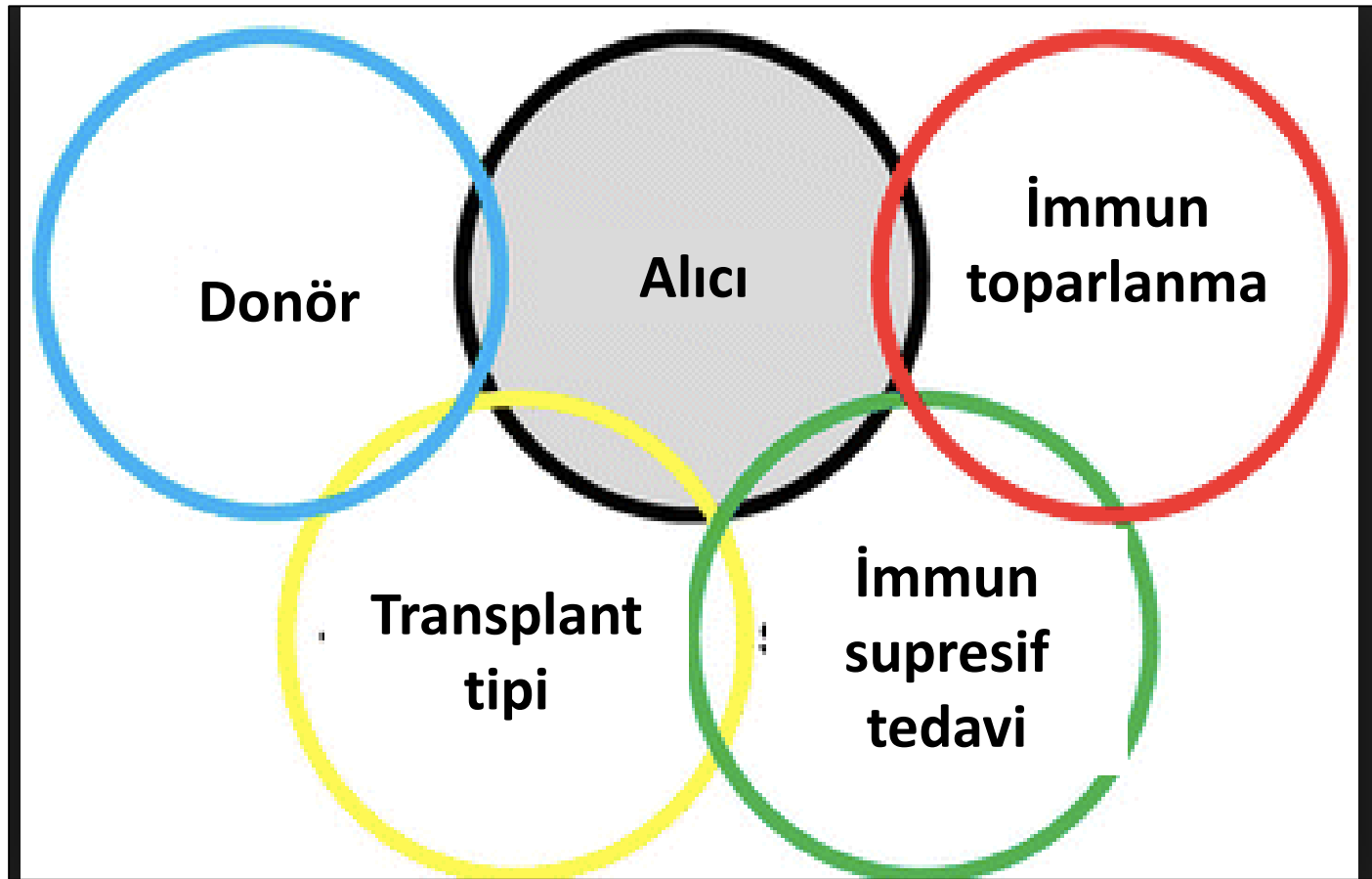
Ekzojen:reinfeksiyon

CMV hastalığı

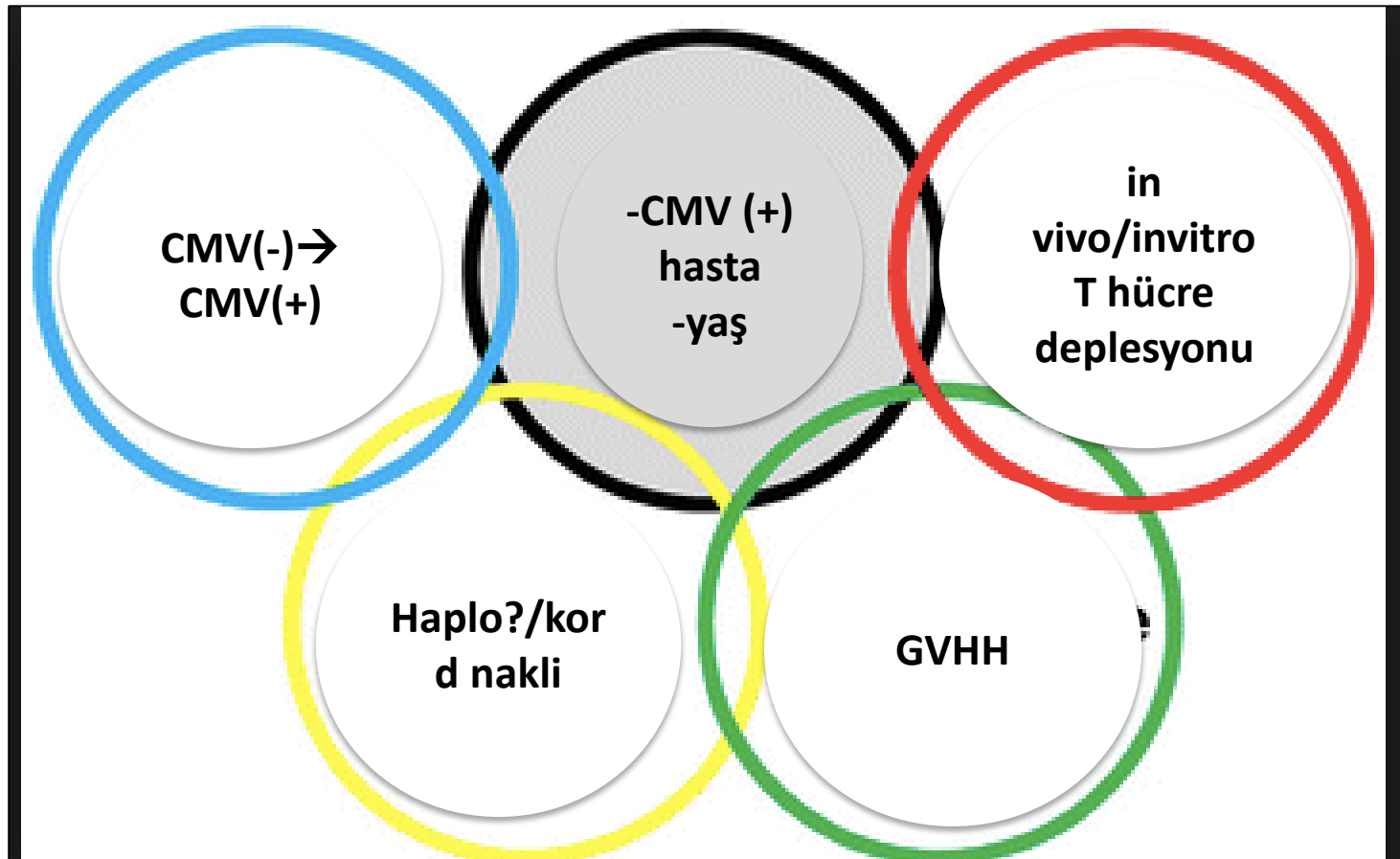
Disease	Proven	Probable	Possible
Pneumonia	Yes	Yes	Yes
Gastrointestinal diseases	Yes	Yes	Yes
Haemolytic anaemia	Yes	Yes	Yes
Recurrent fever	Yes	Yes	Yes
Encephalopathy	Yes	Yes	Yes
Nephritis	Yes	Yes	Yes
Cystitis	Yes	No	No
Myocarditis	Yes	No	No
Pancreatitis	Yes	No	No
Other end-organ diseases	Yes	No	No
Syndrome	No	Yes	No

**APKHN sonrası CMV
hastalığı %1-5**

Kimde risk daha fazla?



Kimde risk daha fazla?



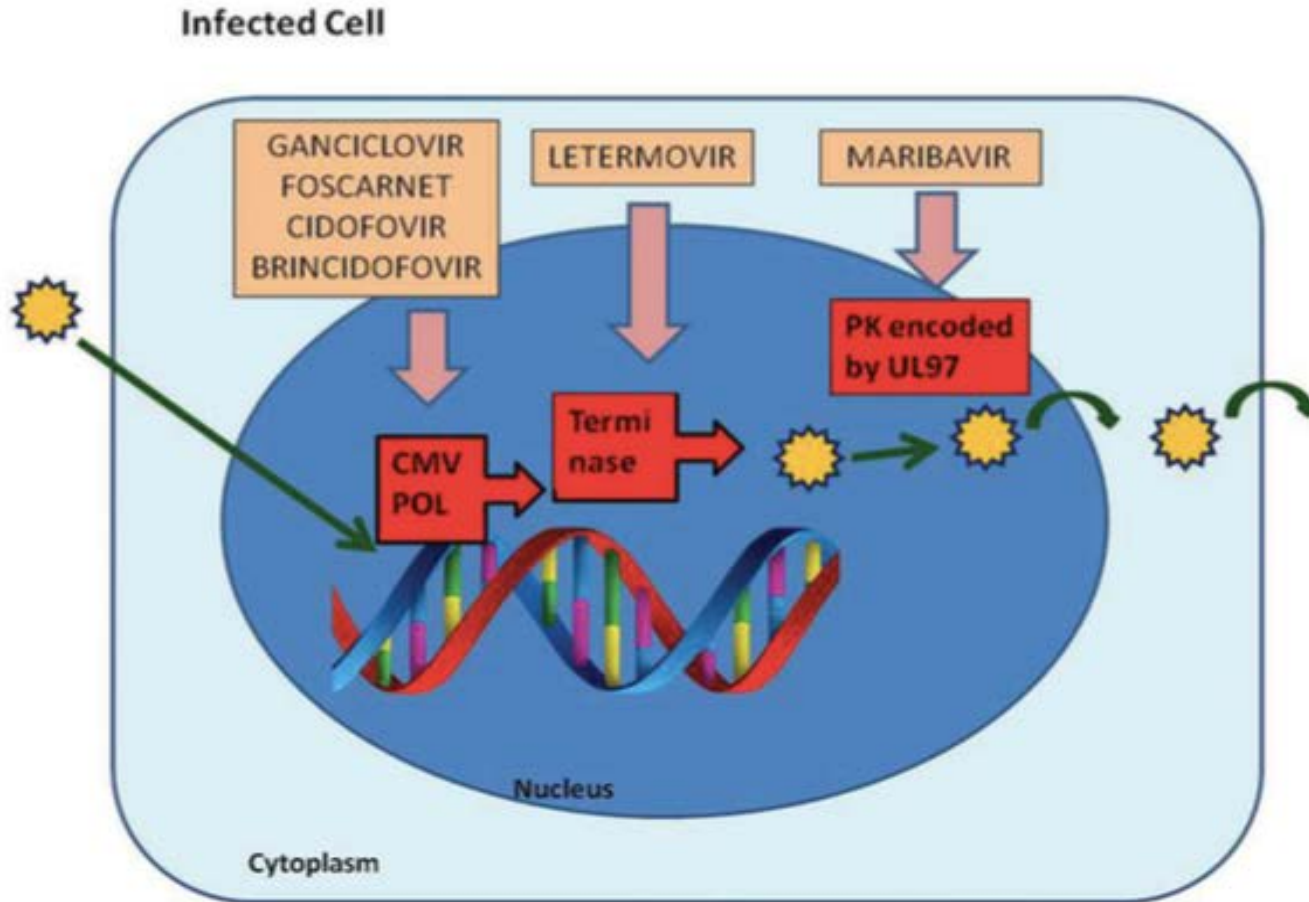
PRE-EMPTİF TEDAVİ

Pre-emptif tedavi

- İlk 100 gün hafada bir CMV monitorizasyon
- PCR,pp65 ag
- Viral yük →cut off??
- En az 2 hafta,viral yüke göre değişir
- 2 kez negatif sonuç elde edilmeli

- SORUN:
 - viremi olmadan hastalık
 - 'escape'infeksiyonlar

CMV infeksiyonu tedavisi



Gansiklovir

- 2x 5 mg/kg/gün en az 2 hafta(indüksiyon)→5 mg/kg/gün 1-2 hafta(idame) veya aynı doz devam
- Daha düşük doz etkili??
- %30 myelotoksisite
- Direnç→UL97 ve UL54 genleri
- İlaç düzeyi takip edilebilir

Boeckh M,BBMT 2015,Emery V,Br J hematol 2013

Park SY,Jantimicrob Hematol 2012,Ljungman P,BMT 1998

Gohring G,J Clin Virol 2013

Valgansiklovir

- Gansiklovir esteri
- 900 mg BID → idame çalışması yok
- Benzer etkinlik
- Benzer güvenlik profili

Chawla JS, Trans Infect Dis 2012
Barkam J, BMR 2012

Foskarnet

- Gansiklovir ile benzer etkinlik
- 2.basamak tedavi
- Gansiklovir ile kombinasyon?
- 60 mg/kg BID →idame çalışması yok
- Myelotoksisite gelişmez
- Nefrotoksisite,elektrolit bozuklukları olur
- Direnç→UL54 geni

Sidofovir

- Nükleotid analogu
- Parenteral tedavi
- Hem inf. hem de hastalıkta etkinliği kanıtli
- Retrospektif çalışma;26/47 CMV tedavi dirençli APKHN hastasında ortalama 22 günde yanıt elde edildi.
- 3-5 mg/kg/gün
- Nefrotoksisite, okuler ve GIS yan etkileri var
- Direnç→UL54 geni

ECIL 7

-ilk basamak-

- CMV nükleik asit veya antijen yöntemi ile preemptif tedavi (AI)
- Gansiklovir veya foskarnet (AI)
- Valganciclovir iv gansiklovir veya foskarnet yerine kullanılabilir (GIS GVHD dışında); (Allu)
- Gansiklovir+Foskarnet (DIII)
- İlaç seçimi HKHN sonrası döneme,toksisiteye ve daha önceki antiviral kullanımına bağlıdır.

CMV antiviral direnç

- Genotipik direnç → UL97 ve UL54 mutasyonları
- Fenotipik direnç
- Klinik direnç
- Tedavide en az 3 gün gecikme viral yükte artışa sebep olabilir.
- Viral yükte 2 hafta ara ile 1log10 artış
- Viral yükte en az 3 haftaya rağmen >1 log 10 düşme olmaması
- CMV hastalığı ve 2 hafta tedaviye rağmen semptomların kötüleşmesi

ECIL 7

-2.basamak-

- Ganciclovir/valganciclovir veya foscarnet (AIIu)
- Sidofovir 2.veya 3.basamak olabilir –BFT dikkat- (BIIu).
- Gansiklovir+foskarnet kombinasyon 2.veya 3. basamak olabilir (CIIu)
- İmmunsupresyon azaltılmalı(BIII)
- Gelişmekte olan ilaçlar ile ilgili öneri yok.
- Leflunomid veya artesunate mevcut ilaçlara dirençlilerde düşünülebilir (CIII)
- i.v Ig önerilmez (DIII)

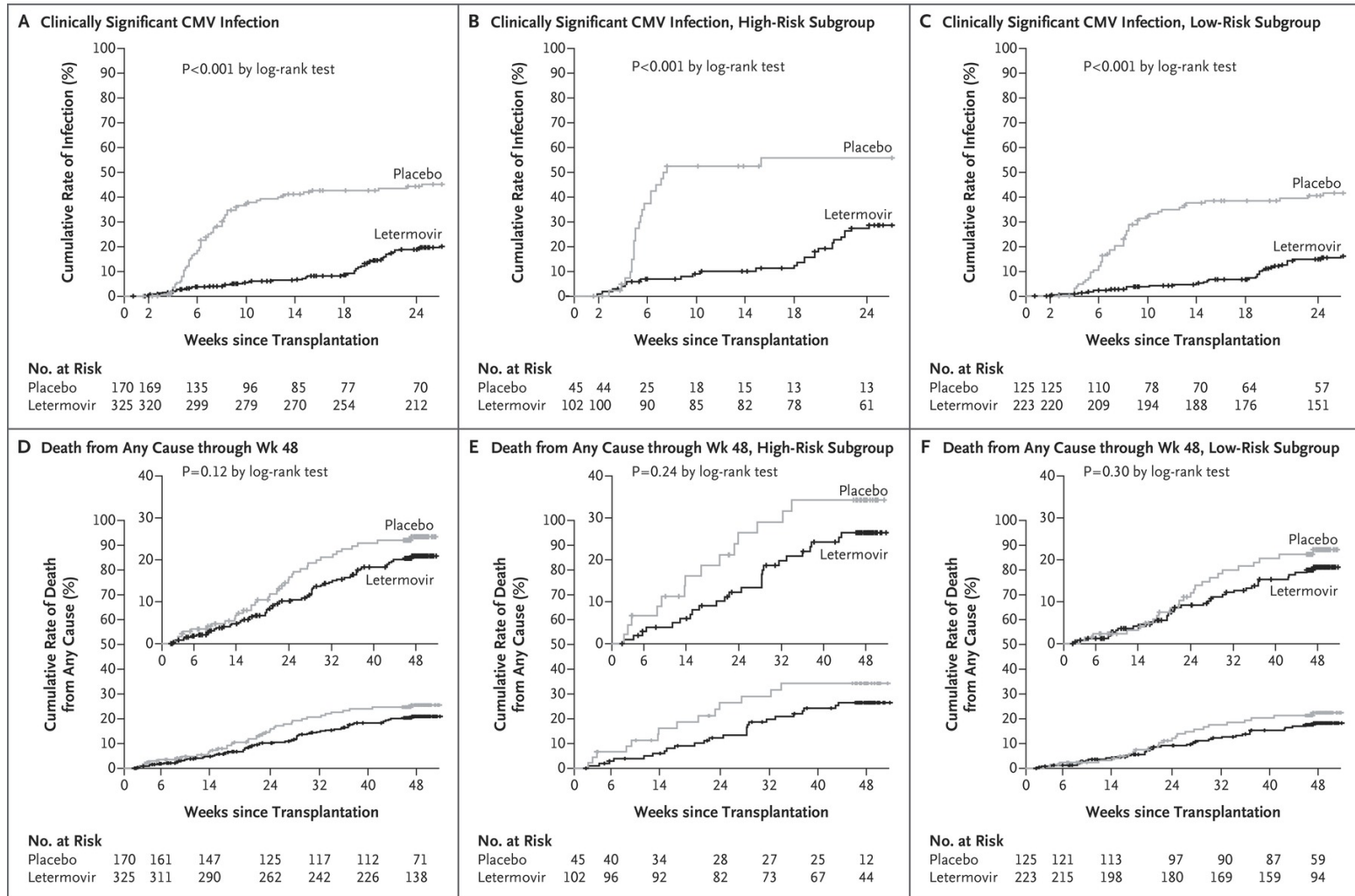
**YENİ AJANLARIN TEDAVİDE YERİ
VAR MI?**

Letermovir

- Terminaz aktivitesini inhibe eder→virion oluşumunu engeller
- 240 mg ile en iyi etkinlik
- Multidirençli CMV suşlarına etkin
- Çarpaz direnç yok
- Tedavide onaylı değil;**böbrek nakli** hastalarında viral yükte azalma
- Profilakside etkisi kanıtlandı.

Letermovir

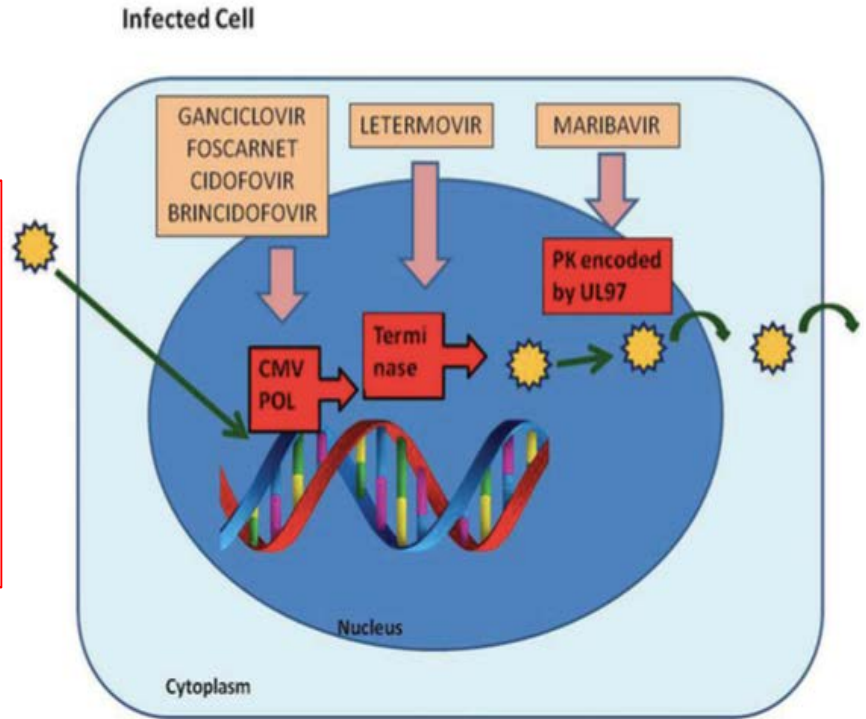
-profilaksi-



Marty F, NEJM 2017

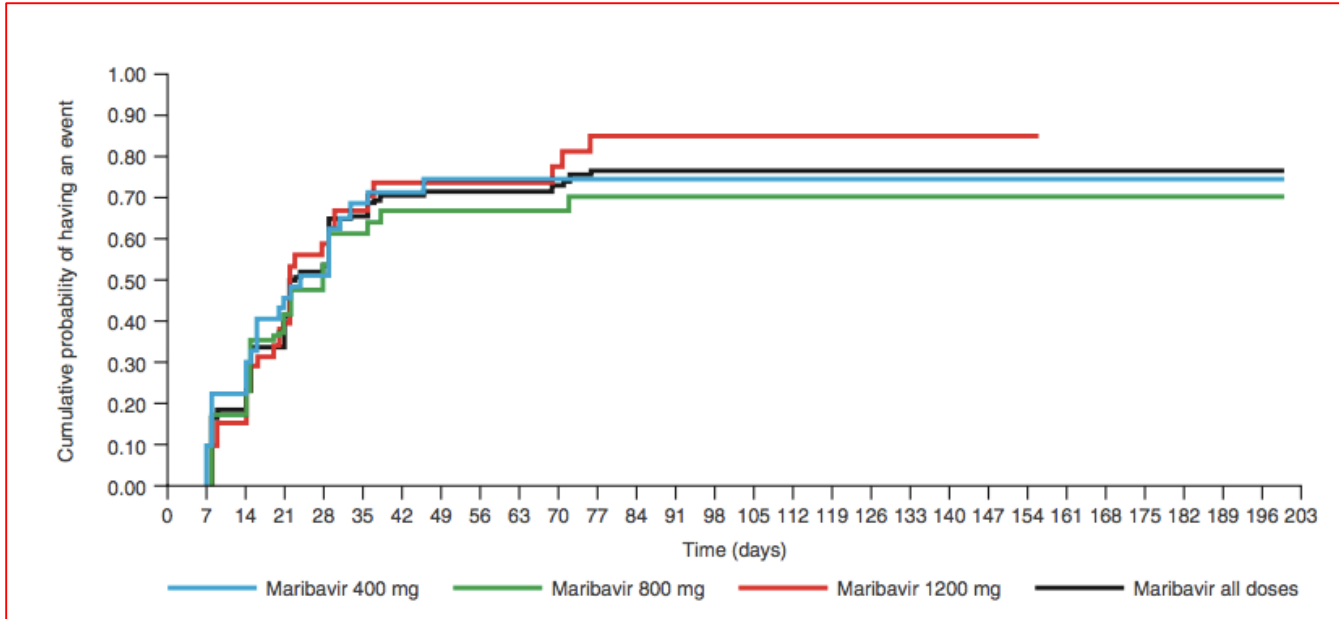
Maribavir

- 100mg 2X1
- Benzimidiazol derivatifi
- Gansiklovir ve sidofovir dirençli suşlara etkili
- Bulantı ,kusma, metalik tat..



Maribavir

-tedavi-



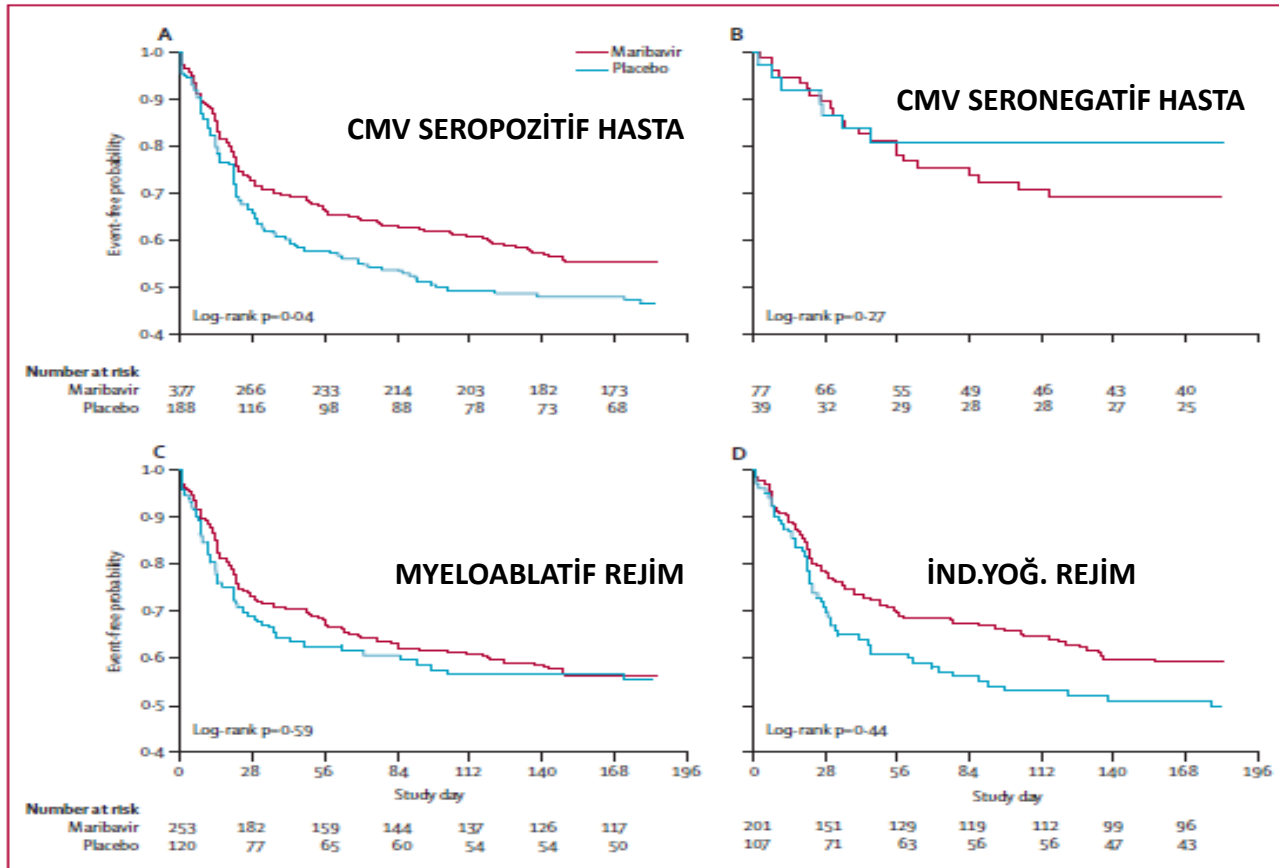
%71 hastada 6.haftada CMV DNA <200 kopya

Yüksek dozlarla rezistans suşlara dikkat!!

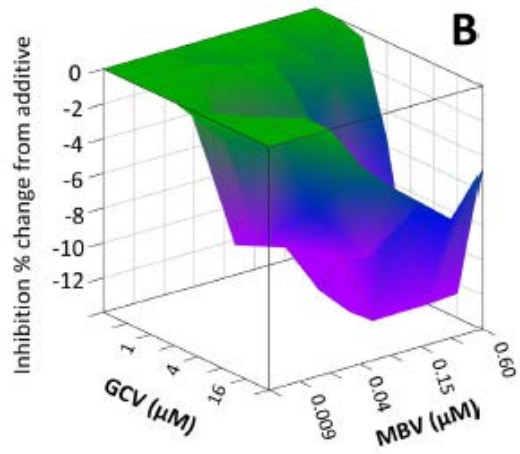
Maribavir

-PROFİLAKSİ-

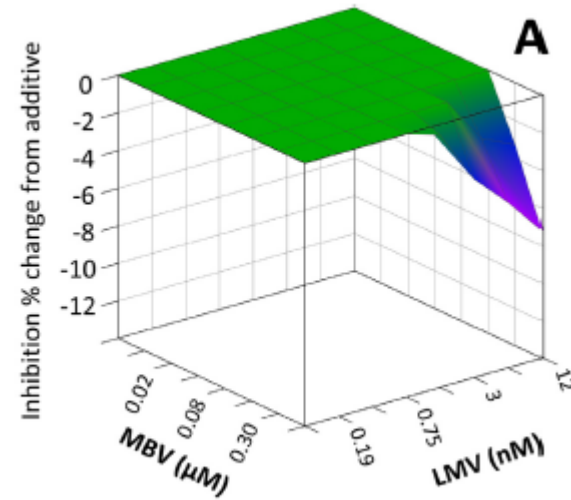
-Faz 3 çalışma-



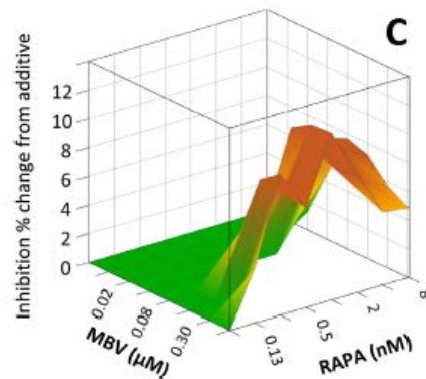
Maribavir



Antagonist



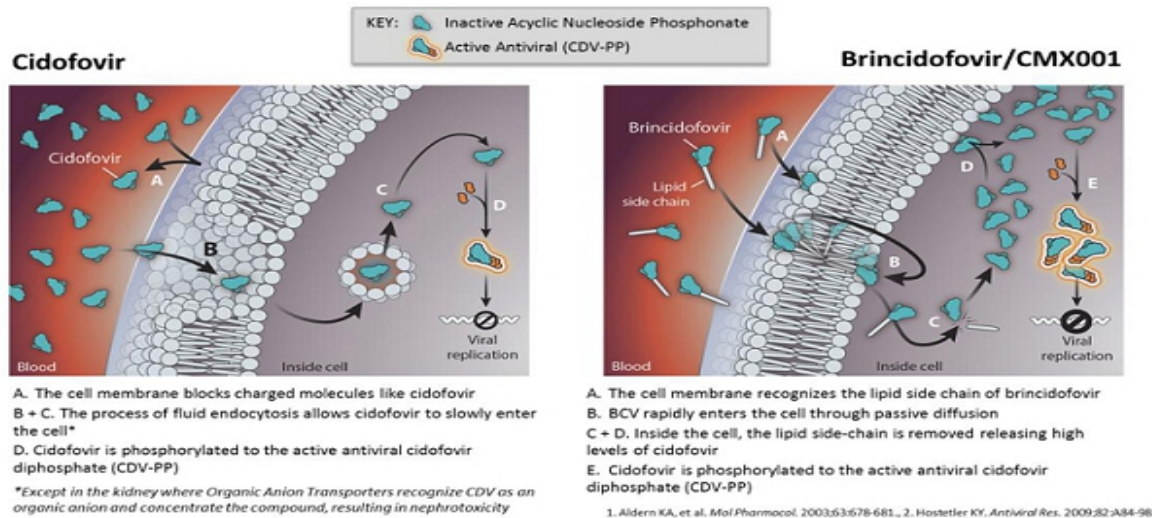
Agonist



Sinerjistik

Brinsidofovir

- Sidofovirin ön ilaç formu→intraselüler Sidofovir difosfat olur
- Haftada 2 kez,oral
- Dirençli suşlar dahil
- Doz ilişkili diare



Hostetler KY, Antiviral Res 2009; Marty FM, NEJM 2013; Marty FM, BBMT 2016

Brinsidofovir

A Randomized, Double-Blind, Placebo-Controlled Phase 3 Trial of Oral Brincidofovir for Cytomegalovirus Prophylaxis in Allogeneic Hematopoietic Cell Transplantation.

Marty FM¹, Winston DJ², Chemaly RF³, Mullane KM⁴, Shore TB⁵, Papanicolaou GA⁶, Chittick G⁷, Brundage TM⁷, Wilson C⁷, Morrison ME⁷, Foster SA⁷, Nichols WG⁷, Boeckh MJ⁸; SUPPRESS Trial Clinical Study Group.

⊕ Author information

Abstract

Cytomegalovirus (CMV) infection is a common complication of allogeneic hematopoietic cell transplantation (HCT). In this trial, we randomized adult CMV-seropositive HCT recipients without CMV viremia at screening 2:1 to receive brincidofovir or placebo until week 14 post-HCT. Randomization was stratified by center and risk of CMV infection. Patients were assessed weekly through week 15 and every third week thereafter through week 24 post-HCT. Patients who developed clinically significant CMV infection (CS-CMVi; CMV viremia requiring preemptive therapy or CMV disease) discontinued the study drug and began anti-CMV treatment. The primary endpoint was the proportion of patients with CS-CMVi through week 24 post-HCT; patients who discontinued the trial or with missing data were imputed as primary endpoint events. Between August 2013 and June 2015, 452 patients were randomized at a median of 15 days after HCT and received study drug. The proportion of patients who developed CS-CMVi or were imputed as having a primary endpoint event through week 24 was similar between brincidofovir-treated patients and placebo recipients (155 of 303 [51.2%] versus 78 of 149 [52.3%]; odds ratio, .95 [95% confidence interval, .64 to 1.41]; $P = .805$); fewer brincidofovir recipients developed CMV viremia through week 14 compared with placebo recipients (41.6% vs 57.1%; $P < .001$). Serious adverse events were more frequent among brincidofovir recipients (57.1% versus 37.6%), driven by acute graft-versus-host disease (32.3% versus 6.0%) and diarrhea (6.9% versus 2.7%). Week 24 all-cause mortality was 15.5% among brincidofovir recipients and 10.1% among placebo recipients. Brincidofovir did not reduce CS-CMVi by week 24 post-HCT and was associated with gastrointestinal toxicity.

PROFILAKSI

Drug	Grading	References	Comment
Aciclovir	CI	Prentice, <i>Lancet</i> 1994 Milano, <i>Blood</i> 2011	Less efficient than valaciclovir
Valaciclovir	BI	Ljungman, <i>Blood</i> 2002 Winston <i>CID</i> 2003 Milano, <i>Blood</i> 2011	Association with preemptive strategy
Ganciclovir/ valganciclovir	CI CIh	Winston, <i>Ann Intern Med</i> 1993 Goodrich, <i>Ann Intern Med</i> 1993 Montesinos, <i>BBMT</i> 2009	Cord blood SCT
Foscarnet	DIIu	Ordemann, <i>Ann Hematol</i> 2000 Bregante et al, <i>BMT</i> 2000	
Letermovir	AI (provisional)	Ljungman, <i>EBMT</i> 2017	

HÜCRESEL TEDAVİ??

Adaptif T hücre tedavisi

DLI → GVHD tetiklenebilir → azaltmak için;

- Alloreaktif T hücre inaktivasyonu
- Selektif ex vivo allodeplesyon
- Selektif in vivo allodeplesyon
- Donör ilişkili virus spesifik T hücreleri

Hanley et al, Blood 2009 Khanna N et al, Blood 2011 Gerdemann U et al, Mol Ther 2013 Prockop SE et al, Blood 2014 ;Leen AM et al, Blood 2013 ;Neuenhahn M et al, Leukemia 2017

ADAPTİF T HÜCRE TEDAVİSİ

Restoration of Viral Immunity in Immunodeficient Humans by the Adoptive Transfer of T Cell Clones

Stanley R. Riddell,* Kathe S. Watanabe, James M. Goodrich, Cheng R. Li, Mounzer E. Agha, Philip D. Greenberg

The adoptive transfer of antigen-specific T cells to establish immunity is an effective therapy for viral infections and tumors in animal models. The application of this approach to human disease would require the isolation and in vitro expansion of human antigen-specific T cells and evidence that such T cells persist and function in vivo after transfer. Cytomegalovirus-specific CD8⁺ cytotoxic T cell (CTL) clones could be isolated from bone marrow donors, propagated in vitro, and adoptively transferred to immunodeficient bone marrow transplant recipients. No toxicity developed and the clones provided persistent reconstitution of CD8⁺ cytomegalovirus-specific CTL responses.

RECONSTITUTION OF CELLULAR IMMUNITY AGAINST CYTOMEGALOVIRUS IN RECIPIENTS OF ALLOGENEIC BONE MARROW BY TRANSFER OF T-CELL CLONES FROM THE DONOR

ELIZABETH A. WALTER, M.D., PHILIP D. GREENBERG, M.D., MARK J. GILBERT, M.D., ROSALYNDE J. FINCH, M.Sc., KATHE S. WATANABE, M.Sc., E. DONNALL THOMAS, M.D., AND STANLEY R. RIDDELL, M.D.

Abstract Background. Cytomegalovirus (CMV) disease in immunocompromised patients correlates with a deficiency of CD8⁺ cytotoxic T lymphocytes specific for CMV. We evaluated the safety and immunologic effects of immunotherapy with clones of these lymphocytes in recipients of allogeneic bone marrow transplants.

Methods. Clones of CD8⁺ cytotoxic T cells specific for CMV proteins were isolated from the blood of bone marrow donors. Fourteen patients each received four intravenous infusions of these clones from their donors beginning 30 to 40 days after marrow transplantation. The reconstitution of cellular immunity against CMV was monitored before and during the period of infusions and for up to 12 weeks after the final infusion. The rearranged genes encoding the T-cell receptor served as markers in evaluating the persistence of the transferred T cells.

Results. No toxic effects related to the infusions were observed. Cytotoxic T cells specific for CMV were

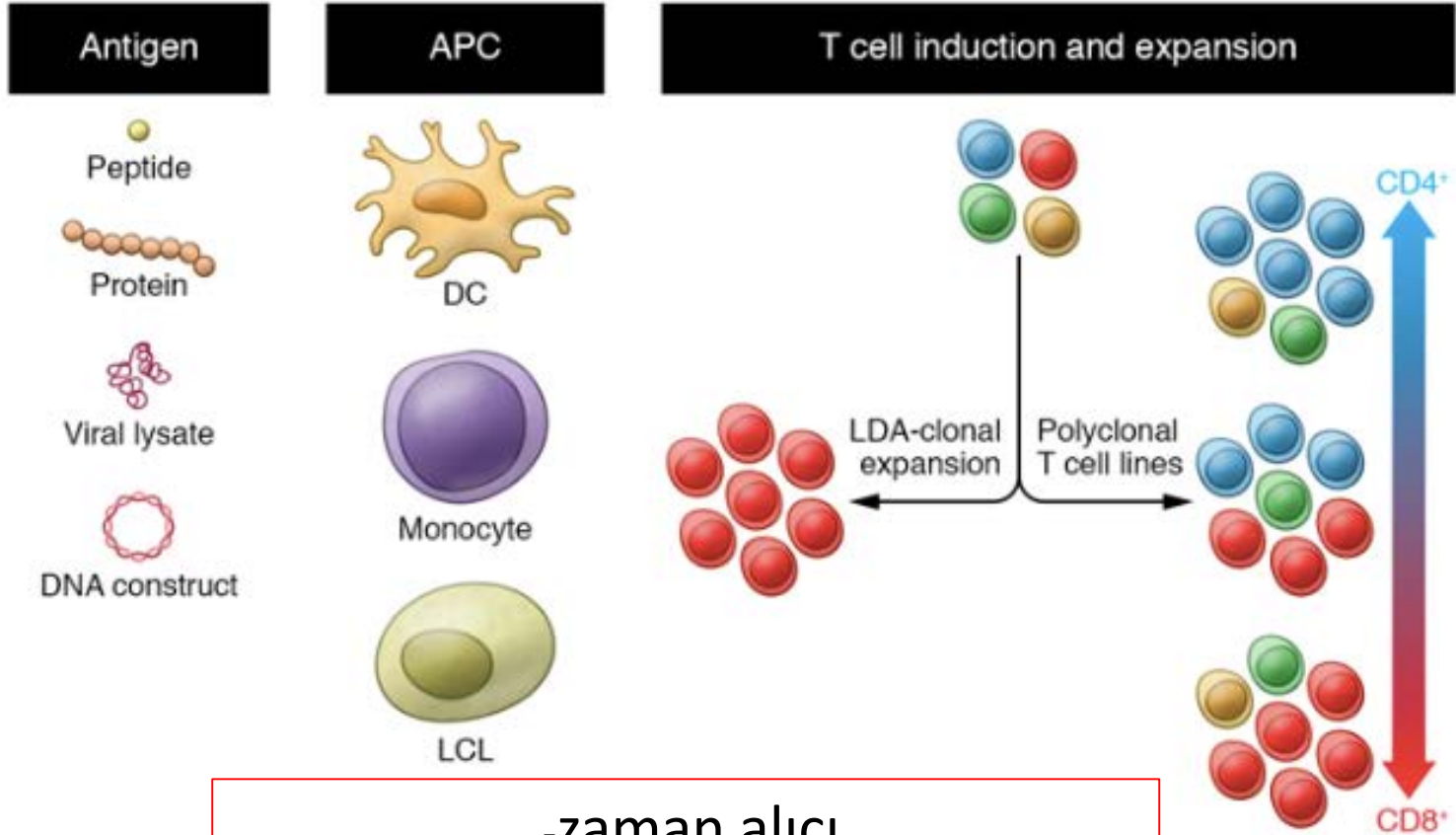
reconstituted in all patients. In vitro measurements showed that cytotoxic activity against CMV was significantly increased ($P < 0.001$) after the infusions in 11 patients who were deficient in such activity before therapy. The level of activity achieved after the infusions was similar to that measured in the donors. Analysis of rearranged T-cell-receptor genes in T cells obtained from two recipients indicated that the transferred clones persisted for at least 12 weeks. Cytotoxic-T-cell activity declined in patients deficient in CD4⁺ T-helper cells specific for CMV, suggesting that helper-T-cell function is needed for the persistence of transferred CD8⁺ T cells. Neither CMV viremia nor CMV disease developed in any of the 14 patients.

Conclusions. The transfer of CMV-specific clones of CD8⁺ T cells derived from the bone marrow donor is a safe and effective way to reconstitute cellular immunity against CMV after allogeneic marrow transplantation. (N Engl J Med 1995;333:1038-44.)

ADAPTİF T HÜCRE TEDAVİSİ

-Donör ilişkili virus spesifik T hücreleri

Ex vivo ekspansiyon-hücre kültürü-



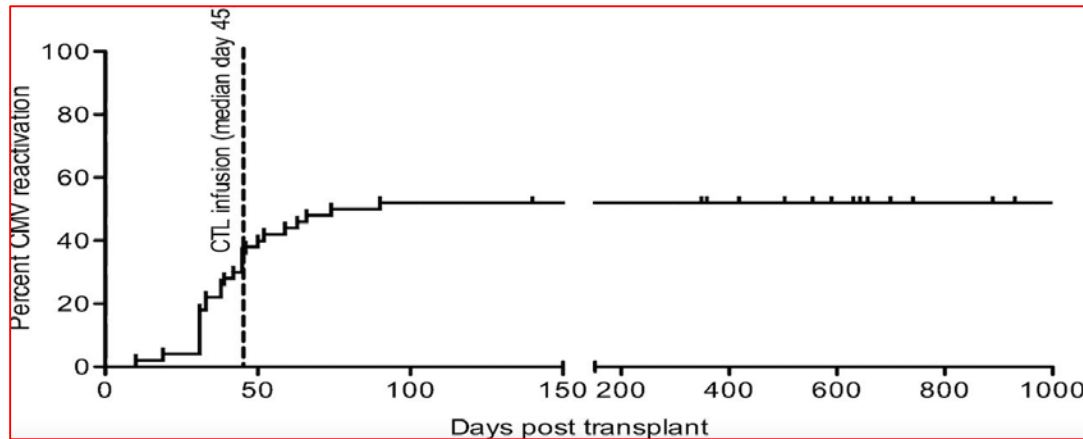
-zaman alıcı
->10e7/kg üzeri T hücre

ADAPTİF T HÜCRE TEDAVİSİ

-Donör ilişkili virus spesifik T hücreleri-

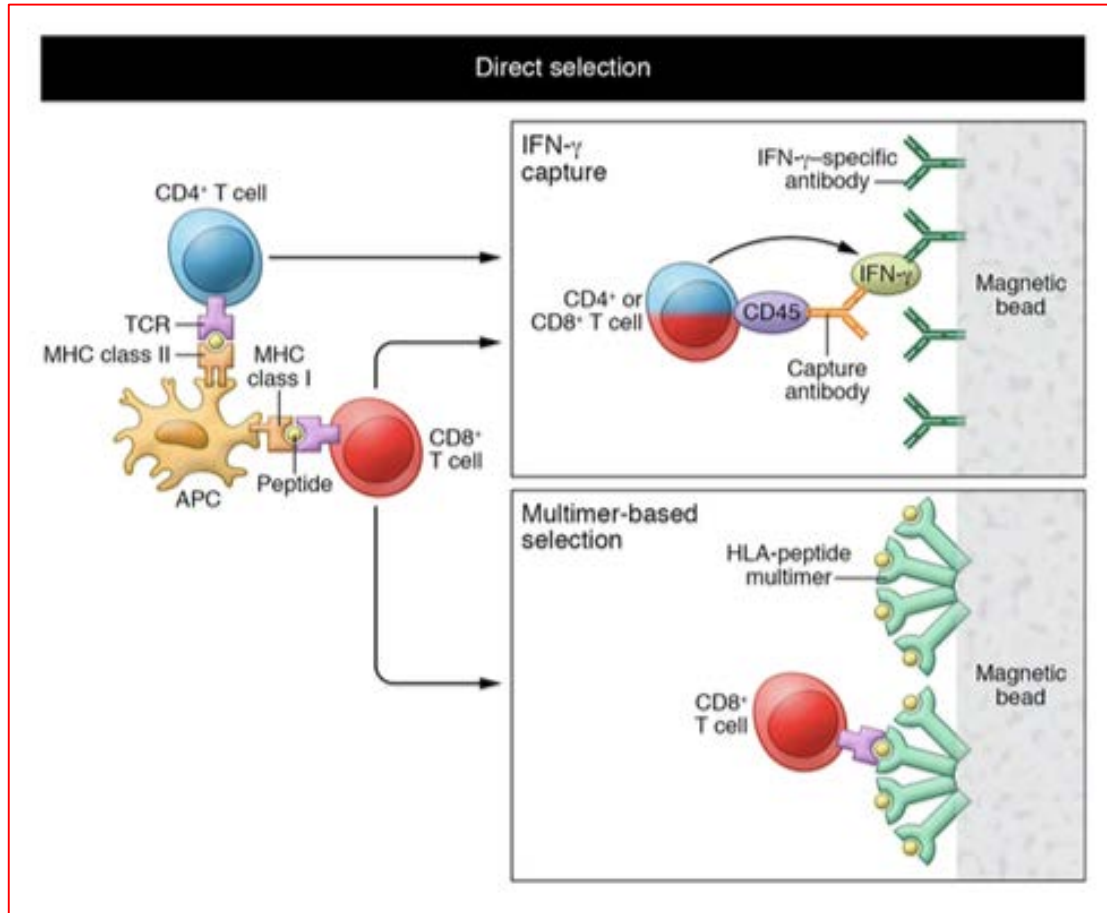
Ex vivo ekspansiyon-hücre kültürü-

→50 hasta,postransplant 28.gün sonrası, 2×10^7 /kg hc
%52 CMV reaktivasyonu,
Antiviral tedavi ihtiyacı ve süresinde azalma
GVHH artışı yok



ADAPTİF T HÜCRE TEDAVİSİ

-Donör ilişkili virus spesifik T hücreleri-



ADAPTİF T HÜCRE TEDAVİSİ

-Donör ilişkili virus spesifik T hücreleri-

-

-*multimer peptid tekniği* → CD8+ hücre

→ CMVIE1 ve pp65 tetramerleri

→ Yüksek miktarda donör kanı gerekir

→ Elde edilen hücre miktarı azdır

-*Uhlin ve ark* → pentamer+immunmanyetik bead

→ HLA peptid/T hücre ilişkisi sonucu klonal bozulma

-*Schmidt ve ark* → septamer

ADAPTİF T HÜCRE TEDAVİSİ

-Donör ilişkili virus spesifik T hücreleri-

- IFN sekresyon tekniği*→CD4+/CD8+ hücreler
- Yüksek miktarda donör kanı gerekir
- Elde edilen hücre miktarı azdır(1×10^4 /kg)
- Faz 1 çalışma→8/18 akut GVHH,3/18 kronik GVHH

ADAPTİF T HÜCRE TEDAVİSİ

- **IM** As of August 2014, all but one patient had completed the study. There were no clinically apparent differences in serious adverse event (SAE) or acute GvHD events between the two arms. Notably, the number of patients experiencing >1 treatment episode was considerably lower than had been predicted in the control group (26% vs 60% predicted). There were fewer CMV reactivations in the ACT arm compared to the control arm (0.75 vs 1.0/patient), and fewer patients experiencing >1 treatment episode (15% vs 26%), although neither reached statistical significance. There was a trend toward reduced overall treatment duration in the ACT arm (Table 2, p=0.14). Preliminary data are summarized below. A complete and final analysis will be available at the time of the conference.
- **AS**
- **dis**

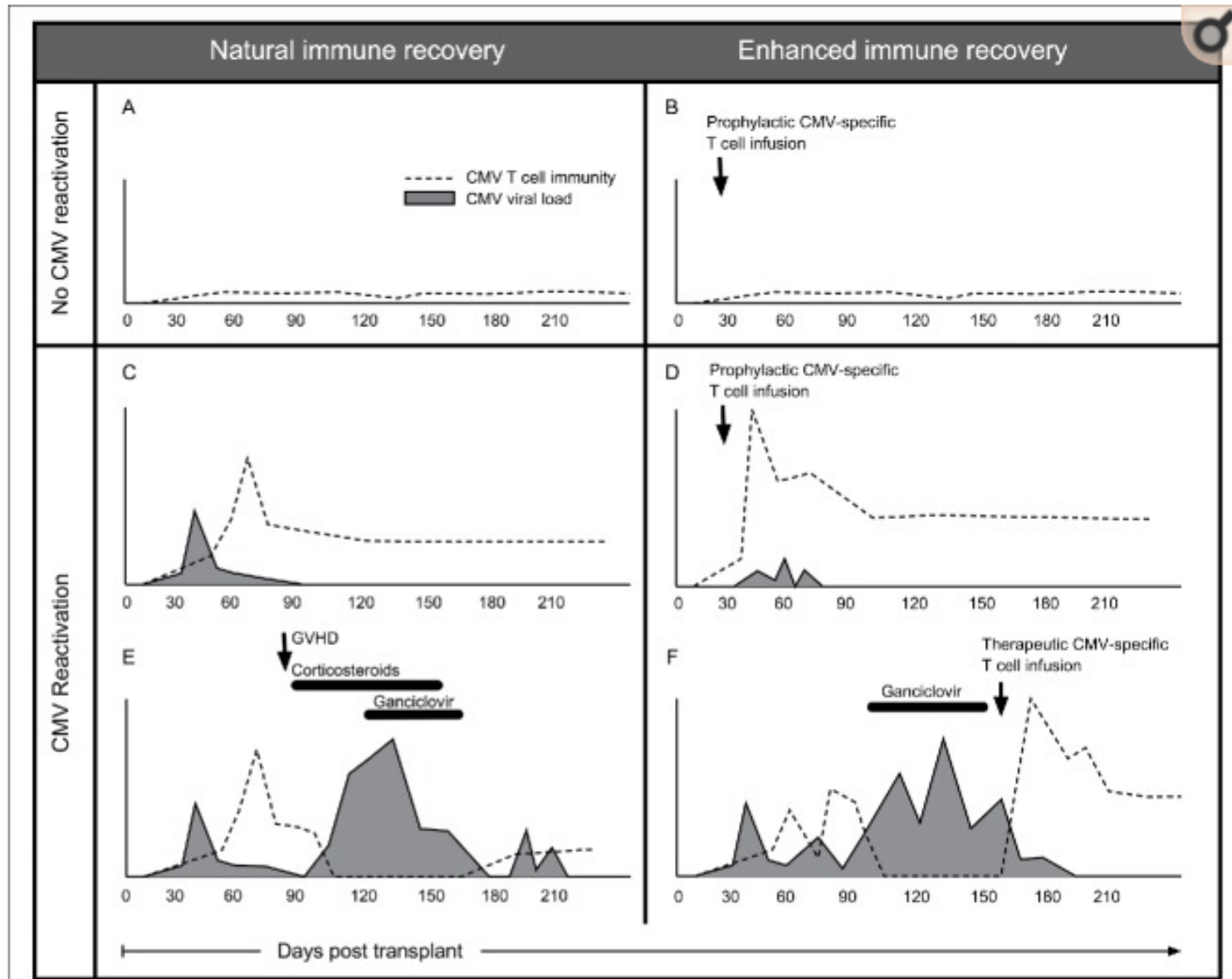
Adaptif CMV tedavisi

Profilaktik? Tedavi?

PROFİLAKSİ

- +28.günde donör spesifik sitotoksik T hücreleri
6/9 hastada CMV reaktivasyonu ancak tedavi ihtiyacı yok!
- DLI→20/31 hastada ilk 100 günde CMV spesifik T hücreler gelişir.

Neden profilaksi çalışmıyor?



Adaptif CMV tedavisi

Profilaktik? Tedavi

TEDAVİ

- Prospektif çok merkezli, Faz I/II, 44 hasta
- 26 T depleasyonu(+) APKHN, 16 T depleasyonu(-) APKHN
- CMV epitop-spesifik T hc. tüm hastalarda gözlemlendi
- Tam virolojik vs kısmi cevap %62 vs %25.
- CMV(-) donörleri olan vakalara verilen 3. kişilerden elde edilen CMV spesifik T hücreler klonal ekspansiyon göstermedi.

Adaptif CMV tedavisi

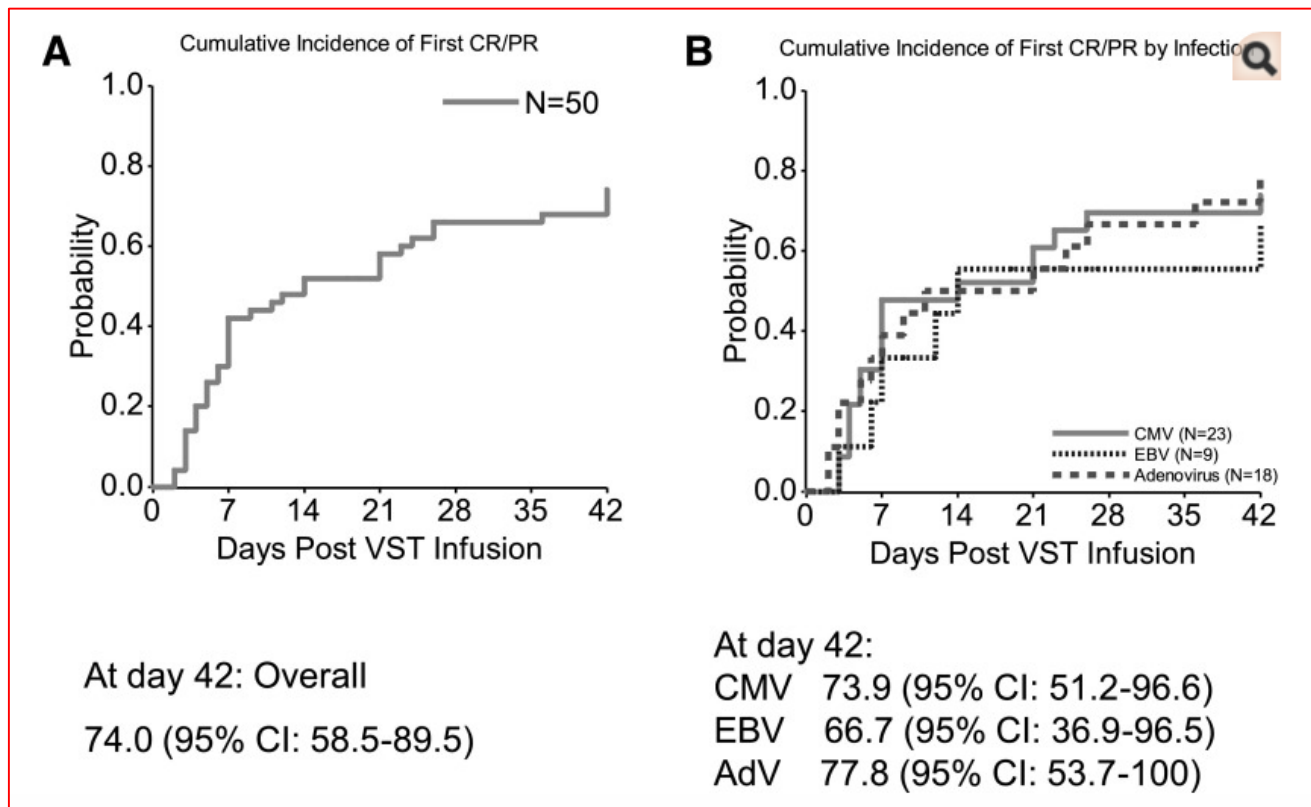
Profilaktik? Tedavi?

- 32 refrakter CMV hastası
- Ex vivo CD8+ CMV spesifik ve daha az oranda CD4+CMV spesifik T hücreleri
- %84 hastada ilk 4 haftada düzelme,viral rekürens yok
- CMV rekürrensi 4.haftadan sonra olan 5 hastada CMV spesifik T hücreleri kantitatif ve fonksiyonel olarak gelişememiş.

Adaptif CMV tedavisi

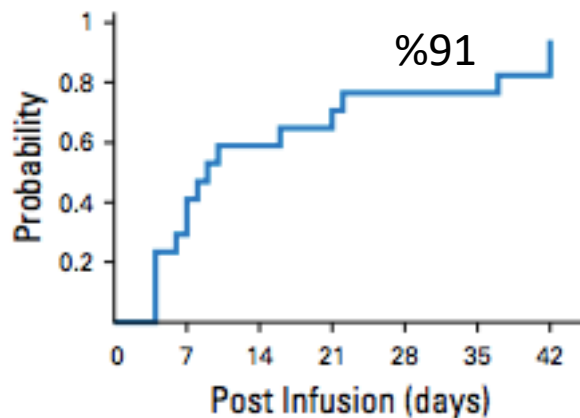
-3RD Party virus sps.T hcleri-

- Kord kanı ve seronegatif vericilerde gerekir
- HLA haplotiplerine göre seçim

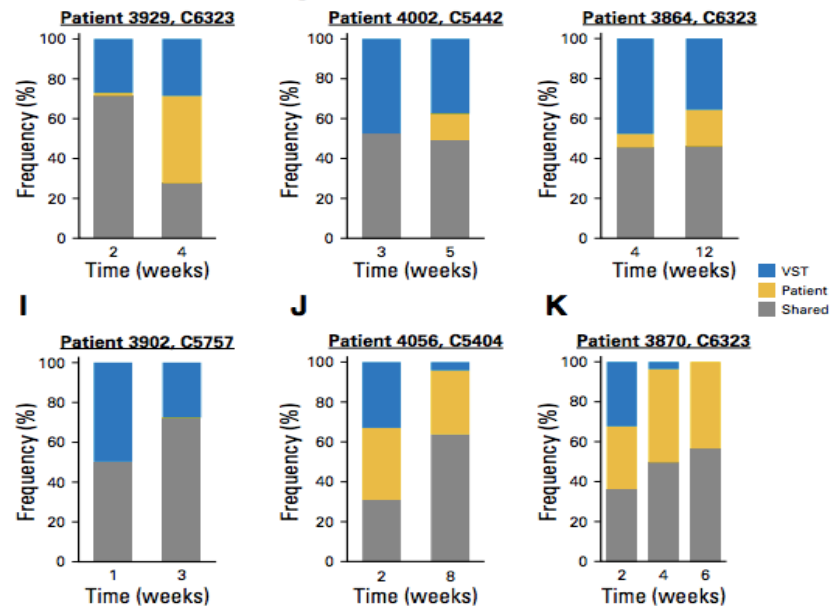


Off-the-Shelf Virus-Specific T Cells to Treat BK Virus, Human Herpesvirus 6, Cytomegalovirus, Epstein-Barr Virus, and Adenovirus Infections After Allogeneic Hematopoietic Stem-Cell Transplantation

Ifigeneia Tzannou, Anastasia Papadopoulou, Swati Naik, Kathryn Leung, Caridad A. Martinez, Carlos A. Ramos, George Carrum, Ghadir Sasa, Premal Lulla, Ayumi Watanabe, Manik Kuvalekar, Adrian P. Gee, Meng-Fen Wu, Hao Liu, Bambi J. Grilley, Robert A. Krance, Stephen Gottschalk, Malcolm K. Brenner, Cliona M. Rooney, Helen E. Heslop, Ann M. Leen, and Bilal Omer



CMV Vokalari



Multispesifik virüs T hücre tedavisi

Cell therapy	No. of patients	Date of study	Activation	Acute GVHD	Dose	CMV-related outcome
EBV, ADV	14	2009	Monocytes/LCLs transduced with ADV vector	3 Skin rashes	5×10^6 to 1.35×10^8 cells/m ²	11 Patients treated prophylactically remain negative; 2/3 ADV infection cleared virus
CMV, EBV	3	2010	DCs pulsed with EBV-LMP2, CMV-pp65, CMV-IE peptides	1 Grade 1 GVHD	Median cell dosage 0.6×10^6 /kg/infusion	2/2 patients cleared virus; 1/1 patient did not reactivate virus (patients treated prophylactically)
CMV-specific or multi-VSTs (CMV, EBV, ADV)	40	2013	pp65-pulsed MoDCs or MoDCs transfected with Ad5f35pp65 adenoviral vector encoding CMV-pp65	No increase in acute or chronic GVHD related to viral-specific CTLs	Dose 2×10^7 cells/m ²	CTL recipients had CMV immune reconstitution and less frequent reactivation with only 1 case requiring pharmacotherapy
Multi-VSTs (CMV, EBV, ADV)	10	2013	DC nucleofection with DNA plasmids encoding viral antigen	1 Grade 1 GVHD	Dose range $0.5-2 \times 10^7$ cells/m ²	Complete viral eradication in 8/10
Multi-VSTs (CMV, EBV, ADV, HHV-6, BK virus)	11	2014	Immunodominant antigen pepmixes	1 Stage II skin GVHD	Dose range 0.5×10^7 to 2×10^7 cells/m ²	94% Virological and clinical response (sustained)
Multi-VSTs (CMV, EBV, ADV, VZV)	10	2015	Ad5f35 encoding CMV-pp65 (+ selected EBNA-1, LMP EBV epitopes; commercial VZV vaccine)	3 Grade 2-4 GVHD	Dose 2×10^7 /m ² VSTs	Reconstitution CMV immunity in 10/10; 6/10 reactivated CMV and 1/10 required antiviral drugs
Multi-VSTs (CMV, EBV, ADV)	26	2015	EBV-LCLs transduced with Ad5f35pp65 adenoviral vector encoding CMV-pp65	2 Skin rashes	5×10^6 /m ² to 1×10^8 /m ²	10/11 cleared CMV; 5/6 cleared ADV; 6/6 cleared EBV; 1 patient progressed
Multi-VSTs (CMV, EBV, ADV)	3	2015	Monocytes/LCLs transduced with Ad5f35pp65 adenoviral vector encoding CMV-pp65	None reported	5×10^6 /m ² to 1×10^7 /m ²	Treatment: 1/1 cleared virus; prophylaxis: 2/2 no reactivation
Multi-VSTs (CMV, EBV, ADV)	6	2016	Immunodominant antigen pepmixes	1× grade 1 and 1× grade 2 GVHD	5×10^5 /m ² to 4.6×10^7 /m ²	Complete response in 2/2 with EBV and 2/5 with CMV

ECIL7

-immunoterapi-

- Farmakoterapiye dirençli CMV infeksiyonunda kullanılabilecek terapötik opsiyondur(Bllu)
- Yüksek doz KS alanlarda etkinliği düşüktür
- Ticari bir ürün bulunmaktadır.

AŞI

CMV vaccines in development.

Type of vaccine	Developer
Attenuated strain (Towne)	Wistar Inst./Med Coll VA
Recombinants with wild virus (Towne-Toledo)	Medimmune
Replication-defective virus	Merck
Vectored:	
Canary Pox	Sanofi
MVA	City of Hope
Adeno	Queensland Inst.
LCMV	Hookipa
VSV	Yale
Recombinant gB glycoprotein with adjuvant	Sanofi Pasteur, GSK
Soluble Pentamers	Redbiotech, GSK, Humabs
DNA plasmids	Astellas, Inovio
Self-replicating RNA	Moderna
Peptides	City of Hope
Dense bodies	Vaccine Project Management (Germany) and Serum Inst. India
Virus-like particles	Variations Bio

Transvax→viremi süresi ve antiviral tedavi kısalmır

AŞI

Investigators initiated the randomized, double-blind, placebo-controlled HELIOS (N = 514) in 2013 to evaluate the efficacy of ASP0113.

“We are disappointed that the results did not demonstrate a significant improvement in overall survival and reduction in CMV end-organ disease,” Bernhardt G. Zeiher, president of Development, Astellas, said in a statement. “We would like to thank the patients and clinicians who participated in this important trial.”

SONUÇ OLARAK

- CMV tedavisinde bugün standart preemtif tedavi
- Letermovir profilaksisi umut verici
- Hücresel tedavilerde donör ilişkili virüs spesifik T hücreleri(3rd party),multispesifik virüs T hücreleri kullanılabilir.
- Aşı sonuçları için henüz erken..