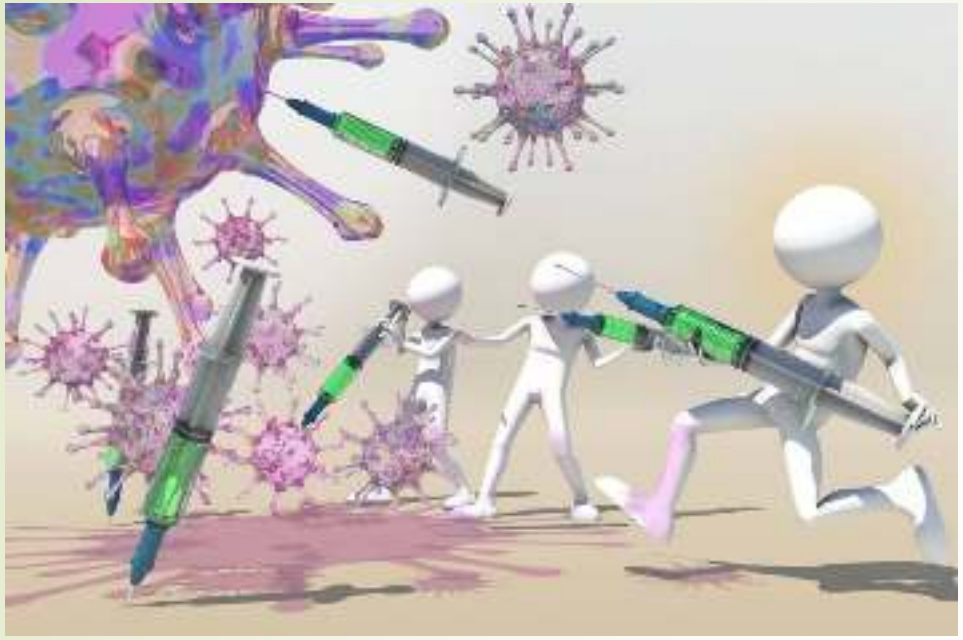

HEMATOPOİETİK KÖK HÜCRE TRANSPLANT ALICILARINDA AŞILAMA

Dr. Behice Kurtaran

Ç.Ü.T.F. Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

Transplant hastalarında immün durumun belirleyicileri

- Önceki aşılanma ve enfeksiyon öyküsü
- Otolog kök hücre alıcıları
  - Alıcının mevcut immünitesinin persistansı
- Allojeneik kök hücre alıcıları
  - Donörden transfer edilen immünite
  - Alıcının mevcut immünitesinin persistansı

İmmünsüpresyonun derecesini transplant tipi belirler

- Allojeneik: alıcının immün sistemi, donörünki ile yer değiştirir
  - Kondisyon rejimi
  - GVHD varlığı
  - Tx sonrası kullanılan immünsüpresif ilaçlar
- Otolog
  - Altta yatan hastalık için daha önce uygulanmış olan RT ve KT'lerin ağırlığı
  - Pretx fludarabin, rituksimab alması

Aşılama ile önlenebilir önemli "erken enfeksiyonlar"

- Pnömokok
- İnfluenza
- HBV
- CMV
- Varicella; primer veya reaktivasyon

Aşılama ile önlenebilir önemli "geç enfeksiyonlar"

- Pnömokok
- İnfluenza
- HBV; reaktivayon
- HIB
- Varicella; primer veya reaktivasyon
- Meningokok
- Kızamık
- Boğmaca
- Papillomavirüs

Diğer enfeksiyonlar/aşılar

- Difteri
- Tetanoz
- Polio
- Tüberküloz
- "Seyahat aşıları"

Tedavi Öncesi Stratejiler

- Rutin şemaların uygulanması
- Seronegatif hastaların immünizasyonu
- Transplant öncesi var olan immünitenin güçlendirilmesi
- Donörün immünizasyonu

Donör Aşılaması

- Alıcının immünitesi üzerine olumlu etkisi gösterilmiştir
  - HIB, tetanoz toksoidi, PCV7, HBV
- Erken post-tx aşılama ile birlikte uygulanmalı

Hasta Aşılanması-Dikkat

- Gerçek etkinlik verisi mevcut değil
- Çoğu aşının toksisite verileri oldukça güçlü
- Tüm etkinlik verileri, immün yanıt olarak değerlendirilmiş
- **"Kanıtın olmayışı, olmadığının kanıtı değildir"**

İnaktive Aşıların Riskleri

- Doğrudan majör yan etkisi yok
- İmmün aktivasyon yan etkisi oldukça düşük
- Rejeksiyon, GVHD, otoimmün reaksiyonlar
- Adjuvanlı aşılar ile riskin arttığına dair kanıt yok

Canlı Aşıların Riskleri

- Özellikle T hücre bağışıklığı düşük hastalarda aşının indüklediği hastalık gelişmesi olasılık dahilinde
- İmmün aktivasyon komplikasyonları
- Mevcut veriler riskin düşük olduğunu göstermek ile birlikte suçiçeği aşılaması sonrası ölüm de bildirilmiş!

GVHD aşı için kontrendikasyon oluşturur mu?

- 1) GÜVENLİK
  - GVHD'nin belirgin kötüleştiğini görülmemiş
  - Ciddi yan etki raporlanmamış
- 2) ETKİNLİK : GVHD immün yanıtı bozar mı?
  - Evet: PPV ve PCV yanıtları azalır
  - Hayır: Konjuge Hib aşı yanıtı bozulmaz

IDSA GUIDELINES

2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

Lorry G. Rubin,[1] Myron J. Levin,[2] Per Ljungman,[3,4] E. Graham Davies,[5] Robin Avery,[6] Marcie Tomblyn,[7] Athos Bousvaros,[8] Shireesha Dhanireddy,[9] Lillian Sung,[10] Harry Keyserling,[11] and Insoo Kang[12]

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An international panel of experts prepared an evidenced-based guideline for vaccination of immunocompromised adults and children. These guidelines are intended for use by primary care and subspecialty providers who care for immunocompromised patients. Evidence was often limited. Areas that warrant future investigation are highlighted.

Keywords. vaccination; immunization; immunocompromised patients; immunosuppression; asplenic patients; immunodeficiency patients

TÜRKİYE ENFEKSİYON HASTALIKLARI VE
KLİNİK MİKROBİYOLOJİ UZMANLIK DERNEĞİ

ERİŞKİN BAĞIŞIKLAMA REHBERİ ÇALIŞMA GRUBU

Pre-Transplant Aşılama

- Alıcıda henüz immünsüpresyon gelişmeden; immün sistemi sağlam bir bireyin aşılanması gereken aşılarını tamamlamalı
  - yaş, aşılanma öyküsü ve temas öyküsüne göre
- Canlı virüs aşıları kondisyon rejiminden ≥ 4 hafta, inaktive aşılar ≥ 2 hafta önce tamamlanmış olmalı

Table 4. Vaccinations Prior to or After Allogeneic or Autologous Hematopoietic Stem Cell Transplant

	Pre-HSCT		Post-HSCT	
Vaccine	Recommendation	Strength, Evidence Quality	Recommendation; Earliest Time Posttransplant; Number of Doses	Strength, Evidence Quality
Haemophilus influenzae b conjugate	U	Strong, moderate	R; 3 mo; 3 doses	Strong, moderate
Hepatitis A	U	Strong, very low	R; 6 mo; 2 doses	Weak, low
Hepatitis B	U	Strong, low	R; 6 mo; 3 doses	Strong, moderate
DTaP, DT, Td, Tdap	U	Strong, low	R; age <7 y: DTaP; 6 mo; 3 doses R; age ≥7 y: DTaP*; 6 mo; 3 doses OR 1 dose Tdap, then 2 doses DT* or Td; 6 mo	Strong, low Weak, very low DTaP: weak, moderate DT, Td: weak, low
Human papillomavirus	U: 11–26 y	Strong, very low	U; 6 mo; 3 doses	Weak, very low
Influenza-inactivated (inactivated influenza vaccine)	U	Strong, low	R; 4 mo	Strong, moderate
Influenza-live attenuated (live attenuated influenza vaccine)	X	Weak, very low	X	Weak, very low
Measles, mumps, and rubella–live	U[a]	Strong, very low	X[b]	Strong, low
Measles, mumps, and rubella–varicella–live	U[a]	Weak, very low	X	Strong, very low
Meningococcal conjugate	U	Strong, very low	R; age 11–18 y; 6 mo; 2 doses	Strong, low
Pneumococcal conjugate (PCV13)	R[c]	Strong, low	R; 3 mo; 3 doses	Strong, low
Pneumococcal polysaccharide (PPSV23)	R[c]	Strong, very low	R; ≥12 mo post if no GVHD	Strong, low
Polio-inactivated (inactivated poliovirus vaccine)	U	Strong, very low	R; 3 mo; 3 doses	Strong, moderate
Rotavirus–live	X	Weak, very low	X	Weak, very low
Varicella–live	U[a]	Strong, low	X[d]	Strong, low
Zoster–live	R[a,e]: age 50–59 y* U[a]: age ≥60 y	Weak, very low Strong, low	X X	Strong, low Strong, low

Abbreviations: DT, diphtheria toxoid, tetanus toxoid, DTaP, diphtheria toxoid, tetanus toxoid, acellular pertussis; GVHD, graft-vs-host disease; HSCT, hematopoietic stem cell transplant; R, recommended—administer if not previously administered or current; such patients may be at increased risk for this vaccine-preventable infection; Td, tetanus toxoid, reduced diphtheria toxoid; Tdap, Tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis; U, usual—administer if patient not current with recommendations for dose(s) of vaccine for immunocompetent persons in risk and age categories; X, contraindicated.

[a] These live vaccines should not be administered unless the vaccine is otherwise indicated based on the annually updated Centers for Disease Control and Prevention recommendations AND the patient is not immunosuppressed AND there will be an interval of ≥4 weeks prior to transplant.

[b] Administer to adolescents and adults (strong, low) and to children (strong, moderate) if measles seronegative, the timing is ≥24 months after transplant, no GVHD is present, and the patient is not receiving immunosuppressive medication. Two doses should be administered.

[c] If not previously administered.

[d] Administer if varicella seronegative, the timing is ≥24 months after transplant, no GVHD is present, and the patient is not receiving immunosuppressive medication. Two doses should be administered (strong, low).

[e] Consider if the patient is not severely immunosuppressed AND the patient is varicella immune as defined by documentation of age-appropriate varicella vaccination, serologic evidence of immunity, documentation of varicella or zoster infection, or birth in the United States before 1980 [45] AND there will be an interval of ≥4 weeks prior to transplant.

*Indicates recommendation for a course of action that deviates from recommendations of the Advisory Committee on Immunization Practices, Centers for Disease Control and Prevention.

Kapsüllü Bakteriler

- *Streptococcus pneumoniae* ve *Haemophilus influenzae* type b (HIB) riski tx sonrası ilk 6 ayda özellikle allojenik alıcılarda ve GVHD olanlarda artar
- Polisakkarid konjuge aşılar HSCT hastalarında konjuge olmayan aşılara iyi bir alternatif
  - Tx alıcıları konjuge olmayan aşılara yeterli antikapsüler polisakkarid antikorları oluşturamazlar; T hücre bağımlı olmayan polisakkarid antijenlerine yanıt zayıf

Pnömokokal Hastalık

- Kök hücre transplantasyonu sonra IPH insidansı
  - Otolog 3.8-5/1000 tx
  - Allojeneik 8.2-9/1000 tx
    - GVHD var ise 20.8/1000 tx
- Bir seride olguların %20'si 100. günden önce

Kapsüllü Bakteriler

78. Three doses of PCV13 should be administered to adults and children starting at age 3–6 months after HSCT (strong, low). At 12 months after HSCT, 1 dose of PPSV23 should be given provided the patient does not have chronic GVHD (strong, low). For patients with chronic GVHD, a fourth dose of PCV13 can be given at 12 months after HSCT (weak, very low).*

- **3 doz konjuge pnömokok aşısını** izleyen **tek doz PPSV 23** aşı koruyucu yanıtı artırmada önerilir
  - PPSV HSCT'den en az 1 yıl sonra
- Kronik GVHD' li hastalarda bunun yerine pnömokok konjuge aşı dördüncü doz olarak önerilebilir
- Takipler sırasında **2- 3 yılda bir revaksinasyon kronik GVHD olan hastalarda önerilmiştir**

Çalışmalar ne diyor?

- Kontrollü olmayan çalışmalar HSCT hastalarında tek doz PCV'nin oldukça zayıf cevap oluşturduğunu göstermiş
- Donörü aşılamak yanıtı arttırabilmekte
- İyi immün yanıt için kaç doz aşı yapılması gerektiğini ortaya koyan kontrollü çalışma yok

MAJOR ARTICLE

Immunogenicity, Safety, and Tolerability of 13-Valent Pneumococcal Conjugate Vaccine Followed by 23-Valent Pneumococcal Polysaccharide Vaccine in Recipients of Allogeneic Hematopoietic Stem Cell Transplant Aged ≥2 Years: An Open-Label Study

Catherine Cordonnier,[1] Per Ljungman,[2] Christine Juergens,[3] Johan Maertens,[4] Dominik Selleslag,[5] Vani Sundaraiyer,[6] Peter C. Giardina,[7] Keri Clarke,[8] William C. Gruber,[7] Daniel A. Scott,[7] and Beate Schmoele-Thoma[3]; for the 3003 Study Group

[1]Hopital Henri Mondor, Assistance Publique-Hopitaux de Paris, and Université Paris-Est-Créteil, France; [2]Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden; [3]Pfizer Pharma GmbH, Berlin, Germany; [4]Universitaire Ziekenhuizen Gasthuisberg, Leuven, and [5]AZ Sint-Jan Brugge-Oostende, Belgium; [6]inVentiv Health Clinical, LLC, Princeton, New Jersey; [7]Pfizer Inc, Pearl River, New York; and [8]Pfizer Inc, Surrey, United Kingdom

Background. Life-threatening *Streptococcus pneumoniae* infections often occur after hematopoietic stem cell transplant (HSCT); vaccination is important for prevention.

Methods. In an open-label study, patients (n = 251) 3–6 months after allogeneic HSCT received 3 doses of 13-valent pneumococcal conjugate vaccine (PCV13) at 1-month intervals, a fourth dose 6 months later, and 1 dose of 23-valent pneumococcal polysaccharide vaccine (PPSV23) 1 month later. Immunogenicity at prespecified time points and vaccine safety were assessed.

Results. In the evaluable immunogenicity population (N = 216; mean age, 37.8 years), geometric mean fold rises (GMFRs) of immunoglobulin G geometric mean concentrations from baseline to postdose 3 showed significant increases in antibody levels across all PCV13 serotypes (GMFR range, 2.99–23.85; 95% confidence interval lower limit, >1); there were significant declines over the next 6 months, significant increases from predose 4 to postdose 4 (GMFR range, 3.00–6.97), and little change after PPSV23 (GMFR range, 0.86–1.12). Local and systemic reactions were more frequent after dose 4. Six patients experienced serious adverse events possibly related to PCV13 (facial diplegia, injection-site erythema and pyrexia, autoimmune hemolytic anemia, and suspected lack of vaccine efficacy after dose 3 leading to pneumococcal infection), PCV13 and PPSV23 (Guillain-Barré syndrome), or PPSV23 (cellulitis). There were 14 deaths, none related to study vaccines.

Conclusions. A 3-dose PCV13 regimen followed by a booster dose may be required to protect against pneumococcal disease in HSCT recipients. Dose 4 was associated with increased local and systemic reactions, but the overall safety profile of a 4-dose regimen was considered acceptable.

Clinical Trials Registration. NCT00980655.

Keywords. 13-valent pneumococcal conjugate vaccine; 23-valent pneumococcal polysaccharide vaccine; hematopoietic stem cell transplant; *Streptococcus pneumoniae* infections.

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METHODS

Study Design

This open-label study was conducted at 37 centers in Europe, Canada, and the United States between January 2010 and May 2013. Approximately 3–6 months after HSCT, 3 doses of PCV13 were administered monthly, a fourth dose of PCV13 was administered 6 months later, and a dose of PPSV23 was administered 1 month later. The study was conducted in compliance with the Declaration of Helsinki and was approved by the responsible institutional review boards and independent ethics committees.

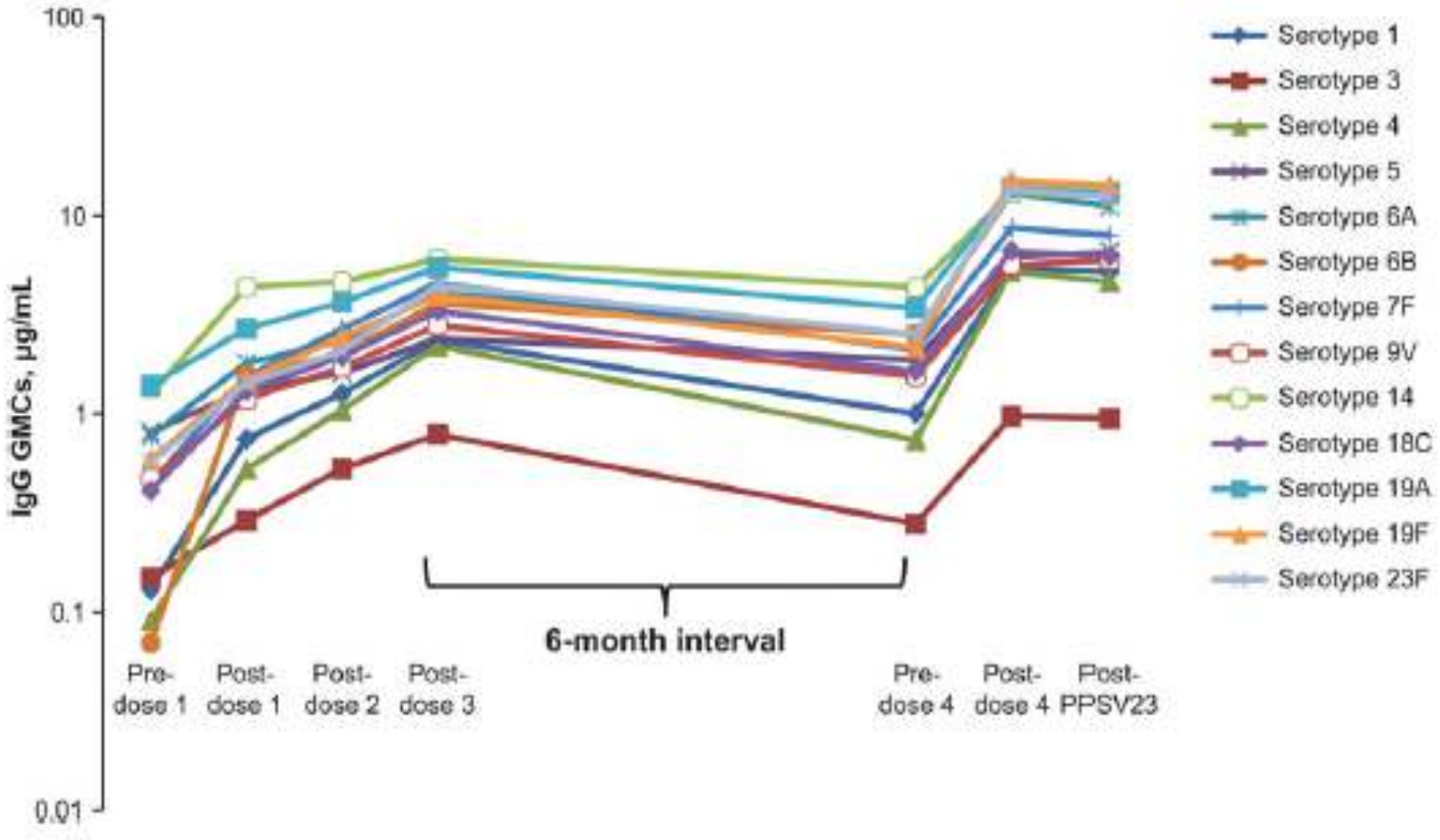

Figure 2. Pneumococcal immunoglobulin G (IgG) geometric mean concentrations (GMCs) in the evaluable immunogenicity population after 3 doses of 13-valent pneumococcal conjugate vaccine (monthly), a booster dose (6 months later), and a dose of 23-valent pneumococcal polysaccharide vaccine (PPSV23) (1 month later).

İNFLUENZA AŞISI

- Aşı enfeksiyonu önler mi?
- Önlemezse ağır geçirilmesini önler mi?
- Tx'den ne kadar süre sonra aşılama yapılmalıdır?
- Aşılamanın riskleri var mıdır?
- Aşının yanıtı nasıl ölçülmelidir?

HSCT alıcılarında immünizasyon

77. One dose of IIV should be administered annually (strong, moderate) to persons aged ≥6 months starting 6 months after HSCT (strong, moderate) and starting 4 months after if there is a community outbreak of influenza as defined by the local health department (strong, very low). For children aged 6 months–8 years who are receiving influenza vaccine for the first time, 2 doses should be administered (strong, low).

- **İnfluenza aşısı**
- HSCT alıcılarında yaşamı tehdit eden enfeksiyon; yarıdan fazlasında pnömoni (%50 mortalite)
- HSCT adaylarına ve HSCT alıcılarına transplantasyon sonrası 4-6 ayda ve yaşam boyunca yıllık inaktive influenza aşısı önerilir
  - Salgın varsa 4.aydan itibaren; ideal >6 ay
  - 6 aydan önce aşılananlarda 2.doz gerekmekte
- Yakın temaslıları ve hastane personelini aşılama
- Canlı aşı uygulanmamalı
- Bazı olgularda kemoprofilaksi uygulanabilir

Brief report

Rituximab blocks protective serologic response to influenza A (H1N1) 2009 vaccination in lymphoma patients during or within 6 months after treatment

Olav Erich Yri,[1] Dag Torfoss,[1] Olav Hungnes,[2] Anne Tierens,[3] Kristian Waalen,[2] Tone Nordøy,[4] Susanne Dudman,[2] Anette Kilander,[2] Karin Fahl Wader,[5] Bjørn Østenstad,[1] Roald Ekanger,[6] Peter Meyer,[7] and Arne Kolstad[1]

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Cancer patients are often encouraged to receive seasonal influenza vaccination. The monoclonal antibody rituximab is widely used in treatment of non-Hodgkin lymphoma. This results in a prolonged depletion of normal B cells, which might impair humoral responses. The aim of the present study was to investigate whether lymphoma patients undergoing rituximab-containing treatment regimens or having received such regimens within the past 6 months were able to mount protective antibody responses to the influenza A(H1N1) 2009 virus vaccine Pandemrix during the 2009 "swine flu" pandemic. Contrary to the control group, where 82% responded adequately to the vaccine, none of the 67 patients achieved protective antibody titers, suggesting that lymphoma patients receiving rituximab-containing regimens might not benefit from this vaccine. It is important that doctors who care for such patients are aware that they may fail to respond not only to the influenza vaccine, but also to other common vaccines. (*Blood*. 2011; 118(26):6769-6771)

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Rituximab-Treated Patients Have a Poor Response to Influenza Vaccination*

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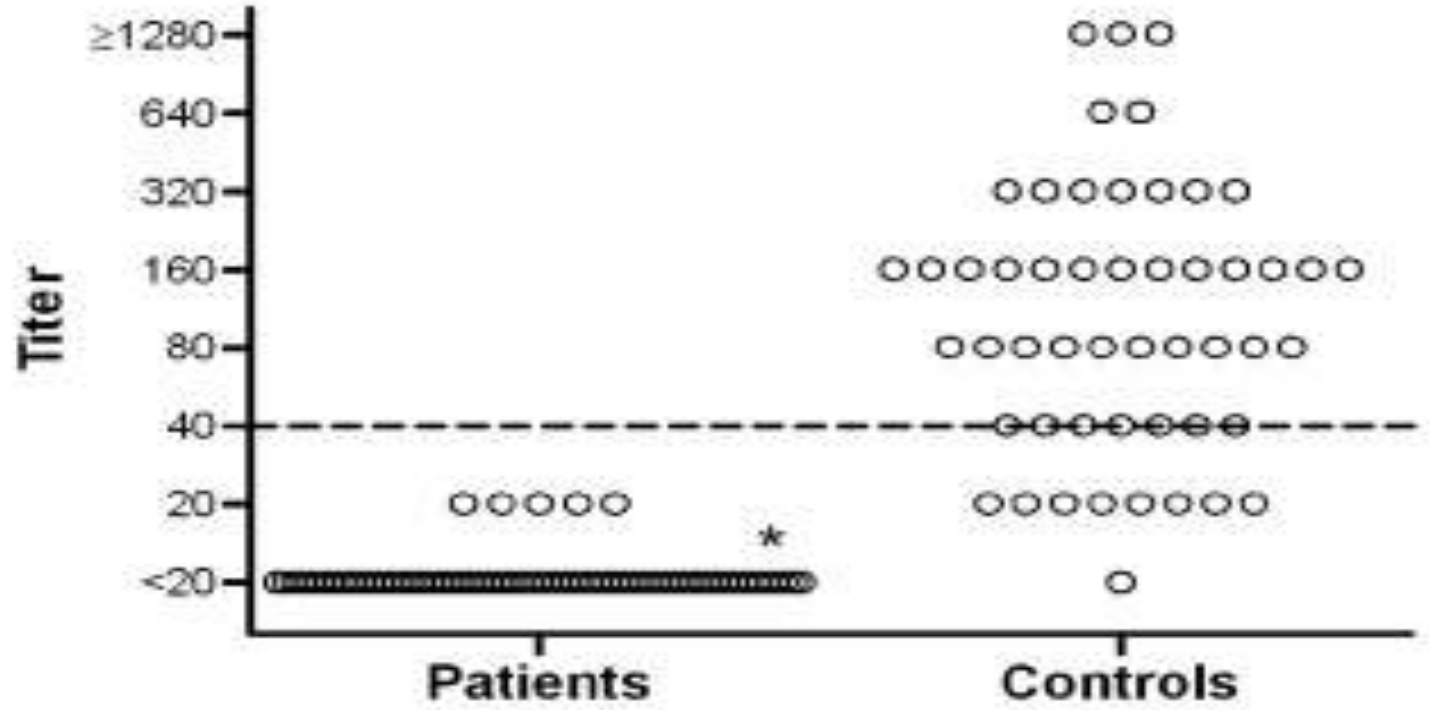

Figure 1. Postvaccination antibody titers in patients and controls. Titers are given as the reciprocal value of the highest dilution inhibiting the hemagglutination reaction. The dotted line indicates the protective antibody level of 40. *A total of 62 patients had an undetectable postvaccination titer.

MAJOR ARTICLE

Influenza Vaccination for Immunocompromised Patients: Systematic Review and Meta-analysis by Etiology

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Many national guidelines recommend annual influenza vaccination of immunocompromised patients, although the decision to vaccinate is usually at clinical discretion. We conducted a systematic review and meta-analyses to assess the evidence for influenza vaccination in this group, and we report our results by etiology. Meta-analyses showed significantly lower odds of influenza-like illness after vaccination in patients with human immunodeficiency virus (HIV) infection, patients with cancer, and transplant recipients and of laboratory-confirmed influenza in HIV-positive patients, compared with patients receiving placebo or no vaccination. Pooled odds of seroconversion and seroprotection were typically lower in HIV-positive patients, patients with cancer, and transplant recipients, compared with immunocompetent controls. Vaccination was generally well tolerated, with variation in mild adverse events between etiological groups. Limited evidence of a transient increase in viremia and a decrease in the percentage of $CD4^+$ cells in HIV-positive patients was found although not accompanied by worsening of clinical symptoms. Clinical judgment remains important when discussing the benefits and safety profile with immunocompromised patients.

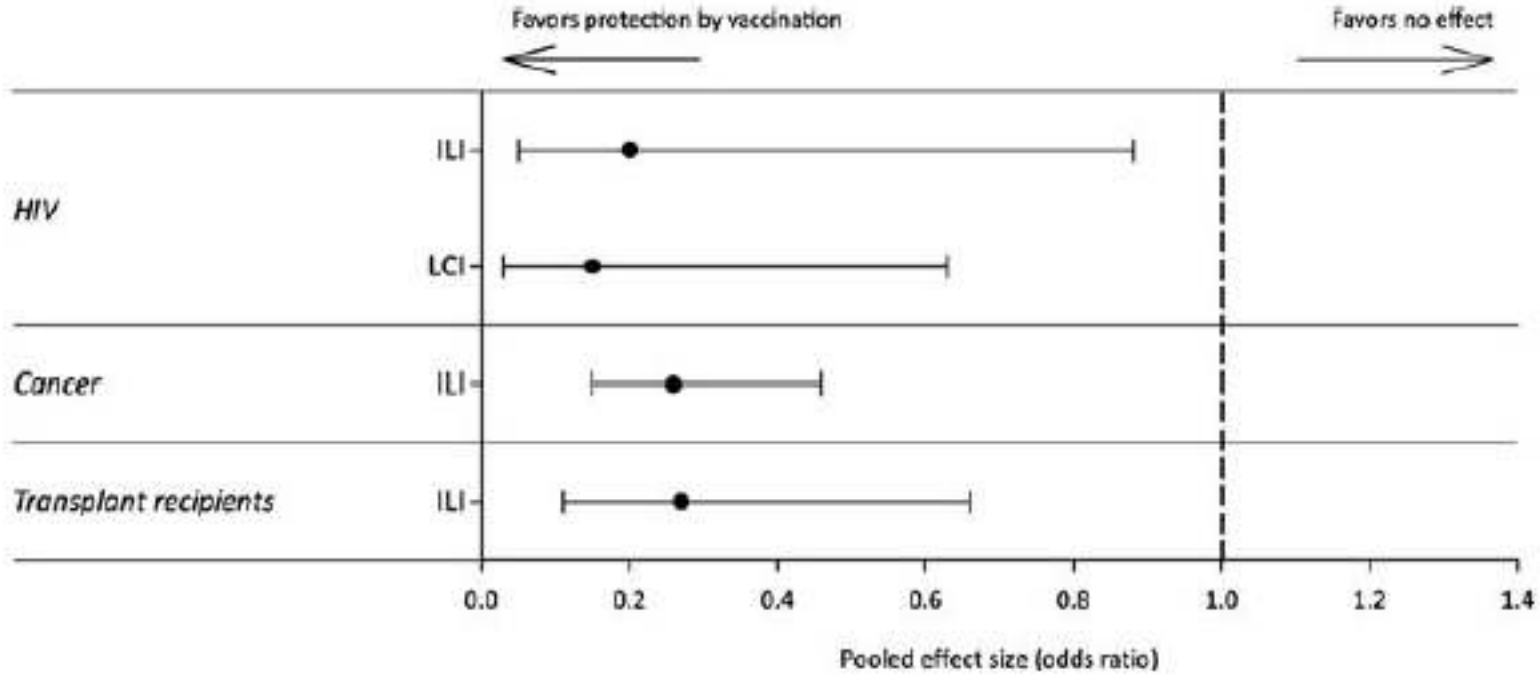

Figure 2. Selected meta-analysis results of influenza-like illness (ILI) and laboratory-confirmed influenza (LCI) by etiology of immunocompromise. Results represent odds of ILI and LCI compared with placebo or no vaccination; error bars show 95% confidence interval around pooled effect size. Abbreviation: HIV, human immunodeficiency virus.

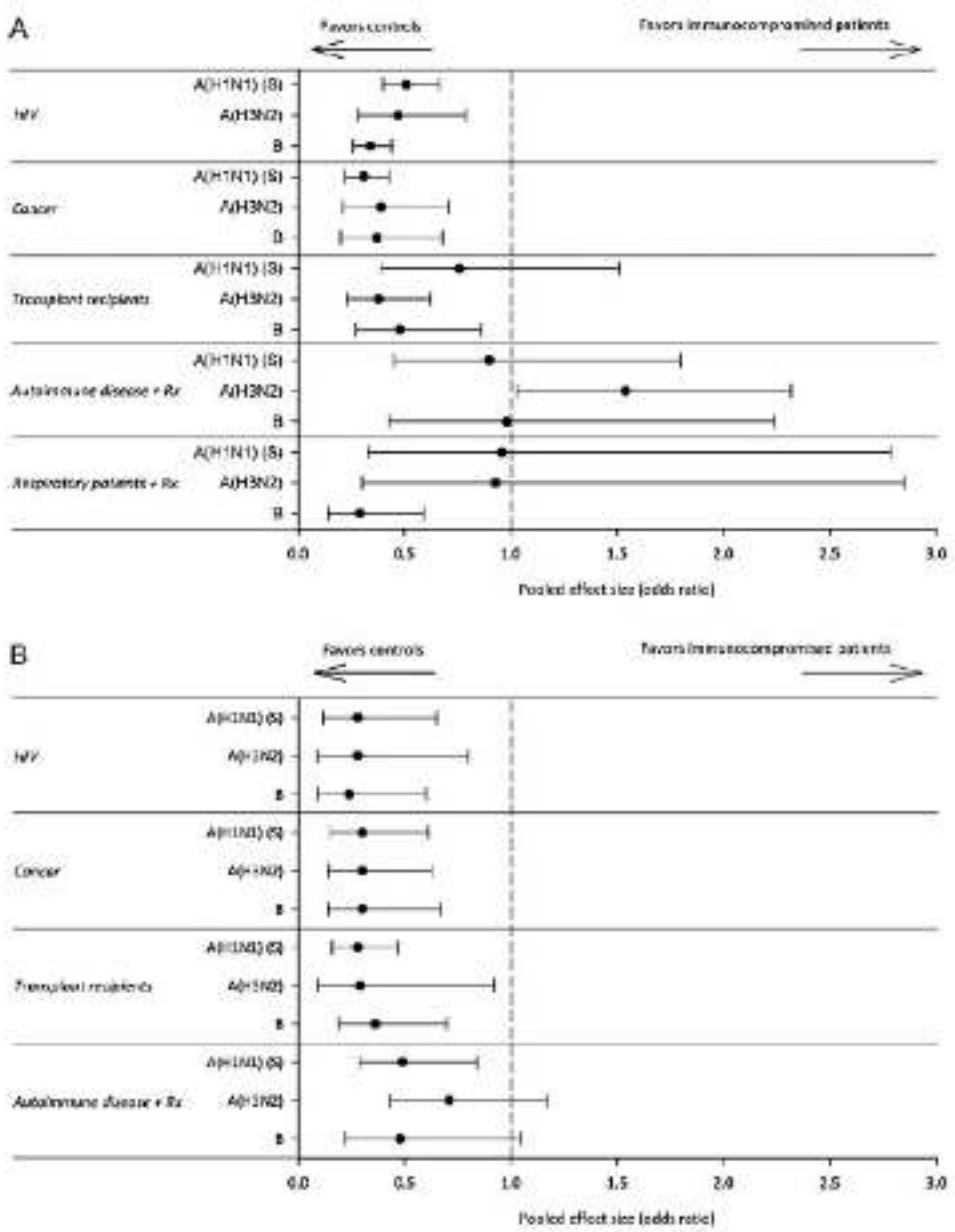

Figure 3. Selected meta-analysis results of serological outcome measures by etiology of immunocompromise. *A*, Odds of seroconversion with ≥4 fold rise in hemagglutination inhibition titer after vaccination, compared with vaccinated immunocompetent controls. *B*, Odds of seroprotection with ≥1:40 hemagglutination inhibition titer after vaccination, compared with vaccinated immunocompetent controls; error bars show 95% confidence interval around pooled effect size. Abbreviations: HIV, human immunodeficiency virus; Rx, treated with immunosuppressants.

Tetanoz-Difteri-Boğmaca Aşıları

- Transplantasyon öncesi Tdap aşısı uygulanmalı
- Transplantasyon sonrası en erken 6. ayda yapılmalı
- 3 doz DTaP veya Tdap sonrası iki doz DT veya iki doz dT
  - Boğmaca aşısının yapılma zamanı ve yapılması konusunda net bir öneri yok
- Doz aralıkları erişkin aşı şemasına benzer; 3 doz
  - 1-3 ay ara ile

Poliovirüs

- Allojenik alıcıların yaklaşık %33'ü, otolog alıcıların %20'si seronegatifleşir
- **İnaktive poliovirus aşısı** HCT sonrası 6-12 ay içerisinde 1-3 ay ara ile tüm alıcılar için önerilir
- **Oral polio aşısı** hastalarda ve yakınlarında, ayrıca bakım veren sağlık personelinde **kullanılmamalı**

HSCT alıcılarında immünizasyon

- **Haemophilus influenza aşısı**
- HIB konjuge aşı HCT alıcılarında iyi tolere edilmiş; immünojenik

- Transplantasyonu izleyen 6-12 aylık dönemde 3 doz HIB konjuge aşı en az 4 hafta aralıklar ile

- **Meningokok aşısı**
- Endikasyonları normalde risk grupları için önerilen koşullarda
- HSCT'yi izleyen 6-12 aylık dönemde iki doz olarak 8-12 hafta ara ile uygulanır
- Muhtemelen konjuge aşı daha etkili

HSCT alıcılarında immünizasyon

- **Hepatit B aşısı,** riski olan tüm HSCT alıcılarına önerilir
- HBV (-) hastalarda tx sonrası 6- 12 aylık dönemde üç doz aşı önerilir
  - Üçüncü dozdan bir ay sonrasında antikor istenmesi önerilir
- Kronik HBV'si olan transplant alıcılarında donör hepatit B aşısı ile aşılanmalı ve erken postransplant dönemde de alıcıya aşı uygulanmalıdır
- **Hepatit A** aşısı genel populasyona benzer koşulda seronegatif HSCT alıcılarına önerilir

HSCT alıcılarında immunizasyon

- **Human papillomavirus**
- Genel populasyona benzer şekilde endikasyonu olan HSCT alıcılarında kullanılabilir,
  - Etkinliği hakkında net veri yok
- **inaktif varisella aşısı** transplantasyondan bir ay önce ve transplantasyondan sonraki 30-60-90.günlerde uygulanmıştır,
  - Uzun süreli etkinliği hakkında daha fazla çalışmaya ihtiyaç var
  - Lisanslı ürün değil

HCT alıcılarında immünizasyon

- **Canlı Aşılar**
- Kızamık, kabakulak, kızamıkçık, suçiçeği HSCT alıcılarında özellikle tx sonrası erken dönemde genellikle önerilmez
- Doğal enfeksiyonu geçirenlerde, aşılananlardan daha az seronegatifleşme
- MMR için seronegatif olan, aktif GVHD'si olmayan veya immünsupresif tedavi almayan HSCT alıcılarına tx sonrası 24. aydan itibaren iki doz halinde

Disseminated, Persistent, and Fatal Infection Due to the Vaccine Strain of Varicella-Zoster Virus in an Adult Following Stem Cell Transplantation

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Live attenuated varicella vaccine is recommended for healthy individuals who are susceptible to varicella. Although the vaccine is safe, effective, and used worldwide, serious adverse events have been reported, mainly in immunocompromised patients who subsequently recovered. Here, we describe the fatality of an immunocompromised patient who received the varicella vaccine. His medical history provides a cautionary lens through which to view the decision of when vaccination is appropriate.

A middle-aged man with non-Hodgkin lymphoma received chemotherapy and a stem cell transplant. He was vaccinated 4 years post-transplantation, despite diagnosis of a new low-grade lymphoma confined to the lymph nodes. Within 3 months of vaccination, he developed recurrent rashes with fever, malaise, weakness, hepatitis, weight loss, and renal failure. The syndrome was eventually determined to be associated with persistent disseminated zoster caused by the vaccine virus. This case illustrates a circumstance when a live viral vaccine should not be used.

Keywords. zoster; vOka; varicella; vaccine; granulomas.

Table 1. Reported Severe Adverse Events Following vOka Vaccination, Proven by Polymerase Chain Reaction

Age, Sex	Underlying Condition	Complication	Reference
Reactions resembling varicella within 42 d after vaccination (n = 11)			
13 mo, M	ADA deficiency	Hepatitis, respiratory distress	[10, 11]
13 mo, M	Di George syndrome	Pneumonia	[12]
15 mo, F	Possible undiagnosed immunodeficiency disease	Severe rash, respiratory compromise, steroids, died	[15]
16 mo, M	Human immunodeficiency virus, 8 CD4 cells/mm^3	Severe rash, encephalopathy	[16]
18 mo, F	Unidentified cell-mediated immune deficit	Severe rash, pneumonia	[17]
4 yr, F	Leukemia, remission 5 mo	Pneumonia, multiorgan failure; died	[18]
5 yr, M	Asthma, cerebral palsy, steroid therapy	Pneumonia	[10, 19]
6 yr, M	iNK cell deficiency	Severe rash, pneumonia	[20]
11 yr, F	iNK cell deficiency	Severe rash, pneumonia	[21]
14 yr, M	Severe combined immunodeficiency	Severe rash, hepatitis	[19]
48 yr, M	Down's syndrome	Pneumonia	[19]
Reactions due to VZV reactivation resembling zoster after vaccination (n = 13)			
1 yr, M	Neuroblastoma	HZ thigh, meningitis[a]; ACV resistance	Reviewed in [13]
21 mo, F	Neuroblastoma	HZ right hand, leg, abdomen, meningitis[a]; ACV resistance	Reviewed in [13]
3 yr, F	Otherwise healthy	HZ face, meningitis, mild encephalitis[a]	Reviewed in [13]
4 yr, M	Leukemia; chemotherapy	HZ arm, meningitis[a]	Reviewed in [13]
4 yr,	Otherwise healthy	HZ arm, meningitis[a]	Reviewed in [13]
7 yr, M	Otherwise healthy	HZ arm, shoulder, meningitis[a]	Reviewed in [13]
8 yr, M	Otherwise healthy	HZ shoulder, meningitis[a]	Reviewed in [13]
9 yr, M	Otherwise healthy	HZ arm, meningitis[a]	Reviewed in [13]
12 yr, F	Otherwise healthy	HZ neck, meningitis[a]	Reviewed in [13]
16 yr, M	Otherwise healthy	Hemorrhagic gastric ulcer	Reviewed in [22]
20 yr,	Common variable immunodeficiency	Progressive outer retinal necrosis	[23]
6 yr,	DOCK 8 syndrome	VZV vasculopathy	[24]
67 yr, M	Lymphoma; Stem cell transplant	Disseminated HZ, death	Current patient

Estimate e > 60 million vaccine doses distributed.

Abbreviations: ACV, acyclovir; ADA, adenosine deaminase; DOCK8, dedicator of cytokinesis 8; HZ, herpes zoster; iNK, invarient natural killer cells; vOka, varicella vaccine; VZV, varicella zoster virus.

[a] VZV Oka DNA demonstrated in cerebral spinal fluid.

- **HSCT alıcılarında kontrendike aşılar**
- BCG,
- Oral poliovirus aşı,
- İntranazal influenza aşısı,
- Kolera aşısı,
- Oral tifo aşısı,
- i.m Tifo aşısı,
- Zoster aşısı

Pasif İmmünizasyon

- Varicella Zoster IG (VZIG)
- GVHD ve immünsüpresif dönemde; ilk 24 ayda
- Varicella seronegatif bireylere;
  - Suçiçeği ve zona geçiren bireyler ile yakın temas halinde
  - Temastan sonraki ilk 10 gün içinde
  - VZIG yoksa temas sonrası valasiklovir
- Varicella seropozitif bireylere;
- Çok ağır immünsüpresyon (T hücre baskılayıcı) veya uzun süre yüksek doz steroid verilmesi halinde VZIG yoksa IVIG veya temas sonrası valasiklovir
- Hepatit A Ig
- Kızamık teması sonrası IVIG
  - 400 mg/kg

Serolojik Testler

- Varicella, Rubella ve Kızamık aşıları yapılmadan testlerine bakılmalı ve hasta seronegatif ise uygulanmalı
- Pnömokok ve HBV aşıları sonrası antikor yanıtına bakılmalı
- 4-5 yılda bir seropozitivite için antikor düzeylerine periyodik olarak bakılmalı
  - HBV, tetanoz, kızamık, difteri, poliovirüs
  - Pnömokok için ek olarak HCT sonrası 2., 4. yıllarda da bakılması önerilmekte

Tablo 14. Erişkinlerde risk gruplarına göre 2016 aşı önerileri (ÖZET TABLO)

Aşı	KHN[1]	İmm. Komp. Hasta.	Aspleni[2]	SOT[3]	Romato. hast.[4]	HIV enf.[5] (CD4<200 /mm³)	HIV enf.[5] (CD4≥200 /mm³)	Sağlık çalışanı[6]	Gebe[7]
Td/Tdap									
İnfluenza									
PCV13									
PPSV23									
Hepatit B									
Hepatit A									
Zoster									
Suçiçeği									
KKK									
Meningokok									
Hib									
HPV									

Td: Tetanoz-difteri; Tdap: Tetanoz-difteri-aselüler boğmaca; Hib: *Haemophilus influenzae* tip b aşısı; HPV: Human papilloma virus aşısı; KHN: Kök hücre nakli; KKK: Kızamık-kızamıkçık-kabakulak aşısı; PCV13: Konjuge pnömokok aşısı; PPSV23: Polisakkarit pnömokok aşısı; SOT: Solid organ transplantasyonu

Uygulanması önerilir.

Diğer risk faktörleri, endikasyonlar ve yaş faktörüne göre uygulanması önerilir.

Kontrendikedir.

Özel bir öneri olmayıp hastanın ve hekimin isteğine göre uygulanabilir.

Tablo 6. Allojeneik ve otolog KHN sonrası aşı önerileri[a,b]

Aşı	Öneri	KHN sonrası aşı zamanı	Doz
Pnömokok (konjuge)	Evet	3-6 ay	3[c]
Tetanoz	Evet	6-12 ay	3
Difteri	Evet	6-12 ay	3
Boğmaca (aselüler)	Evet	6-12 ay	3
Hib (konjuge)	Evet	6-12 ay	3
Meningokok (konjuge)	Ulusal öneri	6-12 ay	1
Polio (inaktive)	Evet	6-12 ay	3
Hepatit B (rekombinant)	Ulusal	6-12 ay	3
Influenza (inaktive)	Yıllık	4-6 ay	1-2
Kızamık	Evet	24 ay	1-2
Kabakulak	Evet	24 ay	1-2
Kızamıkçık	Evet	24 ay	1-2

[a]EBMT önerileri dikkate alınmıştır.

[b]BCG, oral polio, intranasal influenza, kolera, tifo(oral), rota virüs aşısı önerilmez.

[c]12 ve 24. ayda 2 doz polisakkarit aşı ile rapel

NEYE İHTİYAÇ VAR?

- Yeni (daha iyi?) aşılar ile yeni çalışmalara
- Yeni transplant teknikleri ile yeni çalışmalara
- İmmün rekonstitüsyon etkisinin daha iyi anlaşılmasına
- Aşılama konusunun iyileştirilmesine

HEYECANA, UMUDA .....