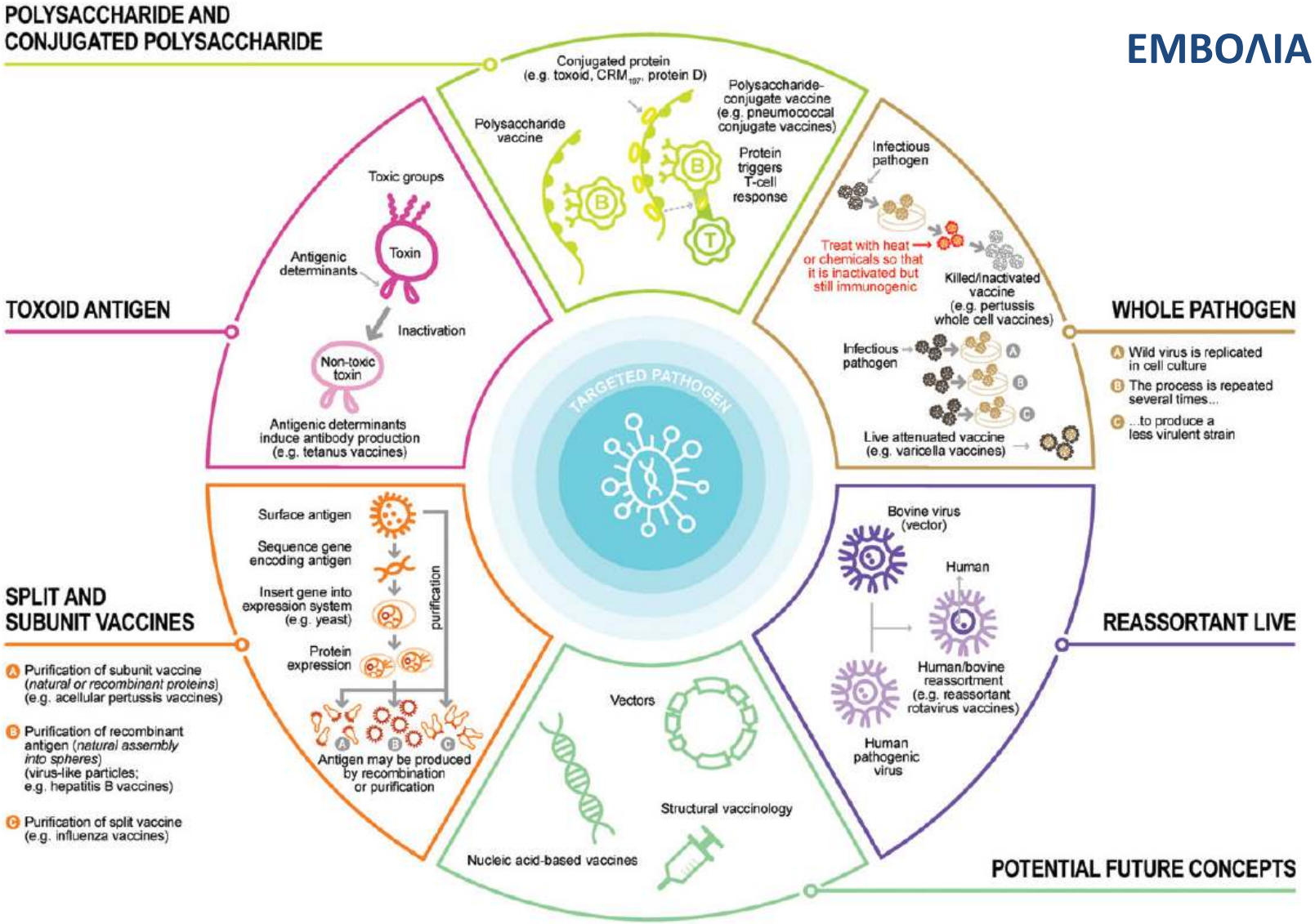
ΕΜΒΟΛΙΑ ΣΕ ΑΝΟΣΟΚΑΤΕΣΤΑΛΜΕΝΟΥΣ ΑΣΘΕΝΕΙΣ

ΛΕΚΚΟΥ ΑΛΕΞΑΝΔΡΑ
ΠΑΘΟΛΟΓΟΣ – ΛΟΙΜΩΞΙΟΛΟΓΟΣ
ΔΙΕΥΘΥΝΤΡΙΑ ΕΣΥ
Πανεπ. Παθολ. Κλινική & Τμήμα Λοιμώξεων
Π.Γ.Ν. ΠΑΤΡΩΝ

ΕΜΒΟΛΙΑ


POLYSACCHARIDE AND CONJUGATED POLYSACCHARIDE
Conjugated protein (e.g. toxoid, CRM197, protein D)
Polysaccharide vaccine
Polysaccharide-conjugate vaccine (e.g. pneumococcal conjugate vaccines)
Protein triggers T-cell response
TOXOID ANTIGEN
Toxic groups
Antigenic determinants
Toxin
Inactivation
Non-toxic toxin
Antigenic determinants induce antibody production (e.g. tetanus vaccines)
TARGETED PATHOGEN
WHOLE PATHOGEN
Infectious pathogen
Treat with heat or chemicals so that it is inactivated but still immunogenic
Killed/inactivated vaccine (e.g. pertussis whole cell vaccines)
Infectious pathogen
Live attenuated vaccine (e.g. varicella vaccines)
A Wild virus is replicated in cell culture
B The process is repeated several times...
C ...to produce a less virulent strain
SPLIT AND SUBUNIT VACCINES
Surface antigen
Sequence gene encoding antigen
Insert gene into expression system (e.g. yeast)
Protein expression
purification
Antigen may be produced by recombination or purification
A Purification of subunit vaccine (natural or recombinant proteins) (e.g. acellular pertussis vaccines)
B Purification of recombinant antigen (natural assembly into spheres) (virus-like particles; e.g. hepatitis B vaccines)
C Purification of split vaccine (e.g. influenza vaccines)
REASSORTANT LIVE
Bovine virus (vector)
Human
Human/bovine reassortment (e.g. reassortant rotavirus vaccines)
Human pathogenic virus
POTENTIAL FUTURE CONCEPTS
Vectors
Structural vaccinology
Nucleic acid-based vaccines

ΤΥΠΟΙ ΕΜΒΟΛΙΩΝ (Ι)

Vaccine type	Benefits [27,68]	Limitations [27,68]	Examples
Live attenuated vaccines	Mimic natural infection and immune response	Contraindicated for immunocompromised individuals and pregnant women	Measles, mumps, rubella, varicella (Priorix Tetra, ProQuad), rotavirus (Rotarix, Rotavac), herpes zoster (Zostavax), influenza (Flumist), oral poliovirus (OPV), yellow fever (Stamaril)
	Elicit both antibodies and cell-mediated immunity	Less stable over time, heat labile	
	Life-long immunity possible after 1 or 2 doses	Possibility to reverse to natural form (e.g. poliovirus)	
Inactivated vaccines	Robust technique for production	Limited immunogenicity, adjuvants may be required	Whole-cell pertussis (Tritanrix), hepatitis A (Havrix, Vaqta), rabies (Rabipur), tickborne encephalitis (Encepur), Japanese encephalitis (Ixiaro), cholera (Dukoral)
	High stability	Multiple primary and booster doses required to obtain long-term protection	
	Impact on carriage		
	No replication of the inactivated pathogen		
	Not contraindicated in immunocompromised individuals and pregnant women		
Split and subunit protein vaccines (natural or recombinant)	Non-infectious	No or limited innate defence triggers	Influenza (Fluarix, Fluarix Tetra, Flulaval, Intanza, Vaxigrip, etc.), acellular pertussis, hepatitis B (Engerix B, Recombivax HB), human papillomavirus (Cervarix, Gardasil, Gardasil 9), meningococcal B (Bexsero, Trumenba), malaria (Mosquirix), herpes zoster (Shingrix)
	Low reactogenicity	Often have reduced immunogenicity compared to whole pathogen vaccines	
		For those vaccines with lower immunogenicity, adjuvants are often needed	
Toxoid vaccines	Vast experience as mature technology	Vaccines only target the toxin and do not prevent infection by the pathogen	Tetanus, diphtheria, acellular pertussis (as part of DTaP combination vaccines: Boostrix, Infanrix, Adacel, etc.)
	Non-infectious	No herd protection	
	Used as carrier proteins due to good immunogenicity	Priming and boosting necessary	

Vetter V, Annals of Med 2018; 50(2): 110–20

ΤΥΠΟΙ ΕΜΒΟΛΙΩΝ (II)

Vaccine type	Benefits [27,68]	Limitations [27,68]	Examples
Polysaccharide vaccines	Easily identifiable target	Weakly immunogenic, elicit only a transient antibody response giving a limited duration of protection Limited immunogenicity in infants Hyporesponsiveness after repeated doses Limited or no impact on carriage	Pneumococcal polysaccharide vaccine (Pneumovax 23), meningococcal polysaccharide vaccine (Mencevax)
Polysaccharide conjugate vaccines	Improved memory responses leading to increased protection in infants Provide a longer duration of protection than polysaccharide vaccines due to B- and T-cell responses Impact on carriage and transmission	Booster doses may be required to attain long-term protection	Meningococcal C (Neisvac), A (MenAfriVac), ACWY (Nimenrix, Menveo, Menactra), pneumococcal conjugate vaccine (Prevnar, Prevnar 13, Synflorix), *Haemophilus influenzae* type b (ACT-HIB)
Reassortant live attenuated	Benefit from a live infection with a non-pathogen strain Cannot cause the original disease, good safety profile Improved tolerability due to combination of low pathogenic virus with antigen from high pathogenic virus	Contraindicated for immunocompromised individuals Risk of re-reassortants, especially when combination of several reassortants [69] Immunogenicity limited to selected antigens	Rotavirus (RotaTeq)

Vetter V, Annals of Med 2018; 50(2): 110–20

ΕΘΝΙΚΟ ΠΡΟΓΡΑΜΜΑ ΕΜΒΟΛΙΑΣΜΩΝ ΕΝΗΛΙΚΩΝ

Εμβόλιο	Κύηση ή λοχεία	Ανοσοκαταστολή (πλην HIV)	HIV λοίμωξη (CD4+ κύτταρα)		Ασπληνία, μόνιμη έλλειψη τελικών κλασμάτων συμπληρώματος	Νεφρική ανεπάρκεια τελικού σταδίου σε αιμοδιύλυση	Χρόνιες καρδιοπάθειες, πνευμονοπάθειες, χρόνιος αλκοολισμός	Χρόνιες παθήσεις του ήπατος	Σακχαρώδης διαβήτης	Υγειονομικό προσωπικό	MSM
			<200	≥200							
Γρίπης	1 δόση ετησίως										
Td/Tdap	1 δόση σε κάθε κύηση	Υποκαταστήστε μία δόσηTd με Tdap ή Tdap-IPV, στη συνέχεια Td κάθε 10 χρόνια									
MMR	Αντενδείκνυται		1-2 δόσεις ανάλογα με την περίπτωση								
VAR	Αντενδείκνυται		2 δόσεις								
HZV	Αντενδείκνυται			1 δόση							
HPV - θήλυ		3 δόσεις μέχρι την ηλικία των 26 ετών									
HPV - άρρεν		3 δόσεις μέχρι την ηλικία των 26 ετών									3 δόσεις μέχρι 26 ετών
PCV13		1 δόση									
PPSV23		1,2 ή 3 δόσεις ανάλογα με τις ενδείξεις									
HepA	2 δόσεις										
HepB	3 δόσεις							3 δόσεις			
MenACWY	1 ή περισσότερες δόσεις ανάλογα με τις ενδείξεις										
MenB		2-3 δόσεις ανάλογα με το εμβόλιο									
Hib		3 δόσεις στους δέκτες σε μεταμόσχευση μυελού			1 δόση						

Συστήνεται για ενήλικες που πληρούν τα ηλικιακά κριτήρια και δεν έχουν αποδεικτικό προηγούμενου εμβολιασμού ή νόσησης

Συστήνεται για ενήλικες με συνοδές ιατρικές καταστάσεις (ομάδες αυξημένου κινδύνου) ή άλλες ενδείξεις

Αντενδείκνυται

Δεν συστήνεται

Πίνακας 1. Εθνικό Πρόγραμμα Εμβολιασμών Παιδιών και Εφήβων, 2019*

Εμβόλιο ▼ / Ηλικία ▶		Γέννηση	1 μηνός	2 μηνών	4 μηνών	6 μηνών	12 μηνών	15 μηνών	18 μηνών	19-23 μηνών	2-3 ετών	4-6 ετών	7-10 ετών	11-12 ετών	13-14 ετών	15-18 ετών
Ηπατίτιδας Β (HepB)[1]	- Έναρξη στη γέννηση	HepB	HepB			HepB, 3 ή 4[1] δόσεις συνολικά				HepB						
	- Όχι έναρξη στη γέννηση			HepB	HepB	HepB, 3 δόσεις συνολικά				HepB						
Διφθερίτιδας, Τετάνου, ακυτταρικό Κοκκύτη (DTaP <7 ετών, Tdap ≥7 ετών)[2]				DTaP	DTaP	DTaP	DTaP	DTaP		DTaP		DTaP	Tdap ή Td	Tdap ή Tdap-IPV	Tdap ή Td	
Πολιομυελίτιδας αδρανοποιημένο (IPV)[3]				IPV	IPV	IPV				IPV		IPV	Tdap ή Td	Tdap ή Tdap-IPV	Tdap ή Td	
Αιμόφιλου ινφλουέντζας τύπου b (Hib)[4]				Hib	Hib	Hib	Hib	Hib		Hib			Hib			
Πνευμονιόκοκκου συζευγμένο (PCV)[5]				PCV	PCV	PCV	PCV	PCV					PCV13			
Πνευμονιόκοκκου πολυσακχαριδικό (PPSV23)[6]											PPSV23					
Μηνιγγιτιδόκοκκου ορομάδας C συζευγμένο (MCC)[7]							MCC 1 δόση	MCC, 1 δόση								
Μηνιγγιτιδόκοκκου ορομάδων A,C,W135,Y συζευγμένο (MenACWY)[7]				Men ACWY	Men ACWY			MenACWY, 1 δόση						MenACWY 1 δόση	MenACWY 1 δόση	
Μηνιγγιτιδόκοκκου ορομάδας Β πρωτεϊνικό (MenB-4C ή MenB-fHbp)[8]				MenB-4C										MenB-4C ή MenB-fHbp		
Ιλαράς, Παρωτίτιδας, Ερυθράς (MMR)[9]							MMR 1η δόση			MMR	MMR 2η δόση					
Ανεμευλογιάς (VAR)[10]							VAR 1η δόση			VAR	VAR 2η δόση					
Ηπατίτιδας Α (HepA)[11]											HepA 2 δόσεις					
Ιού ανθρωπίνων θηλωμάτων (HPV)[12]														Θ: HPV 2 δόσεις		
														Θ & Α: HPV, 3 δόσεις		
Φυματίωσης (BCG)[13]		BCG														
Γρίπης[14]						Ετησίως σε ομάδες αυξημένου κινδύνου										
Ρότα ιού (RV1 ή RV5)[15]				RV1 ή RV5	RV1 ή RV5	RV5										

* Τα πολυδύναμα εμβόλια πρέπει να προτιμώνται των ολιγοδυνάμων.

Σημειώσεις: Το εμβόλιο κάτω από τη διπλή γραμμή δεν περιλαμβάνεται στο Εθνικό Πρόγραμμα Εμβολιασμών και συνταγογραφείται με συμμετοχή. Θ: θήλεις, Α: άρρενες (για εμβόλιο HPV).

Συστήνονται για όλα τα άτομα με την ανάλογη ηλικία που δεν έχουν ένδειξη ανοσίας.

Συστήνονται σε άτομα που καθυστέρησαν να εμβολιασθούν.

Συστήνονται σε άτομα που ανήκουν σε ομάδες αυξημένου κινδύνου (βλέπε ομάδες αυξημένου κινδύνου).

Δεν συστήνονται.

Ανοσοκατεσταλμένοι ασθενείς – Ετερογενής ομάδα

Immunocompromised persons vary:

- Nature of immunodeficiency
- Degree of immunosuppression
- Response to immunization
- Susceptibility to infection

→Vaccine safety and vaccine efficacy
→Vaccine benefit
→**Recommendations**

Common Community Respiratory Viruses in Patients with Cancer

More than Just "Common Colds"

Krystal L. Hicks, Pharm.D.[1]
Roy F. Chemaly, M.D.[2]
Dimitrios P. Kontoyiannis, M.D., Sc.D.[2]

[1] Department of Bone Marrow Transplantation, The University of Texas M. D. Anderson Cancer Center, Houston, Texas.

[2] Department of Infectious Diseases, Infection Control, and Employee Health, The University of Texas M. D. Anderson Cancer Center, Houston, Texas.

Community respiratory viruses long have been recognized as primary respiratory pathogens among infants and young children. More recently, it has become clear that these viruses cause a considerable disease burden throughout life. The consequences of repeated infections are most evident in elderly and immunocompromised persons. Even in otherwise healthy persons, reinfections often require medical attention but generally are undiagnosed and unrecognized. These reinfections may spread from healthy persons to those at highest risk. Control requires a multifaceted approach combining vaccination, chemoprophylaxis, and aggressive early antiviral treatment of high-risk individuals, as well as education of all populations affected by these viruses. Cancer 2003;97:2576–87.

DOI 10.1002/cncr.11353

- In immunocompromised hosts, **30 – 60% of patients with pneumonia remained without a clear-cut diagnosis**
- Some of these undiagnosed cases of idiopathic pneumonia actually were infections involving community-acquired respiratory viruses (influenza, respiratory syncytial virus (RSV), parainfluenza virus (PIV)
- **Immunocompromised hosts have the highest risk of developing life-threatening respiratory infections**

Cancer 2003;97:2576 – 87

Επιδημιολογικά δεδομένα

Increased risk of invasive pneumococcal disease in haematological and solid-organ malignancies

A. WONG[1*], T. J. MARRIE[1], S. GARG[2], J. D. KELLNER[3], G. J. TYRRELL[4,5] and the SPAT Group

Rates of invasive pneumococcal disease (IPD) in patients with underlying malignancy, 2000–2004

Malignancy	IPD cases 2000–2004/cases of specified malignancy	Incidence rate/100 000 per year (95% CI)	OR (95% CI) compared to general population	*P* value (two-tailed Fisher's exact test)
Lung cancer	29/20 198	143·6 (91·36–195·80)	13·41 (9·30–19·35)	<0·001
Multiple myeloma	18/2671	673·9 (363·63–984·18)	62·83 (39·56–99·80)	<0·001
Chronic lymphocytic leukaemia	11/8039	124·4 (47·34–201·45)	12·61 (7·02–22·65)	<0·001
Acute myeloid leukaemia or acute lymphoblastic leukaemia	10/7740	129·2 (49·17–209·23)	11·90 (6·45–21·97)	<0·001
Hodgkin's lymphoma	4/8383	47·8 (0·97–94·47)	4·37 (1·70–11·26)	0·014
Non-Hodgkin's lymphoma	12/18 905	63·5 (27·57–99·38)	5·846 (3·34–10·25)	<0·001

OR, Odds ratio; CI, confidence interval.

Epidemiol. Infect. (2010), 138: 1804-10

Clinical Infectious Diseases

MAJOR ARTICLE

Outcomes of Immunocompromised Adults Hospitalized With Laboratory-confirmed Influenza in the United States, 2011–2015

Jennifer P. Collins,[1,2] Angela P. Campbell,[3] Kyle Openo,[2] Monica M. Farley,[2,4] Charisse Nitura Cummings,[2] Mary Hill,[5] William Schaffner,[6] Mary Lou Lindegren,[8] Ann Thomas,[7] Laurie Billing,[8] Nancy Bennett,[9] Nancy Spina,[10] Marisa Bargsten,[11] Ruth Lynfield,[12] Seth Eckel,[13] Patricia Ryan,[14] Kimberly Yousey-Hindes,[15] Rachel Herlihy,[16] Pam Daily Kirley,[17] Shikha Garg,[3] and Evan J. Anderson[1,2,4]

[1]Emory University School of Medicine, Department of Pediatrics, Atlanta, [2]Emerging Infections Program, Atlanta VA Medical Center, [3]Influenza Division, US Centers for Disease Control and Prevention, Atlanta, and [4]Emory University School of Medicine, Department of Medicine, Atlanta, Georgia, [5]Salt Lake Valley Health Department, Salt Lake City, Utah; [6]Vanderbilt University School of Medicine, Nashville, Tennessee; [7]Oregon Public Health Division, Portland; [8]Ohio Department of Health, Columbus; [9]University of Rochester Medical Center, New York; [10]New York State Department of Health, Albany; [11]New Mexico Department of Health, Santa Fe; [12]Minnesota Department of Health, St Paul; [13]Michigan Department of Health and Human Services, Lansing; [14]Maryland Department of Health and Mental Hygiene, Baltimore; [15]Connecticut Emerging Infections Program, Yale School of Public Health, New Haven; [16]Colorado Department of Public Health and Environment, Denver; and [17]California Emerging Infections Program, Oakland

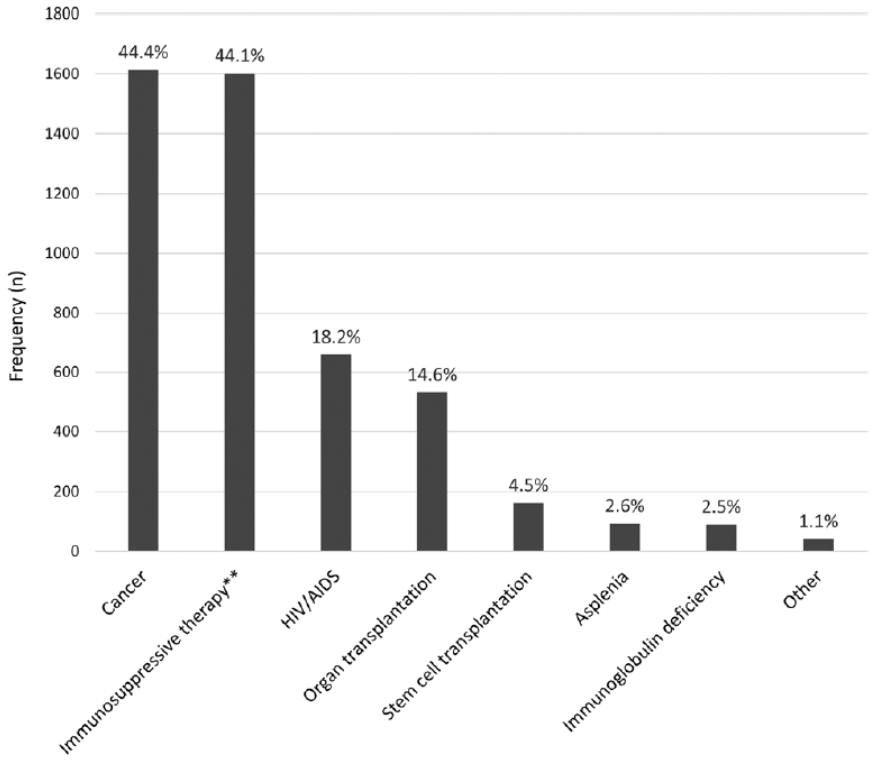
Background. Hospitalized immunocompromised (IC) adults with influenza may have worse outcomes than hospitalized non-IC adults.

Methods. We identified adults hospitalized with laboratory-confirmed influenza during 2011–2015 seasons through CDC's Influenza Hospitalization Surveillance Network. IC patients had human immunodeficiency virus (HIV)/AIDS, cancer, stem cell or organ transplantation, nonsteroid immunosuppressive therapy, immunoglobulin deficiency, asplenia, and/or other rare conditions. We compared demographic and clinical characteristics of IC and non-IC adults using descriptive statistics. Multivariable logistic regression and Cox proportional hazards models controlled for confounding by patient demographic characteristics, pre-existing medical conditions, influenza vaccination, and other factors.

Results. Among 35 348 adults, 3633 (10%) were IC; cancer (44%), nonsteroid immunosuppressive therapy (44%), and HIV (18%) were most common. IC patients were more likely than non-IC patients to have received influenza vaccination (53% vs 46%; $P < .001$), and ~85% of both groups received antivirals. In multivariable analysis, IC adults had higher mortality (adjusted odds ratio [aOR], 1.46; 95% confidence interval [CI], 1.20–1.76). Intensive care was more likely among IC patients 65–79 years (aOR, 1.25; 95% CI, 1.06–1.48) and those >80 years (aOR, 1.35; 95% CI, 1.06–1.73) compared with non-IC patients in those age groups. IC patients were hospitalized longer (adjusted hazard ratio of discharge, 0.86; 95% CI, .83–.88) and more likely to require mechanical ventilation (aOR, 1.19; 95% CI, 1.03–1.36).

Conclusions. Substantial morbidity and mortality occurred among IC adults hospitalized with influenza. Influenza vaccination and antiviral administration could be increased in both IC and non-IC adults.

Frequency of various immunocompromising conditions among immunocompromised adults hospitalized with laboratory-confirmed influenza



**Nonsteroidal immunosuppressive therapy included chemotherapy for cancer (within 2 weeks of admission), antibody-based agents (alemtuzumab, basiliximab, daclizumab, trastuzumab, rituximab, infliximab, and/or muromonab-CD3), immunosuppressants (cyclosporine, azathioprine, and/or leflunomide), and antirejection medications (tacrolimus, sirolimus, mycophenolate mofetil, and/or antithymocyte globulin).

CID 2019

NCBI Resources How To

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed

Advanced

Format: Abstract

Send to

J Clin Virol. 2011 Mar;50(3):212-6. doi: 10.1016/j.jcv.2010.11.013. Epub 2010 Dec 17.

Evaluation of pandemic H1N1 (2009) influenza vaccine in adults with solid tumor and hematological malignancies on active systemic treatment.

Mackay HJ[1], McGee J, Villa D, Gubbay JB, Tinker LM, Shi L, Kuruvilla J, Wang L, MacAlpine K, Oza AM.

Author information

Abstract

BACKGROUND: Over 85% of healthy individuals vaccinated with the pandemic H1N1 (pH1N1) vaccine achieve seroprotection.

OBJECTIVES: We evaluated the safety and immunogenicity of pH1N1 vaccine in patients undergoing chemotherapy for hematological and solid tumor malignancies.

STUDY DESIGN: Adult patients, receiving chemotherapy undergoing pH1N1 vaccination at our institution had blood samples drawn for CBC (baseline only) and serology prior to and ≥ 21 days post vaccination. HAI antibody testing was performed for pH1N1 (A/California/7/2009 strain) and seasonal H1 (A/Brisbane/59/07 strain). Seroprotection was defined as a pH1N1 antibody titre ≥ 1:40 and seroconversion as an antibody titre >4 × baseline. Patients completed a symptom diary card.

RESULTS: Paired samples were available for 46 patients (20 solid tumor, 26 hematological), median age 56 (range 23-76) years. The seroprotective rate post-vaccination for solid tumors was 50% compared to 27% for hematological malignancy (p=0.11), respective seroconversion rates were 45% and 19% (p=0.06). In patients with solid tumors vaccination mid cycle resulted in the highest pH1N1 titres, although timing and blood count were not associated with seroconversion or seroprotection. For hematological patients, a normal leukocyte count and vaccination at the beginning of a cycle were associated with higher rates of seroconversion ($p \leq 0.05$). Addition of rituximab to chemotherapy resulted in a failure to seroconvert (p=0.05). Vaccination was well tolerated by all patients.

CONCLUSIONS: Although well tolerated, the seroprotection rate following pH1N1 vaccination is lower than that would be expected. Further investigation into immunization strategies in patients receiving chemotherapy is required.

PMID: 21168361 DOI: 10.1016/j.jcv.2010.11.013

Αποτελεσματικότητα των εμβολίων σε ανοσοκατεσταλμένους

frontiers in Immunology

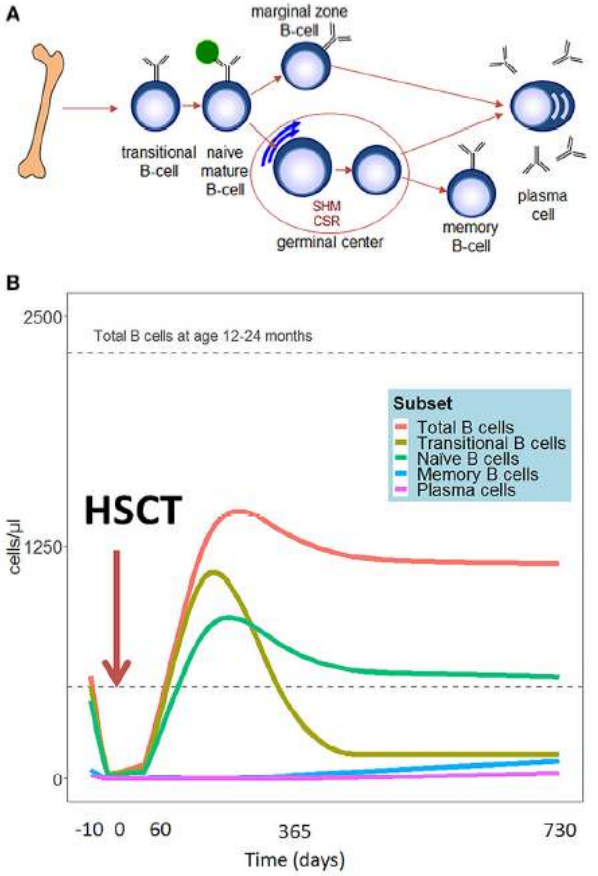
MINI REVIEW
published: 12 April 2019
doi: 10.3389/fimmu.2019.00782

B Cell Reconstitution and Influencing Factors After Hematopoietic Stem Cell Transplantation in Children

*Nicolaas G. van der Maas, Dagmar Berghuis, Mirjam van der Burg and Arjan C. Lankester**

Willem-Alexander Children's Hospital, Department of Pediatrics and Laboratory for Pediatric Immunology, Leiden University Medical Center, Leiden, Netherlands

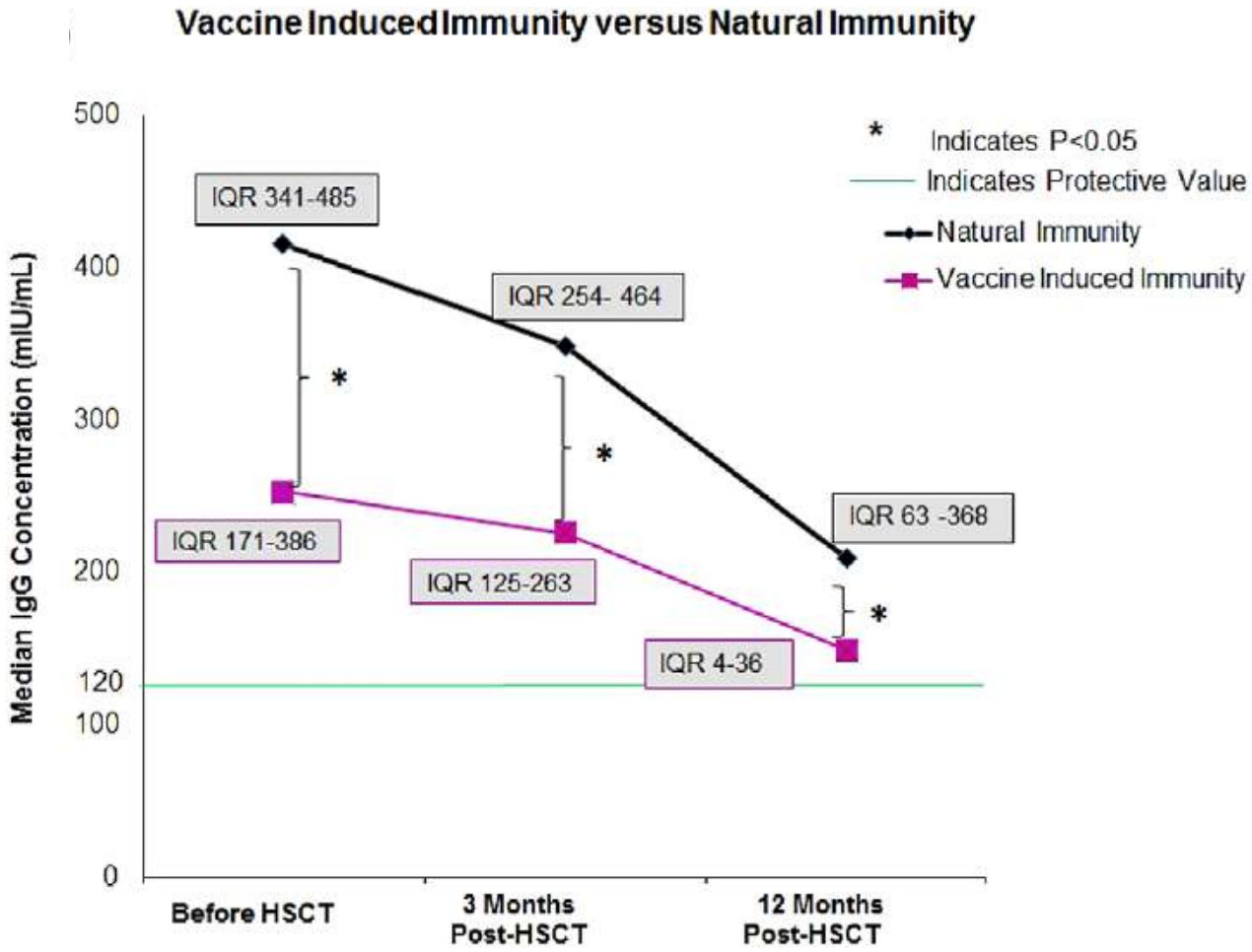
- **Risk of pneumococcal invasive disease** is increased both early and late after HSCT, reaching **30-fold higher risks** compared to the general population after 10 years
- Correlates with presence/occurrence of GVHD



A. Schematic representation of peripheral B-cell development.
B. Hypothetical scheme of B cell subset reconstitution after HSCT

Front. Immunol2019;10:782.doi: 10.3389/fimmu.2019.00782

Early loss of immunity against measles following allogeneic hematopoietic stem cell transplantation



Decline in measles-specific IgG levels before and after allogeneic HSC

Garrido G, AJH 2019

ΠΡΩΤΟΠΑΘΕΙΣ ΑΝΟΣΟΑΝΕΠΑΡΚΕΙΕΣ - ΕΜΒΟΛΙΑ

Type of PID	Type of infectious risk	Recommended vaccines	Contraindicated vaccines
Phagocytic cell defects	Bacterial and fungal infections	Inactivated vaccines	Live attenuated bacterial vaccines in chronic granulomatous disease. Live attenuated viral and bacterial vaccines in leucocyte adhesion deficiency and cytotoxic granule-release defect.
Complement deficiencies	Bacterial infections	All (probably effective)	None
TLR and IL-12/IFN-gamma signalling pathway defects.	Viral infections (HSV) Bacterial infections (Non-tuberculous Mycobacteria, non-typhoidal Salmonella)	Inactivated vaccines	Live attenuated should be given after evaluating immune system efficiency
Minor antibody deficiencies (IgA deficiency, IgG subclass deficiency, SPAD, ATS)	Viral infections (Enterovirus) Bacterial infections	All	None
Major antibody deficiencies (X-linked agammaglobulinemia, CVI, ataxia-telangiectasia DiGeorge syndrome, Wiskott–Aldrich syndrome)	Viral, bacterial and fungal infections	Inactivated influenza vaccines and vaccines based on bacterial polysaccharides	Live attenuated vaccines (except to MMRV in ptz with CD4 ≥ 500 cells/ L, CD8 ≥200 cells/ L and a normal mitogen response or with CD4 cells/L ≥25%)

Principi N, Vaccine 2014;32(30)

ΔΕΥΤΕΡΟΠΑΘΕΙΣ ΑΝΟΣΟΑΝΕΠΑΡΚΕΙΕΣ - ΕΜΒΟΛΙΑ

Type of SID	Type of infectious risk	Recommended vaccines	Contraindicated vaccines
HIV	Viral, bacterial and fungal infections	All	Live attenuated vaccines if CD4<200 cells/μl
Hematological and solid malignancies	Viral, bacterial and fungal infections	All inactivated vaccines. Live attenuated vaccines in low-level ID ptz.	Live attenuated vaccines during chemotherapy
HSCT	Viral, bacterial and fungal infections	All inactivated vaccines.	MMR-ZV up to 24mo post transplant, up to 3mo after immunosuppressive therapy in chronic GVHD.
Solid organ tranplant	Viral, bacterial and fungal infections	All inactivated vaccines. Live attenuated vaccines in low-level ID ptz.	Live attenuated vaccines.
Immunosuppressive therapy in AI diseases	Viral, bacterial and fungal infections	All inactivated vaccines. Live attenuated vaccines in low-level immunosuppression: to be considered.	Live attenuated vaccines in high-level immunosuppressed pt (4ws before to 4ws after high-dose cortcosteroid therapy; 4ws before to 3mo after biological modifiers therapy).
Asplenia	Bacterial infections	All	LAIV

Eibl MM & Wolf HM, 2015; IDSA, 2014

Vaccination and haematological malignancies 1

Vaccination of patients with haematological malignancies who did not have transplantations: guidelines from the 2017 European Conference on Infections in Leukaemia (ECIL 7)

Malgorzata Mikulska, Simone Cesaro, Hugues de Lavallade, Roberta Di Blasi, Sigrun Einarsdottir, Giuseppe Gallo, Christina Rieger, Dan Engelhard, Thomas Lehrnbecher, Per Ljungman, Catherine Cordonnier, on behalf of the European Conference on Infections in Leukaemia group

ECIL 7 recommendations for vaccination of patients with myeloid diseases

	Inactivated influenza vaccine	Pneumococcal vaccines	Other inactivated vaccines	Comments
AML and MDS	At the end of intensive chemotherapy in patients with AML or MDS, a single dose is recommended yearly as long as the patient is considered immunocompromised (B II u)	3–6 months after the end of chemotherapy, patients with AML or MDS should be (re) vaccinated according to age and country recommendations	In countries with high HBV prevalence where a high risk of HBV transmission during chemotherapy exists, HBV vaccination starting before and continuing during chemotherapy can be administered (C II u). 3–6 months after the end of chemotherapy, patients with AML or MDS should be (re) vaccinated according to age and country recommendations	Patients with MDS who do not receive any specific treatment should have their vaccine programme revised according to age and country recommendations
CML	Patients with CML should receive one dose yearly (B II u)	Patients with CML should be vaccinated against *Streptococcus pneumoniae* (C II t). Although there are no data on the response to PCV, it is recommended to give one dose of PCV followed 2 months later by one dose of PPSV23	According to age and country recommendation	The expected response rate during dasatinib or bosutinib treatment might be lower than with the other tyrosine kinase inhibitors
Other chronic myeloproliferative neoplasms	According to age and country recommendation	According to age and country recommendation	According to age and country recommendation	There are no data on the vaccine response under ruxolitinib

Lancet Infect Dis 2019; 19: e188–99

Chronic myeloid leukaemia (CML) - Inactivated influenza vaccine

- Seroprotection rate of H1N1 adjuvanted vaccine in 32 patients with CML receiving imatinib or dasatinib was 85% after one dose, which was not different from that in healthy controls (100%).
- Geometric mean concentrations of specific antibodies were significantly lower than those in controls.
- **The second dose did not provide a significant benefit.**

Haematologica 2011; 96: 307–14
Blood 2013; 122: 227–38

Other vaccination data in AML:
paediatric population, summary and impact on adult AML patients

- Loss of previous immunity is less pronounced in AML than in ALL children (in line with adult setting, e.g. tetanus)
- However, **if revaccinated, both groups mount a satisfactory response once treatment is finished**
- Extrapolation to adult population: revaccination of selected adult AML patients after completion of chemotherapy might be successful and may have clinical benefit, for example given low residual immunity to tetanus following AML chemotherapy

Hammarstrom et al. Support Cancer Care 1998; Bochennek et al., Vaccine 2014; Patel et al. CID 2007; Cheng et al. Arch Dis Child 2012; Patel et al. Arch Dis Child 2012; Spickermann et al. Leukemia and Lymphoma 1994

ΧΜΘ – Επηρεάζει την αποτελεσματικότητα των εμβολίων?

Infection incidence in CML patients on Tyrosine Kinase Inhibitors (TKI)

- CML patients in pre TKI era had an increased risk of respiratory and skin infections *(Titmarsh 2014)*
- TKIs further increase this risk, but precise data not available
  - Risk of reactivations of hepatitis B with TKIs have been repeatedly reported leading to a recommendation of the EMA to screen all patients for HBV before starting TKI
  - Case reports on dasatinib-induced opportunistic infection *(Chang, IJID 2014)*
- **TKI treatment might lower the vaccine efficacy**
- Response to pneumococcal vaccination was lower than in healthy controls
- Reponses to influenza vaccination (inactivated and adjuvanted) was similar to healthy controls

Titmarsh et al. Cancer Epidemiology 2014; Rubin et al. CID 2013; Chang et al. Int J Infect Dis. 2014; de Lavallade et al. Blood 2013; de Lavallade et al. Haematologica 2011

2017

Myeloproliferative disorders (MPD) and ruxolitinib

- Data suggest no increased risk of infection in patients with MPDs in the pre-JAKi era
- Ruxolitinib is associated with an increased risk of infections, and in particular HZ and opportunistic infections
- **JAKi treatment might lower the vaccine efficacy**
- No data on the efficacy of vaccination in patients on JAKi

2017

ECIL 7 recommendations for vaccination of patients with lymphoproliferative diseases

	Inactivated influenza vaccine	Pneumococcal vaccines	Other inactivated vaccines	Comments
Multiple myeloma	Yearly vaccination (one dose) is strongly recommended (A II u) as long as the patient is considered immunocompromised	One dose of PCV13 followed by one dose of PPSV23, at least 8 weeks later, is recommended (B II u), preferably before treatment or during maintenance	Other inactive vaccines should be considered 3–6 months after the end of treatment, according to age, comorbidities, and country recommendations	LAVs are contra-indicated until at least 3 months after the end of chemotherapy (D III)
Lymphoma	Yearly vaccination (one dose) is strongly recommended (A II u) as long as the patient is considered immunocompromised, except in patients receiving intensive chemotherapy or who are receiving or have received anti-CD20 antibodies in the previous 6 months	One dose of PCV13 followed by one dose of PPSV23, at least 8 weeks later, is recommended (B II t), preferably before treatment or during maintenance, except in patients who are receiving high-dose chemotherapy or who are receiving or have received anti-CD20 antibodies in the previous 6 months	Human papillomavirus vaccine is recommended in healthy adolescents and young adults according to country recommendations for age after the end of treatment (B II t). Other inactive vaccines should be considered 3–6 months after the end of treatment, according to age, comorbidities, and country recommendations	In patients who are receiving or have received anti-CD20 antibodies in the previous 6 months, any inactivated vaccine should be delayed for at least 6 months after the last dose (B II u for IIV). LAVs are contra-indicated until at least 3 months after the end of chemotherapy (D III)
Chronic lymphocytic leukaemia	Same recommendation as for lymphoma patients	One dose of PCV13 followed by one dose of PPSV23, at least 8 weeks later, are recommended (B II u), preferably before treatment	Same recommendation as for lymphoma patients	Same recommendation as for lymphoma patients. Novel drugs might significantly impair the vaccination response

ECIL 7=2017 European Conference on Infections in Leukaemia. LAVs=live-attenuated vaccines. PCV13=pneumococcal conjugate 13-valent vaccine. PPSV23=pneumococcal polysaccharide 23-valent vaccine

Lancet Infect Dis 2019; 19: e188–99

ΠΟΛΛΑΠΛΟΥΝ ΜΥΕΛΩΜΑ - ΑΠΟΤΕΛΕΣΜΑΤΙΚΟΤΗΤΑ ΕΜΒΟΛΙΩΝ

MM and pneumococcal vaccination, summary

Response rate to PPSV23: between **33-57%.** However:

- Most patients off therapy or during plateau phase > not representative of current treatments
  - » *Chapel Lancet 1994; Hargreaves J Clin Pathol 1995, Robertson Br J Cancer 2000; Hinge APMID 2012*

Response rate to PCV: a single study: **MM: 63% vs controls 100%**

- **Ab function test (OPA): MM: 8% vs** controls: **55%**
  - » *Karlsson Trials in Vaccinology 2013*

Response to vaccination variable, possibly better on lenalidomide
  - » *Noonan Clin Cancer Res 2012*

No safety issues

No data on the duration of immunity induced by vaccination

2017

MM and influenza vaccination, summary

Risk of influenza increased in MM: HR=6.1
  - » *Blimark et al. Haematologica 2015*

Trivalent inactivated vaccine (TIV)

Seroconversion **0% to 83%** (5/6 pts), most frequently approx. **20-25%***

Robertson et al. Br J Cancer 2000; Rapezzi et al. Eur J Haematol 2003; Ljungman et al. Br J Haematology 2005; Hahn et al. Haematologica 2015; Cherif et al. Eur J Haematol 2013; Sanada et al. Japanese Journal of Clinical Oncology 2016;

Improving efficacy:

- **No clear benefit of 2nd dose of TIV or of an adjuvanted vaccine**

Ljungman et al. Br J Haematol. 2005; Sanada et al. Jap J Clin Oncol 2016; Monkman et al. Leuk Lymph 2011

- **Possible benefit of 2 doses of high dose or adjuvanted vaccine**

Cherif et al. Eur J Haematol 2013; Branagan et al. Clin LymphMyel Leuk. 2017

No safety issues

2017

Risk of infections in lymphoma

Very heterogenous disease

Increased risk of invasive pneumococccal disease: 5-10 fold

Lindstrom et al. Infect Dis 2016; Wong et al. Epidemiol Infect 2010

Increased risk of influenza

Increased risk of Herpes Zoster: 2-3.5 fold

Hansson et al. Br J Cancer 2017, Yenikomshian et al. BMC Infect Dis 2015, Forbes et al. BMJ 2014

HBV: In low endemicity settings de novo infections rare, while reactivation is more frequent, thus appropriate screening and prophylaxis or treatment should be provided

HPV: increased risk, particularly in case of HD or pelvic irradiation

Klosky et al. Cancer 2009

Pneumococcal vaccination and lymphoma

PPSV23

- Many data from splenectomised patients: good response (45%, 72%, 80%), similar to other patients undergoing splenectomy, if vaccinated before CT

Petrasch et al. Clin Diagn Lab Immunol 1997; Landgren et al. J Intern Med 2004, Cherif et al. Vaccine 2006, Grimfors et al. Eu J Haematol 1990; Ammann et al. Rev Infect Dis 1981

- Titres waned at 3 years > revaccination at 2 years might be beneficial
  - » *Grimfors et al. Eu J Haematol 1990*

PCV

- Better response to conjugate HiB than polysaccharide vaccine to PPSV23
  - » *Svensson et al. Br J Haematol 2012*
- No data in lymphoma with PCV7 or PCV13
- The benefit of the conjugated vaccine in this population is expected

2017

Response to influenza vaccination in lymphoma, summary of 15 studies

- **Response to TIV highly variable (3%-95%, in median approx. 30%*), lower than controls**

  Nordøy et al. Medical Oncology 2002; Rapezzi et al. Eu J Haematol 2003; Ljungman et al. Br J Haematol 2005; Mazza et al. Clin Med Res 2005; Brydak et al. Vaccine 2006; Centkowski et al. Clin Immunol 2007; Bedognetti et al. J Immunol 2011; Ide et al. Human Vaccines & Immunother. 2014; Sanada et al. Japanese Journal of Clinical Oncology 2016

- **Similar response to TIV and an adjuvanted vaccine**

  Mackay et al. JCV 2011; Monkman et al. Leuk & Lymph 2011; Villa et al. Leuk & Lymph 2013; De Lavallade et al. Haematologica 2011; Yri et al. Blood 2011

- **Possible benefit of a 2nd dose, particularly of an adjuvanted vaccine**

  Ide et al. Human Vaccines & Immunother. 2014; De Lavallade et al. Haematologica 2011; Villa et al. Leuk & Lymph 2013; Hottinger et al. Oncologist 2012

- **Not affected by chemotherapy, but no clear data on high intensity regimens**
  - *Centkowski et al. Clin Immunol 2007, Hottinger et al. Oncologist 2012*
- **Response strongly impaired by rituximab (ongoing and at least during the previous 6-10 months): no response at all reported in most studies**
  - *Ljungman 2005, Yri 2011, De Lavallade 2011, Ide 2014*

2017

Pneumococcal vaccination in CLL

Response to PPSV23:

- Poor, ranging from 0% to 21%
- Always lower than controls
- Better in early stage disease
  - » *Hartkamp et al. Vaccine 2001; Sinisalo et al. BJH 2001; Van der Velden et al. Eur J Haem 2007; Safdar et al. Cancer 2008*
- No benefit of ranitidine or of GM-CSF
  - » *Van der Velden et al. Eur J Haem 2007; Safdar et al. Cancer 2008*

Response to PCV: better

- PCV7: 20-47%, better in early stage disease *(Sinisalo et al. Vaccine 2007)*
- PCV13: 58% in patients naïve of any treatment *(Pasiarski et al. PLOS One 2014)*
- Poor in case of ibrutinib, but very experienced pts *(Andrick BJH 2017)*

ΧΛΛ- Εμβολιασμός ΠΡΙΝ την έναρξη της θεραπείας

Influenza vaccination in CLL

Response to TIV was low in two studies: **5-30%**; but as high as **72%-95%** in a single study, which included, among others, 60 CLL patients, mainly **treatment naïve**

Van der Velden Eu J Inter Med 2001, Rapezzi Eur J Haematol 2003, Centkowski J Clin Immunol 2007

Little benefit of 2nd dose of TIV but good response to 2 doses of adjuvanted vaccine, particularly in early stage CLL

Van der Velden Eu J Inter Med 2001, Ljungman Br J Haematol 2005<; De Lavallade Haematologica 2011

Poor response (8%-26%) to TIV in patients treated with **ibrutinib, even in case of high dose TIV**

Sun JAMA Oncology 2016; Douglas Haematologica 2017

ΟΛΛ – ΑΝΤΑΠΟΚΡΙΣΗ ΣΕ ΕΜΒΟΛΙΑ

Wide range of response to vaccination with **TIV during maintenance:** H1N1 **22%** - 72%; H3N2 34% - 88%; B 35% - **88%**

Shahgholi E 2012 Pediatr Blood Cancer; Hsieh YC 2002 J Formos Med Assoc; Chisholm 2001 Arch Dis Child; Relly A 2010 J Pediatr Hematol Oncol; Porter CC2004 Pediatr Blood Cancer; Wong-Chew RM 2012 Oncol Lett; Brydak LB 1997 Leuk Lymphoma

✓Seropositivity rates after vaccination **during (mainly maintenance) chemotherapy :**

PCV 7, 2 doses:	86%-100% (depending on serotypes) [7]
PCV 10 , 1 dose:	33%-89% (depending on serotypes) [1]
PCV 13, 1 dose (50% pts with ALL):	46%-87% (depending on serotypes) [6]

✓Seropositivity rates after vaccination **post -chemotherapy**:

PCV 13, 1 dose:	64%-100% (depending on serotypes) [6]

1- Crawford 2015 Vaccine Reports; 2- Lehrnbecher 2011 British J Haematol
3- Patel SR 2010 BMJ; 4- Ridgway 1993 Leukemia and lymphoma
5- Wang 2010 Epidemiol Infect; 6- Hung TY 2017 Cancer; 7- Cheng FW 2010 Arch Dis Child

✓**Countries with high prevalence of HBV**

- ✓ High incidence of de novo HBV infection in, mainly related to hospitalization (unsafe transfusions, in-hospital transmission,…) [1]
- ✓ HBV infection results in delaying full CT course and a reduction of doses with higher mortality rates (7-40%) [2]

1- Hwang JP 2017 cancer; Al-Jadiry MF 2013 East Mediterr Health; 2- Guruprasad 2014 Pediatr Bood Cancer; 3- Karaman S 2011 Ann audi Med; 4- Zignol M 2005 Cancer; Fioredda F 2005 Eur J Haematol

ECIL 7 guidelines for vaccination of children with ALL
INDUCTION and REINDUCTION PHASES

Vaccine	Timing and doses	ECIL 7 recommendation	Comment
In the setting of **high HBV prevalence** and **high risk of acquiring HBV infection during CT**			
HBV in HBsAb and HBcAb seronegative patients	Double dose	**B II u**	Different schedules of 3-5 doses can be used
Co-administration of HBV specific HBIg might improve protection		**C II u**	
All live vaccines (including VZV) are contraindicated		**D II u**	

^ Better response might be obtained administering a 2nd dose and/or using an adjuvanted* or high dose vaccine**
**Data from monovalent pandemic vaccine; no data from regular adjuvanted vaccine. **Unavailable in Europe*
One dose unless specified otherwise

ECIL 7 guidelines for vaccination of children with ALL

MAINTENANCE THERAPY

Vaccine	Timing and doses	ECIL 7 recommendation
Inactivated vaccines are feasible but suboptimal response might be present > most vaccinations should be postponed to 3-6 months after the end of CT in order to achieve better and longer lasting protection		
Inactivated influenza vaccine	Yearly 2 doses if ≤ 9 years	**A II u,** **t for dose**
PCV13	1 dose	**B II u**
VZV	CT suspended for at least 1 week before and after, longer if vaccine-related rash	**C II u**
Postpone VZV vaccination to 3-6 months after CT, and provide alternative protective measures during maintenance therapy (acyclovir, isolation, vaccination of household contacts, etc.), in consideration of the potential risk of ALL relapse		**A III**
Live vaccines other than VZV are contraindicated		**D II u**

ECIL 7 guidelines for vaccination of children with ALL

3-6 MONTHS FROM THE END OF CHEMOTHERAPY

Vaccine	Dose	ECIL 7 recommendation
Inactivated influenza	From the end of maintenance CT and as long as considered immunocompromised	**B II u**
Patients fully vaccinated before ALL diagnosis		
DTaP, IPV, HiB	Irrespective of Ab titres* 1 dose **	**A II u**
HBV	Irrespective of Ab titres* 1 dose according to country recommendations	**A II u**
PCV13	1 dose	**A II u**
MenC/ACWY	1 dose according to country recommendations	**B III**
MenB	1 dose according to country recommendations	**C III**
HPV	According to country recommendations	**B III**
VZV in seronegative patients	2 doses (or 2° only if seronegative 4 weeks after 1st)	**A II u**
MMR	Irrespective of Ab titres or when seronegative 1 dose in previously vaccinated	**A II u**
Patients not vaccinated before CT should be revaccinated with full courses, according to country's recommendations		**A II u**

*Titres may decline over time; ** In high risk patients, suboptimal response to 1 dose might occur

Vaccination and haematological malignancies 2

Vaccination of haemopoietic stem cell transplant recipients: guidelines of the 2017 European Conference on Infections in Leukaemia (ECIL 7)

Catherine Cordonnier, Sigrun Einarsdottir, Simone Cesaro, Roberta Di Blasi, Malgorzata Mikulska, Christina Rieger, Hugues de Lavallade, Giuseppe Gallo, Thomas Lehrnbecher, Dan Engelhard, Per Ljungman, on behalf of the European Conference on Infections in Leukaemia group

Invasive pneumococcal disease (IPD) after HSCT

Mainly pneumonia and bacteremia, 21 - 57% occurring during the first 12 months after transplant

Mortality rate after HSCT # 11-22%

The risk correlates with the decrease of specific Abs (IgG, especially IgG2 and IgG4, and IgM) levels and opsonic activity (OPA) after HSCT.

Although HSCT recipients are at higher risk after Allo than after Auto, **all HSCT patients are at risk**.

Main risk factors:

- After allo: chronic GVHD
- After auto: total body irradiation (TBI)

Lancet Infect Dis 2019;19:e200-12
Winston DJ, Ann Int Med 1979
Sheridan JF, Blood 1990

Immune response rates to the PCV vaccines *(PCV7 and PCV13)* *in prospective studies* after allogeneic SCT

Ref.erence	Vaccine	No. Pts (No. evaluable pts)	Immunization schedule	Definition of response	% of responders and comments
Molrine *Blood 2003*	**PCV7**	**96** **(65)**	**3 doses at 3, 6, 12 mo** **(+/- donor (D) vaccination)**	≥ 0.5 µg/mL for all 7 serotypes	At 13 months: **64-75%** Benefit of D vaccination for the response to the first 2 doses, not for the 3rd
Kumar *CID 2007*	**PCV7**	**64** **(44)**	**1 dose of either PPV23 or PCV7 at 6 mo** **(1 dose of PPV23 or PCV7 to the D), assessed at 12 mo**	≥ 0.35 µg/mL for ≥ 1 serotype	**38.6%** after PCV7 *0% after PPV23* Better immunogenicity of PCV7 vs PPV23
Meisel *Blood 2007*	**PCV7**	**53 ped.** **(43)**	**3 doses at 1 mo. interval from 6-10 mo**	≥ 0.5 µg/mL for all 7 serotypes	**74%**
Cordonnier *CID 2009*	**PCV7**	**158** **(114)**	**3 doses: Early (3, 4, 5 mo.) *or Late* (9, 10, 11 mo) after HSCT**	≥ 0.15µg/mL ≥ 0.5 µg/mL for all 7 serotypes	**79** (E) vs **82** (L) % **56** (E) vs **54** (L) % **Early not inferior to late**
Cordonnier *CID 2015*	**PCV13**	**251** **(207)**	**3 doses from 4 mo, then a 4th dose at 9 mo.**	IgG GMFR and > 0.35 µg/mL for all 13 serotypes	**89.7%–98.0%** *No ≠ betwen MA and non-MA conditioning regimens*

GMFR: Geometric Mean Fold Rise; MA: myeloablative

Pneumococcal vaccination
ECIL7 guidelines for autologous HSCT recipients

From 3 months after transplant

3 doses of PCV13 at 1 month interval **B III**

At 12 months:

1 dose of PPSV23 **B III**

No large data to support recommendations after the initial program

The assessment of Ab titers to the main conjugate and PS vaccine serotypes may help in defining the best option at a given time for a patient

Pneumococcal vaccination

ECIL 7 guidelines for allogeneic HSCT recipients

From 3 months after transplant

3 doses of PCV13 at 1 month interval — A I

A 4th dose given 6 months after the 3rd one can be considered in case of GVHD — B II r

At 12 months:

- 1 dose of PPSV23 * if no GVHD — B I

** No earlier than 8 weeks after the last PCV*

No large data to support recommendations after the initial program

The assessment of Ab titers to the main conjugate and PS vaccine serotypes may help in defining the best option at a given time for a patient

Immune response to Hib vaccination after allogeneic HSCT

- Although the subclass Ig response is different, the overall response to 1 dose of Hib-conjugate was not different at 6-8 or at 18-20 months *(Parkkali T et al. BMT 1996; Parkkali T et al. BMT 1999)*
- The response rates (#85%) to 2 doses starting between 4-9 months or between 10-17 months were not different *(Barra et al. JID 1992)*
- After 3 doses given over the first 2 years, the response rate varied between 47-81% *(Molrine et al. Blood 1996; Parkkali et al. BMT 2007)*
- A 3rd dose increases the GMCs of specific Abs *(Molrine et al. Blood 1996. Parkkali et al. BMT 2007)*

Anti-Hib vaccination

ECIL 7 guidelines for HSCT recipients

Considering the timing of Hib infections after transplant and that patients can respond to the vaccine from 3 months, it is recommended to give **3 doses of conjugate vaccine at 1 month interval from 3 months after transplant** **BII r**

In order to give a combined vaccine and decrease the overall number of vaccine doses, an alternative is to give 3 doses of a DTP-Hib vaccine from 6 months **B II r**

Meningogoccal vaccination after HSCT

- After 1 dose of MCV-4 given a median time of 2.3 (0.6-5.2) y after transplant: (retrospective study, 46 allo-HSCT aged 9-25y), only 65% responded either to the 4 (15%) or ≥ 1 (31-56%) serogroup. In the 16 non-responders, a second dose elicited a response in 8 of them *(Malher MB BBMT 2012)*

- After 3 doses of MCV-C given at 1 month interval: (prospective trial, 23 patients aged 2-17y) from 12 (auto) or 18 months (allo) after transplant, the response rate was 100% both in auto- and allogeneic HSCT recipients *(Patel SR CID 2007)*

- No data on the MenB vaccines after HSCT sofar

ECIL 7 recommendations

Neisseria meningitidis vaccines*	From 6 months after transplantation at least two doses of either a monovalent or tetravalent C vaccine (B II u) and meningococcal B vaccine (B III), in accordance with country recommendations for a given age and particularly for at-risk groups such as students living in campus, travellers, or soldiers

Diphtheria-Tetanus vaccination

- 3 doses are needed *(Ljungman et al. JID 1990).* Excellent tolerance, no SAE.
- Excellent response (85-100%) after 3 doses given at 1-2 months interval from 6-12 months.
- Comparable response after Allo *(Ljungman et al. JID 1990; Parkkali et al. BMT 1997; Parkkali et al. BMT 2007; Inaba et al. BJH 2012)* or Auto HSCT *(Vance et al. BMT 1998)* , except in NHL patients who had received Rituximab before and/or after Auto *(Small T et al. BBMT 2009)*
- Comparable responses after RIC *(Meerveld-Eggink et al. BBMT 2009)* or cord blood transplant when vaccinated at 7-45 months *(Shah et al. BBMT 2015)*
- No difference in response when vaccinated early (6, 8, 14 months) or late (18, 20, 26 months)*(Parkkali et al. BMT 1997)*
- Responses are not or only weakly affected by GVHD

ECIL 7 recommendations

Tetanus-diphtheria vaccine*	From 6 months after the transplant three doses at 1–2-month intervals (B II u); DT vaccines should be preferred over Td vaccines both in children and adults (C III); booster doses should be administered according to country recommendations

Acellular Pertussis vaccine

Reference	Vaccine (Pertussis Toxoid content/ µg)	No. evaluable patients Type of HSCT (age range)	Immunization schedule	Definition of response	% of responders
Papadopoulos Blood 2008 (Abstract ASH)	Tdap (2.5)	41 pts ALLO *(1)* (10-64y)	1 dose, at a median of 4.5 y post-transplant	≥ 2 fold Ab titers from pre-vaccine titers	7/41 (17%)
Small BBMT 2009	Tdap (2.5)	28 pts AUTO *(2)* (20-73y)	1 dose, at a median of 4.5 y post-transplant	«	2/28 (7%)
Inaba BJH 2012	DTaP (25)	30 children ALLO < 7 y evaluable for long-term FU with 3 Ab assessments	3 doses planned at 12, 15 and 18 months *(4)*	EIA index values> 1.19	Each of the 3 doses increased Ab titers At 5 years post-HSCT: only 5/16 (31%) were protected
Shah BBMT 2016	Tdap (8) in adults DTaP (25) in children	63 pts ALLO Cord Blood (0.9-64)	2 or 3 doses at 1 month interval, started at a median of 17 (range: 7-45) months*(3)*	Seroconversion in a seroneg patient or >2 fold rise Ab titer	Children (n=16): 100% Adults (n= 44): 54%

ECIL 7 recommendations

Acellular pertussis vaccine*

The addition of pertussis toxoid to the diphtheria-tetanus vaccine, three doses at 1–2-month intervals, should be considered (C III); although there is no specific study with DTaP in adult HSCT recipients, considering the poor response to TdaP, the DTaP that contains a higher dose of pertussis toxoid than the Tdap should be preferred both in children and adults (C III)

Vaccination and haematological malignancies 2

Vaccination of haemopoietic stem cell transplant recipients: guidelines of the 2017 European Conference on Infections in Leukaemia (ECIL 7)

Catherine Cordonnier, Sigrun Einarsdottir, Simone Cesaro, Roberta Di Blasi, Malgorzata Mikulska, Christina Rieger, Hugues de Lavallade, Giuseppe Gallo, Thomas Lehrnbecher, Dan Engelhard, Per Ljungman, on behalf of the European Conference on Infections in Leukaemia group

Inactivated influenza vaccine(IIV) – HSCT Patients

	Recommendation and (grading) in allogeneic HSCT	Recommendation and grading in autologous HSCT
Inactivated influenza vaccine IIV†	From 6 months after transplantation a seasonal IIV dose should be administered annually at the beginning of flu season, after the first years following transplant, and at least until 6 months after stopping any immunosuppressor and as long as the patient is judged to be immunocompromised (A II r) or life-long (B II r); a second dose administered 3–4 weeks after the first one could be considered in patients with severe GvHD or low lymphocyte counts (B II r); in the setting of a community outbreak, IIV can be administered 3 months after transplantation, in which case, a second dose administered 3–4 weeks later is likely to be beneficial (B II r)	From 6 months: annual seasonal IIV, 1 dose, at the beginning of influenza season, at least as long as the patient is judged to be immunocompromised (B II r); in the setting of a community outbreak, IIV can be administered 3 months after transplant, in which case, a second dose administered 3–4 weeks later is likely to be beneficial (B II r)

HSCT Patients -Inactivated influenza vaccine(IIV)

Predictors of poor immune response to IIV after HSCT

- **Shorter time between transplant and vaccination-***(Natori 2017, Engelhard 1993, Mohty 2011, Issa 2011, Karras 2013)*
- **Low lymphocyte counts at vaccination** *(Engelhard 2011, Fukatsu 2016)*
- **Low IgG, IgA or IgM at vaccination** *(Fukatsu 2016, Mohty 2011)*
- **Chronic GVHD** *(Fukatsu 2017)*
- **Use of of calcineurin inhibitors or other immunosuppressive drugs** *(Mohty 2011, Natori 2017)*
- **Use of rituximab last 12 months** *(Issa, 2011)*

❖ **Second dose** might be beneficial in patients that cumulate factors of poor response or during outbreaks in patients vaccinated within 6 months of transplantation.

Hepatitis B virus vaccine(HBV) – HSCT Patients

	Recommendation and (grading) in allogeneic HSCT	Recommendation and grading in autologous HSCT
HBV vaccine*	Before transplant patients who are negative for all HBV markers that are transplanted with a graft from an anti-HBc positive donor should be vaccinated if possible (B III) and could additionally receive anti-HBV immunoglobulins; 6 months after transplantation patients who were negative for HBV before transplantation and patients who were vaccinated before transplant but lost their immunity at 6 months should be vaccinated according to country recommendation (6–12 months after transplantation 3 doses should be administered 0, 1, and 6 months apart), (B II t); patients infected with HBV before HSCT (HBsAg negative and anti-HBc positive) should be assessed regularly for anti-HBs antibody titres and should be vaccinated if they have unprotective titres (B III); if anti-HBs titres are <10 mIU/mL 1–2 months after the initial series of three vaccine doses, an additional series of three doses should be considered	6 months after transplantation: patients who were negative for HBV before transplantation and patients who were vaccinated before transplantation but lost their immunity after 6 months should be vaccinated according to country recommendation and age (6–12 months after transplantation 3 doses should be administered 0, 1, and 6 months apart)(B II t); patients infected with HBV before HSCT (HBsAg negative and anti-HBc positive) should have anti-HBs antibody titres assessed regularly and be vaccinated if they have unprotective titres (B III); if anti-HBs titres are <10 mIU/mL 1–2 months after the initial series of three vaccine doses, an additional series of three doses should be considered

ECIL 7 recommendations

Anti-HBc (+) donor can transmit HBV to the recipient.
ECIL group recommend vaccinating the recipient before transplantation.
Accelerated schedule of vaccination (day 0, 10, and 21)(?)
In previously HBV-infected recipients (in addition to antivirals) vaccination might prevent reverse seroconversion.

Lancet Infect Dis 2019;19:e200-12
Marchou B, J Infect Dis 1995;172:258-60
Le Q, Biol Blood Mar Transplatation 2009; 15:886-87

Human papillomavirus vaccine(HPV) – HSCT Patients

MacIntyre et al. Vaccine 2016

59 immunocompromised children (5-18y) including 20 HSCT recipients

3 doses of quadrivalent vaccine from 6 months after transplant, within 2-6 months

Seroconversion rate after 3 doses: 89 to 100% according to type

ECIL 7 recommendations

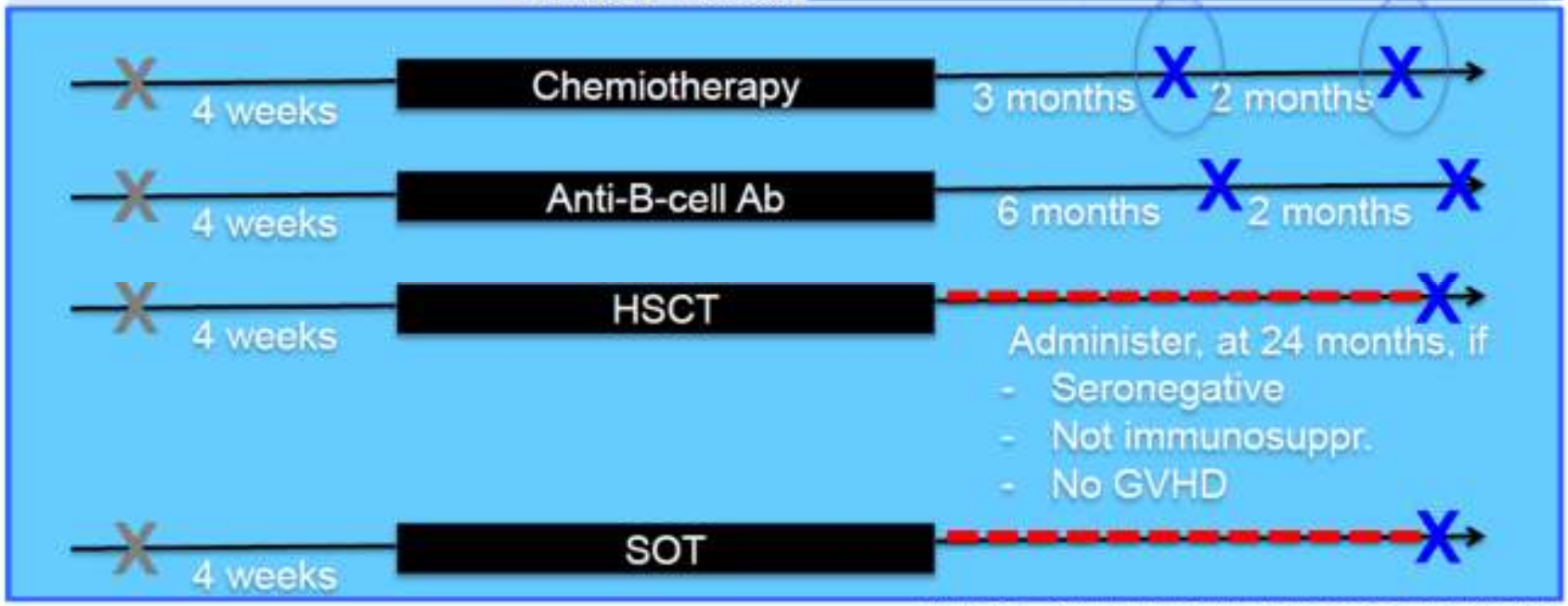
- Follow recommendations for general population in each country from 6-12 months after transplant

BIIu

Varicella vaccine – Ανοσοκατεσταλμένοι ασθενείς

Indications	*Schedule*	*Recommendation, Strength of Recommendation and Quality of Evidence*
All immunocompromised patients	Not licensed	Potential risk of severe disease
PID disorder without defective T-cell–mediated immunity	2-dose schedule separated by a 3-month i	**Recommended (not administered**
HSCT		
Pre-HSCT	See later	
Post-HSCT	See later	

U – patient not current with recommendation for immunocompetent individuals

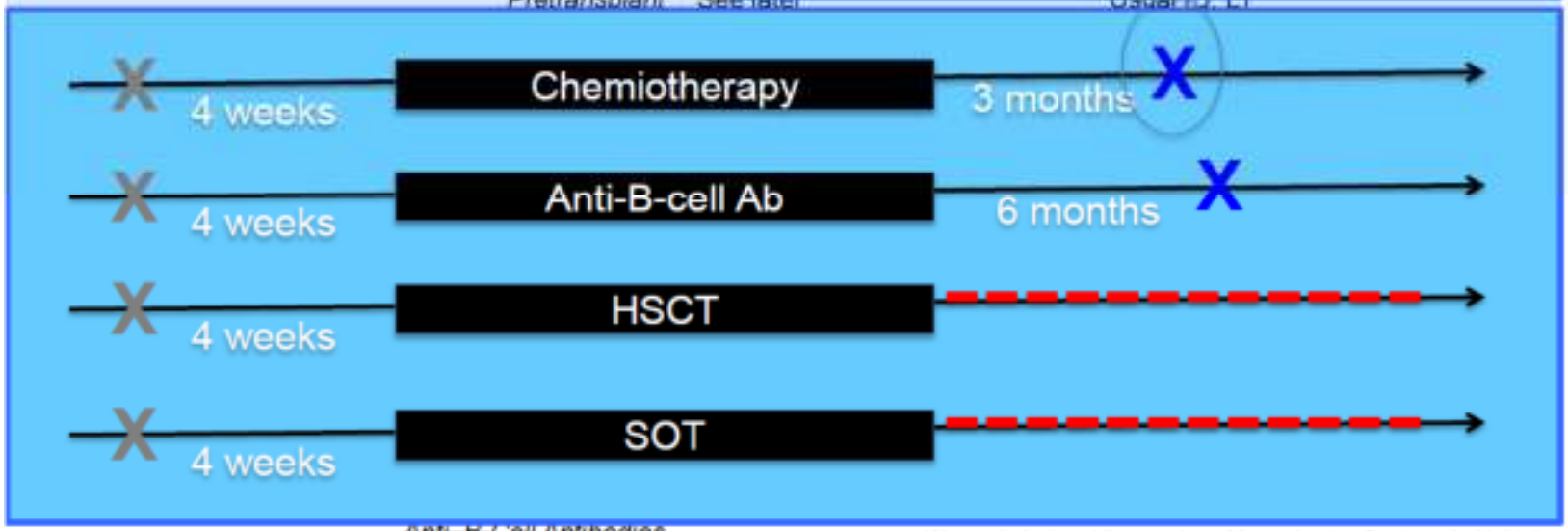


W=weak; L=low; VL=very low; M=moderate; S=strongh; H=high

Live Zoster virus vaccine – Ανοσοκατεσταλμένοι ασθενείς

Indications	*Schedule*	*Recommendation, Strength of Recommendation and Quality of Evidence*
All immunocompromised subjects	Not licensed	Potential risk of severe disease
Subject aged ≥ 50 years	4 weeks before beginning immunosuppressive therapy	Should be considered 50-59 years (W, L) >60 years (S, L)
PID		
HSCT		
Pre-HSCT	Se	
Post-HSCT	Se	
SOT recipients		
Pretransplant	See later	Usual Dx, Tx

U – patient not current with recommendation for immunocompetent individuals



Anti–B-Cell Antibodies

W=weak; L=low; VL=very low; M=moderate; S=strongh; H=high

NCBI Resources How To

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed

Advanced

Format: Abstract

Send to

Lancet. 2018 May 26;391(10135):2116-2127. doi: 10.1016/S0140-6736(18)30631-7. Epub 2018 May 24.

Inactivated varicella zoster vaccine in autologous haemopoietic stem-cell transplant recipients: an international, multicentre, randomised, double-blind, placebo-controlled trial.

Winston DJ[1], Mullane KM[2], Cornely OA[3], Boeckh MJ[4], Brown JW[5], Pergam SA[4], Trociukas I[6], Žák P[7], Craig MD[8], Papanicolaou GA[9], Velez JD[10], Panse J[11], Hurtado K[12], Fernsler DA[12], Stek JE[12], Pang L[12], Su SC[12], Zhao Y[12], Chan ISF[12], Kaplan SS[12], Parrino J[12], Lee I[12], Popmihajlov Z[12], Annunziato PW[12], Arvin A[5]; V212 Protocol 001 Trial Team.

Collaborators (135)

Author information

Abstract

BACKGROUND: Recipients of autologous haemopoietic stem-cell transplants (auto-HSCT) have an increased risk of herpes zoster and herpes zoster-related complications. The aim of this study was to establish the efficacy and safety of an inactivated varicella zoster vaccine for the prevention of herpes zoster after auto-HSCT.

METHODS: In this randomised, double-blind, placebo-controlled phase 3 trial, participants were recruited from 135 medical centres (ie, stem-cell transplant centres and hospitals) in North America, South America, Europe, and Asia. Patients were eligible if they were aged 18 years or older, scheduled to receive an auto-HSCT within 60 days of enrolment, and had a history of varicella infection or were seropositive for antibodies to varicella zoster virus, or both. Exclusion criteria included a history of herpes zoster within the previous year of enrolment, and intended antiviral prophylaxis for longer than 6 months after transplantation. Participants were randomly assigned according to a central randomisation schedule generated by the trial statistician, to receive either the inactivated-virus vaccine from one of three consistency lots, a high-antigen lot, or placebo, stratified by age (<50 vs ≥50 years) and intended duration of antiviral prophylaxis after transplantation (≤3 months vs >3 to ≤6 months). Participants, investigators, trial staff, and the funder's clinical and laboratory personnel were masked to group assignment. Participants were given four doses of inactivated vaccine or placebo, with the first dose 5-60 days before auto-HSCT, and the second, third, and fourth doses at about 30, 60, and 90 days after transplantation. The primary efficacy endpoint was the incidence of herpes zoster, confirmed by PCR or adjudication by a masked clinical committee, or both, assessed in all participants randomly assigned to the vaccine consistency lot group or placebo group who received at least one dose of vaccine and had auto-HSCT. Safety was assessed in all randomised participants who received at least one dose of vaccine and had follow-up data. A prespecified vaccine efficacy success criterion required the lower bound of the 95% CI be higher than 25% for the relative reduction of the hazard ratio of herpes zoster infection in participants given the vaccine from one of the consistency lots compared with those given placebo. This trial is registered on ClinicalTrials.gov (NCT01229267) and EudraCT (2010-020150-34).

FINDINGS: Between Dec 7, 2010, and April 25, 2013, 560 participants were randomly assigned to the vaccine consistency lot group, 106 to the high-antigen lot group, and 564 to the placebo group. 249 (44%) of patients in the vaccine consistency lot group, 35 (33%) in the high-antigen lot group, and 220 (39%) in the placebo group discontinued before study end, mostly because of death or withdrawal. 51 participants were excluded from the primary efficacy endpoint analyses because they did not undergo auto-HSCT or were not vaccinated, or both (22 [4%] in the vaccine consistency lot group, and 29 [5%] in the placebo group). Mean follow-up for efficacy was 2·4 years (SD 1·3) in the vaccine consistency lot group and 2·3 years (SD 1·3) in the placebo group. 42 (8%) of 538 participants in the vaccine consistency lot group (32·9 per 1000 person-years) and 113 (21%) of 535 in the placebo group (91·9 per 1000 person-years) had a confirmed case of herpes

Recombinant Zoster vaccine (RZV)-Autologous HSCT

- Double-blind, placebo-controlled phase 3 trial
- 135 medical centers
- Scheduled to receive an auto-HSCT within 60 days
- **The estimated vaccine efficacy was 63·8%** (95% CI 48·4-74·6)

Lancet 2018;391:2116-27

Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in adults with haematological malignancies: a phase 3, randomised, clinical trial and post-hoc efficacy analysis

*Alemnew F Dagnew, Osman Ilhan, Won-Sik Lee, Dariusz Woszczyk, Jae-Yong Kwak, Stella Bowcock, Sang Kyun Sohn, Gabriela Rodriguez Macías, Tzeon-Jye Chiou, Dimas Quiel, Mickael Aoun, Maria Belen Navarro Matilla, Javier de la Serna, Samuel Milliken, John Murphy, Shelly A McNeil, Bruno Salaun, Emmanuel Di Paolo, Laura Campora, Marta López-Fauqued, Mohamed El Idrissi, Anne Schuind, Thomas C Heineman, Peter Van den Steen, Lidia Oostvogels, on behalf of the Zoster-039 study group**

Lancet Infect Dis 2019; 19: 988–1000

Published Online August 6, 2019 http://dx.doi.org/10.1016/S1473-3099(19)30163-X

This online publication has been corrected. The corrected version first appeared at thelancet.com/infection on December 3, 2019

See Comment page 921

*Members are listed in the appendix

GSK, Rockville, MD, USA (A F Dagnew MD, A Schuind MD); Department of Hematology, Ankara University Medicine Faculty, Ankara, Turkey (Prof O Ilhan MD); Department of Hemato-Oncology, Internal Medicine, Inje University Busan Paik Hospital, Busan, South Korea (Prof W-S Lee MD); Department of Haematology, University of Opole, Provincial Hospital, Opole, Poland (D Woszczyk MD); Department of Internal Medicine, Chonbuk National University Medical School and Hospital, Jeonju, South Korea (Prof J-Y Kwak MD); Department of Haematological Medicine, King's College Hospital, London, UK

Summary

Background The adjuvanted recombinant zoster vaccine (Shingrix) can prevent herpes zoster in older adults and autologous haemopoietic stem cell transplant recipients. We evaluated the safety and immunogenicity of this vaccine in adults with haematological malignancies receiving immunosuppressive cancer treatments.

Methods In this phase 3, randomised, observer-blind, placebo-controlled study, done at 77 centres worldwide, we randomly assigned (1:1) patients with haematological malignancies aged 18 years and older to receive two doses of the adjuvanted recombinant zoster vaccine or placebo 1–2 months apart during or after immunosuppressive cancer treatments, and stratified participants according to their underlying diseases. The co-primary objectives of the study were the evaluation of safety and reactogenicity of the adjuvanted recombinant zoster vaccine compared with placebo from the first vaccination up to 30 days after last vaccination in all participants; evaluation of the proportion of participants with a vaccine response in terms of anti-glycoprotein E humoral immune response to the adjuvanted recombinant zoster vaccine at month 2 in all participants, excluding those with non-Hodgkin B-cell lymphoma and chronic lymphocytic leukaemia; and evaluation of the anti-glycoprotein E humoral immune responses to the vaccine compared with placebo at month 2 in all participants, excluding those with non-Hodgkin B-cell lymphoma and chronic lymphocytic leukaemia. We assessed immunogenicity in the per-protocol cohort for immunogenicity and safety in the total vaccinated cohort. The study is registered with ClinicalTrials.gov, number NCT01767467, and with the EU Clinical Trials Register, number 2012-003438-18.

Findings Between March 1, 2013, and Sept 10, 2015, we randomly assigned 286 participants to adjuvanted recombinant zoster vaccine and 283 to placebo. 283 in the vaccine group and 279 in the placebo group were vaccinated. At month 2, 119 (80·4%, 95% CI 73·1–86·5) of 148 participants had a humoral vaccine response to adjuvanted recombinant zoster vaccine, compared with one (0·8%, 0·0–4·2) of 130 participants in the placebo group, and the adjusted geometric mean anti-glycoprotein E antibody concentration was 23132·9 mIU/mL (95% CI 16642·8–32153·9) in the vaccine group and 777·6 mIU/mL (702·8–860·3) in the placebo group (adjusted geometric mean ratio 29·75, 21·09–41·96; p<0·0001) in all patients, excluding those with non-Hodgkin B-cell lymphoma and chronic lymphocytic leukaemia. Humoral and cell-mediated immune responses persisted above baseline until month 13 in all strata and, as expected, vaccine was more reactogenic than placebo (within 7 days after vaccination pain was reported by 221 [79·5%] of 278 vaccine group participants and 45 [16·4%] of 274 placebo group participants; fatigue was reported by 162 [58·3%] of 278 vaccine group participants and 102 [37·2%] of 274 placebo group participants). Incidences of unsolicited or serious adverse events, potential immune-mediated diseases, disease-related events, and fatal serious adverse events were similar between the groups.

Geometric mean anti-glycoprotein E antibody concentration was 23 132·9 mIU/mL in the vaccine group and 777·6 mIU/mL in the placebo group(p<0·0001) in all patients, excluding those with non-Hodgkin B-cell lymphoma and chronic lymphocytic leukaemia

Measles Mumps Rubella vaccine – HSCT Patients

	Recommendation and grading for allogeneic HSCT	Recommendation and grading for autologous HSCT	Paediatric specificities
MMR§	From 24 months after HSCT, recipients should have MMR antibody titres tested (B II u); consider vaccination only in patients with no GvHD, no immunosuppression, no relapse of the underlying disease, and treatment with immunoglobulins during the previous months‡; seronegative patients for measles should receive one dose of MMR (B II u); HSCT recipients who are women, seronegative for rubella, and of childbearing potential should receive one dose of MMR with the same precautions (C II u); in case of a measles outbreak, MMR vaccination could be considered 12 months after transplantation in patients with low-grade immunosuppression (C III)	Same recommendation as after allogeneic HSCT	Because of a lower response in children, two doses—instead of one in adults—should be considered in children, at least 4 weeks apart

- Probability of becoming seronegative 5 years after allogeneic HSCT is 60% for measles, 73% for mumps, and 52% for rubella;
- Response rates: 65–100% for measles, 50–87% for mumps, and 75–100% for rubella.
- **Patients with ongoing GvHD or immunosuppression should not be vaccinated.**

Lancet Infect Dis 2019;19:e200-12
Blood 2002; 99: 83–87

Biology of Blood and Marrow Transplantation
journal homepage: www.bbmt.org

Position statement

Preventing Measles in Immunosuppressed Cancer and Hematopoietic Cell Transplantation Patients: A Position Statement by the American Society for Transplantation and Cellular Therapy

Steven A. Pergam[1,2,3,*], Janet A. Engl
Joshua A. Hill[1,2,3], Bipin Savani[8], Roy
Jeffery Duchin[3,13], Paul A. Carpenter

Criteria for Early MMR Vaccine among High-Risk HCT Recipients and Patients Receiving CAR-T Cell Therapy

Criteria	Allogenic HCT	Autologous HCT	CAR-T Cell Therapy
Timing	>1 year post	>1 year post	>1 year post, but can consider as early as 6 months in the context of acute community clustering or during outbreaks
Immunosuppressive therapy	Single agent: tacrolimus with serum trough level <5 ng/mL *or* cyclosporine with serum trough level <120 ng/mL *or* sirolimus with serum trough level of <2 ng/mL	No post-transplantation chemotherapy, unless lenalidomide or bortezomib for maintenance therapy • no data exist for novel chemotherapy agents (eg, ibrutinib) • risk for agents such as rituximab	No post-CAR-T cell therapy chemotherapy • no data exists for novel chemotherapy agents (eg, ibrutinib) • risk for agents such as rituximab
Steroid use	≤5 mg prednisone daily (for secondary adrenal insufficiency; not for GVHD)	≤5 mg prednisone daily (for secondary adrenal insufficiency)	≤5 mg prednisone daily (for secondary adrenal insufficiency)
Cell counts	Total lymphocyte count of $\geq 1 \times 10^3$ μL *or* CD4 >200/μL and CD19 > 20/μL	Total lymphocyte count of $\geq 1 \times 10^3$ μL *or* CD4 >200/ μL and CD19 >20/μL	Total lymphocyte count of $\geq 1 \times 10^3$ μL *or* CD4 >200/μL and CD19 >20/μL
Immunoglobulin level	Unsupported IgG >400 mg/dL and measurable IgA >6 mg/dL	Unsupported IgG >400 mg/dL and measurable IgA >6 mg/dL	Unsupported IgG >400 mg/dL and measurable IgA >6 mg/dL
Additional	No active systemic GVHD requiring immunosuppression beyond topical agents		Patients who received allogeneic or autologous HCT before CAR-T cell therapy should meet both the HCT and CAR-T cell parameters.

Biol Blood Marrow Transplant 25 (2019) e321e330

SPECIAL ISSUE-TRANSPLANT INFECTIOUS DISEASES

Clinical TRANSPLANTATION WILEY

Vaccination of solid organ transplant candidates and recipients: Guidelines from the American society of transplantation infectious diseases community of practice

Lara Danziger-Isakov[1] | Deepali Kumar[2] | On Behalf of The AST ID Community of

- **Inactivated vaccines** should be given at least **2 weeks prior to transplant**.
- **Live-attenuated vaccines** should be given at least **4 weeks prior to transplant**.
- **In the post-transplant setting**, inactivated vaccines can be administered starting **at 3-6 months post-transplant except influenza vaccine which can be given as early as 1 month post-transplant**.

- **Influenza vaccination** is recommended for all SOT transplant candidates and recipients. In the post-transplant setting, either high-dose or booster dosing in the same season has greater immunogenicity over a single standard dose and may be preferred over standard dosing.
- Both PCV13 and PPSV23 **pneumococcal vaccines** should be administered to transplant candidates and recipients.

Recommendations for pneumococcal vaccination of SOT recipients

Previous dose	Recommendations[47]	
Unvaccinated or any incomplete schedule (<3 doses)	Two doses PCV13	First dose ≥8 wk after most recent dose Second dose ≥8 wk later
Any incomplete schedule of three doses	One dose of PCV13	≥8 wk after most recent dose
Four doses of PCV7 or other age-appropriate complete PCV7 schedule	One dose of PCV13	≥8 wk after most recent dose

Clinical Transplantation. 2019;33:e13563.

Clinical Infectious Diseases

REVIEW ARTICLE

A Systematic Review of Safety and Immunogenicity of Influenza Vaccination Strategies in Solid Organ Transplant Recipients

Pearlie P. Chong,[1] Lara Handler,[2] and David J. Weber[3,4]

[1]Division of Infectious Diseases, Department of Medicine, University of Texas Southwestern Medical Center, Dallas; [2]Health Sciences Library and [3]Division of Infectious Diseases, University of North Carolina, and [4]Hospital Epidemiology, UNC Health Care, Chapel Hill, North Carolina

(See the Major Article by Natori et al on pages 1698–704.)

Immunogenicity from seasonal inactivated influenza vaccine (IIV) remains suboptimal in solid organ transplant recipients (SOTRs). We conducted a systematic review that compared the safety and immunogenicity of nonstandard influenza vaccination strategies with single-dose IIV in SOTRs. Booster doses and possibly high-dose (HD) influenza vaccination strategies seem to hold promise for improving vaccination immunogenicity in SOTRs. Administration of intradermal and MF59-adjuvanted trivalent IIV (IIV3) did not improve vaccine immunogenicity compared with single-dose intramuscular IIV. Alternative vaccine strategies were generally well tolerated; SOTRs who received HD, intradermal or adjuvanted IIV3 had a higher frequency of infection site reactions, while systemic adverse events were more frequent in SOTRs who received HD IIV3. Allograft rejection rates were similar in both groups. SOTRs should continue to receive standard-dose IIV annually in accordance with current recommendations, pending future studies to determine the optimal timing, frequency, and dosage of IIV using the booster-dose strategy.

Keywords. influenza vaccination; solid organ transplants; immunogenicity; immunization.

CID 2018:66(11):1802–11

The immunogenicity of influenza vaccine in this group is variable but has been lower than that of the general population and is dependent on various factors including type of transplant and immunosuppression. Lung transplant recipients have traditionally had the lowest levels of seroconversion and range from 7–26%.[44,45] The main barrier to immunogenicity is lifelong immunosuppression given to this population. Mycophenolate mofetil (MMF) has been shown to have a dose-dependent response where higher doses especially those ≥2 grams daily were correlated with lower seroconversion rates.[46–50] A recent meta-analysis confirmed this correlation with MMF and lower rates of seroconversion compared to other immunosuppressants. No significant correlation of low immunogenicity was detected with tacrolimus, sirolimus, cyclosporine, and azathioprine.[51] Induction immunosuppression may not impact vaccine immunogenicity. In a kidney transplant cohort in which thymoglobulin or basiliximab was used as induction therapy, 60 patients were evaluated for the immune response to IIV. There were no significant differences in geometric mean titers for any of the three viral strains between groups.[52] A recent study also showed that immune responses were not significantly different between groups that received basiliximab or ATG in heart and kidney transplant recipients although reported that the median number of influenza-specific memory B-cell (IgG-MBC) did not increase after vaccination.[53]

SPECIAL ISSUE-TRANSPLANT INFECTIOUS DISEASES

Clinical TRANSPLANTATION WILEY

Vaccination of solid organ transplant candidates and recipients: Guidelines from the American society of transplantation infectious diseases community of practice

Lara Danziger-Isakov[1] | Deepali Kumar[2] | On Behalf of The AST ID Community of

- **Hepatitis B vaccine** series should be offered pretransplant.
- Accelerated schedules such as 0,1,2 months or 0,7,21 days can be used.
- A higher dose (40 µg) vaccine can be used in end-stage renal disease.
- **Hepatitis B high-dose (40 µg) vaccine is recommended in the post-transplant setting**

- Transplant candidates ≥50 years of age should receive **herpes zoster vaccination**. **Subunit** vaccination is preferred to avoid delays in transplant. Post-transplant patients ≥50 years can also receive subunit vaccine. **Transplant candidates and recipients <50 years of age could be considered for herpes zoster vaccine.**

Clinical Transplantation. 2019;33:e13563

SPECIAL ISSUE-TRANSPLANT INFECTIOUS DISEASES

Clinical TRANSPLANTATION WILEY

Varicella zoster virus in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice

Steven A. Pergam[1,2,3] | Ajit P. Limaye[1] | on behalf of the AST Infectious Diseases Community of Practice

	Pre-transplant	Post-transplant	Dosing	Comments
Vaccination				
Varicella vaccine (Varivax®)	Yes, if seronegative (Strong, moderate)	Generally, contraindicated, but can be used with caution if seronegative in select populations (Weak, low)	Varivax® 0.5 mL administered SQ	• Vaccination has been shown to be safe in ESRD and ESLD patients • Minimum recommended age for vaccine is ≥6 mo of age • Do not give if <1 mo to transplant • Seroconversion rate reduced in immunosuppressed individuals • Caution should be used in post-transplant patients since live virus vaccine; education and close follow-up recommended. • Second dose can be given 4-8 wk after first dose (see package insert for guidelines)
Inactivated adjuvanted subunit herpes zoster vaccine (Shingrix®)	Yes, known seropositive and on minimal immunosuppression ≥50 y age (Strong, high), populations <50 y of age on minimal immunosuppression can be considered for vaccination (Weak, low)	Safety and efficacy studies ongoing (Weak, moderate)	Shingrix® 0.5 mL administered IM Two doses at 0 and 2-6 mo	• Currently only FDA approved for patients ≥50 y of age • Side effects are common, and frequently include pain at injection site, fever and chills/myalgias • Data demonstrate vaccine immunogenicity and safety in carefully selected renal transplant patients on immunosuppressive therapy at low risk for rejection, Efficacy data are not available to date • Patients with primary autoimmune diseases (eg, systemic lupus erythematous, etc) and or at moderate/high risk for rejection were excluded from the trial so data on safety is unknown • Prospective studies have not been done in children <18 y of age.
Live-attenuated herpes zoster vaccine (Zostavax®)	Alternative to Inactivated Adjuvanted Vaccine for >50, if not severely immunosuppressed (Strong, high)	Contraindicated (Strong, low)	Zostavax® 0.5 mL administered SQ	• Follow label indications, as no evidence that vaccine is safe in severe organ dysfunction or post-transplant • If patient meets label indications can be considered, but should be given at least 3-4 wk prior to transplant.

Clinical Transplantation. 2019;33:e13622

Hepatitis A virus (HAV) vaccination

Indications	*Schedule*	*Recommendation, Strength of Recommendation and Quality of Evidence*
HIV *Low-level or no immunosuppression* *High-level immunosuppression*	2-doses	Usual (S, M) Usual (S, M)
Solid or hematologic cancer *Prior to or During Chemotherapy* *Starting ≥3 mo Postchemotherapy and ≥6 mo Post Anti–B-Cell Antibodies*	2-doses	 Usual (W, L) Usual (S, VL)
Chronic inflammatory diseases on Immunosuppressive Medications	2-doses	Usual (S, L-M)
Asplenia and sickle cell disease	2-doses	Usual (S, M)
HSCT *Pre-HSCT* *Post-HSCT*	 2 doses 2 doses; 6 mo	 Usual (S, VL) Recommended (W, L)
SOT recipients *Pretransplant* *Starting 2-6 mo Posttransplant*	2 doses pre-transplantation or 6 months after transplantation	Recommended (S, M) Recommended (S, M

W=weak; L=low; VL=very low; M=moderate; S=strongh; H=high

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Vaccination against the human cytomegalovirus

Stanley A. Plotkin[a,*], Suresh B. Boppana[b]

[a] University of Pennsylvania, Vaccinonk, 4650 Wismer Rd., Doylestown, PA 18902, United States
[b] UAB School of Medicine, CVB 324, 1600 7th Avenue South, Birmingham, AL 35233, United States

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

Vaccine 37 (2019) 7437–7442

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Vaccination in immunocompromised host: Recommendations of Italian Primary Immunodeficiency Network Centers (IPINET)

Baldassarre Martire, Chiara Azzari, Raffaele Badolato, Clementina Canessa, Emilia Cirillo, Vera Gallo, Simona Graziani, Tiziana Lorenzini, Cinzia Milito, Raffaella Panza, Viviana Moschese, with Italian Network for Primary Immunodeficiencies (IPINET)

Vaccination and Steroid therapy

Children receiving either a dose of prednisone ≥ 2 mg/kg/day or a total dose of 20 mg/day if they weigh more than 10 kg **must not be vaccinated with live viruses before** 2 weeks (if they have undergone therapy for less than 14 days), or 4 weeks (if they have undergone therapy for >14 days).

In individuals using:

- steroids <2 mg/kg) for less than 2 weeks
- steroids replacement therapy
- topical, intra-articular, conjunctival steroids or steroid aerosol

all the necessary vaccinations can be carried out during treatment, including those with live attenuated viruses

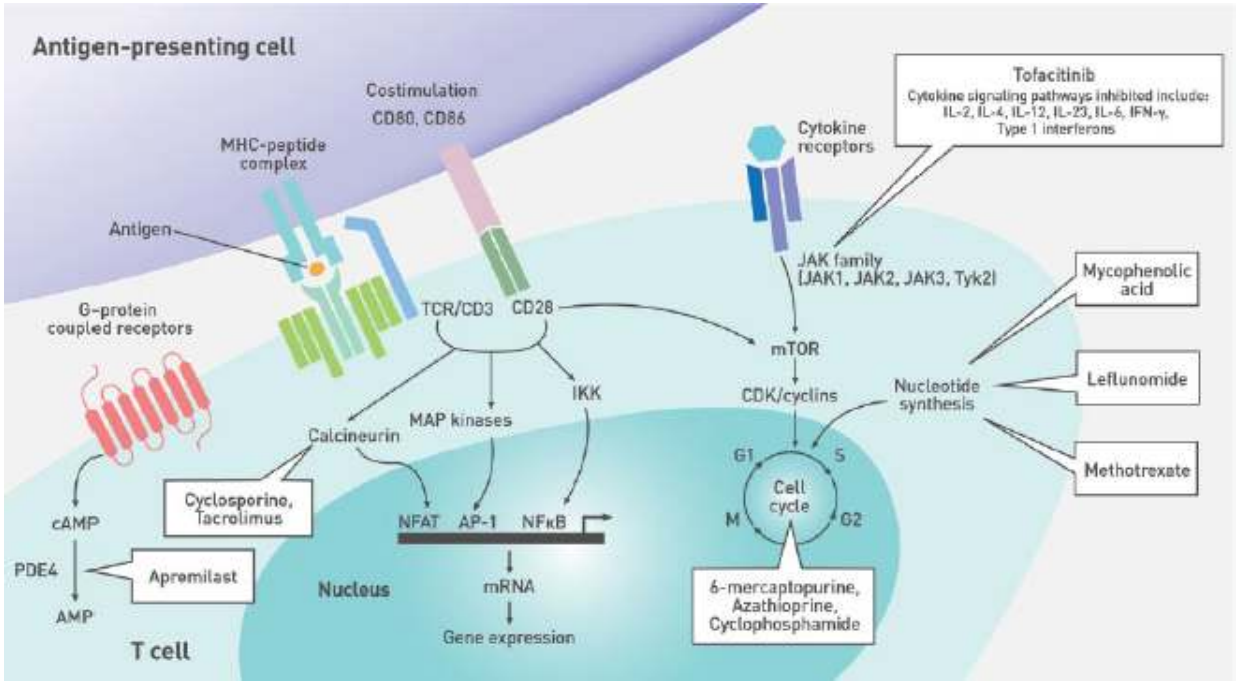
Vaccine 36 (2018) 3541–3554

Vaccination Guidelines for Patients With Immune-Mediated Disorders on Immunosuppressive Therapies

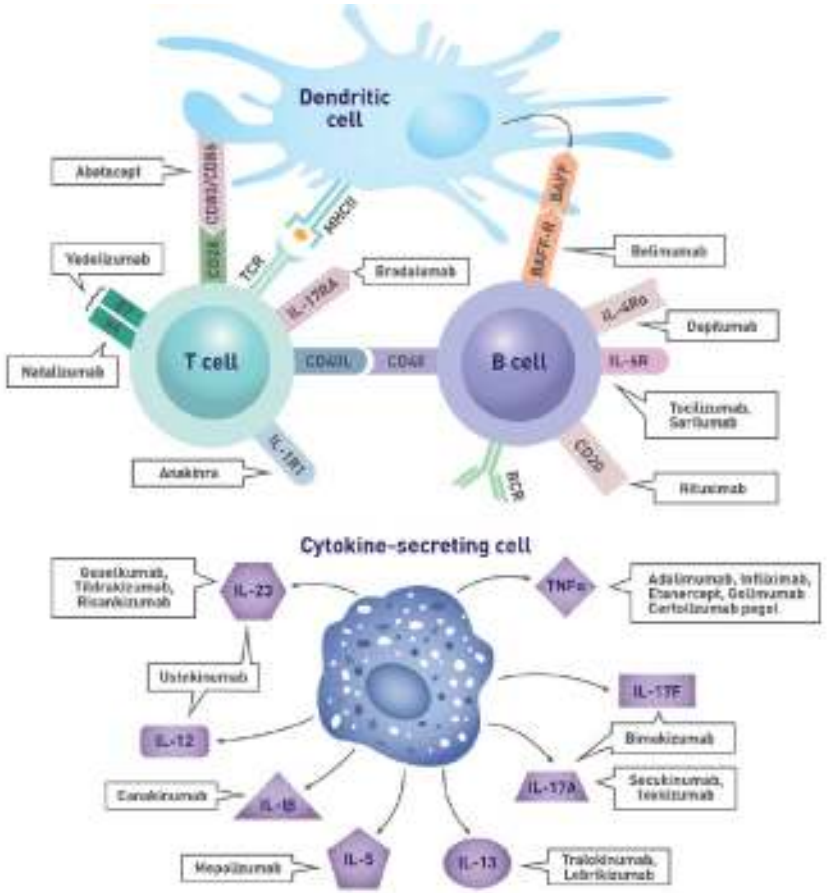
Kim A. Papp[1,2], Boulos Haraoui[3], Deepali Kumar[4,5], John K. Marshall[6], Robert Bissonnette[7], Alain Bitton[8], Brian Bressler[9,10], Melinda Gooderham[2,11], Vincent Ho[9], Shahin Jamal[12], Janet E. Pope[13,14], A. Hillary Steinhart[5,15], Donald C. Vinh[8,16], and John Wade[9,17]

Journal of Cutaneous Medicine and Surgery
2019, Vol. 23(1) 50–74

DOI: 10.1177/1203475418811335
journals.sagepub.com/home/jcms
Canadian Dermatology Association
Association canadienne de dermatologie
CME



Immune pathways targeted by nonbiologic disease-modifying antirheumatic drugs



Immunological targets of biologic agents

Journal Cut Medicine & Surgery 2019;23(1)

Vaccination Guidelines for Patients With Immune-Mediated Disorders on Immunosuppressive Therapies

Kim A. Papp[1,2], Boulos Haraoui[3], Deepali Kumar[4,5], John K. Marshall[6], Robert Bissonnette[7], Alain Bitton[8], Brian Bressler[9,10], Melinda Gooderham[2,11], Vincent Ho[9], Shahin Jamal[12], Janet E. Pope[12,14], A. Hillary Steinhart[5,15], Donald C. Vinh[8,16], and John Wade[9,17]

- To optimize the immunogenicity **of inactivated vaccines** in treatment-naive patients with immune-mediated conditions, we suggest that immunization be performed **at least 2 weeks prior to initiation of immunosuppressive therapy**.
- Immunosuppressive treatment not be interrupted for administration of inactivated vaccines.
- **In patients treated with rituximab** who require optimal vaccine immunogenicity: immunization be deferred to **⩾5 months after the last dose and at least 4 weeks prior to the subsequent dose of rituximab.**
- To optimize the immunogenicity of the **live attenuated herpes zoster vaccine** in treatment-naive patients: immunization be performed **at least 2 to 4 weeks prior to initiation of immunosuppressive therapy.**
- Live attenuated herpes zoster vaccine can be safely administered to patients at risk, but the **subunit vaccine is the preferred alternative**.

Journal Cut Medicine & Surgery 2019;23(1)

Vaccination Guidelines for Patients With Immune-Mediated Disorders on Immunosuppressive Therapies

Kim A. Papp[1,2], Boulos Haraoui[3], Deepali Kumar[4,5], John K. Marshall[6], Robert Bissonnette[7], Alain Bitton[8], Brian Bressler[9,10], Melinda Gooderham[2,11], Vincent Ho[9], Shahin Jamal[12], Janet E. Pope[12,14], A. Hillary Steinhart[5,15], Donald C. Vinh[8,16], and John Wade[9,17]

Journal of Cutaneous Medicine and Surgery
2019, Vol. 23(1) 68–74

DOI: 10.1177/1203475418811335
journals.sagepub.com/home/jcm

Table 6. Length of Viremia Following Vaccination With Live Attenuated Vaccines.

Vaccine	Length of Viremia
Varicella (Oka strain)	The vaccine strain could not be isolated up to 14 days postvaccination in children,[225] but 1 study detected the vaccine strain by PCR up to 5 weeks after immunization in 5 of 166 (3%) asymptomatic children given the varicella vaccine.[226]
Herpes zoster (Oka strain)	Varicella zoster virus DNA can be detected by PCR analysis in 16% (11/67) of individuals 2 weeks postvaccination[227] and up to 4 weeks in 6% (2/36) of individuals >60 years old.[71]
Yellow fever	Viremia after primary immunization wanes within 7 days postimmunization[228] and is generally cleared within 2 weeks of vaccination.[229]
Measles	The vaccine strain has not been isolated from human blood after immunization of healthy children,[230] but a study on macaques has shown the persistence of the Schwarz vaccine strain 7 to 9 days postvaccination.[231]
Mumps	There is a low risk of viremia with the mumps vaccine strains; however, the incidence of aseptic meningitis occurring 2 to 3 weeks after vaccination suggests that the potential is maintained in some vaccine strains. The frequency of vaccine-associated aseptic meningitis varies from approximately 1 in 1.8 million doses for the Jeryl Lynn strain to as high as 1 in 336 for the Urabe AM9 strain.[232]
Rubella	Viremia was documented 7 to 21 days postvaccination in some adults receiving the primary vaccination but not in children.[233]
Live polio (type 2 Sabin)	In adults, free virus is present in the serum between 2 and 5 days after vaccine administration, with antibody-bound virus being present up to 8 days after vaccination.[234] In children aged ≤17 months, free virus can be detected up to 8 days after vaccination.[235]

In treatment-naive patients who are vaccinated with **live attenuated vaccines**, we recommend that the **duration of viremia** following immunization be considered when determining the **optimal time to initiate immunosuppressive therapy.**

Journal Cut Medicine & Surgery 2019;23(1)

Recommendation

2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases

Victoria Furer [1,2] Christien Rondaan,[3,4] Marloes W Heijstek,[5] Nancy Agmon-Levin [2,6] Sander van Assen,[7] Marc Bijl,[8] Ferry C Breedveld,[9] Raffaele D'Amelio,[10] Maxime Dougados [11] Melliha Crnkic Kapetanovic [12] Jacob M van Laar [13] A de Thurah [14] Robert BM Landewé [15,16] Anna Molto [11] Ulf Müller-Ladner,[17] Karen Schreiber,[18,19] Leo Smolar,[20] Jim Walker,[21] Klaus Warnatz,[22] Nico M Wulffraat [23] Ori Elkayam [1,2]

Recommendation

Table 1 Overarching principles for vaccination in adult patients with AIIRD

	Overarching principles	Level of Agreement (%)
1.	The vaccination status and indications for further vaccination in patients with AIIRD should be assessed yearly by the rheumatology team.	100%
2.	The individualised vaccination programme should be explained to the patient by the rheumatology team, providing a basis for shared decision-making, and be jointly implemented by the primary care physician, the rheumatology team and the patient.	94%
3.	Vaccination in patients with AIIRD should preferably be administered during quiescent disease.	94%
4.	Vaccines should preferably be administered prior to planned immunosuppression, in particular B cell depleting therapy.	100%
5.	Non-live vaccines can be administered to patients with AIIRD also while treated with systemic glucocorticoids and DMARDs.	100%
6.	Live-attenuated vaccines may be considered with caution in patients with AIIRD.	53%

AIIRD, autoimmune inflammatory rheumatic diseases; DMARDs, disease-modifying antirheumatic drugs.

Furer V, et al. Ann Rheum Dis 2020;79:39–52

Recommendation

2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases

Victoria Furer,[1,2] Christien Rondaan,[3,4] Marloes W Heijstek,[5] Nancy Agmon-Levin,[2,6] Sander van Assen,[7] Marc Bijl,[8] Ferry C Breedveld,[9] Raffaele D'Amelio,[10] Maxime Dougados,[11] Melina Crnkic Kapetanovic,[12] Jacob M van Laar,[13] A de Thurah,[14] Robert BM Landewé,[15,16] Anna Molto,[11] Ulf Müller-Ladner,[17] Karen Schreiber,[18,19] Leo Smolar,[20] Jim Wal Klaus Warnatz,[22] Nico M Wulffraat,[23] Ori Elkayam[1,2]

Table 2 Recommendations for vaccination in adult patients with AIIRD with level of evidence for the incidence/prevalence of VPI, efficacy, immunogenicity and safety of vaccines, strength of recommendations (SoR) and level of agreement for each recommendation

Recommendation	Infection rate	Efficacy	Immuno-genicity	Safety	SoR*	Level of agreement: average/ range (0–10), %≥8
1. Influenza vaccination should be strongly considered for the majority of patients with AIIRD.	2b	2b	2a	2b	B	9.4 7–10 93%
2. Pneumococcal vaccination should be strongly considered for the majority of patients with AIIRD.	2b	4	2a	4	C	8.7 6–10 93%
3. Patients with AIIRD should receive toxoid tetanus vaccination in accordance with recommendations for the general population. Passive immunisation should be considered for patients treated with B cell depleting therapy.	NA	NA	2b	4	B D	9.5 8–10 100%
4. Hepatitis A and hepatitis B vaccination should be administrated to patients with AIIRD at risk. In specific situations booster or passive immunisation is indicated.	HAV – NA HBV 2b	NA	2b	4	B C	9.6 8–10 100%
5. Herpes zoster vaccination may be considered in high-risk patients with AIIRD.	2b	2b	2b	4	B	9.1 7–10 93%
6. Vaccination against yellow fever should be generally avoided in patients with AIIRD.	NA	NA	2b	4	D	9.2 6–10 85.7%
7. Patients with AIIRD, in particular patients with SLE, should receive vaccinations against HPV in accordance with recommendations for the general population.	2b	NA	2b	4	C	9.5 8–10 100%
8. Immunocompetent household members of patients with AIIRD should be encouraged to receive vaccines according to national guidelines with the exception of the oral polio vaccines.	NA	NA	NA	NA	D	9.1 7–10 93%
					D	9.5 8–10 100%

9. Live-attenuated vaccines should be avoided during the first 6 months of life in newborns of mothers treated with biologics during the second half of pregnancy.

Furer V, et al. Ann Rheum Dis 2020;79:39–52

2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

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

Vaccination of Persons With Asplenia or a Sickle Cell Disease, Cochlear Implants, or Cerebrospinal Fluid Leak

	Asplenia or a Sickle Cell Disease		Cochlear Implants[a] or Cerebrospinal Fluid Leak	
Vaccine	Recommendation	Strength, Evidence Quality	Recommendation	Strength, Evidence Quality
Haemophilus influenzae b conjugate	U: age <5 y R: age ≥5 y	Strong, moderate weak, low	U	Strong, moderate
Hepatitis A	U	Strong, moderate	U	Strong, moderate
Hepatitis B	U	Strong, moderate	U	Strong, moderate
Diphtheria toxoid, tetanus toxoid, acellular pertussis; tetanus toxoid, reduced diphtheria toxoid; tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis	U	Strong, moderate	U	Strong, moderate
Human papillomavirus	U	Strong, moderate	U	Strong, moderate
Influenza-inactivated (inactivated influenza vaccine)	U	Strong, moderate	U	Strong, moderate
Influenza-live attenuated (live attenuated influenza vaccine)	X	Weak, very low	U	Strong, moderate
Measles, mumps, and rubella–live	U	Strong, moderate	U	Strong, moderate
Measles, mumps, and rubella–varicella–live	U	Strong, moderate	U	Strong, moderate
Meningococcal conjugate	R: age 2–55 y[b]	Strong, low	U	Strong, moderate
Meningococcal polysaccharide	R: age >55 y[b]	Strong, low	U	Strong, moderate
Pneumococcal conjugate (PCV13)	U: age <6 y[c] R: age ≥6 y[d]	Strong, moderate Strong, very low	U: age <6 y[c] R: age ≥6 y[d]	Strong, moderate strong, low
Pneumococcal polysaccharide (PPSV23)	R: age ≥2 y[e]	Strong, low	R: age ≥2 y[e]	Strong, moderate
Polio-inactivated (inactivated poliovirus vaccine)	U	Strong, moderate	U	Strong, moderate
Rotavirus–live	U	Strong, moderate	U	Strong, moderate
Varicella–live	U	Strong, moderate	U	Strong, moderate
Zoster–live	U	Strong, moderate	U	Strong, moderate

PLWH- Vaccination schedule

- Vaccinate according to national guidelines for healthy population, preferably after having achieved suppressed viraemia and immune reconstitution (CD4 count > 200 cells/µL)
- Consider repeating vaccinations performed at CD4 count < 200 cells/µL (< 14%) or unsuppressed viraemia once adequate immune reconstitution is achieved (HIV-VL undetectable and CD4 count > 200 cells/µL)
- As vaccine responses may be significantly lower in PLWH (i.e. lower seroconversion rates, faster titer decline), do not use rapid schedules and consider antibody titers to assess their effectiveness if vaccinated at CD4 count < 200 cells/µL or unsuppressed viremia (e.g. rabies, tick-borne encephalitis, HAV, meningococci)
- Avoid polysaccharide vaccination
- For background data, see http://www.bhiva.org/vaccination-guidelines.aspx

- For attenuated live vaccines(i)
  (in addition to restrictions for general population):
  - *__Varicella, measles, mumps, rubella, yellow fever__
    Contraindicated if CD4 count < 200 cells/µL (14%) and/or AIDS.
    Impaired protection after vaccination with unsuppressed viraemia
  - __Oral live typhoid__
    Contraindicated if CD4 count < 200 cells/µL (14%): give inactivated parenteral polysaccharide vaccine. Preferred if CD4 count > 200 cells/µL (> 14%)

PLWH- Vaccination schedule

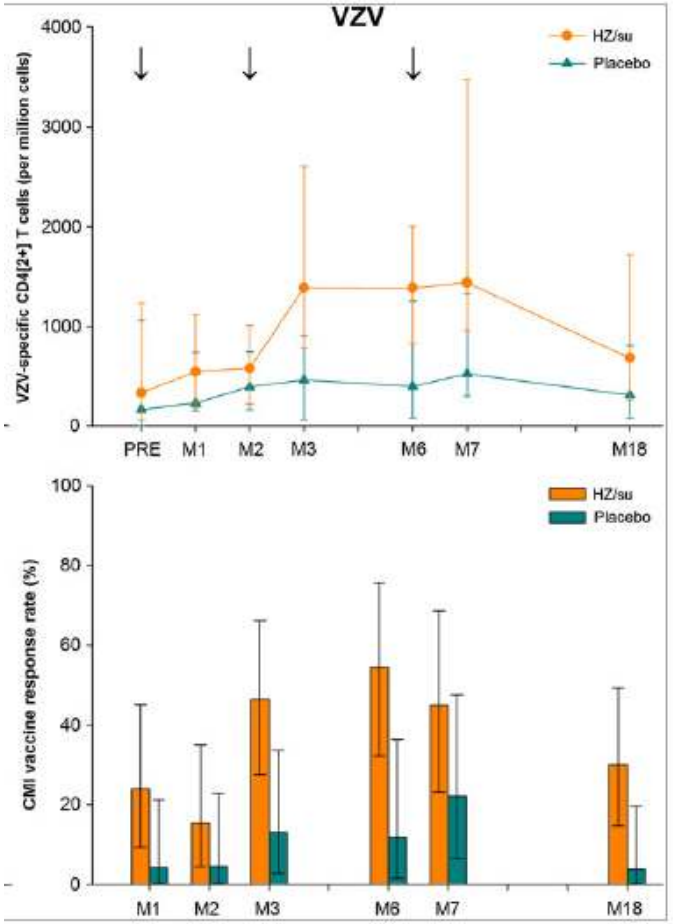
Infection	Vaccination rationale in PLWH	Comment
Influenza Virus	Higher rate of pneumonia. Explicitly recommended in all PLWH	Yearly
Human Papilloma Virus (HPV)	Shared risk with HIV of contracting infection. Higher rate of cervical and anal cancer	Vaccinate all PLWH with 3 doses between ages 9 and 40 (health insurance coverage differs by country according to age, sex, sexual orientation). Use 9-valent vaccine if available. Persons treated for high grade cervical dysplasia could benefit from a full course vaccination for secondary prevention
Hepatitis B Virus (HBV)	Shared risk with HIV of contracting infection. HIV accelerates liver disease progression	Vaccinate if seronegative. Repeat doses until anti-HBs antibodies ≥ 10 IU/L / ≥ 100 IU/L according to national guidelines. In order to reach ≥ 100 IU/L in non-responders repeat 3 doses if anti-HBs < 10 IU/L, 1 dose if anti-HBs < 100 IU[ii]; consider double dose (40 µg) in particular with low CD4 count and high HIV-VL. See page 95
Hepatitis A Virus (HAV)	According to risk profile (travel, close contact with children, MSM, IVDU, active hepatitis B or C infection, chronic liver disease)	Vaccinate if seronegative. Consider checking antibody titres in PLWH with high risk. Weaker immune response expected with HAV/HBV co-vaccine. See page 95
Neisseria meningitidis	According to risk profile (travel, close contact with children, MSM)	Use conjugated[iii] 4-valent vaccine (2 doses 1-2 months apart) if available. Booster every five years if exposure continues. Polysaccharide vaccine not recommended anymore
Streptococcus pneumoniae	Higher rate and severity of invasive disease. Vaccine explicitly recommended for all PLWH	One dose of conjugated[iii] 13-valent vaccine (CPV-13) for all PLWH, also if pre-vaccinated with PPV-23 polysaccharide vaccine. No general recommendation for any booster dose. Some national guidelines consider one dose of PPV-23 at least 2 months after CPV-13 for all PLWH
Varicella Zoster Virus (VZV)	Higher rate and severity of both chicken-pox and zoster	Perform serology if exposure history negative. Vaccinate if seronegative. For contraindications, see*. To prevent shingles consider adjuvant sub-unit vaccine rather than live-attenuated vaccine according to national guidelines
Yellow Fever Virus	Mandatory for travel to selected countries (provide exemption letter if no true risk of exposure)	Contraindicated if past or current haematological neoplasia or thymus affection (thymoma, resection/radiation) For other contraindications, see*. Booster q 10 years
Rabies		For PLWH with CD4 count < 200 cells/µL or unsuppressed viremia consider pre-exposure vaccination with 3 doses (0, 7, 28 days) and titer control 14 days later as well as post-exposure immunoglobulins for all non-vaccinated

MAJOR ARTICLE

Safety and Immunogenicity of an Adjuvanted Herpes Zoster Subunit Candidate Vaccine in HIV-Infected Adults: A Phase 1/2a Randomized, Placebo-Controlled Study

Elchonon M. Berkowitz,[1] Graeme Moyle,[2] Hans-Jürgen Stellbrink,[4] Dirk Schürmann,[5] Stephen Kegg,[3] Matthias Stoll,[6] Mohamed El Idrissi,[7] Lidia Oostvogels,[7] and Thomas C. Heineman[3]; for the Zoster-015 HZ/su Study Group*

- Median cell-mediated immune responses peaked after dose 2.
- No vaccination-related serious adverse events were reported.
- No sustained impact on HIV load or CD4+ T-cell count



Cell-mediated immune (CMI) vaccine response rate.
Data are percentages with 95% confidence intervals

JID 2015;211:1279–87

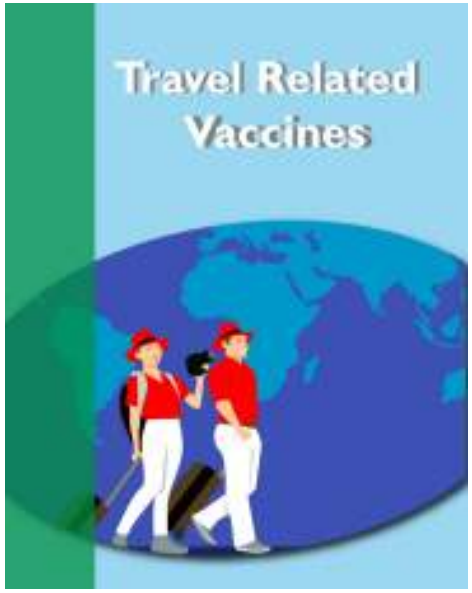
Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Review

Revisiting Role of Vaccinations in Donors, Transplant Recipients, Immunocompromised Hosts, Travelers, and Household Contacts of Stem Cell Transplant Recipients

Aneela Majeed[1], Zoey Harris[2], Eric Brucks[2], Alyssa Hinchman[3], Arafat Ali Farooqui[4], Muhammad Junaid Tariq[5], Kavin Tamizhmani[2], Irbaz bin Riaz[6], Ali McBride[7], Azka Latif[8], Vikas Kapoor[9], Raheel Iftikhar[10], Sherif Mossad[1], Faiz Anwer[10,*]



Vaccination Recommendations for HSCT Recipients before Travel

Vaccine	Adult
General inactivated vaccines	As recommended (IDSA 2013, Aung et al. 2015)
Yellow fever	No unless endemic (IDSA 2013, ASBMT 2009) For endemic areas, >12 months after autologous transplant and >24 months after allogeneic transplant (Aung et al. 2015)
General live vaccines (MMR, BCG, polio, typhoid, rotavirus, live influenza, smallpox)	No (IDSA 2013, Aung et al. 2015)
Tick-borne encephalitis	No unless endemic (ASBMT 2009, Aung et al. 2015)
Japanese B encephalitis	No unless endemic (ASBMT 2009) For >1 month in endemic area or short-term with high-risk itinerary (Aung et al. 015)
Meningococcal polysaccharide	Meningitis belt in sub-Saharan Africa in Dec-June (Aung et al. 2015)
Meningococcal conjugate	Meningitis belt in sub-Saharan Africa in Dec-June (Aung et al. 2015)
Cholera	Optional for endemic areas (Aung et al. 2015) Use if indicated ≥6 months post-HSCT (Canadian 2018)
Hepatitis A	For travel/endemic areas (EBMT 2005)

Majeed A, Biol Blood Marrow Transplant 2020;26: e38-e50

Yellow Fever

Indications	*Schedule*	*Recommendation, Strength of Recommendation and Quality of Evidence*
All immunocompromised subjects	A single dose	**Contraindicated (S, M)**
In asymptomatic HIV-infected adults with CD4 T-cell lymphocyte count ≥200 cells/mm^3 who travel to an endemic area	A single dose	**Administration (W, L)**

Patients (no immunosuppression for 2 years, no active GvHD, normal CD4 counts and IgG levels) were vaccinated at a median of 3–9 years after transplantation, with no SAE.
(J Infect Dis 2017; 217: 494–97, J Travel Med 2009; 16: 365–67)

ECIL 7 recommendations for family and close contacts of stem cell transplant recipients by vaccine

	Recommendation	Grading
General recommendation	It is recommended that family members and close contacts of HSCT recipients be immunised or vaccinated according to the age and country recommendation	..
IIV	It is recommended that family members and close contacts of HSCT recipients be vaccinated with IIV at the start of autumn before transplantation and first season after, and annually as long as the patient is considered immunocompromised	A II t and C III
LAV influenza	The nasal LAV influenza vaccine is contraindicated in close contacts of HSCT recipients during the first months after transplantation or if the patient has GvHD	B III
Varicella or MMR vaccine to a close contact of the patient	In case a close contact of an HSCT recipient needs varicella or MMR LAV because he or she is seronegative, he or she should be seperated from the HSCT recipient, because of the risk of developing post-vaccine disease	..
Rotavirus vaccine in close infants	Within 4 weeks after rotavirus vaccination of infants, HSCT recipients should have no contact with the stools or diapers of the vaccinated infants because there is a risk of contracting the vaccine virus	..

IIV=influenza inactivated vaccine. LAV=live-attenuated vaccine. GvHD=graft-versus-host disease. MMR=measles-mumps-rubella. For the evidence-based medicine grading system (A II t, B III, C III) see appendix.

Lancet Infect Dis 2019;19:e200-12

Benefit of donor vaccination before harvest on the recipient response to inactivated vaccines

Vaccine	Benefit	Comments	References
Tetanus	Yes	Improves the response of early (d-1, d50) R vaccination	*Storek 2004*
Diphtheria	Yes	Improves the Ab concentrations	*Storek 2004, Parkkali 2007*
Polio	No	Good response in the group with no D vaccination	*Parkkali 2007*
Pertussis	*Unknown*		
PPV23	No		*Storek 2004, Kumar 2007*
PCV	Yes	Improved after early vaccination, no more significant at 12 months	*Molrine 2003, Kumar 2007*
Hib	Yes	Improves the response of early (d-1, d50) R vaccination	*Storek 2004*
Influenza	No	No difference on Flu Abs of the R during the first 6 months after transplant . No improved response of the R when vaccinated at 6 months	*Ambati 2015*
HBV	Conflicting results	Poor response to HBsAg with or without D vaccination in Storek et al. Improved response to KLH in Wimperis et al.	*Storek 2004* *Wimperis 1990*

Συμπεράσματα

- **Οι εμβολιασμοί αποτελούν αποτελεσματική στρατηγική για την πρόληψη λοιμώξεων σε ανοσοκατεσταλμένους ασθενείς.**
- **Τα εμβόλια με ζώντες ιούς πρέπει να αποφεύγονται.**
- **Παρακολούθηση της ανοσιακής κατάστασης των ασθενών για πιο σωστή λήψη θεραπευτικών αποφάσεων.**
- **Ανεπάρκεια δεδομένων σχετικά με τον ρόλο των εμβολίων σε ασθενείς που λαμβάνουν νεώτερες ανοσοτροποποιητικές αγωγές.**
- **Απαιτούνται επιπλέον μελέτες για τον προσδιορισμό της αποτελεσματικότητας των εμβολίων αναλόγως της υποκείμενης νόσου/ ανοσοκατασταλτικής αγωγής.**