Name of the Presentation

Pneumococcal vaccination

Per Ljungman, MD, PhD
Karolinska University Hospital, Karolinska Institutet
Stockholm, Sweden

Content

Will talk about:

- Stem cell and SOT patients
- Cancer patients

Will not talk about

- Primary immunodeficiencies
- HIV

Why /why not vaccinate?

+	-
Risk for infection	Side effects
Risk for severe disease	Cost

Incidence of invasive pneumococcal disease (IPD) in immunocompromised hosts

Adults, ABCs database on 7 american states, 1999-2000

Group	Incidence (CI 95%) / 100 000 persons
Healthy subjects	*8.8 (8.5-9)*
Diabetes	51.4 (49.2-53.9)
Chronic respiratory failure	62.9 (59.8-66.3)
Chronic heart disease	93.7 (87.4-100.9)
Alcoholism	100.4 (94.1-107.7)
Solid tumor	**300.4 (272.6-334.6)**
HIV infection	**422.9 (378.3-479.4)**
Hematological malignancy	**503.1 (422.2-622.3)**

Kyaw MH et al. J Infect Dis 2005

Incidence of IPD after solid organ transplantation

Prospective survey of 2976 adults with solid organ transplants 1995-2004, Canada. 21 cases observed.

Type of transplant	No. cases / 100 000 patients / year
Normal population	*11.5*
Kidney	104
Lung	239
Liver	354
Heart, pancreas	0
All SOT	**146**

Kumar D et al. Am J Transplant 2007

Incidence of IPD after stem cell transplant

Engelhard D et al. 2002
n=8547
51 cases
1994-1997

Incidence / 1,000 SCT
Auto: 3.8
Allo: 8.2
Allo with GVHD: 18.8
7/51 cases before d35
#20% before d100

Youssef S et al. 2005
n=7888 patients
54 cases
1989-2005

Incidence / 1,000 SCT,
Auto: 5
Allo: 9
4 / 54 cases before d100
Bacteriemic pneumonia more frequent in case of GVHD

Children with cancer/leukemia

Antibody levels are generally low in children treated for acute leukemia – lower than age-matched unvaccinated controls.

It was not due to low Ig levels (Lehrnbecher et al Br. J. Haematol 2009)

Few if any patients have "protective" levels to all serotypes included in the PCV7 (Patel et al Arch Dis Child 2012)

What determines immune status in secondary immunodeficency

Previous vaccination and infection history

Underlying disease

Given immunosuppression
- Type
- Intensity

Allogeneic SCT recipients
- Transfer of immunity from the donor
- Persistence of existing recipient immunity

Why is the immunity lost?

No. of antigen specific cells in the patient

Eradication of patient memory B-cells by therapy

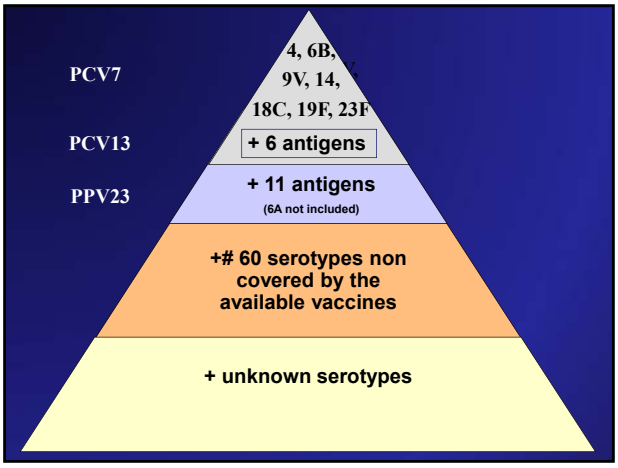
- Graft-vs-host (lymphocyte) reaction?
- Cytotoxic chemo-radiotherapy?
- Anti-B-cell therapy

(No. of antigen specific cells in the donor graft)

S. Pneumoniae vaccines

Polysaccharide vaccines
- Non T-cell dependent response
- Poor primary response
- No memory = no boost effect

Conjugate vaccines
- Obtained by covalent coupling of the PS with a protein
- T-cell dependent response
- Better primary response, boost effect



Doses, intervals, and vaccine types

How should we use these vaccines?

When can we start?

Number of doses?

Intervals between doses?

Safety

How to define immune response to pneumococcal vaccine in immunocompromised patients?

By the reduction of incidence rate? unfeasible

By a biological parameter ?

- GMC of specific Abs : which ones: all vaccine Ag, or only some?
- Geometric mean fold rise of specific Abs
- Specific Ab serum level ≥ 0.35µg/mL? One Ag? All vaccine Ag?
- Opsonophagocytic activity (OPA) ?

When to assess the immune response ?

-> No consensus on what is the best parameter to assess protection in these populations

Risks with inactivated vaccines

No evident major risks for direct side effects

- Local side effects
- Systemic side effects

Is there a risk for immune activation complications (rejection, GVHD, autoimmune phenomena)?

- Existing data suggest the risks are very low

Increased risk with adjuvanted vaccines?

When should vaccinations be performed

When is the patient at risk for infection?

What is the likelihood for an adequate immune response after therapy?

Can we vaccinate before initiation of therapy?

If not, when is it

a) safe

b) effective

Immunocompromised patients are poorly immunized!

Examples of pneumococcal vaccination coverage

- Before transplantation:
  - 62% before lung transplant *(Gasink et al. 2006)*
  - 13% before liver transplant *(Chesi et al 2009)*
- In high-risk adults in the US 2007-2010 (Medicaid):
  - Overall: 6.2% of 57,089 medicaid-enrollees
  - 7.6% in chronic renal disease
  - 4.2% in cancer
  - 3.7% in transplant patients

Yang HK et al., 9th ISPPD, Hyderabad, India, 9-13th Mar 2014 (#0438)

What are the possible pre-therapy strategies?

Complete routine schedules

Immunize seronegative patients

Boost existing pre-transplant immunity

Immunize the donors (HSCT)

Pretherapy vaccination - cancer patients

It is unlikely that patients needing intensive therapy can wait for vaccinations before start of therapy

Patients who can wait are unlikely to become very immunosuppressed.

Possible exceptions

- low malignant lymphomas or CLL given anti-B cell antibodies
- patients requiring splenectomy
- myeloma patients early in the stage of the disease
- patients only treated with surgery or local irradiation

This possible strategy of vaccination followed by therapy has not been tested

Pre-transplant vaccinations - HSCT

Usually undergo cytotoxic chemotherapy limiting the possibilities to perform pre tx vaccinations.

Vaccination efficacy during chemotherapy usually poor

Pre-transplant immunity is frequently lost

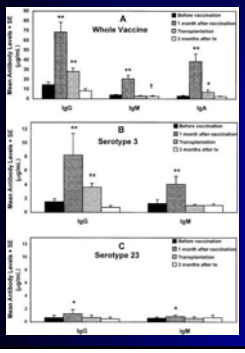
However in patients not receiving chemotherapy, pre-transplant vaccination can be considered for example against varicella.

What about the donor?

- *S. pneumoniae* PPV23 *(Molrine 1996, Storek 2004)* NO
- Conjugate Hib vaccine *(Molrine 1996, Storek 2004)* YES
- Tetanus (Vance 1998, Storek 2004) YES
- *S pneumoniae* PCV7 *(Molrine 2003)* YES

In routine: practically, and ethically difficult !!

Is immunization while on the waiting list, enough to protect?



45 patients on the waiting list for liver transplant

1 dose of PPV23 before transplant

25 of 45 patients were transplanted

91% of the patients responded to vaccine

But .. 3 months after transplant, Ab levels were below the pre vaccination levels

McCashland TM, JID 2000

Karolinska Institutet

IDSA GUIDELINES

2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

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

[1]Division of Pediatric Infectious Diseases, Steven and Alexandra Cohen Children's Medical Center of New York of the North Shore-LIJ Health System, New Hyde Park; [2]Section of Pediatric Infectious Diseases, University of Colorado Denver Anschutz Medical Campus, Aurora; [3]Department of Hematology, Karolinska University Hospital; [4]Division of Hematology, Department of Medicine Huddinge, Karolinska Institutet, Stockholm, Sweden; [5]Department of Immunology, Great Ormond Street Hospital & Institute of Child Health, London, United Kingdom; [6]Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, Maryland; [7]Department of Blood and Marrow Transplant, H. Lee Moffitt Cancer Center and Research Institute, University of South Florida, Tampa; [8]Department of Gastroenterology and Nutrition, Children's Hospital Boston, Massachusetts; [9]Department of Allergy and Infectious Diseases, University of Washington, Seattle; [10]Division of Hematology-Oncology, Hospital for Sick Children, Toronto, Ontario, Canada; [11]Division of Pediatric Infectious Diseases, Emory University of School of Medicine, Atlanta, Georgia [12]Section of Rheumatology, Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut

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

CID 2014: 58; 309-318; e44-100

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IDSA - cancer

70. PCV13 should be administered to newly diagnosed adults with hematological (strong, very low) or solid malignancies (strong, very low) and children with malignancies (strong, very low) as described in recommendations 27a-c. PPSV23 should be administered to adults and children aged ≥2 years (strong, low) at least 8 weeks after the indicated dose(s) of PCV13.

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IDSA - SOT

91. Adult SOT candidates; adults with end-stage kidney disease; and pediatric patients who are SOT candidates; are aged <6 years and have end-stage kidney, heart, or lung disease; or are aged 6–18 years and have end-stage kidney disease should receive PCV13 as in recommendations 27a-c (strong, very low).

92. Adults and children aged ≥2 years who are SOT candidates or have end-stage kidney disease should receive PPSV23 if they have not received a dose within 5 years and have not received 2 lifetime doses (strong, moderate). Patients with end-stage kidney disease should receive 2 lifetime doses 5 years apart (strong, low). Adults and children aged ≥2 years with end-stage heart or lung disease as well as adults with chronic liver disease, including cirrhosis, should receive a dose of PPSV23 if they have never received a dose (strong, low). When both PCV13 and PPSV23 are indicated, PCV13 should be completed 8 weeks prior to PPSV23 (strong, moderate).

What do the recommendations say?

Children should receive age appropriate vaccinations

What about adults?

- What vaccine should be used?
- What schedule should be used?
- When should vaccines be given?

Patient vaccination: Caveat!

No true efficacy data does exist

Toxicity data quite robust for many vaccines

”All” efficacy data is on surrugate endpoints e.g immune responses!

but

Absence of Evidence is not Evidence of Absence

Patients with hematological malignancies

A very heterogeneous group

A long list of therapeutic drugs and strategies

The ones with the higher need for protection are mostly those with the lower response to vaccine

A big issue: timing!

What do the studies say?

Very few studies have looked at PCV in hemat malignancies

One randomized study in which one dose of PCV7 was compared to one dose of PPSV23 in pateints with Hodgkin lymphoma.

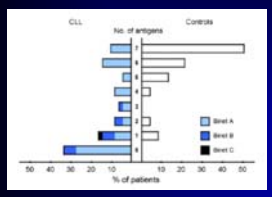
One dose of PCV7 gave lower antibody level increases than one dose of PPSV23.

Molrine et al Ann Intern Med 1996

A subgroup of the PCV7 patients received 12 months later a PPSV23 dose and responded with higher antibody levels than the patients in the original study that got only PPSV23

Chan et al, JID 1996

One dose of conjugate vaccine, CLL



Sinisalo et al, Vaccine 1997

PCV 13 one dose in untreated patients

58% of CLL patients responded (better response in lower stages)

100% of controls responded

Pasiarski et al 2014

Responses after rituximab treatment

Table I. Patient characteristics and responses to vaccines.

Age (years)	Lymphoma type	Therapy	Time of vaccination after rituximab (months)	% CD19⁺ + CD19⁺ CD20⁺ of total WBC at vaccination/4 weeks after vaccination	Response to Pneumo 23®	Response to Act-HIB®
63	Follicular grade 2 stage II	R 4 + 4	6	0·04/0·22	No	No
			12 revaccination	1·26/1·7	No	No
59	Follicular grade 3A stage III	R + CHOP × 8	6	0·54/1·0	No	No
			no revaccination			
57	Marginal zone stage IV	R 4 + 4	6	0·26/0·7	Yes	Yes
63	Follicular grade 2 stage III	R 4+4	12	0·6/0·83	No	Yes
73	Mantle cell stage IV	R + CHOP × 8	12	0·32/0·24	No	Yes
63	Follicular grade 2 stage III	R 4	12	0·6/0·57	No	No
			18 revaccination	1·1/0·95	No	No
56	Follicular grade 2 stage III	R 4 + 4	6	0·42/0·82	No	Yes
61	Follicular grade 2 stage III	R 4 + 4	12	1·0/0·9	No	Yes

R, rituximab; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisolone; WBC, white blood cells.

Svensson et al BJH 2012

Name of the Presentation

Brief report

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

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

[1]Clinic for Surgery and Cancer Medicine, Department of Oncology, Oslo University Hospital, Oslo, Norway; [2]Division of Virology, Norwegian Institute of Public Health, Oslo, Norway; [3]Clinic for Diagnostics and Intervention, Department of Pathology, Oslo University Hospital, Oslo, Norway; [4]Department of Oncology, University Hospital of Northern Norway, Tromsø, Norway; [5]Department of Oncology, St Olaf's University Hospital, Trondheim, Norway; [6]Department of Oncology, Haukeland University Hospital, Bergen, Norway; and [7]Department of Hematology and Oncology, Stavanger University Hospital, Stavanger, Norway

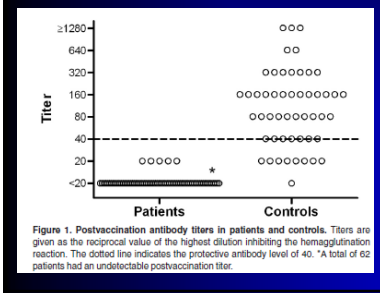


Figure 1. Postvaccination antibody titers in patients and controls. Titers are given as the reciprocal value of the highest dilution inhibiting the hemagglutination reaction. The dotted line indicates the protective antibody level of 40. *A total of 62 patients had an undetectable postvaccination titer.

2013 IDSA guidelines

Rubin et al. Clin Infect Dis

Bortezomib?

Lenalidomide?

TKI ?

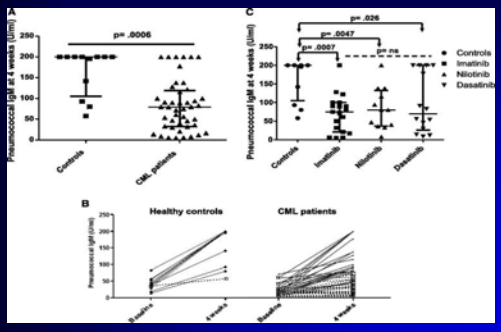
High-l… in cancer patients

- C…
- Co… weigh<10 kg)
  of pr…
- C… imab

Low-l…

- Corti… oid therapy < 20 mg (o… e-day
- Methotrexate ≤ 0.4 mg/kg/w
- Azathioprine ≤ 3 mg/kg/d
- 6-mercaptopurine ≤ 1.5 mg/kg/d

Pneumococcal IgM response following PPV23 vaccination in CML patients receiving TKI



de Lavallade et al. Blood 2013;122:227-238

Children with cancer/leukemia

Antibody levels are generally low in children treated for acute leukemia – lower than age-matched unvaccinated controls.

It was not due to low Ig levels (Lehrnbecher et al Br. J. Haematol 2009)

Few if any patients have "protective" levels to all serotypes included in the PCV7 (Patel et al Arch Dis Child 2012)

No good data regarding efficacy of pneumococcal vaccination in children with cancer/leukemia

UK recommendations – PCV13

Severely immunocompromised children diagnosed from five years onwards and adults

Severely immunocompromised children aged at least five years and adults – including bone marrow transplant patients, patients with acute and chronic leukaemia, multiple myeloma or genetic disorders affecting the immune system (e.g. IRAK-4, NEMO, compliment deficiency) – should be offered a single dose of PCV13 followed by PPV23 at least two months later (irrespective of their routine childhood vaccinations).

For leukaemia patients, PCV13 should be given from six months after completion of chemotherapy, and for bone marrow transplant patients, PCV13 should be offered 9-12 months following transplantation.

Severely immunocompromised patients who have already received PPV23 should be offered PCV13 with an interval of at least six months following the dose of PPV23 to reduce the risk of pneumococcal serotype-specific hypo-responsiveness.

Vaccination of Patients With Cancer — Starting ≥3 mo Postchemotherapy and ≥6 mo Post Anti–B-Cell Antibodies for Inactivated Vaccines; See Each Live Vaccine for Interval

Vaccine	Recommendation	Strength, Evidence Quality
Haemophilus influenzae b conjugate	U	Strong, moderate
Hepatitis A	U	Strong, very low
Hepatitis B	U R: adults	Strong, moderate Strong, very low
Diphtheria toxoid, tetanus toxoid, acellular pertussis; tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis	U: age 0–18 y R: adults with acute lymphoblastic leukemia or lymphoma	Strong, moderate Weak, very low
Human papillomavirus	U	Strong, very low
Influenza-inactivated (inactivated influenza vaccine)	U[b]	Strong, moderate
Influenza-live attenuated (live attenuated influenza vaccine)	U	Strong, low
Measles, mumps, and rubella–live	Starting at 3 mo: U	Strong, low
Measles, mumps, and rubella–varicella–live	Starting at 3 mo: U	Weak, very low
Meningococcal conjugate	U	Strong, low
Pneumococcal conjugate-13 (PCV13)	U	Strong, low
Pneumococcal polysaccharide (PPSV23)	U	Strong, low
Polio–inactivated (inactivated poliovirus vaccine)	U	Strong, low
Rotavirus–live	Not applicable	
Varicella–live	Starting at 3 mo: U[c]	Weak, very low
Zoster–live	Starting at 3 mo: U[c]	Weak, very low

HSCT. What do the studies say?

Uncontrolled studies show that only one dose PCV gives quite poor response also in HSCT recipients.

Donor vaccination might improve the results

No controlled study have compared one vs. three doses of PCV

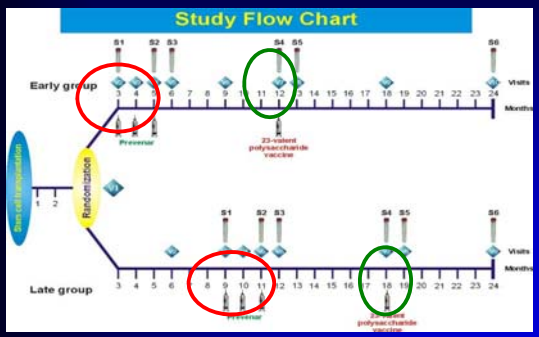
No controlled study has investigated the efficacy of the prime – boost strategy with 1 dose PCV followed by 1 dose PPSV23

Influence of Immunization Timing on the Response to Conjugate-Pneumococcal Vaccine after Allogeneic Stem Cell Transplantation; the *IDWP01 trial*

CID 2009

C Cordonnier, M Labopin, V Chesnel, P Ribaud, R da la Camara, R Martino, A Ullmann, T Parkkali, A Locasciulli, K Yakouben, K Pauksen, D Niederwieser, J Apperley, E Bonnet, H Einsele, P Ljungman,
for the EBMT Infectious Diseases Working Party

IDPW01: Timing of immunization



Percentage of responders at the cut-off of ≥ .5µg/mL for all the 7 antigens of Prevnar ®

	EARLY GROUP n=75	LATE GROUP n=83	P=
S1 (before)	8% 6/74	2% 1/64	.08
S3 (1 mo after 3 doses)	56% 32/57	54% 31/57	0.64
S6 (24 mo)	34% 15/44	55% 23/42	.06

S1 and S6: no difference
S3 (test of non-inferiority): we are 95% sure that the results in the early arm are not more than 13.5% worse than the results in the late arm.

Impact of transplant factors on the responders (> .5 µg/mL)

(uni and multivariate analysis)

Factor	Yes / No	p	Multivariate
Donor age > 37y	63% v. 34%	.003	.03
Acute GvHD before S3	25% v. 45%	.03	ns
Gammaglobulines >4g/L	85 % v. 68%	.044	ns
cGVHD before S3	29% v. 60%	.002	.009

No impact of recipient age, sex, diagnosis, status at transplant, source of stem cells, lymphocyte counts

Response to PPSV23 given at 12 or 18 months after HSCT

Pn 1	Time	Early group	Late group	
positive > 0.5	S4	4/51 (8%)	1/52 (2%)	0.16
	S5	21/50 (42%)	28/47 (60%)	0.08
	S6	17/44 (39%)	21/42 (50%)	0.29

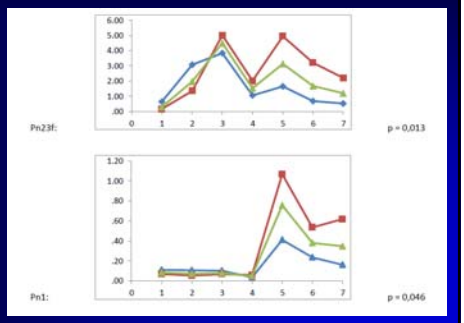
41% of non-responders to PCV7 responded

The serotype coverage was extended

Cordonnier et al Vaccine 2010

Long-term immunity in the IDWP01 study

All
Late
Early



Cordonnier et al; BMT 2015

Clinical Infectious Diseases Advance Access published May 27, 2015

MAJOR ARTICLE

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

Catherine Cordonnier,[1] Per Ljungman,[2] Christine Juergens,[3] Johan Maertens,[4] Dominik Selleslag,[5] Vasi Sundarajan,[6] Peter C. Giardina,[7] Keri Clarke,[8] William C. Gruber,[7] Daniel A. Scott,[7] and Beate Schmoele-Thoma[9]; for the 3003 Study Group

We honor the memory of Dr Trudy Small, who contributed to the design and conduct of the study from a US perspective

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Study Design and Endpoints

Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8
PCV13	PCV13 28–42 days after visit 1	PCV13 28–42 days after visit 2	28–42 days after visit 3	PCV13 182–224 days after visit 3	PPSV23 28–42 days after visit 5	28–42 days after visit 6	168–196 days after last PCV13

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Name of the Presentation

Patient characteristics

All Patients Assigned to Study	Age 2<18 n=61	Age ≥ 18 n=190	All (age ≥2) N=251
All Available Immunogenicity Population	**n=60**	**n=189**	**N=249**
Demographics at baseline			
Median age, y (min, max)	10 (2,17)	47 (18,71)	42 (2,71)
Sex: M/F, %	55/45	61/39	59/41
Transplant details			
Conditioning: myeloablative/reduced intensity, %	82/18	55/46	61/39
Donor HLA: matched/mismatched, %	92/8	93/7	92/7
Source: marrow/PBSC*/cord blood, %	57/33/10	10/87/3	21/74/4
Median time between HSCT and PCV13 dose 1, d (min, max)	175 (97, 209)	146 (96, 208)	152 (96, 209)
Underlying disease, n (%)			
Acute myeloid leukaemia	8 (13)	95 (50)	103 (41)
Acute lymphocytic leukaemia	16 (27)	16 (9)	32 (13)
Aplastic anaemia	14 (23)	8 (4)	22 (9)
Myelodysplastic syndrome	4 (7)	17 (9)	21 (8)
Other haematologic conditions	18 (30)	53 (28)	71 (29)
Baseline medications, n (%)†			
Systemic corticosteroids	11 (18)	55 (29)	66 (26)
Cyclosporine	24 (39)	114 (60)	138 (55)
Tacrolimus	4 (7)	29 (15)	33 (13)

*One additional adult patient had PBSC (confirmed by site after the study).
† Assessed using the "All Assigned Patients" population.

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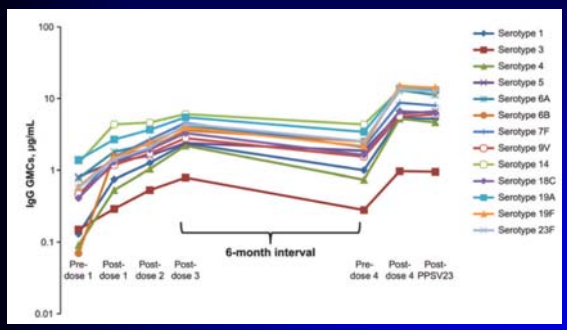
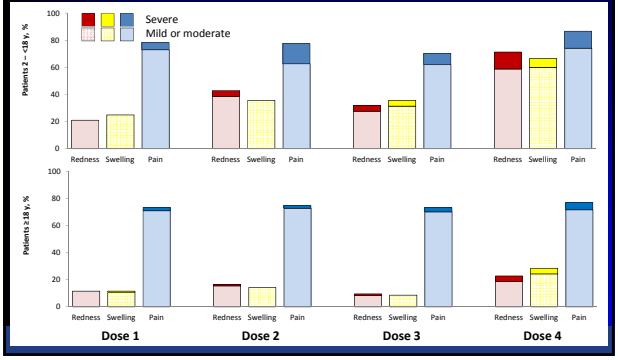
Pneumococcal IgG GMCs



Percentage of Patients with Local Reactions Following PCV13



Vaccine differently in different groups of patients?

Few or no specific data, and no comparative data

In the PCV13 (3003) study *(Cordonnier et al. CID 2015)* : no difference in the immune response between:

- Myeloablative and reduced intensity conditioning
- Bone marrow vs peripheral blood SC vs Cord blood

⇒ *Guidelines: « …same vaccination schedule for all HSCT recipients, until additional data are published… »*

Is GVHD a contra-indication to vaccination?

1) SAFETY

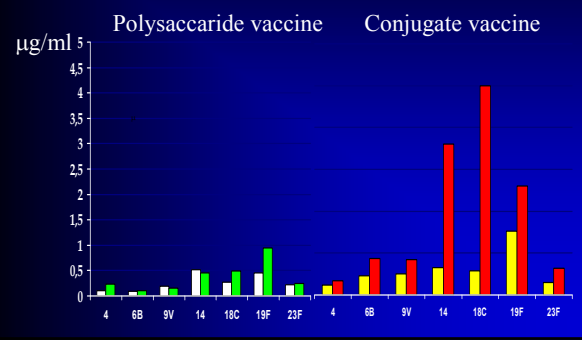
- no significant worsening of GVHD
- no serious side effect reported

2) EFFICACY: does GVHD impair the immune response?

- Yes for pneumococcal PPV and conjugate vaccine
- No for conjugate Hib vaccine

Rubin et al. CID 2014

PCV7 in patients with ch GVHD



IDSA - HSCT

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

Immune response to PPV23 after solid organ transplant

Very close to the one of healthy subjects when vaccinated BEFORE transplant *(Mc Cashland 2000)* *or* SEVERAL YEARS LATER*(Dengler TJ 1998, Blumberg EA 2001)*

But much lower if vaccinated earlier after transplant (13-40% if PPV23 given 1.2 y after renal transplant) *(Kumar D 2003)*

Variable response according to the serotype: ex: only 50% for serotype 3 *(Dengler TJ 1998)*

The response may be lost 3-5 years later *(Danzinger-Isakov L 2009)*

Immune response to PCV7 in renal transplant adult recipients

Randomized study PCV7 versus PPV23, in 60 renal transplant adults 3 mo to 3 y after transplant

Response criteria: Ab level ≥ 1µg/mL *and* GMFR ≥ x 2 for ***at least one*** vaccine serotype 2 months after immunization

Results:

Comparable response (73.3% vs 53.3%)

A trend for better response after PCV7, significant only for serotypes 23F and 6B

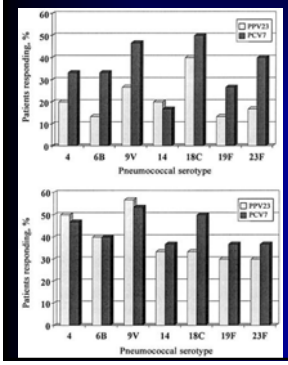
No graft rejection

Considerations:

- The patients were vaccinated between 13-15 months after transplant
- All parameters favor PCV7

Kumar D et al JID 2003

PCV7 vs PPV23 after renal transplantation



Percentage of subjects responding to each serotype in the 2 groups when compared by the quantitative antibody response

Percentage of subjects responding to each serotype in the 2 groups when compared by the opsonophagocytic response

Kumar D et al. J Infect Dis. 2003;187:1639-1645

Immune response to PCV7 in adult liver transplant recipients

Randomized study in 113 liver transplant recipients

PCV7 + PPV23 (2 mo interval) *versus* placebo + PPV23

Response criteria: Ab level ≥ .35µg/mL *and* GMFR ≥ x 2 for at least one vaccine serotype, 2 months after immunization

Results:

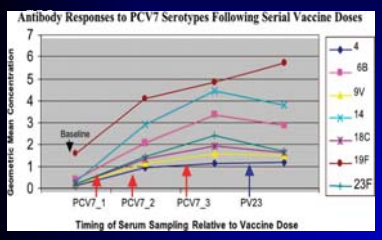
- Responses not different (including on OPA test): 85.7% vs 91.2%

Considerations:

- Response criteria: debatable
- Patients immunized between 2.6 to 3.4 years after transplant

Kumar D et al CID 2008

Immunization with PCV7 followed by PPV23 in SOT children



81 children with SOT

- Heart: 31
- Kidney: 27
- Liver: 18
- Lung: 5

Median age: 7.8 y (0.6-17.5y)

Vaccinated at a median of 1.3 y after transplant (0.3-6y)

Barton et al; Ped Infect Dis J 2009

Prime – boost strategy in renal transplanted adults

Randomized study

PCV 7 + PPV23 (1 yr) vs. PPV23

40 patients in each group

No difference in response between the two groups in response rate or response in number of serotypes

Tobutic et al, PLOSone 2012

Guidelines for immunization against pneumococcal infection in SOT recipients

Before transplant: 1 PCV13+1 PPV23 (if no PPV23 during the last 5 y)

After transplant:

- If not administered before SOT, PCV13 should be administered 2 to 6 months after SOT, with the timing based on the patient's degree of immunosuppression, then one dose of PPV23 2 months later
- If PCV13 before transplant: one dose of PPV23

Vaccination SHOULD BE withheld from SOT recipients during intensified immunosuppression, including the first 2 months post-transplant period, because of the likelihood of inadequate response .

Vaccination SHOULD NOT be withheld due to concerns about rejection

Rubin LG, Levin MJ, Ljungman P et al. CID 2013

Are recommendations followed?

663 HSCT recipients reviewed between December 2010 through February 2013 revealed that:

252 (38%) patients received the first series of recommended vaccinations by 6 months

398 (60%) received them by 1 year after HSCT

Ariza-Heredia EJ et al, Transplant ID 2015