VaccHemInf cohort

Vaccination efficacy after allogeneic haematopoietic stem cell transplantation: importance of haematological characteristics for vaccine immunogenicity

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Introduction

Recipients of allogeneic haematopoietic stem cell transplantation (allo-HSCT) are at high risk of developing infections preventable by vaccinations.
An important heterogeneity in vaccine immunogenicity is expected, as immune response may vary according to haematological characteristics and transplant-related complications.

The objective of this study is to assess vaccination efficacy after allo-HSCT

Material and Methods

Single-centre, prospective, observational study from jan. 2014 to nov. 2016 including a consecutive cohort of allo-HSCT recipients referred to the vaccination unit of our infectious disease department.

Patients received the following vaccines: the 13-valent **pneumococcal** conjugate vaccine, the penta- or the hexavalent combination vaccine : **diphtheria, tetanus, pertussis, poliomyelitis, *Haemophilus influenzae* b** and **hepatitis B virus** (HBV) in seronegative recipients.

Vaccine immunogenicity at baseline (before vaccination) and at 4 months post-vaccination was assessed with the measurement of serum antibody titres (ELISA) against pneumococcus, *Haemophilus*, tetanus, diphteria, and HBV.

In addition, were measured from patient's whole blood samples at baseline (before vaccination) and at 4 months post-vaccination the **T, B** and **NK cell counts**.

The following haematological characteristics were collected :

- underlying disease,
- conditioning regimen (myeloablative or reduced intensity conditioning, use of anti-thymocyte globulins [ATG]),
- type of donor (related, unrelated),
- stem cell source (bone marrow [BM], peripheral blood (PB), umbilical cord blood [UCB]).

The following transplant-related complication data were collected: chronic graft-*versus*-host disease (G*v*HD) alone or treated by extracorporeal photochemotherapy

Wilcoxon matched-pairs signed rank test was used to compare antibody titres before and after vaccination, and Mann-Whitney U test assessed differences between the study groups, as appropriate. A p-value < 0.05 was significant.

Results

Characteristics of the study population are shown in **Table 1**. Patient's flow chart is shown in **Figures 1**. Examples of results of antibody titers are displayed in **Figures 2, 3 and 4**, respectively.

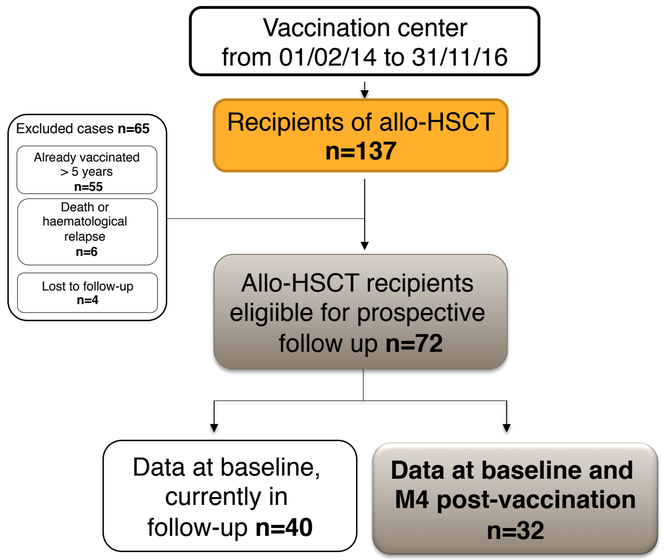


Figure 1

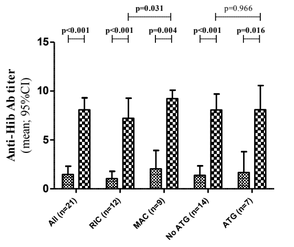
Patient's characteristics	n (%) / mean (95% confidence interval [CI])
gender (male)	19 (59.4)
age at allo-HSCT (years)	45.9 [95%CI, 40.5-51.2]
Underlying disease	
acute leukaemia	21 (65.6)
myelodisplasic syndrome, myelo/ lymphoproliferative disorders	7 (21.9)
others	4 (12.5)
Myeloablative conditioning	19 (59.4)
ATG	12 (37.5)
Donor	
related geno-identical	17 (53.1)
unrelated pheno-identical matched	7 (21.9)
Unrelated pheno-identical mismatched	8 (25)
Stem cell source	
BM	12 (37.5)
PB	14 (43.8)
UCB	6 (18.8)
Chronic G*v*HD	16 (50)
extra corporeal photochemotherapy	7 (21.8)
Immune modulation	
intravenous immunoglobulins	< 3-months 4 (12.5)
	< 6-months 11 (34.4)
Donor lymphocyte infusion	6 (18.8)

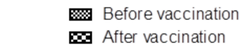
Table 1

Patients received the first vaccine at a mean delay of 14.9 (95%CI, 11.8-18.0) months after allo-HSCT. Main reasons for delay in recipient's inclusion in the vaccination schedule were chronic G*v*HD (n=12, 37.5%), infectious complications (n=10, 31.3%), intravenous immunoglobulin administration (n=9, 28.1%) and completion of immunosuppressive treatment (n=2, 6.3%). Immunogenicity evaluation was performed 3.9 (95%CI, 3.4-4.3) months after the last vaccine injection.

Upon vaccination, normalized counts of T CD4$^+$, T CD8$^+$, B and NK cells were observed in 13 (40.6%), 27 (84.4%), 26 (92.9%) and 23 (82.1%) of recipients, respectively.

Conditioning



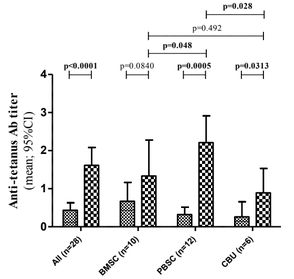


Myeloablative conditioning impacts vaccination response against *H. influenza* b. Other valences were not affected by conditioning or ATG.

ATG, Antithymocyte globulins; MAC, Myeloablative conditioning; RIC, Reduce intensity conditioning.

Figure 2

Stem cell source

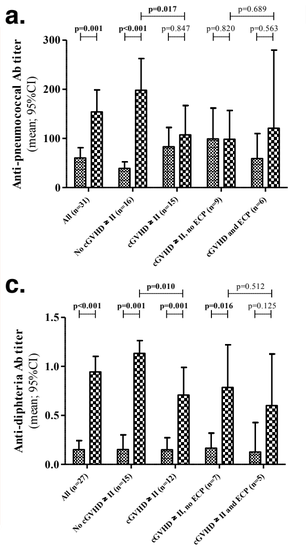


CBU recipients had a reduced response to tetanus vaccination *vs.* PB recipients. Although not reaching significance, response to pneumococcus and diphteria was reduced as well.

BMSC; Bone marrow stem cells; CBU, Cord blood unit; PBSC, Peripheral blood stem cells.

Figure 3

Transplant-related complications



Chronic G*v*HD decreases immunization response against most vaccine targets. A trend toward a lower response was obersved in patients receiving extracorporeal photo-chemotherapy.

cGvHD, Chronic graft versus host disease; ECP, Extracorporeal photochemotherapy.

Figures 4

Conclusion

Haematological characteristics and transplant-related complications reduce vaccine immunogenicity after allo-HSCT. Chronic G*v*HD critically decreases immunization response to most vaccine targets, despite delayed initiation of vaccination schedule. Specific vaccination schedules should be considered in case of chronic G*v*HD after allo-HSCT.

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