



HAL
open science

H1N1 in allogeneic stem cell recipients: courses of infection and influence of vaccination on graft-versus-host-disease (GVHD)

Markus Ditschkowski, Ahmet H. Elmaagacli, Dietrich W. Beelen

► **To cite this version:**

Markus Ditschkowski, Ahmet H. Elmaagacli, Dietrich W. Beelen. H1N1 in allogeneic stem cell recipients: courses of infection and influence of vaccination on graft-versus-host-disease (GVHD). *Annals of Hematology*, 2010, 90 (1), pp.117-118. 10.1007/s00277-010-0971-8 . hal-00554986

HAL Id: hal-00554986

<https://hal.science/hal-00554986>

Submitted on 12 Jan 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Editorial Manager(tm) for Annals of Hematology
Manuscript Draft

Manuscript Number: AOHE-D-10-00190R1

Title: H1N1 in allogeneic stem cell recipients: courses of infection and influence of vaccination on graft-versus-host-disease (GVHD)

Article Type: Letter to the Editor

Keywords: Allogeneic hematopoietic stem cell transplantation 1;
Chronic graft-versus-host-disease 2;
Influenza 3;
H1N1 4;
Immunocompromised host 5

Corresponding Author: Dr. Markus Ditschkowski, M.D.

Corresponding Author's Institution:

First Author: Markus Ditschkowski, M.D.

Order of Authors: Markus Ditschkowski, M.D.; Ahmet H Elmaagacli, Prof.; Dietrich W Beelen, Prof.

Abstract: Seasonal influenza causes substantial morbidity and mortality in immunocompromised allogeneic blood stem cell recipients. In view of 2009 pandemic influenza A (H1N1) and against the background of the preventive nationwide availability of the vaccine Pandemrix™ (GlaxoSmithKline) in Germany since October 2009, the question was raised if patients after allogeneic hematopoietic stem cell transplantation (HSCT) should be vaccinated or not. A major concern against the use of an adjuvant containing vaccine was the apprehension of chronic graft-versus-host-disease (GVHD) exacerbation or deterioration.

Response to Reviewers: All suggestions by the reviewers were considered in the revised version and the addressed points were changed.

1
2
3
4 H1N1 in allogeneic stem cell recipients: courses of infection and influence of
5
6
7 vaccination on graft-versus-host-disease (GVHD)
8
9

10
11
12
13
14 Markus Ditschkowski, M.D.

15
16
17 Ahmet H ElmaagacI, M.D.

18
19 Dietrich W. Beelen, M.D.
20
21
22
23
24
25
26
27

28
29 Department of Bone Marrow Transplantation

30
31 University Hospital of Essen, Germany.
32
33
34
35
36
37
38
39
40

41 Correspondence to:

42
43 Markus Ditschkowski, M.D. (e-mail: markus.ditschkowski@uk-essen.de)

44
45
46 Department of Bone Marrow Transplantation, University Hospital of Essen,

47
48 Hufelandstr. 55, 45122 Essen, Germany.
49

50
51 Phone: +49-201-723-3136

52 Fax: +49-201-723-5961
53
54
55
56
57
58
59
60
61
62
63
64
65

1
2 It is well known that seasonal influenza causes substantial morbidity and mortality in
3 immunocompromised allogeneic blood stem cell recipients. ¹ In view of 2009 pandemic influenza A
4 (H1N1) and against the background of the preventive nationwide availability of the vaccine
5 Pandemrix™ (GlaxoSmithKline) in Germany since October 2009, the question was raised if
6 patients after allogeneic hematopoietic stem cell transplantation (HSCT) should be vaccinated or
7 not. ² A major concern against the use of an adjuvant containing vaccine was the apprehension of
8 chronic graft-versus-host-disease (GVHD) exacerbation or deterioration.
9

10
11 Out of 370 HSCT-recipients with ambulatory clinic visits between October 2009 and February 2010
12 10 (2,7 %) presented with mild to moderate flu-like symptoms and positive throat swab. Median
13 post-transplant follow up was 10 months and all patients were under moderate systemic
14 immunosuppressive medication for GVHD management (n=5) or primary GVHD prophylaxis (n=5).
15 Immediate initiation of oseltamivir at a dose of 75 mg twice a day resulted in remission of clinical
16 symptoms in 5 patients without sequel but 2 required non-invasive and 3 invasive mechanical
17 ventilation emerging disastrous and finally lethal in two cases. Seven patients needed to be
18 hospitalized.
19

20
21 On the other hand 55 patients (14,9 %) with a median post-transplant follow up of 20 (3-192)
22 months underwent single dose 3,75 µg antigen (A/California/7/2009 (H1N1)v-like strain (X-179A))
23 vaccination formulated with the adjuvant system AS03 (Pandemrix™). Local and systemic events
24 were generally mild and adjuvant vaccination was not associated with acute worsening of GVHD
25 symptoms in 31 HSCT recipients suffering from limited (n=19) or extensive (n=12) chronic GVHD.
26 Patients without chronic GVHD (n=24) did not develop de novo vaccine-related allo-immune
27 phenomena within 3 months of post interventional surveillance. Except one patient who got
28 infected with H1N1 4 days after vaccination none of the vaccinated subjects presented with signs
29 of influenza manifestations in the sequel.
30
31

32
33 These single centre experiences during the peak of 2009 H1N1 pandemic in Germany confirm the
34 anticipated potentially serious outcome of H1N1 infection in immunodeficient high risk population
35 groups. The experiences demonstrate that by taking all available measures it might be possible to
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

1 prevent even patients highly susceptible to any kind of infection from epidemic fatalities Apart from
2 the fact that the effectiveness of vaccination needs to be evaluated by verifying immune responses
3 on the laboratory scale the application of vaccines with adjuvant formulation primarily does not
4 seem to have any adverse immune stimulating effects.^{3, 4} Therefore, besides common reasonable
5 precautions active vaccination of allogeneic HSCT recipients may provide a safe strategy to
6 conquer new healthcare challenges.
7
8
9
10
11
12
13
14

15 **References:**

- 16
17 1. Martino R, Porrás RP, Rabella N, et al. Prospective study of the incidence, clinical features,
18 and outcome of symptomatic upper and lower respiratory tract infections by respiratory
19 viruses in adult recipients of hematopoietic stem cell transplants for hematologic
20 malignancies. *Biol Blood Marrow Transplant.* 2005 Oct;11:781-96.
21
22
- 23 2. Kharfan-Dabaja MA, Velez A, Richards K, et al. Influenza A/pandemic 2009/H1N1 in the
24 setting of allogeneic hematopoietic cell transplantation: a potentially catastrophic problem in
25 a vulnerable population. *Int J Hematol.* [Epub ahead of print]
26
27
- 28 3. Avetisyan G, Aschan J, Hassan M, et al. Evaluation of immune responses to seasonal
29 influenza vaccination in healthy volunteers and in patients after stem cell transplantation.
30 *Transplantation.* 2008 Jul 27;86:257-63.
31
32
- 33 4. Roman F, Vaman T, Gerlach B, et al. Immunogenicity and safety in adults of one dose of
34 influenza A H1N1v 2009 vaccine formulated with and without AS03(A)-adjuvant:
35 Preliminary report of an observer-blind, randomised trial. *Vaccine.* 2009 Dec 22. [Epub
36 ahead of print]
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

***Conflict of interest**

[Click here to download Conflict of interest: Conflict of Interest Disclosure Form.doc](#)