Community-acquired respiratory paramyxovirus infection after allogeneic hematopoietic stem cell transplantation: a single-center experience

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Background

- Respiratory syncytial virus (RSV), parainfluenza virus (PIV) and human metapneumovirus (hMPV)

- Progression rate to lower RTI up to 84% and mortality rate up to 80% after allogeneic HSCT[1,2]

- Risk factors for progression/mortality[3]:
  - ≥ 40 years
  - Allogeneic HSCT, particularly myeloablative regimens
  - Neutro- and Lymphopenia
  - Preengraftment or early posttransplant status (< 1 month)
  - Graft-versus-Host-Disease (GvHD)
  - Systemic corticosteroid use

1 Shah JN, Chemaly RF. Management of RSV infections in adult recipients of hematopoietic stem cell transplantation. Blood. 2011;117(10):2755-63.
2 Nichols WG, Gooley T, Boeckh M. Community-acquired respiratory syncytial virus and parainfluenza virus infections after hematopoietic stem cell transplantation: the Fred Hutchinson Cancer Research Center experience. Biol Blood Marrow Transplant. 2001;7 Suppl:11S-5S.
3 Chemaly RF, Shah DP, Boeckh MJ. Management of respiratory viral infections in hematopoietic cell transplant recipients and patients with hematologic malignancies. Clin Infect Dis. 2014;59 Suppl 5:S344-51.

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Objectives

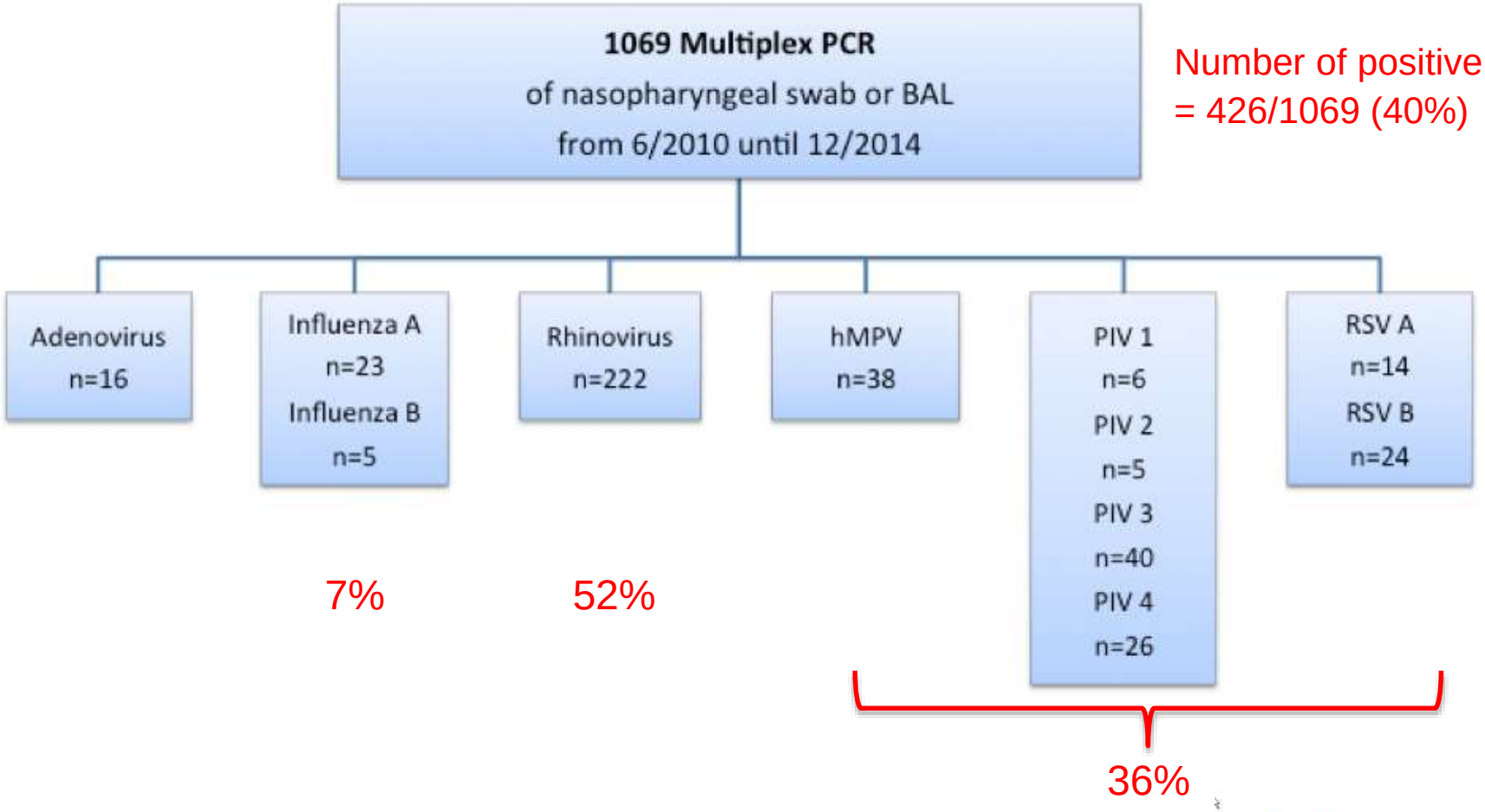
- Comparison regarding occurrence, course, treatment and outcome

- Evaluation of our RTI management according to moderate and severe immunodeficiency (ID)

- Outcome:
  - median duration of viral shedding
  - progression to lower RTI
  - hospitalisation
  - admission to intensive care unit (ICU)
  - mortality

Patient Population

- Retrospective single center study



PCR=polymerase chain reaction; BAL=bronchoalveolar lavage; hMPV=human metapneumovirus; PIV=parainfluenza virus; RSV=respiratory syncytial virus.

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Definitions

- Upper RTI:
  - respiratory virus detection with URTI symptoms

- Lower RTI:
  - respiratory virus detection with LRTI symptoms and pulmonary infiltrates

- Severe immunodeficiency (SID):
  - Allogeneic HSCT ≤ 6 months
  - GvHD grade ≥ 2
  - Leucopenia ≤ 1.0 x 10^9/l or neutropenia < 0.5 x 10^9/l
  - Lymphopenia ≤ 0.1 x 10^9/l
  - Hypogammaglobulinemia <4.5 g/l
  - T-cell or B-cell depletion ≤ 3 months ago

- Very severe immunodeficiency (vSID)
  - fulfilling ≥ 2 SID criteria

Khanna N, Widmer AF, Decker M, Steffen I, Halter J, Heim D, et al. Respiratory syncytial virus infection in patients with hematological diseases: single-center study and review of the literature. Clin Infect Dis. 2008;46(3):402-12.

Episode characteristics at RTI diagnosis

	All episodes (n=103)	PIV (n=48)	RSV (n=33)	hMPV (n=22)
Age, median years (range)	52 (20, 71)	52 (22, 68)	53 (20, 71)	54 (28, 69)
Female, n (%)	31 (30)	14 (29)	9 (27)	8 (36)
HLA-matched related, n (%)	42 (41)	24 (50)	12 (36)	6 (27)
Peripheral blood stem cells, n (%)	102 (99)	47 (98)	33 (100)	22 (100)
GvHD, n (%) - **GvHD grade ≥ 2**	64 (62) 37 (36)	29 (60) 17 (35)	19 (58) 9 (27)	16 (73) 11 (50)
Cyclosporin A, n (%) **Steroids**, n (%)	33 (32) 49 (48)	14 (29) 24 (50)	11 (33) 14 (42)	8 (36) 11 (50)

PIV=parainfluenza virus; RSV=respiratory syncytial virus; hMPV=human metapneumovirus; HLA=human leucocyte antigen; RTI=respiratory tract infection; GvHD=Graft-versus-host disease.

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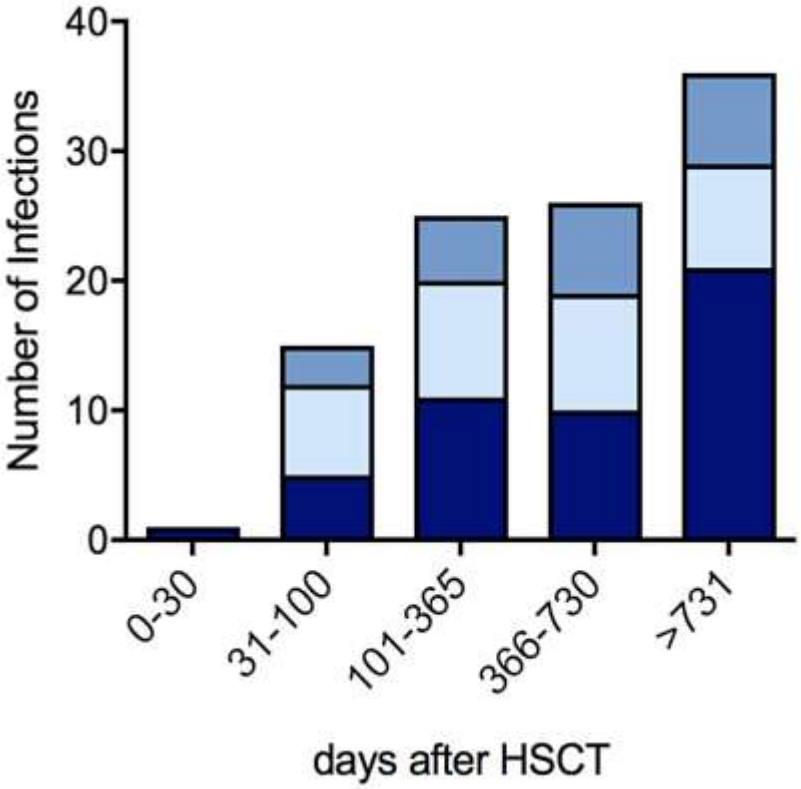
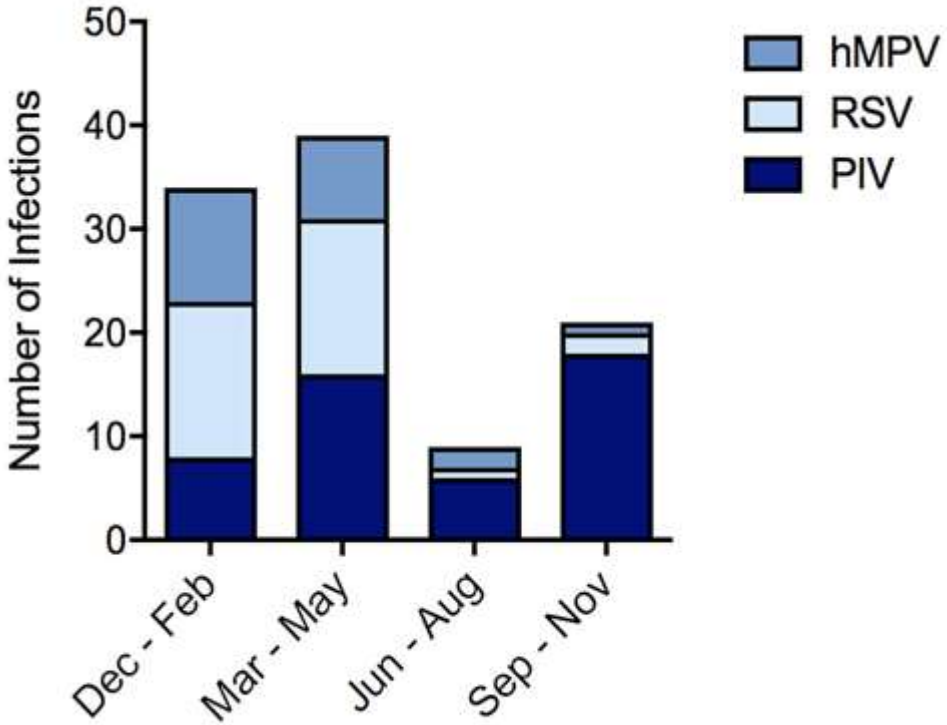
Occurrence of RTIs





- Median post-HSCT time: RSV 382 days, PIV 628 days, hMPV 504 days
- RSV and hMPV RTIs in winter, PIV RTIs in autumn (p-value≤0.001)

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Clinical presentation

	All episodes (n=103)	PIV (n=48)	RSV (n=33)	hMPV (n=22)
Upper RTI, n (%)	59 (57)	27 (56)	21 (64)	11 (50)
Lower RTI, n (%)	37 (36)	19 (40)	8 (24)	10 (46)

- No difference between RSV, PIV and hMPV

Grade of immunodeficiency

	All episodes (n=103)	PIV (n=48)	RSV (n=33)	hMPV (n=22)
MID, n (%)	40 (39)	22 (46)	13 (39)	5 (23)
SID, n (%)	63 (61)	26 (54)	20 (61)	17 (77)

- 63 (61.2%) episodes occured in patients with severe ID
  - 19 (30.2%) very SID (fulfilled ≥ 2 SID criteria)
- No difference between RSV, PIV and hMPV

MID=moderate immunodeficiency, SID=severe immunodeficiency.

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Intervention

	All episodes (n=103)	PIV (n=48)	RSV (n=33)	hMPV (n=22)
Ribavirin + IVIG, n (%)	39 (38)	3 (6)	20 (61)	16 (73)
IVIG only, n (%)	24 (23)	19 (40)	3 (9)	2 (9)
None, n (%)	40 (39)	26 (54)	10 (30)	4 (18)

IVIG=intravenous immunoglobulin.

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Intervention

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None, n (%)	40 (39)	26 (54)	10 (30)	4 (18)

	MID (n=40)	SID (n=63)	vSID (n=19)
Ribavirin + IVIG, n (%)	9 (23)	30 (48)	12 (63)
IVIG only, n (%)	7 (18)	17 (27)	5 (26)
None, n (%)	24 (60)	16 (25)	2 (11)

- Treatment of PIV RTIs less frequently with RBV + IVIG (p-value≤0.001), but PIV RTIs were more often treated with IVIG only
- Any intervention rather than no intervention in episodes with SID (p-value=0.001)

IVIG=intravenous immunoglobulin.

Outcome

- No difference in median duration of viral shedding
  - RSV (21 days), PIV (17 days) and hMPV (32 days)
  - with and without intervention
  - immunodeficiency
- Progression to lower RTI in 6%
- Hospitalisation more often in episodes with lower RTI (25/37; p-value <0.001)
- Overall mortality rate 6%
  - no difference between RSV, PIV and hMPV

Very severe ID

- Trend of higher progression rate (p-value=0.075)
  - 3/6 vSID
- Increased hospitalisation (p-value <0.001)
  - 16/40 vSID
- Increased transfer to the ICU (p-value <0.001)
  - 5/6 vSID
- Increased mortality (p-value <0.001)
  - 6/6 vSID

Conclusion

- Occurrence > 100 days post-HSCT and community-acquired
  → precautions pre-HSCT and early post-HSCT
  → long follow-up of patients

- No difference in outcome between RSV, PIV and hMPV but according to immunodeficiency

- Lower progression to lower RTI and mortality as previously reported
  → few risk factors
  → high awareness
  → timely diagnosis and early initiation of treatment

- Benefit of antiviral treatment unclear, but seems to be useful in patients with SID and vSID

Strengths and Limitations

Strengths

- Large cohort of hematologic patients
- Standardized guidelines on diagnostic and therapeutic regimens particularly for RSV

Limitations

- Retrospective and single centre study
- No clear definition of the antiviral treatment duration
- Lack of a proper randomized control group

Thank you for your attention

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