Virological Surveillance in Paediatric HSCT Recipients

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Important viral reactivations / diseases in children receiving HSCT

I. Cytomegalovirus

- CMV reactivation occurs in 40–70% of HSCT recipients who are seropositive or have a seropositive donor
- Viraemia can be associated with organ disease, including pneumonitis, hepatitis, colitis and retinitis

II. EBV disease

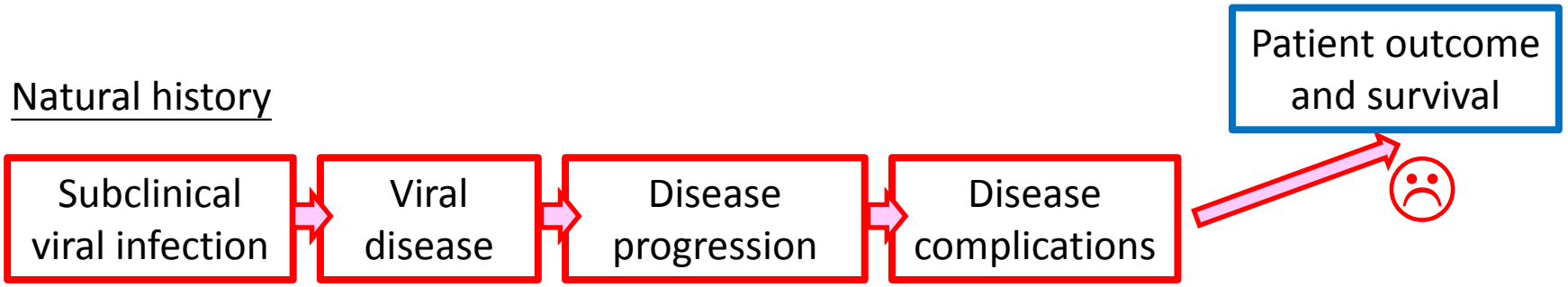
- Historically (before the introduction of Rituximab therapy) 11–26% of transplant recipients developed EBV-related lymphoproliferative disease

III. Adenovirus disease

- Serotypes B and C is particularly problematic in children
- Positive detection of adenovirus: varies widely 8-50% in pediatric SCT recipients (depending on the diagnostic methods and screening schedules), disseminated ADV: 10%
- AdV related mortality ranges between 3.2% and 6.0%
- Disseminated infection leading to pneumonitis, hepatitis, and colitis and associated with mortality rates of up to 50%

Viral surveillance in HSCT

Goal: to detect subclinical viral infection that triggers an intervention



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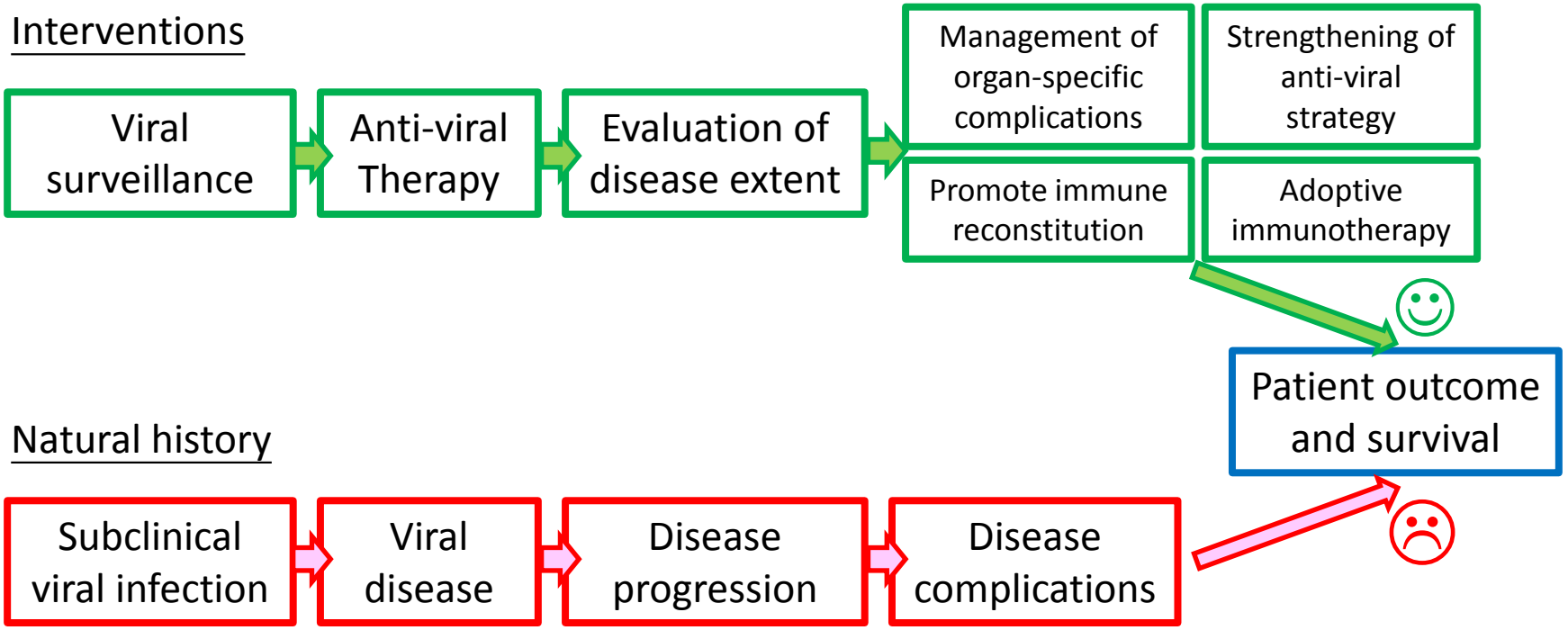

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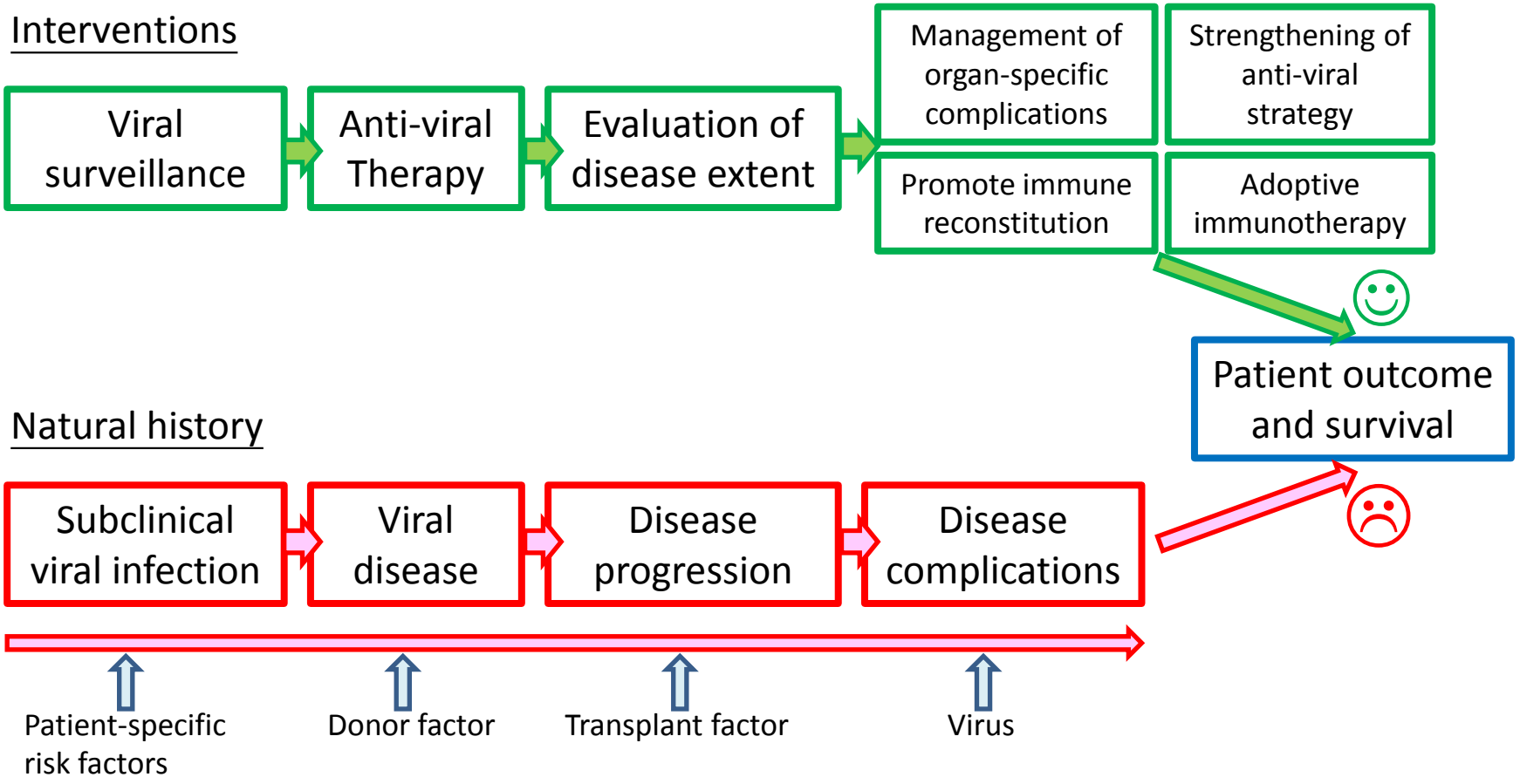

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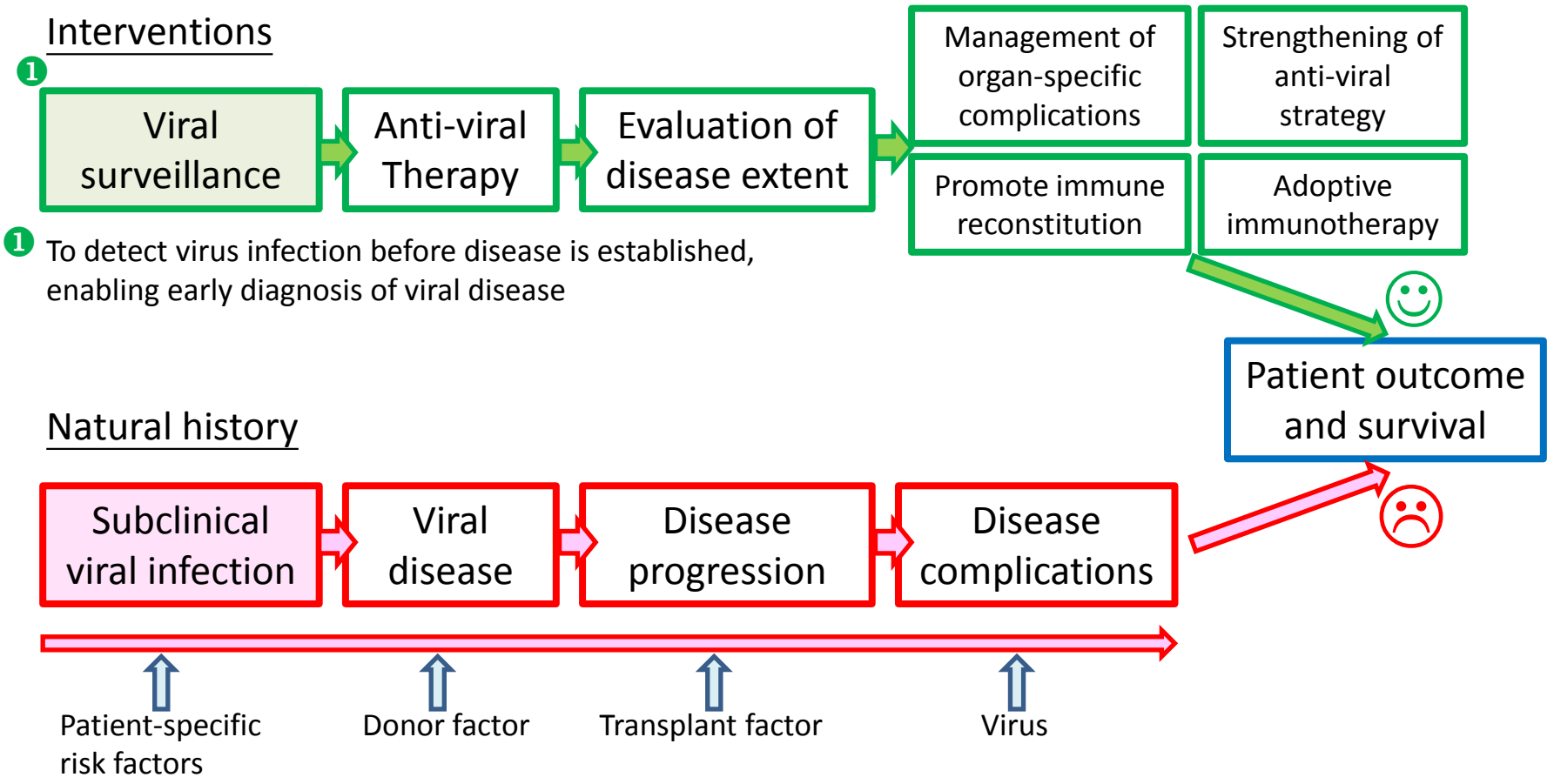

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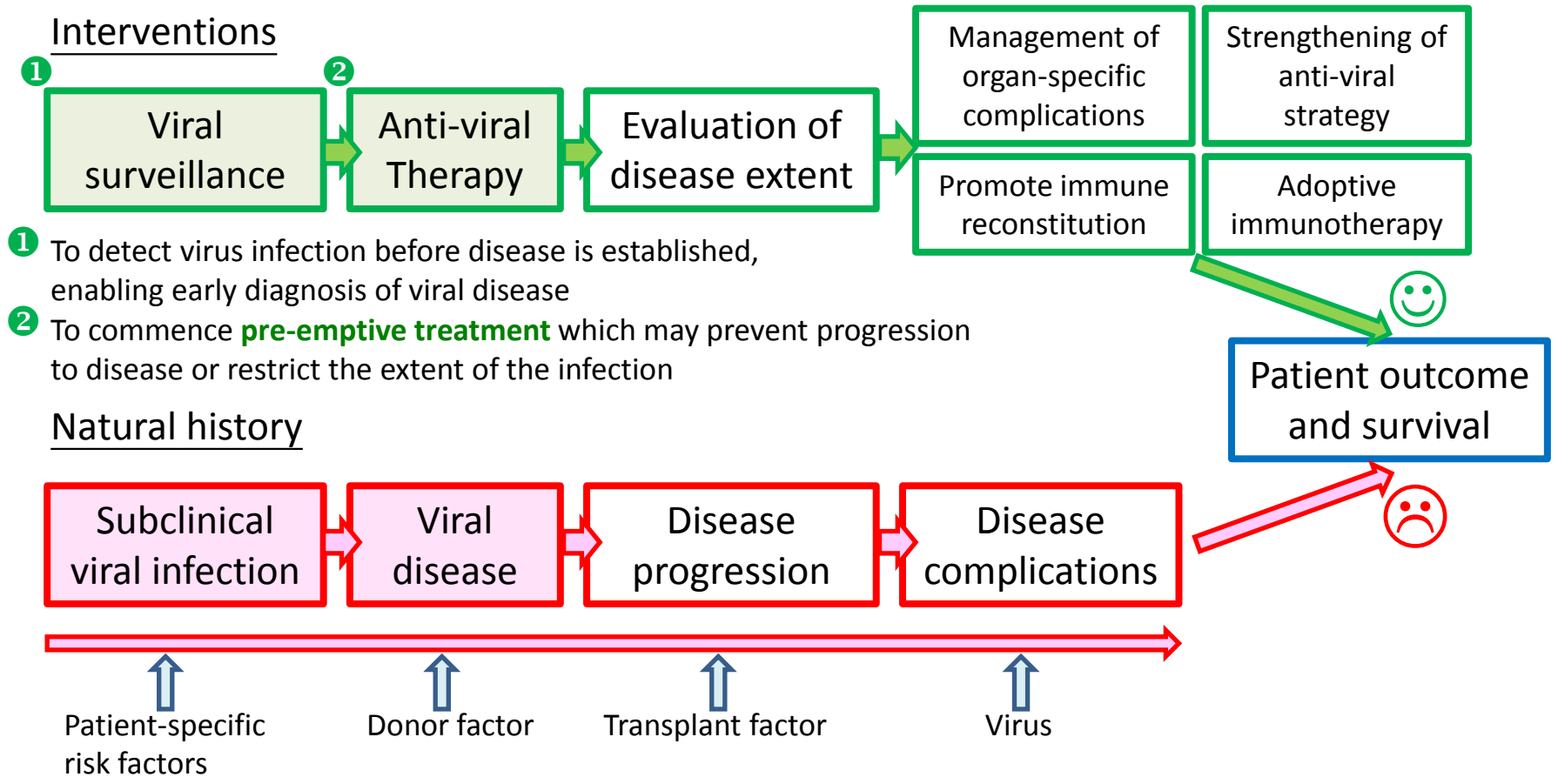
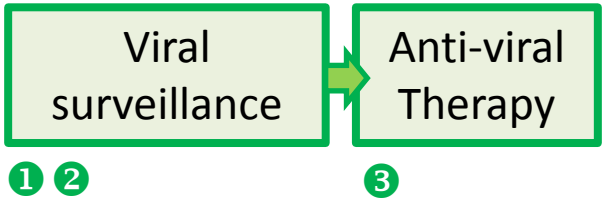


Viral surveillance in HSCT

Goal: to detect subclinical viral infection that triggers an intervention

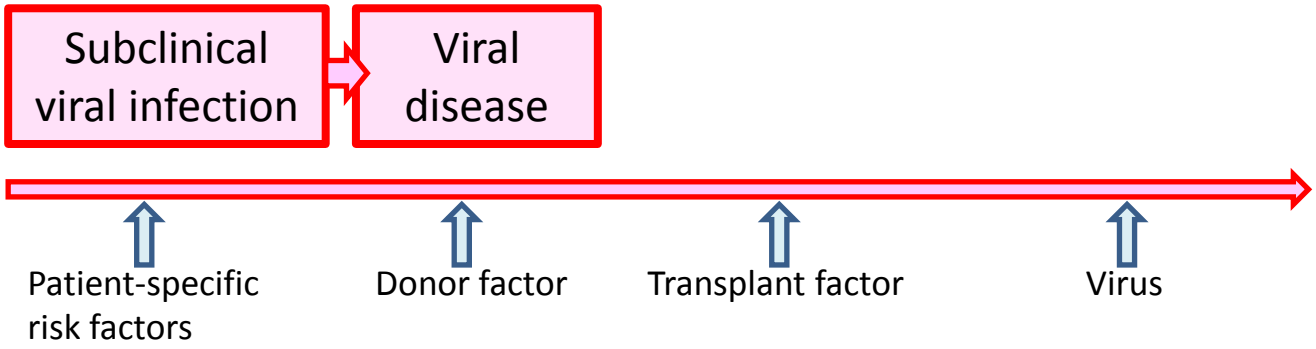
Interventions



Prerequisites for an effective surveillance programme:

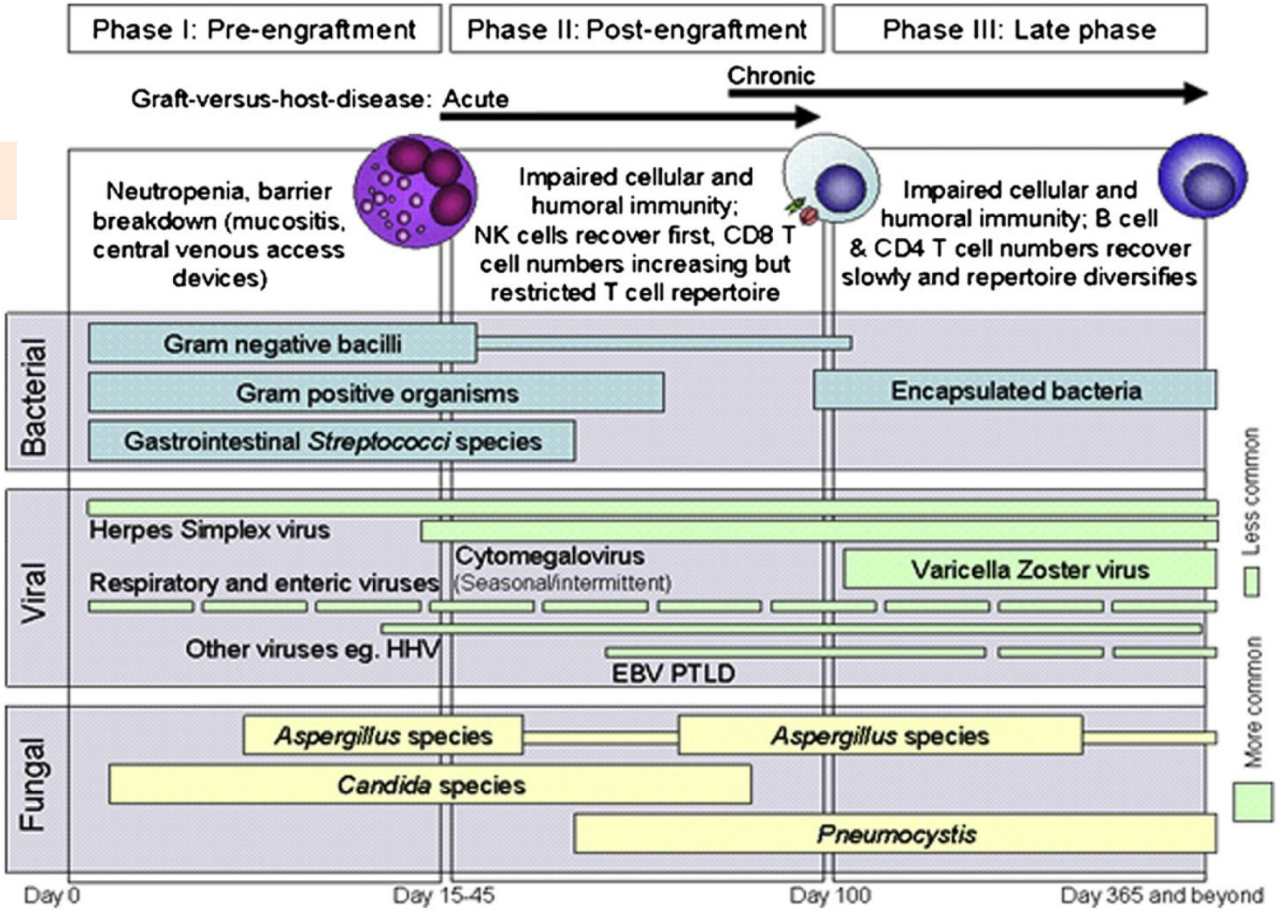
1. Adherence to testing schedule
2. Appropriate frequency of testing
3. Start treatment according to a pre-determined viral load threshold or trend

Natural history



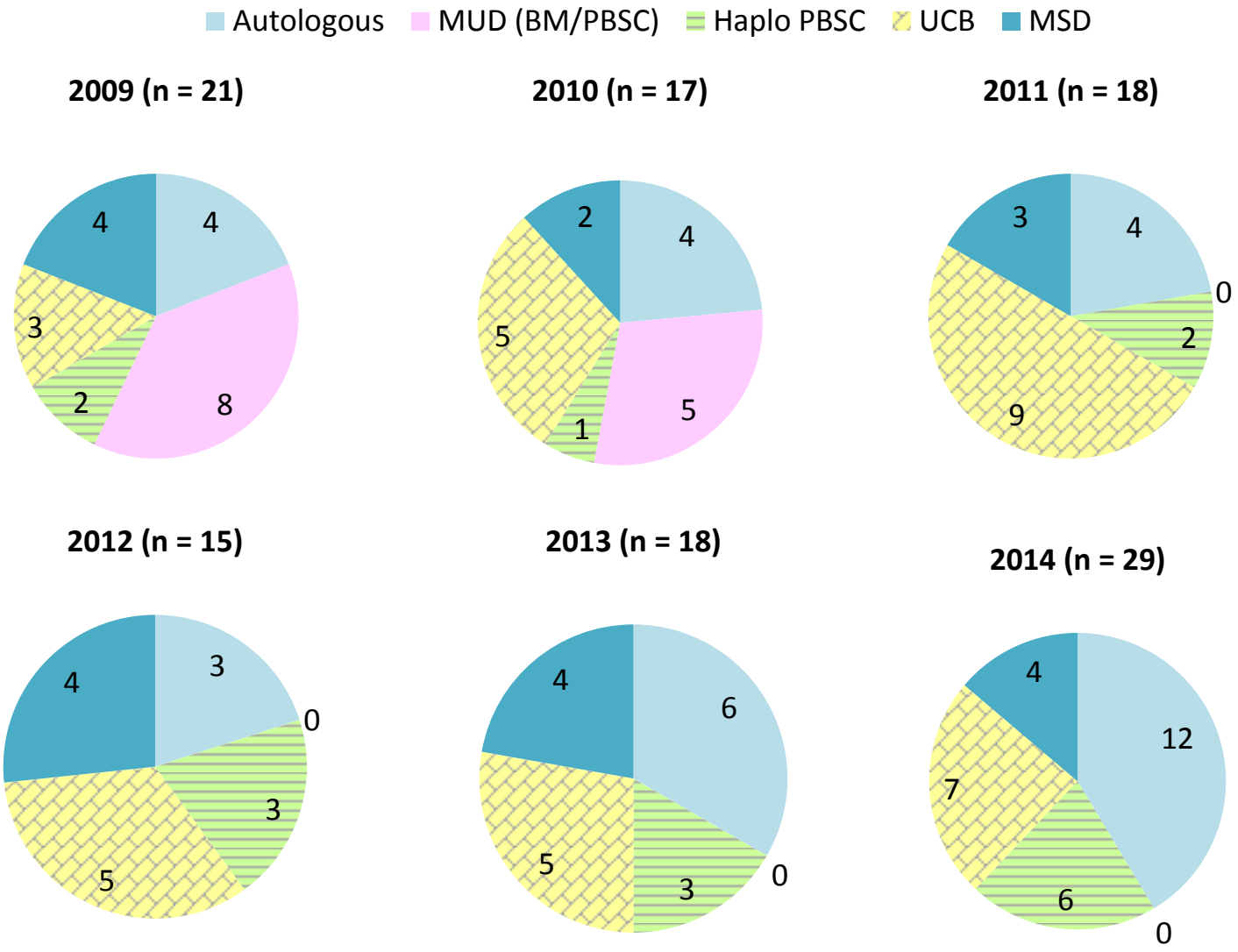
Factors influencing the strategy of viral surveillance

Timing



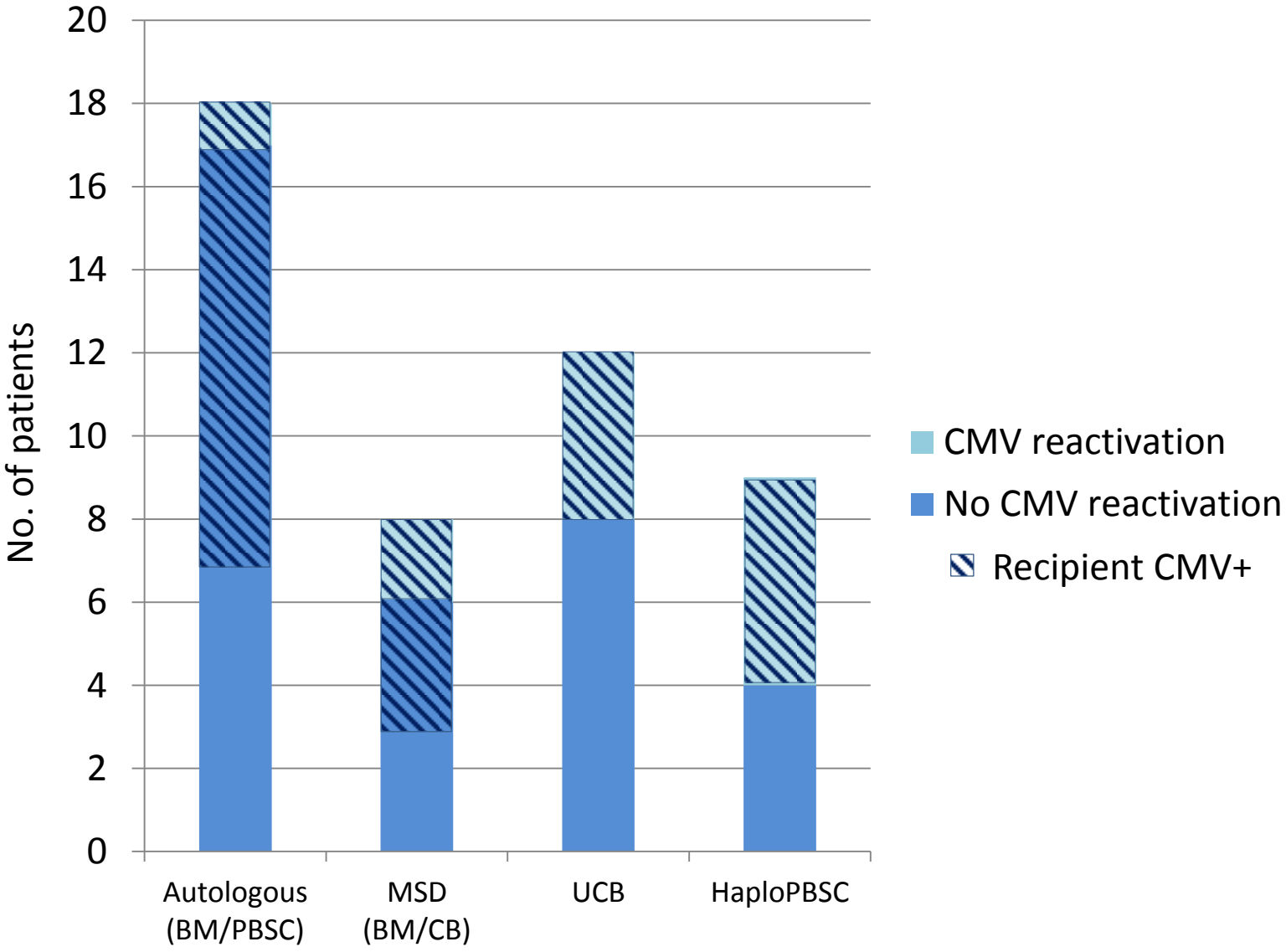
Recipient factor	Donor / graft factor	Transplant factor
Pre-existing viral infections Pre-transplant immunosuppression / underlying immunodeficiency	Donor serostatus Graft manipulation Mismatched / haploidentical donors	Conditioning intensity Immunosuppression GVHD Delayed engraftment

HSCT performed in Department of Paediatrics & Adolescent Medicine, QMH, HKU (2009 – 2014)



Cumulative number of HSCT performed since 1991: 342

CMV surveillance in paediatric HSCT recipients, QMH, 2013 - 2014



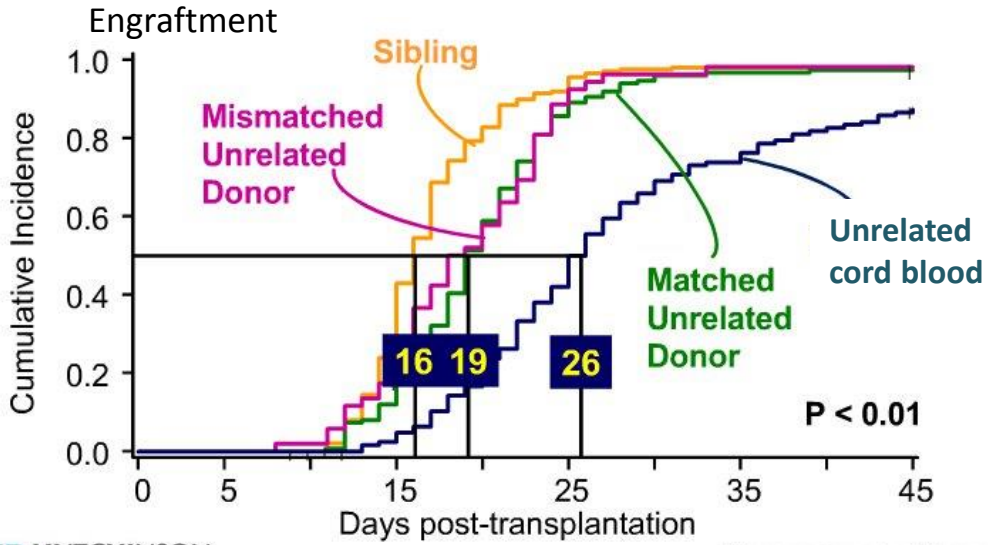
Stem cell source is an important determinant of engraftment and immune reconstitution

Table 1: Number of cells according to stem cell source

	Volume collected	Med CD34 content	Med CD3 content	Target cell dose
Bone marrow	10–20 mL/kg	2–3 x 10^6/kg*	25 x 10^6/kg	>2 x 10^8 TNC/kg
Peripheral blood	150–400 mL	8 x 10^6/kg	250 x 10^6/kg	5–10 x 10^6 $CD34^+$/kg
Umbilical cord blood	80–160 mL	0.2 x 10^6/kg	2.5 x 10^6/kg	>3 x 10^7 TNC/kg

**per kg recipient body weight*

EBMT Handbook 2012



The journey of immune reconstitution

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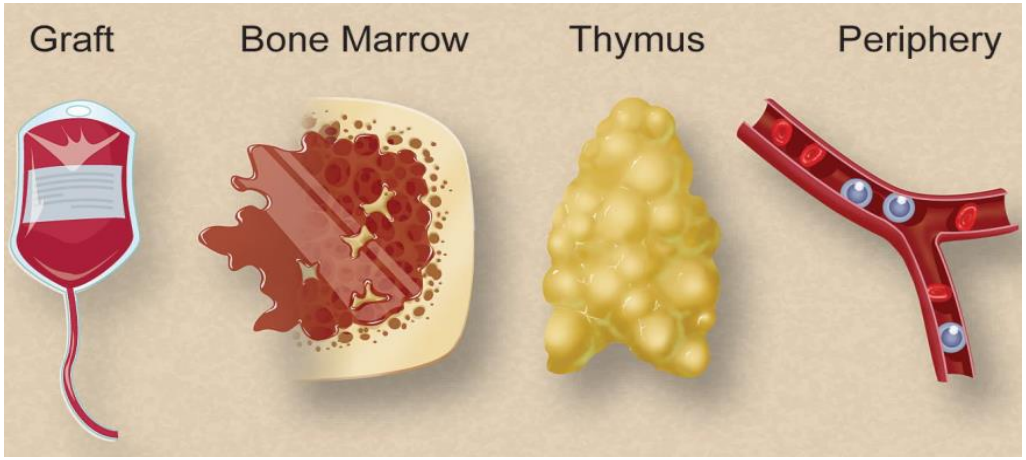
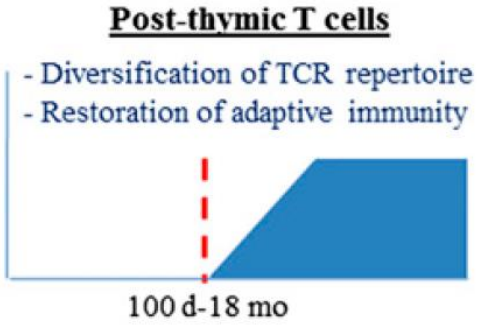


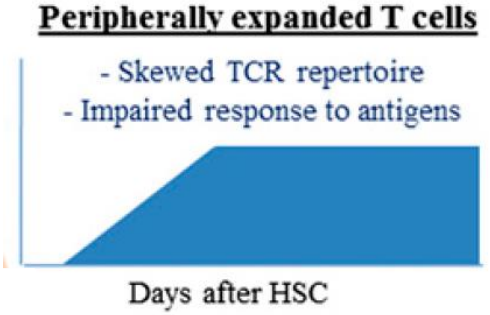
Cell dose
Viability

Engraftment
Development & differentiation of lymphoid precursors

'Education': Positive & negative selection

Antigen-driven expansion of T-cells



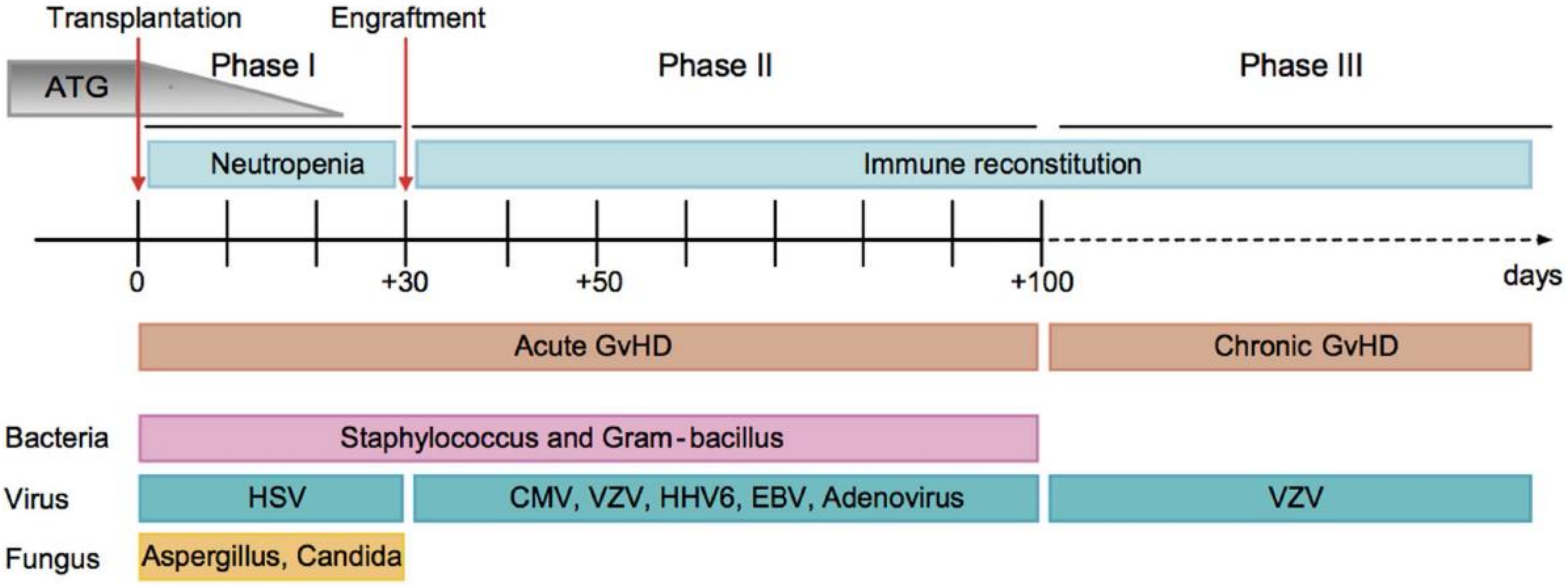


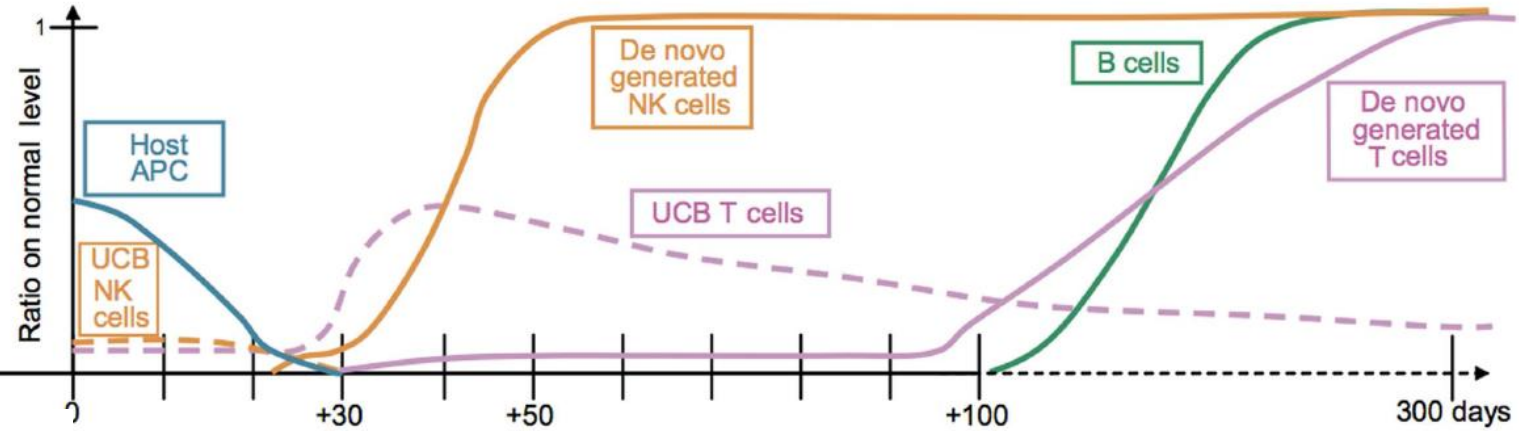
Umbilical cord blood as a stem cell source for transplant

Quantitative and qualitative differences of UCB grafts:

- Each unit contains 1-2 log lower TNC (and T-cell number) compared to BM and PBSC
- Vast majority of T-cells in UCB are naïve T-cells
  - Less responsive to allogeneic stimulation
  - Reduced expression of transcription factors for T-cell activation
  - Activated T-cells produce lower levels of effector cytokines
- UCB contains more immunoregulatory cells e.g. Tregs with immunosuppressive functions
- Dendritic cells in UCB are functionally immature with lower antigen presenting activity, reduced expression of co-stimulatory molecules and cytokine production

Kinetics of engraftment and immune reconstitution following UCB transplantation

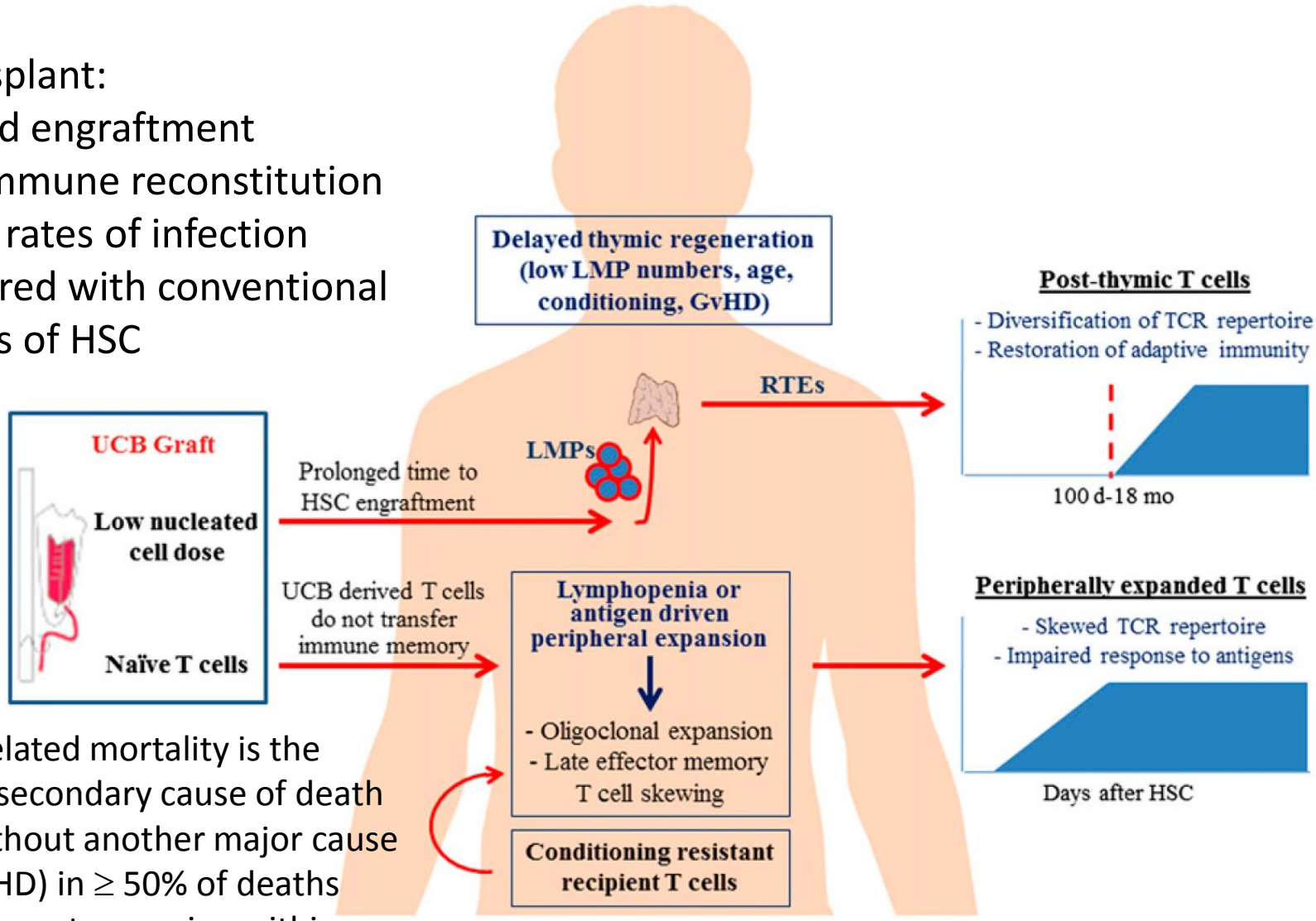




Immune reconstitution in UCBT – The role of thymus

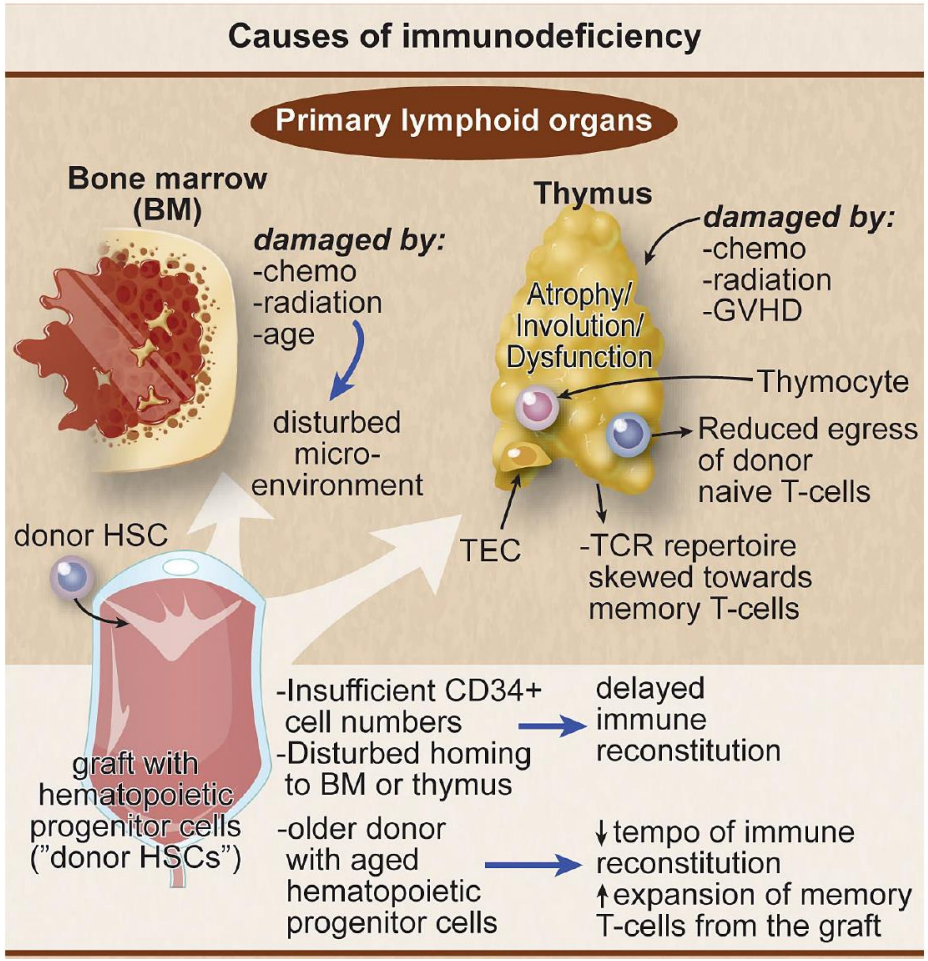
UCB transplant:

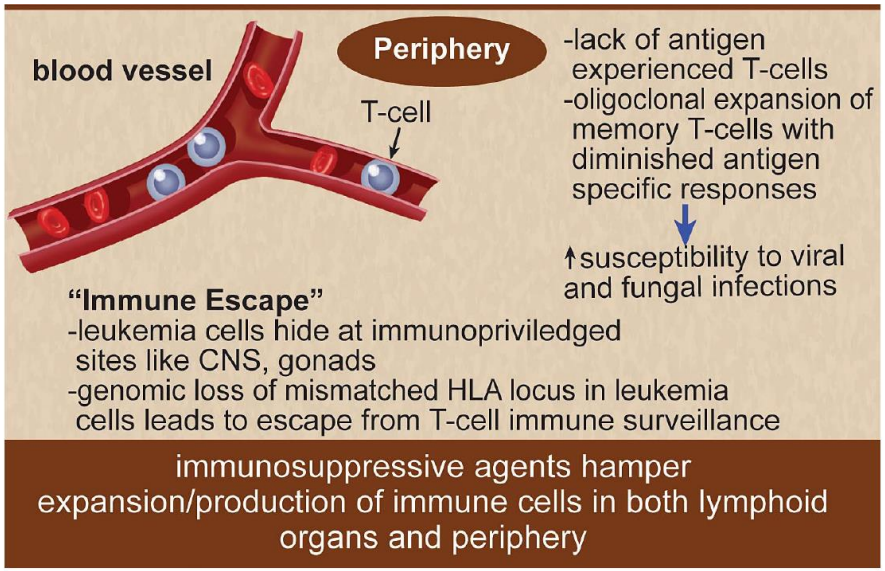
- Delayed engraftment
- Slow immune reconstitution
- Higher rates of infection compared with conventional sources of HSC



Infection-related mortality is the primary or secondary cause of death (with or without another major cause such as GVHD) in ≥ 50% of deaths after UCBT, most occurring within D+100

Transplant factors impacting on immune reconstitution





Seggewiss and Einsele. Immune reconstitution after allo-SCT and expanding options for immunomodulation: an update.
BLOOD, 13 MAY 2010 • VOLUME 115, NUMBER 19

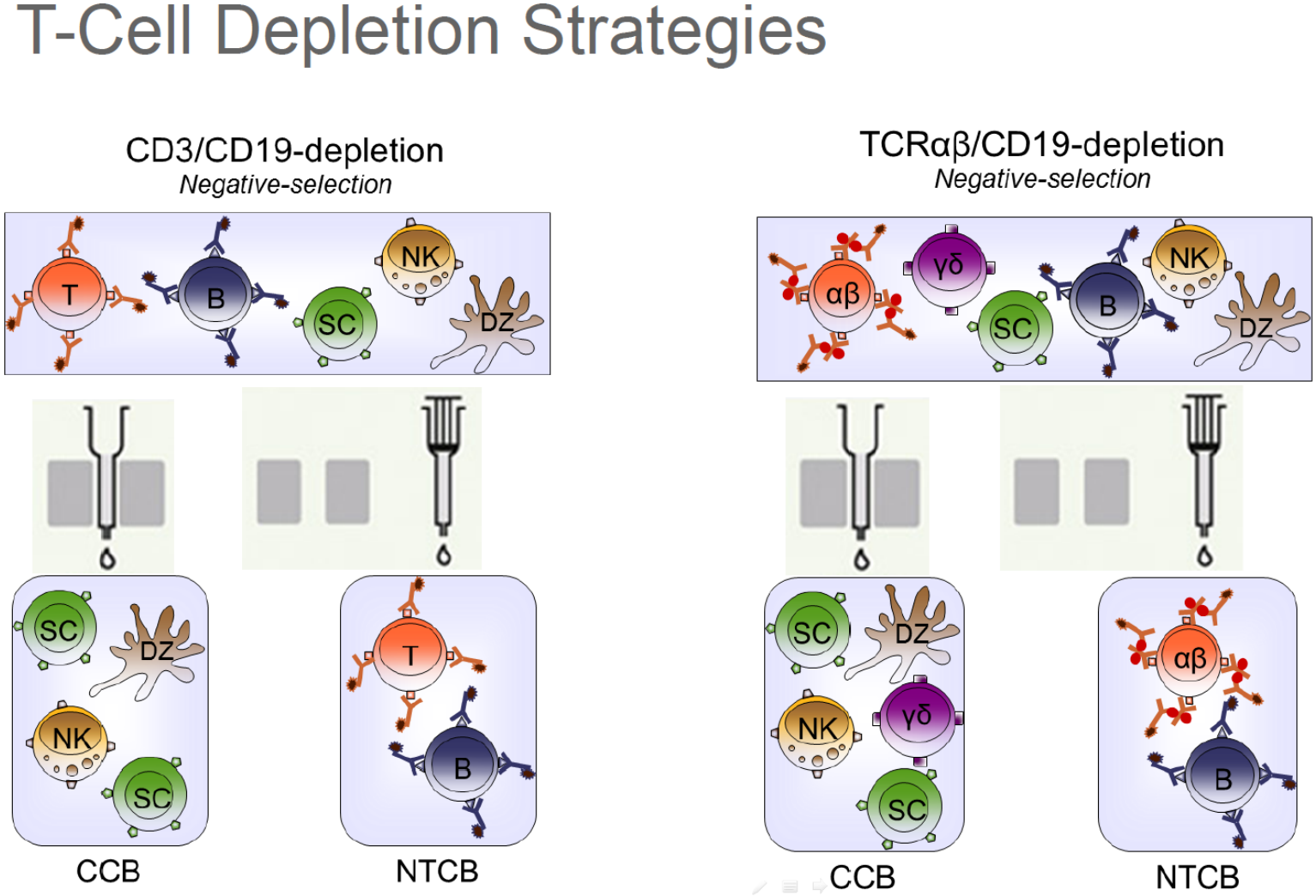
Haploidentical stem cell transplant

- Immediate availability of donors (parents, siblings, offsprings)
- Optimistic chance to obtain high CD34+ stem cell dose
- There is a choice of donor selection according to the donor's killer cell immunoglobulin-like receptor (KIR) phenotype or donor KIR haplotype
- In the case of mixed chimerism, impending relapses or refractory viral diseases, or to accelerate immune recovery, post-transplant donor-derived adoptive therapeutic strategies can rapidly be initiated, including:
  - adoptive transfer of purified donor-derived NK (natural killer) cells
  - adoptive transfer of T lymphocytes or T-lymphocyte subsets
  - minor histocompatibility antigen (mHA)–specific T lymphocytes
  - leukemia-specific T lymphocytes
  - adoptive transfer of CD4+/CD25+ regulatory T lymphocytes
  - adoptive transfer of virus-specific T cells directed against adenovirus, cytomegalovirus, Epstein-Barr virus or other donor-derived effector cells to be identified in future research

Lena Oevermann & Rupert Handgretinger

Pediatric RESEARCH Volume 71 | Number 4 | April 2012

T-cell depleted haploidentical stem cell transplant



Peter Bader, EBMT 2014 (slide accessed on-line)

Transplantation of CD3/CD19 depleted allografts from haploidentical family donors in paediatric leukaemia

British Journal of Haematology, 2014, **165**, 688–698

Peter Lang,[1]* Heiko-Manuel Teltschik,[1]* Tobias Feuchtinger,[1] Ingo Müller,[1] Matthias Pfeiffer,[1] Michael Schumm,[1] Martin Ebinger,[1] Carl P. Schwarze,[1] Bernd Gruhn,[2] Andre Schrauder,[3] Michael H. Albert,[4] Johann Greil,[5] Christian Urban[6] and Rupert Handgretinger[1]

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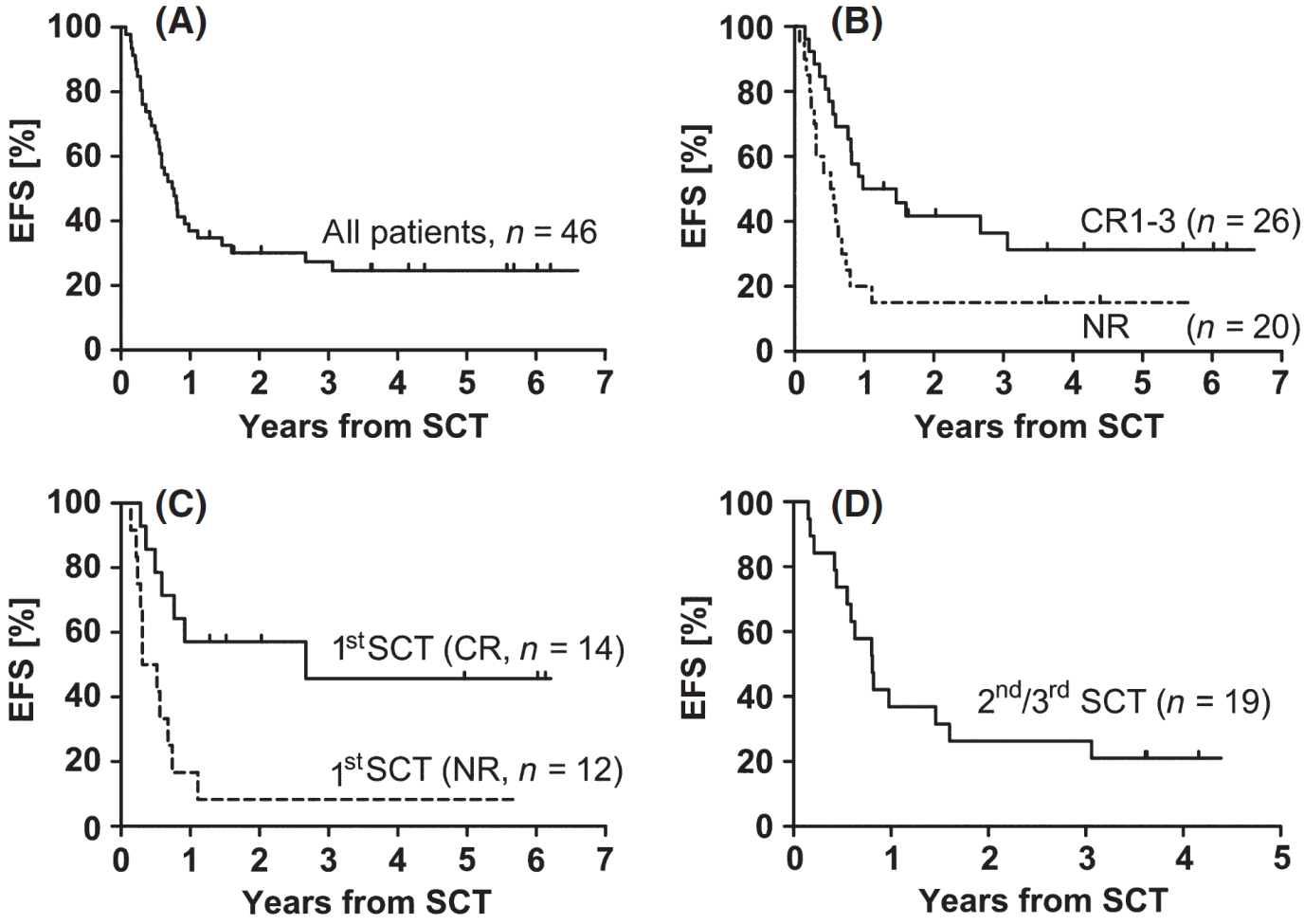

CR, complete remission at the time of transplant
NR, non-remission (active disease) at the time of transplant

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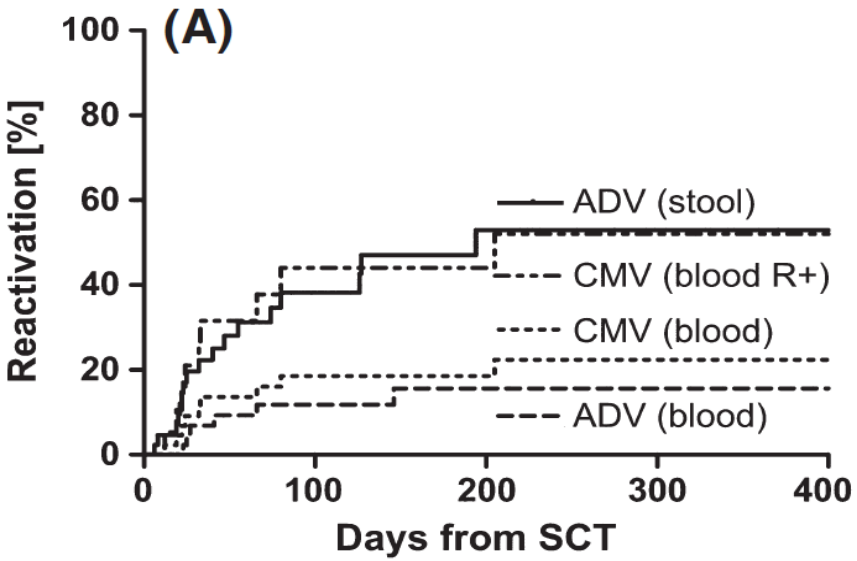
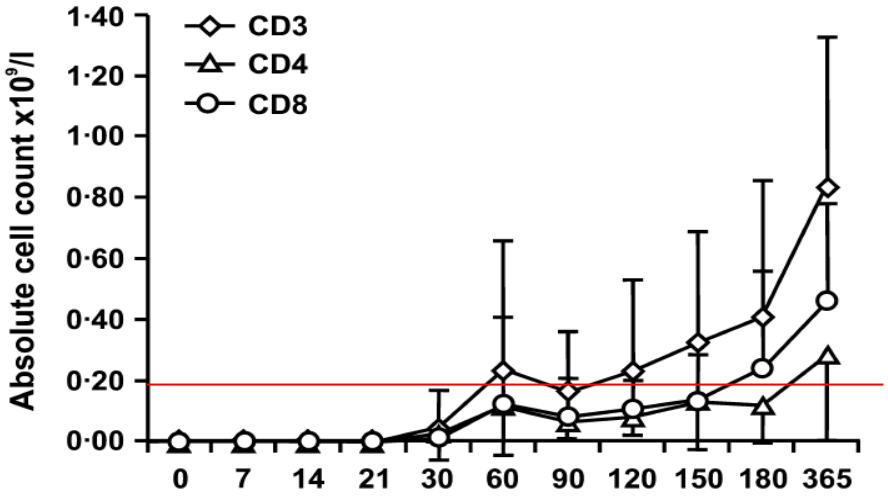
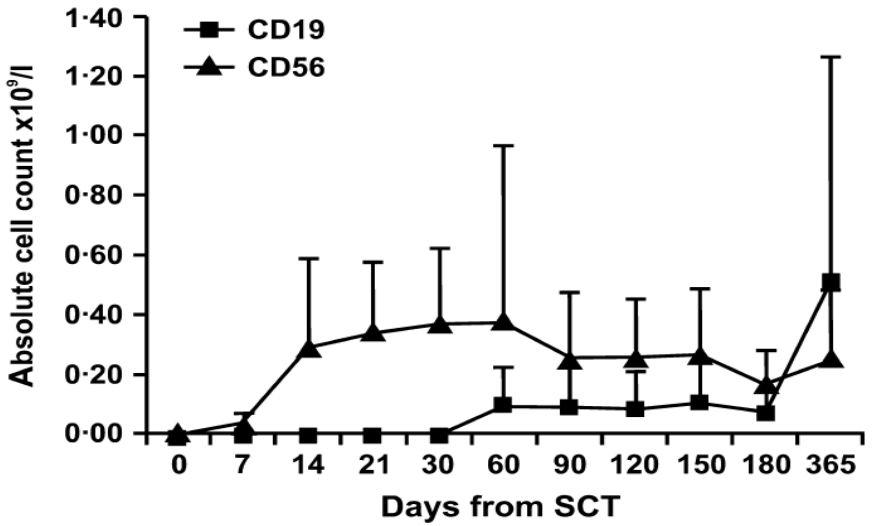


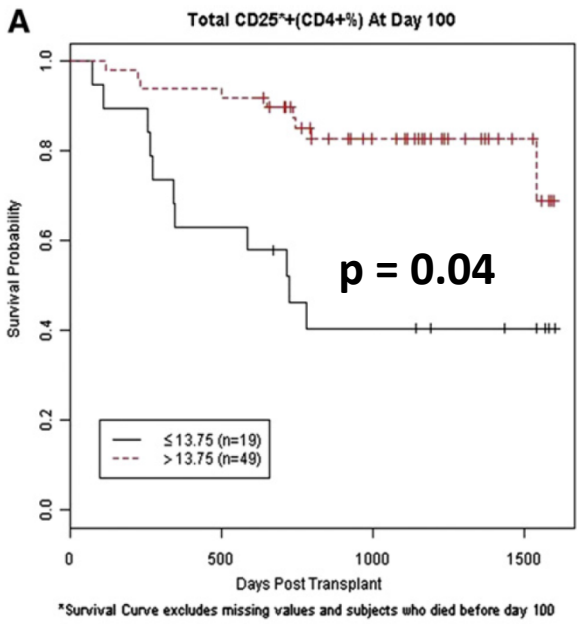




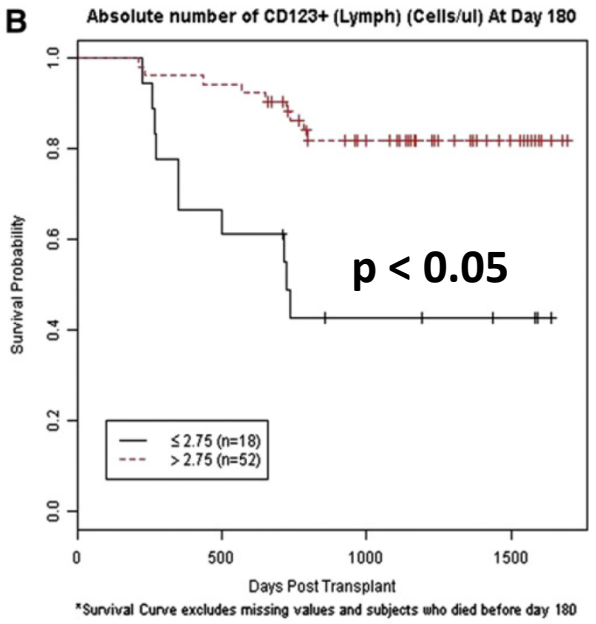
Immune recovery as predictors of survival

NCI, NHLBI/PBMTC First International Conference on Late Effects After Pediatric Hematopoietic Cell Transplantation: Persistent Immune Deficiency in Pediatric Transplant Survivors *Biol Blood Marrow Transplant 18: 6-15 (2012)*

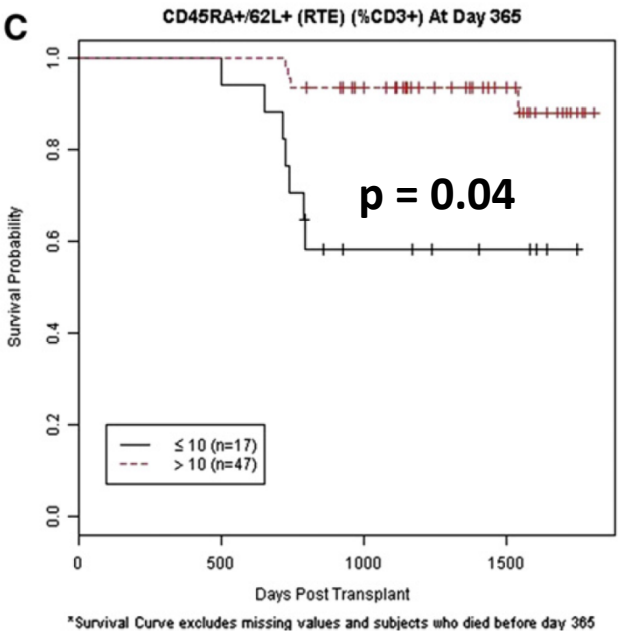
- 93 children who received single cord UCBT with myeloablative conditioning at Duke University
- Median age = 2.1 years, OS at 2 years = 76%



T-regulatory cells



Plasmacytoid dendritic cells



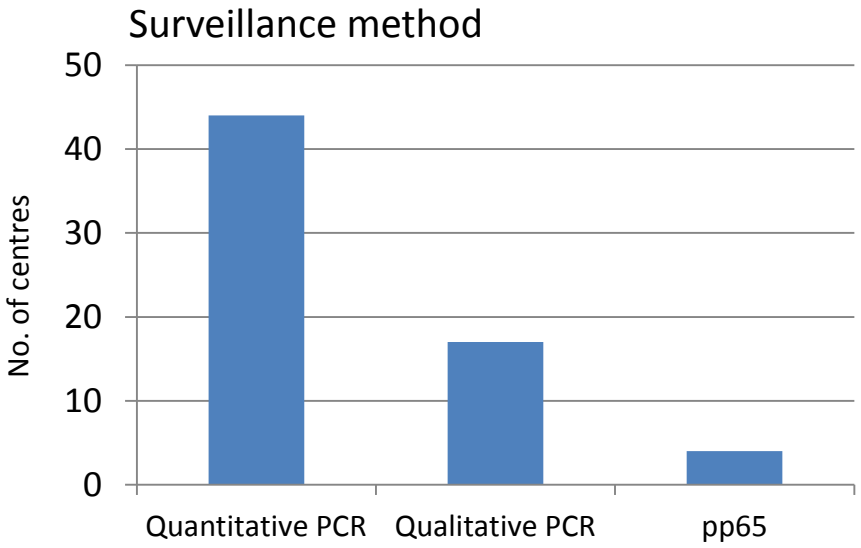
Recent thymic emigrant

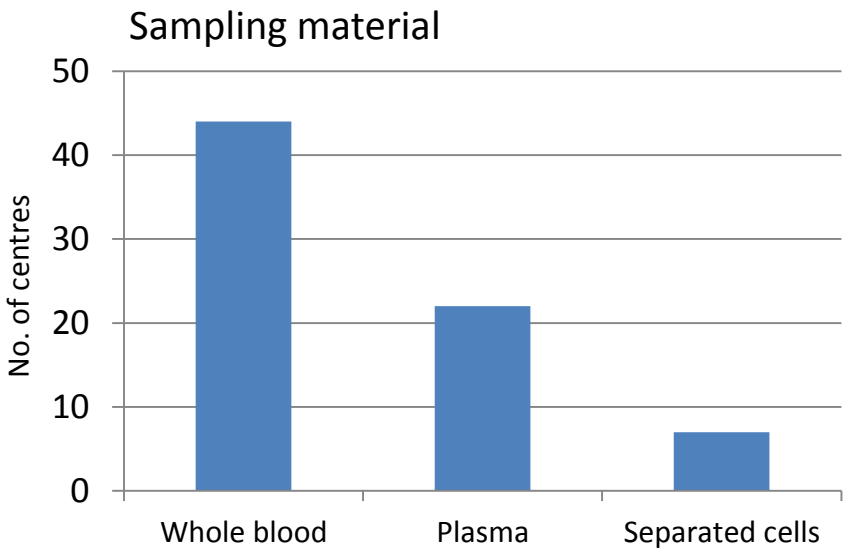
ORIGINAL ARTICLE

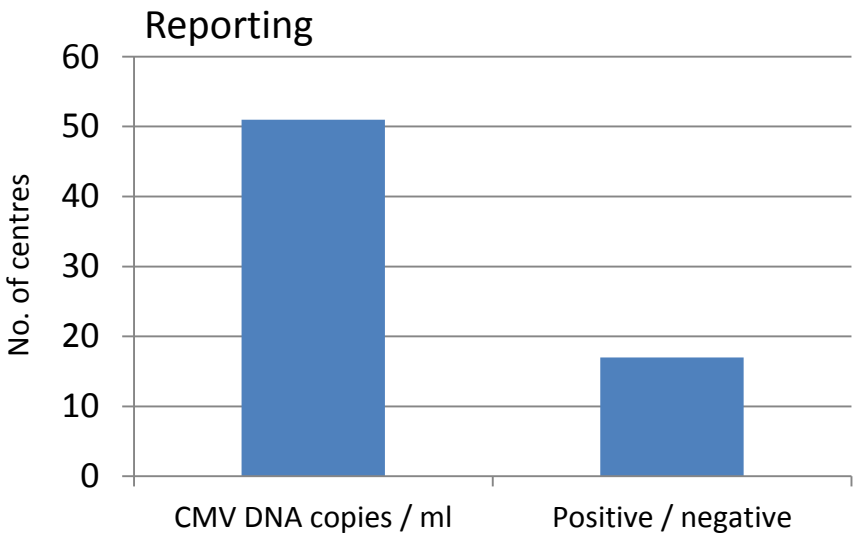
Bone Marrow Transplantation (2014) **49,** 276–279

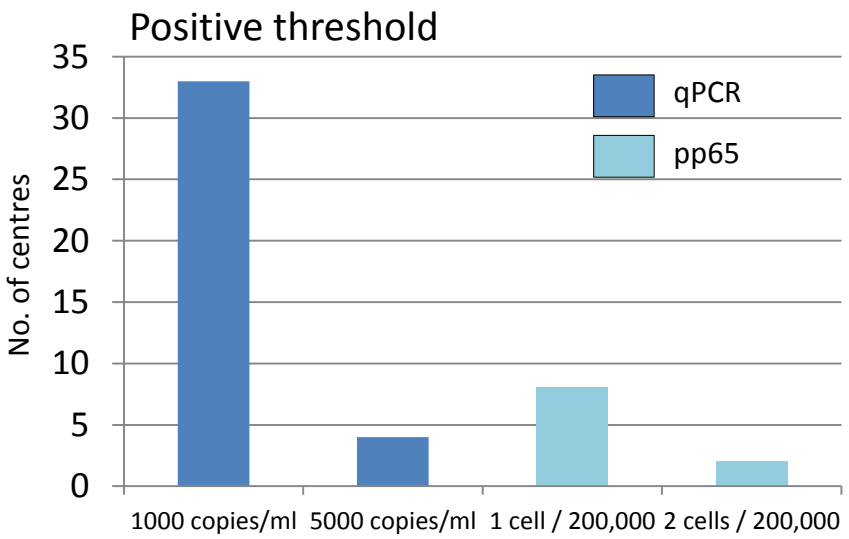
Survey of CMV management in pediatric allogeneic HSCT programs, on behalf of the Inborn Errors, Infectious Diseases and Pediatric Diseases Working Parties of EBMT

T Bontant[1], P Sedlaçek[2], A Balduzzi[3], B Gaspar[4], S Cesaro[5], H Einsele[6], C Peters[7] and J-H Dalle[1]









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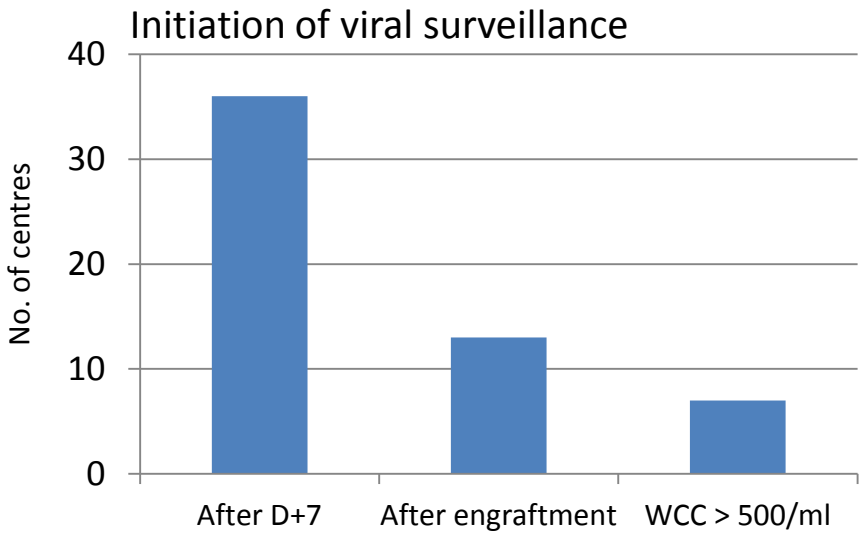
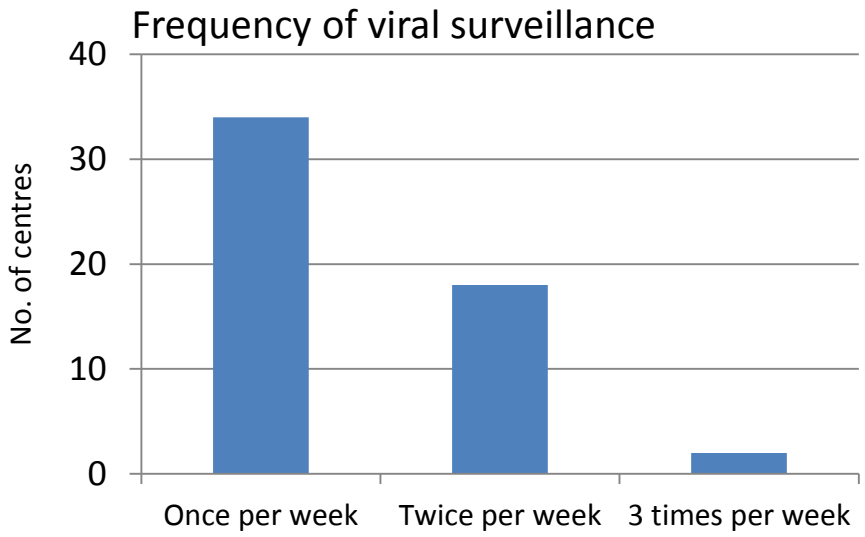
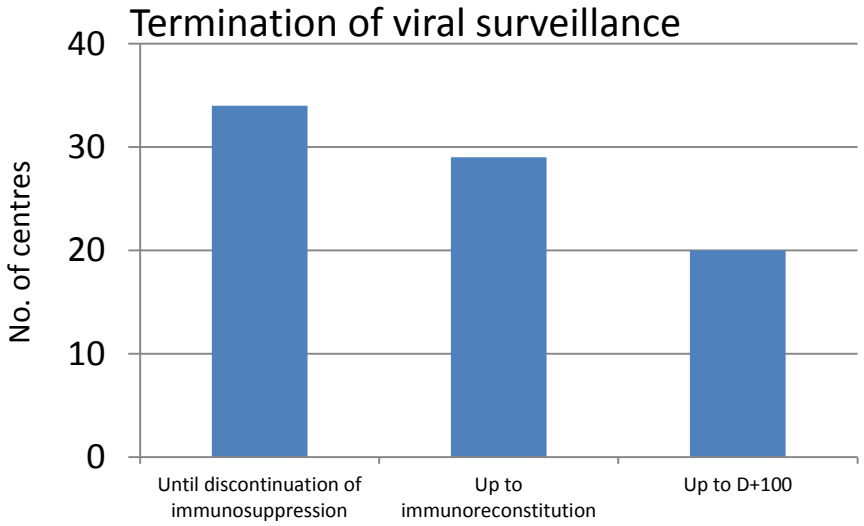


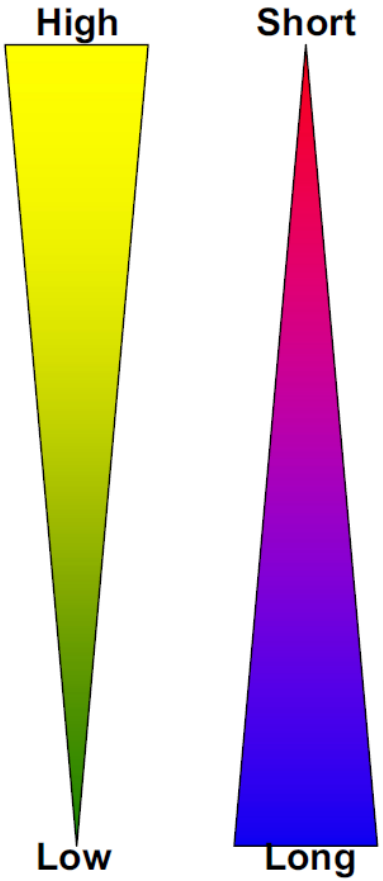




How I treat cytomegalovirus in hematopoietic cell transplant recipients

BLOOD, 4 JUNE 2009 • VOLUME 113, NUMBER 23

Michael Boeckh[1] and Per Ljungman[2]



Immuno-suppression	CMV doubling time	Risk Groups	CMV Plasma DNA Level to Start PET at FHCRC*	CMV Whole Blood DNA Level to Start PET at Karolinska Institute**
High	Short	Cord blood	Any level	1000 copies
		Allograft - High-dose steroids+ - T cell depletion - Anti-T cell antibodies - CD34 selection	> 100 copies/mL	1000 copies
		Allograft - Low dose steroids - No T cell depletion or anti T cell antibodies	> 500 copies/mL > or 5-fold ⇑ †	1000 copies
Low	Long	Allograft - after day 100	> 1000 copies/mL > or 5-fold ⇑ †	1000 copies if GVHD Other individual assessment based on ⇑

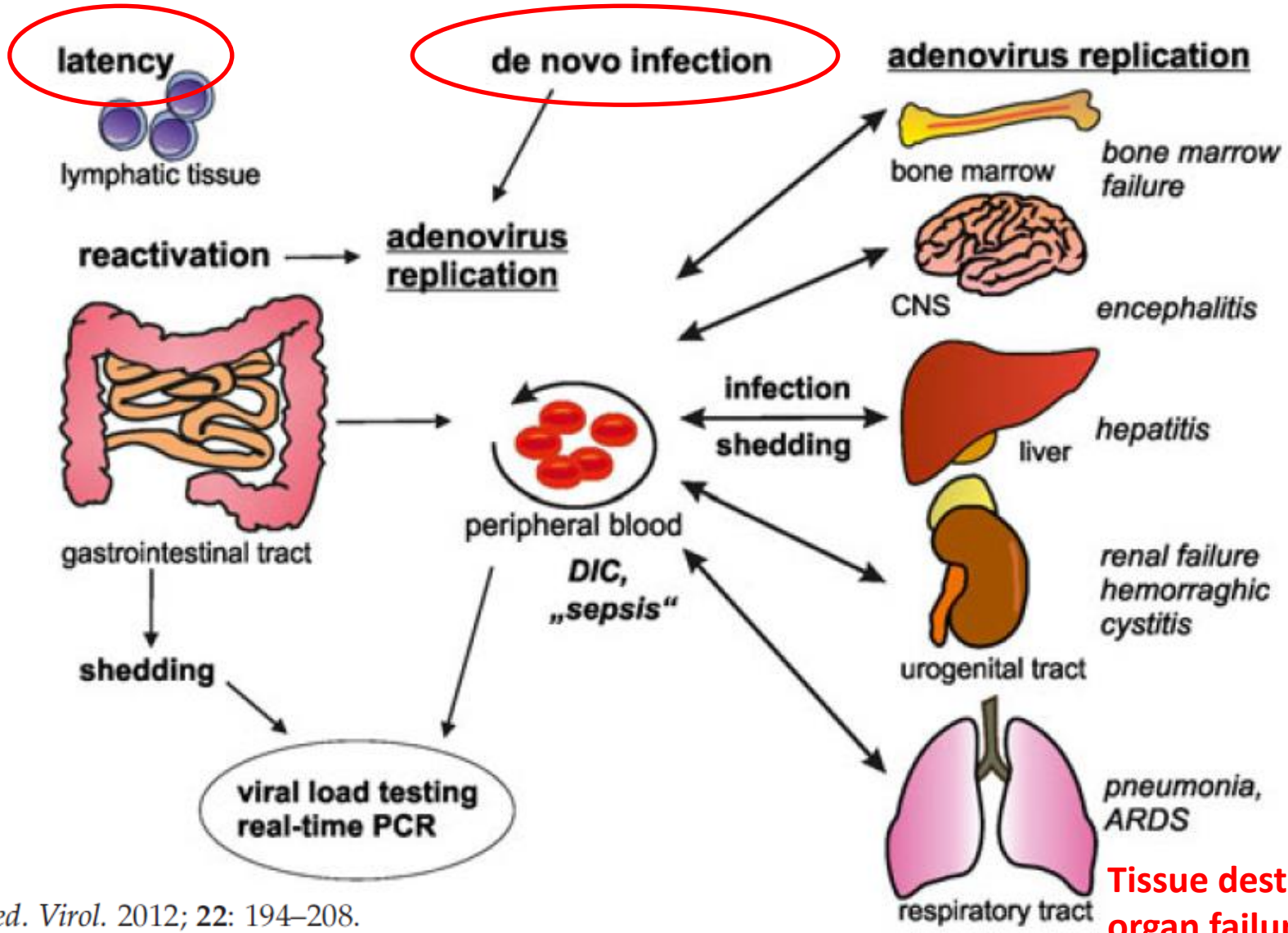
* Assays performed weekly or twice weekly (highest risk); limit of detection 25 copies/mL
+ 1 mg per kg of prednisone or higher
† If initial level is less than threshold
** Assays performed weekly, limit of detection 50 copies/mL

Figure 1. CMV viral load to start preemptive therapy (PET) used at the FHCRC in Seattle, WA, and the Karolinska Institute, Stockholm, Sweden.

Human Adenovirus reactivation in paediatric HSCT

- Human adenovirus (HAdV) PCR positivity in paediatric HSCT recipient: 8-21%, compared with 2-5% in adults
- Caused by reactivations from asymptomatic adenovirus carriage in the upper respiratory tract, gut and / or urinary tract
- Overall HAdV-related mortality ranges from 3.2% to 6.0% (compared with 0-1% in adults)
- Disseminated HAdV disease carries up to 100% mortality
- As high HAdV load in blood is a major risk factor of disseminated disease, monitoring for HAdV by qPCR is recommended for paediatric HSCT recipients

HAdV reactivation in paediatric HSCT



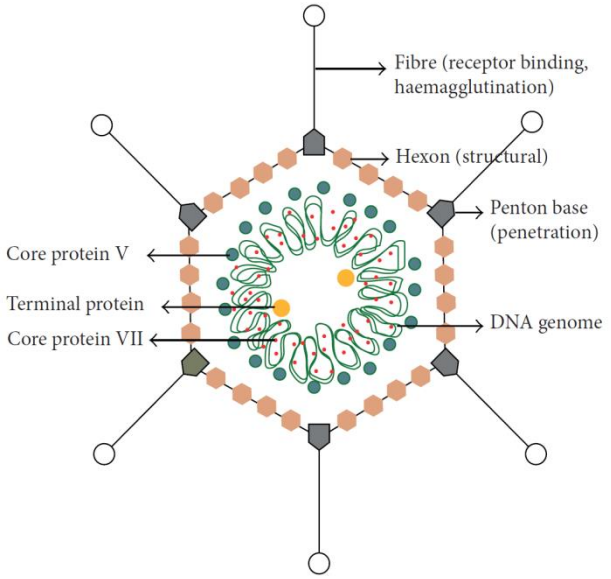
Rev. Med. Virol. 2012; **22**: 194–208.
DOI: 10.1002/rmv

Human Adenovirus

- High genetic diversity of HAdV, >50 types
- 80% of pediatric patients carry species HAdV-C in their nasopharyngeal tissues
- HAdV DNA positivity in nasopharyngeal aspirate prior to transplant is a very strong risk factor for HAdV viremia

Table 1: Classification of human adenoviruses and their sites of infection.

Subgroup	Serotype	Sites of infection
A	12, 18, 31	Gastrointestinal
B1	3, 7, 16, 21, 50	Respiratory
B2	11, 14, 34, 35	Urinary tract/renal
C	1, 2, 5, 6	Respiratory
D	8, 9, 10, 13, 15, 17, 19, 20, 22–30, 32, 33, 36, 37, 38, 39, 42–48, 49, 51	Eye
E	4	Respiratory
F	40, 41	Gastrointestinal



Patient, Virus, and Treatment-Related Risk Factors in Pediatric Adenovirus Infection after Stem Cell Transplantation: Results of a Routine Monitoring Program

ASBMT™ American Society for Blood and Marrow Transplantation

- 238 consecutive pediatric patients undergoing allogeneic HSCT between 1st Jan 2003 and 28th Feb 2012
- Malignant diseases, n = 130; non-malignant diseases, n = 108
- Adenoviral monitoring:
  - Routine adenoviral qPCR from peripheral blood performed weekly from the time of admission till discharge, then monthly thereafter till day +180
  - Lower quantification limit of qPCR: 1000 copies/ml
  - After Jul 2008: routine adenoviral qPCR from stool performed weekly till discharge
- Pre-emptive treatment if:
  - Adenovirus PCR > 10,000 copies/ml
  - rising copy numbers > 1,000 copies/ml on at least 2 occasions

Patient, Virus, and Treatment-Related Risk Factors in Pediatric Adenovirus Infection after Stem Cell Transplantation: Results of a Routine Monitoring Program

ASBMT
American Society for Blood and Marrow Transplantation

- Adenoviremia detected in 120/238 patients (50.4%)
- 27/238 (11.3%) were symptomatic infections
  - Enteropathy: 24/27
  - ARDS / sepsis: 4/27
  - disseminated disease: 5/27
  - 26/27 occurred before D+100
  - 26/27 had received T-cell depletion
- Peak adenovirus level > 10,000 copies / ml was an independent risk factor for poor overall survival

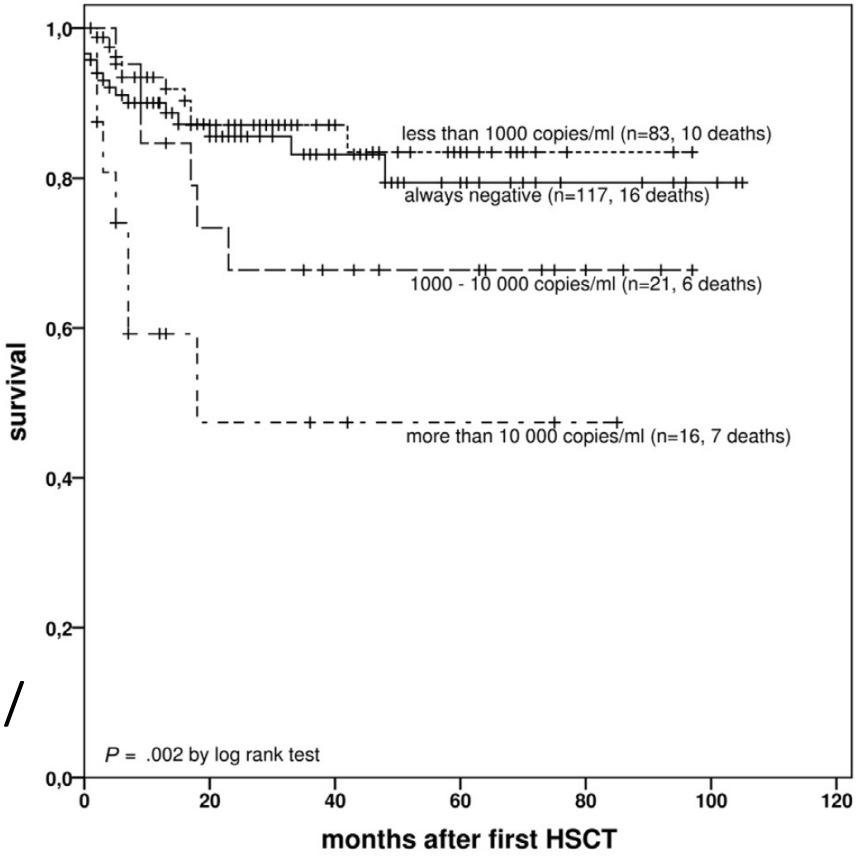


Figure 1. Overall survival after pediatric hematopoietic stem cell transplantation stratified by peak blood HAdV load.

Adenovirus reactivation in paediatric HSCT

European guidelines for diagnosis and treatment of adenovirus infection in leukemia and stem cell transplantation: summary of ECIL-4 (2011)

Risk factors for human adenovirus infection and disease

Children

- Allo-hematopoietic stem cell transplant (HSCT) with *in vivo* or *ex vivo* T-cell depletion (II)
- Allo-HSCT with unrelated donor graft (II)
- Allo-HSCT with unrelated cord blood graft (II)
- Severe (grade III–IV) graft-versus-host disease (II)
- Severe lymphopenia (<200 cells/μL PB) (II)

Adults

- Allo-HSCT with haploidentical donor or unrelated cord blood graft (III)
- Severe (grade III–IV) graft-versus-host disease (III)
- Severe lymphopenia (<200 cells/μL PB) (III)
- Treatment with alemtuzumab (III)

PB, peripheral blood.

DOI: 10.1111/tid.12022
Transpl Infect Dis 2012: **14:** 555–563

Adenovirus reactivation in paediatric HSCT

European guidelines for diagnosis and treatment of adenovirus infection in leukemia and stem cell transplantation: summary of ECIL-4 (2011)

Monitoring of patients for human adenovirus (HAdV)

Allogeneic HSCT recipients

- Monitoring HAdV loads is not routinely recommended in standard-risk patients, such as those receiving HLA-identical sibling transplants (BII)
- Monitoring with quantitative PCR of HAdV load in peripheral blood is recommended on at least a weekly basis for patients with at least 1 risk factor (see Table 2) (AII children/BIII adults)
- The duration of monitoring should be adapted to duration of risk according to degree of immune reconstitution (BIII children/CIII adults)

Autologous SCT and chemotherapy

- Routine monitoring is not recommended (CII)
- Quantitative PCR should be performed in case of clinical suspicion of HAdV infection/disease (CII)

HSCT, hematopoietic stem cell transplantation; HLA, human leukocyte antigen; PCR, polymerase chain reaction.

DOI: 10.1111/tid.12022
Transpl Infect Dis 2012: **14:** 555–563

ORIGINAL ARTICLE

Impact of viral reactivations in the era of pre-emptive antiviral drug therapy following allogeneic haematopoietic SCT in paediatric recipients

Bone Marrow Transplantation (2012), 1–6

P Hiwarkar[1,2], HB Gaspar[1], K Gilmour[1], M Jagani[3], R Chiesa[2], N Bennett-Rees[2], J Breuer[4], K Rao[2], C Cale[5], N Goulden[2], G Davies[5], P Amrolia[2], P Veys[2] and W Qasim[1,5]

Table 1. Transplant characteristics

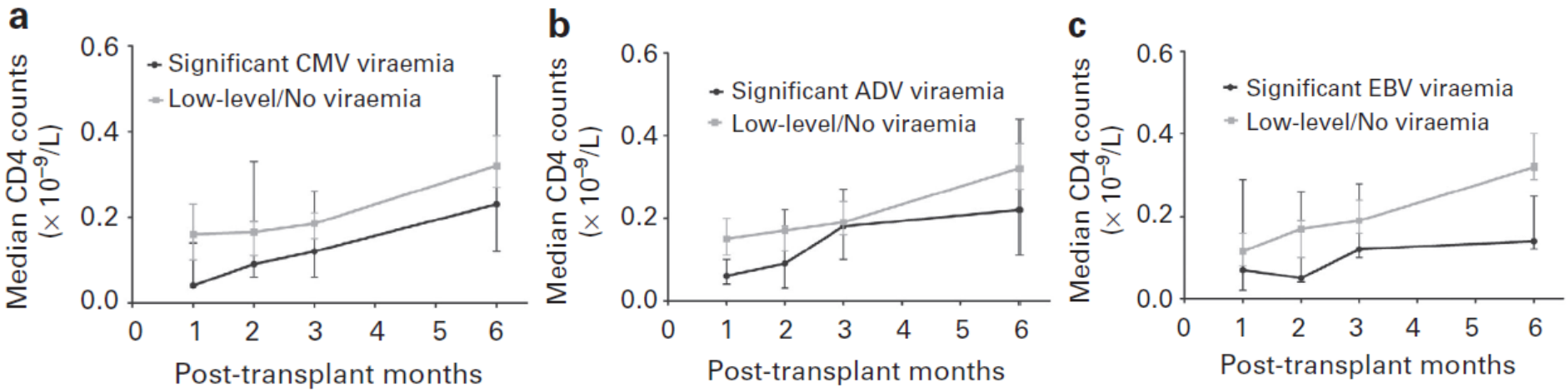
Characteristics	*Number*	
Number of patients	278	
Median age (months) at transplant (range)	33 (0.5–197) months	
Diagnostic category		
Haematological	115 (41%)	
Inherited immune deficiencies	147 (54%)	
Metabolic	16 (5%)	
Number of transplants	291	
HLA match		
HLA-matched related	99 (34%)	
HLA-matched unrelated	90 (31%)	
Mismatched grafts	102 (35%)	
Stem cell source	*Serotherapy*	*No serotherapy*
BM	65 (22%)	75 (26%)
Cord blood	10 (4%)	44 (15%)
Peripheral blood	88 (30%)	9 (3%)
Conditioning		
Myeloablative	159 (55%)	
Non-myeloablative	109 (37%)	
Unconditioned	23 (8%)	

All unrelated donor grafts (matched or mismatched) were performed with serotherapy irrespective of graft type.

Cord blood transplants undertaken after 2006 were performed without serotherapy

A small number of children (n = 9) underwent ex-vivo T-cell depletion by CD34+ stem cell selection for haploidentical transplants and were not included in this study

	n = 278
CMV viraemia (≥10 000 copies per mL)	16% (n=46)
ADV viraemia ≥ 1000 copies per mL in whole blood on two consecutive occasions)	15% (n=44)
EBV viraemia (≥ 40 000 copies per mL)	11% (n=32)



Median CD4 T-cell count (and 95% CI of mean), following HSCT and the development of (a) CMV (b) ADV and (c) EBV viraemia.

At 1 month, children developing significant CMV and ADV viraemia had significantly lower CD4 T-cell counts compared with those developing insignificant (untreated) viraemia or no viraemia.

In first 2 months, CD4 T-cell counts were $\leq 0.15 \times 10^9$/L in children with significant CMV and ADV viraemia, whereas in those with significant EBV viraemia, CD4 T-cell counts continued to be $\leq 0.15 \times 10^9$/L until 6 months following HSCT.

In the case of EBV, CD4 T-cell counts were significantly lower at 6 months.

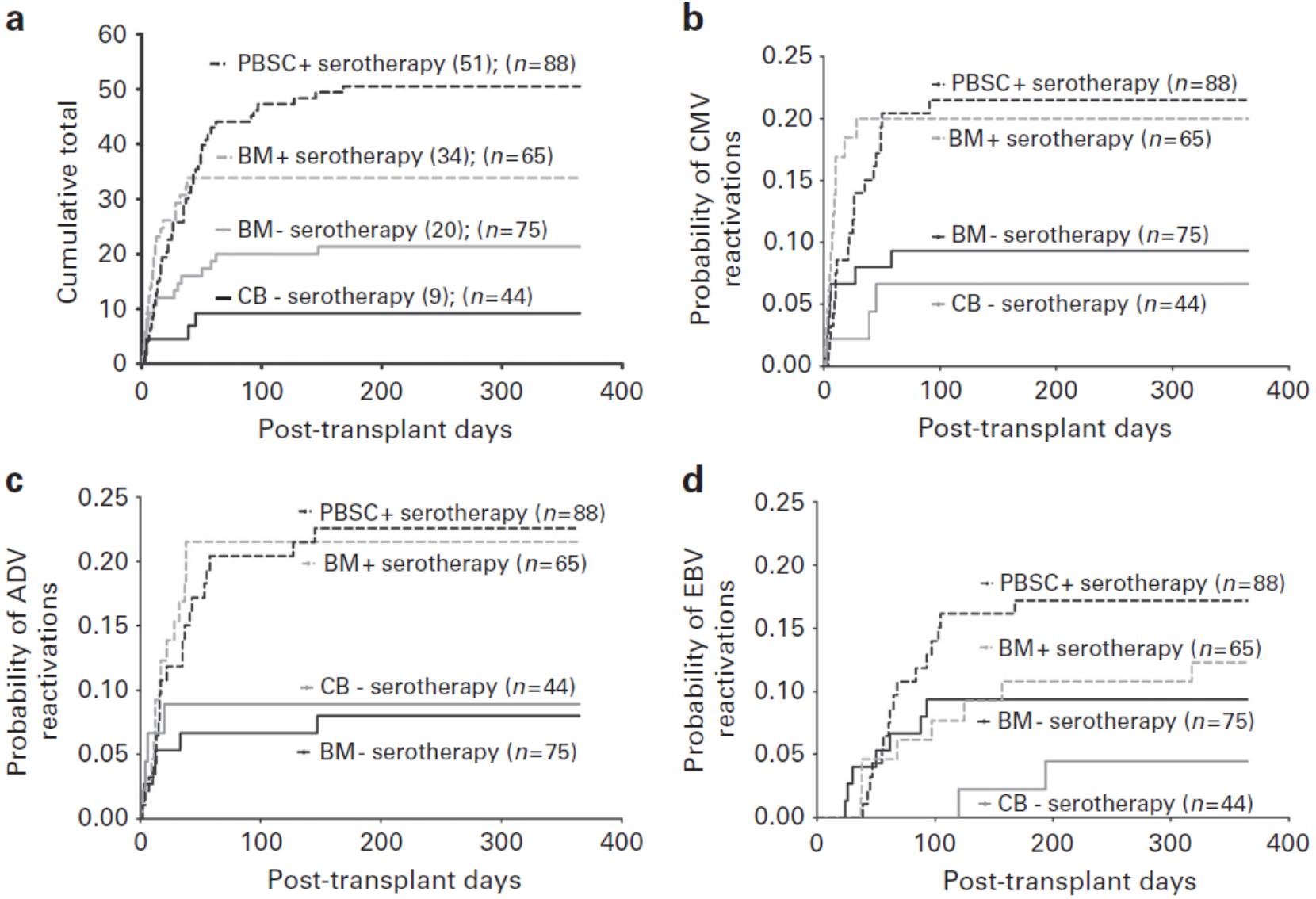
Bone Marrow Transplantation (2012), 1–6

Table 2. Significant risk factors for CMV, ADV and EBV reactivations

Risk factors	*CMV*	*ADV*	*EBV*
Positive donor and recipient serology (CMV or EBV) or host adenoviral infection	OR = 3.7, $P<0.0001$[a]	OR = 13.4, $P<0.0001$[a]	OR = 4.6, $P<0.0001$[a]
Serotherapy	OR = 1.9, $P<0.05$	OR = 3.8, $P<0.0001$	OR = 2.2, $P<0.05$
PBSC as graft source	OR = 1.9, $P<0.05$[a]	OR = 1.6, P = NS	OR = 1.8, P = NS
⩾1 Ag HLA mismatch	OR = 1.2, P = NS	OR = 1.8, $P<0.05$	OR = 2.2, $P<0.05$
Reduced-intensity conditioning	OR = 1.7, P = NS	OR = 1.4, P = NS	OR = 2.1, $P<0.05$
Acute GVHD ⩾grade II	OR = 1.5, P = NS	OR = 2.2, $P<0.01$[a]	OR = 3.6, $P<0.001$[a]

Abbreviations: OR = odds ratio. [a]indicates risk factors, which remained significant on multivariable analysis.

On multivariable analysis [apart from pre-existing viral infection (ADV) or seropositivity (CMV, EBV)],
the use of PBSC as a graft source remained a significant risk factor for CMV reactivation;
whereas for ADV and EBV reactivation, the association with acute GVHD (≥ grade II) remained significant.



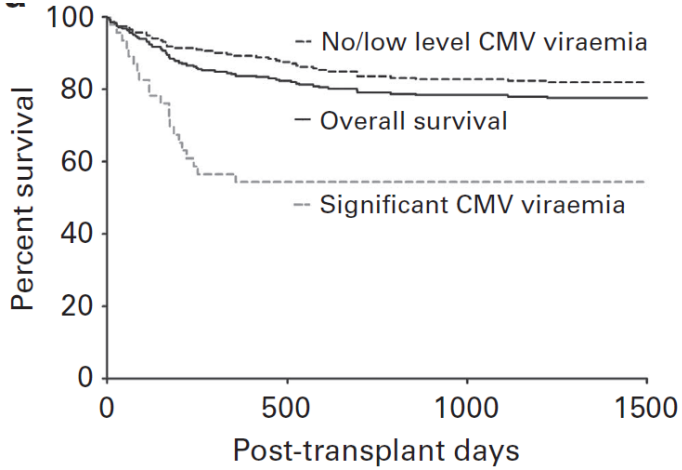
Total numbers of CMV, ADV or EBV reactivation episodes requiring treatment were higher following grafts undertaken with serotherapy, in particular when PBSC grafts were used. Reactivation was lowest, following cord blood transplants undertaken without serotherapy, a routine approach at our centre in recent years.

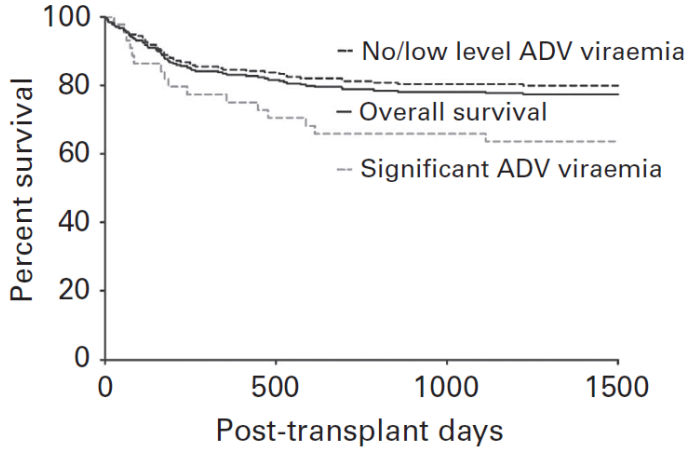
The probability of (b) CMV reactivation (c) ADV reactivation and (d) EBV reactivation was over 20% when serotherapy was used, compared with <10% in grafts performed without serotherapy.

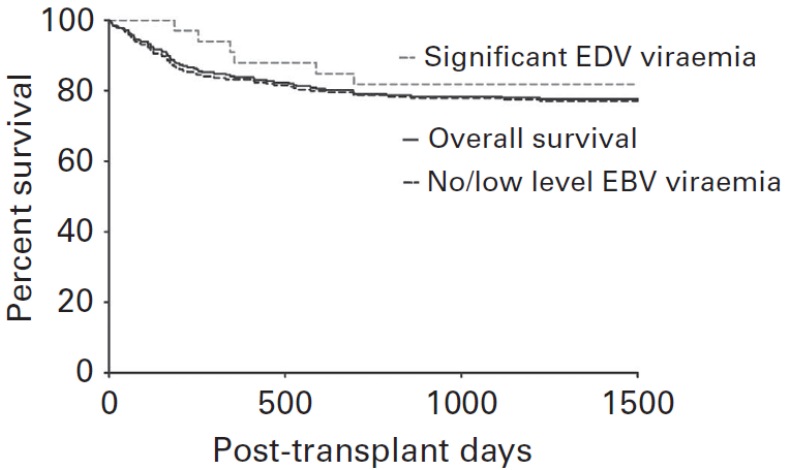
Impact of viral reactivations on overall survival

- The probability of overall survival was 77.1% (CI95 71.2–82.2) at median follow-up of 33 months (6–71 months)
- Viral reactivation of CMV, ADV or EBV infections accounted for 9/63 (15%) of deaths
- An additional six deaths were attributed to respiratory viruses (RSV, parainfluenza 2 and 3)
- Overall, around 24% of post-transplant mortality can be directly linked to viral disease

Bone Marrow Transplantation (2012), 1–6







In univariate analysis, the risk of death was significantly increased with
(i)CMV reactivation [(p<0.0001, OR 3.4 (CI95 1.6–6.9)]
(ii)ADV reactivation [(p<0.01, OR 2.4 (CI95 1.1–5]
(iii)acute GVHD (grade III–(IV) [(p<0.01, OR 2.5 (CI95 1.1–5.4)]

Overall survival was observed to be significantly decreased in patients with
CMV [54.4% vs 81.9% (p<0.0001)) and
ADV reactivations (63.6% vs 79.7% (p<0.05)],
but not with EBV reactivations

CMV and ADV reactivations
remained significant for increased risk of death in logistic regression

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Economic burden of viral reactivation

- Children with viral reactivation remained in hospital for significantly longer periods (127 vs 87 days, $p<0.01$)
- Children with GVHD ≤grade II with viral reactivation requiring therapy had extended hospital stay compared with children not requiring antiviral therapy
- On the basis of routine inpatient costs of £ 800 per day following HSCT, and adding the cost of antiviral drugs, the estimated viral reactivation costs is around £22 500 per patient (not including outpatient visitation costs, additional investigations such as radiology, opthalmology or endoscopy and hospitalization or medications prescribed elsewhere)

Bone Marrow Transplantation (2012), 1–6

HHV6

- Double-stranded enveloped DNA virus
- A member of the β herpesvirus subfamily
- 2 variants: HHV6A and HHV6B
- Almost universally acquired in early childhood (90% by 18m of age) as primary infection ⇨ roseola infantum
- A neurotropic virus
- Rarely causes rombencephalitis in immunocompetent children; rapid progression with poor outcome
- HHV6 remains latently in the host lymphocytes, salivary glands and brain after primary infection ⇨reactivates when enters into immunocompromised state

Post-transplant HHV6 reactivation

- Reactivation of endogenous HHV6, mostly variant B, occurs in 40-60% of transplant recipients,
- CD4+ T-cells and monocytes are the primary targets of HHV6 replication
- Median time to viremia: 23-27 days
- Complications
  - Myelosuppression and graft failure
  - Graft-versus-host disease
  - Interstitial pneumonitis
  - Encephalitis
  - Hepatitis
  - increased transplant-related mortality

Anti-viral therapy for HHV6 reactivation is rarely indicated except for encephalitis

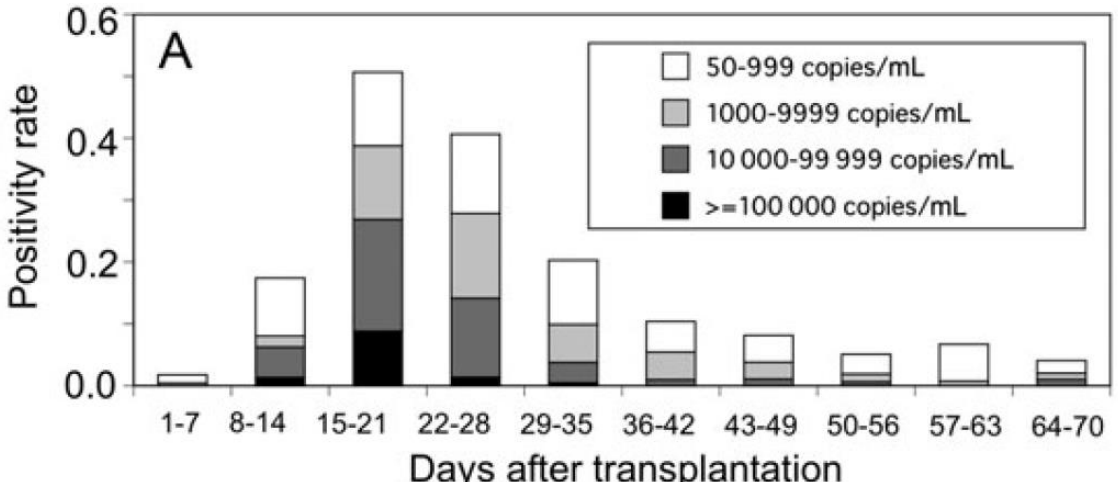
- **Ganciclovir:** good in vitro activity, effective in majority of patients
- **Foscarnet:** excellent in vitro activity, effective in majority of patients
- **Cidofovir:** the best in vitro activity,
  used as second-line agent due to nephrotoxicity
- **Acyclovir:** not effective

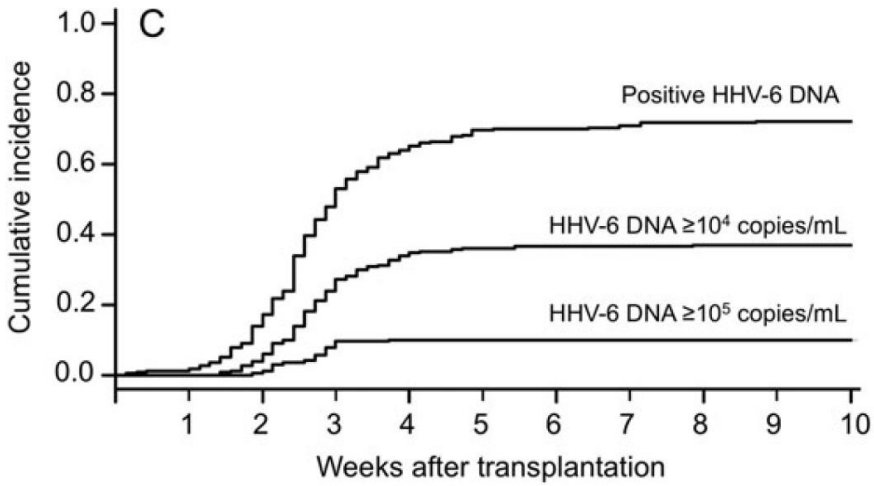
Human Herpesvirus 6 (HHV-6) Reactivation and HHV-6 Encephalitis After Allogeneic Hematopoietic Cell Transplantation: A Multicenter, Prospective Study

CID 2013:57 (1 September) • Ogata et al

Masao Ogata,[1] Takako Satou,[1] Jun-ichi Kadota,[1] Noriyuki Saito,[2] Takashi Yoshida,[3] Hirokazu Okumura,[3] Toshimitsu Ueki,[4] Koji Nagafuji,[5] Shinichi Kako,[6] Nobuhiko Uoshima,[7] Mitsuru Tsudo,[8] Hidekazu Itamura,[9] and Takahiro Fukuda[10]

- 230 allo-HCT recipients
- Age: 15 – 71 years (median = 49 years)
- Plasma HHV6 qPCR (HHV6A and HHV6B) monitored twice per week
- Treatment threshold: >10^4 copies /ml plasma





UCBT is a significant risk factor for HHV6 reactivation and encephalitis

Table 3. Multivariate Analysis of Factors Affecting Human Herpesvirus 6 Reactivation

Variable	Unfavorable Factors	HR (95% CI)	*P*
Positive plasma HHV-6 DNA			
Conditioning regimen	MAC	1.5 (1.1–2.0)	.01
Type of transplanted cells	CB	1.8 (1.3–2.5)	.0003
HHV-6 DNA ≥10 000 copies/mL			
Conditioning regimen	MAC	1.9 (1.2–2.9)	.004
Sex	Male	1.6 (1.0–2.5)	.04
Type of transplanted cells	CB	2.0 (1.3–3.0)	.003

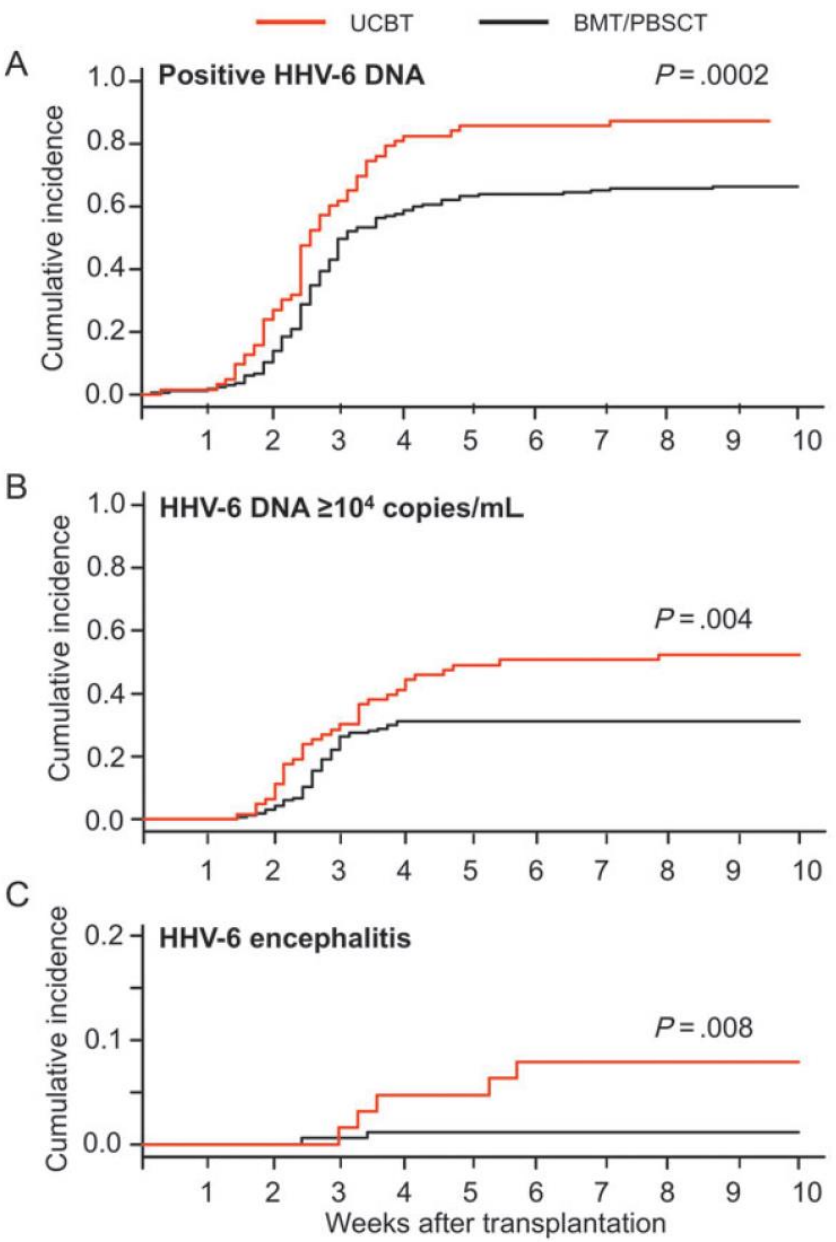
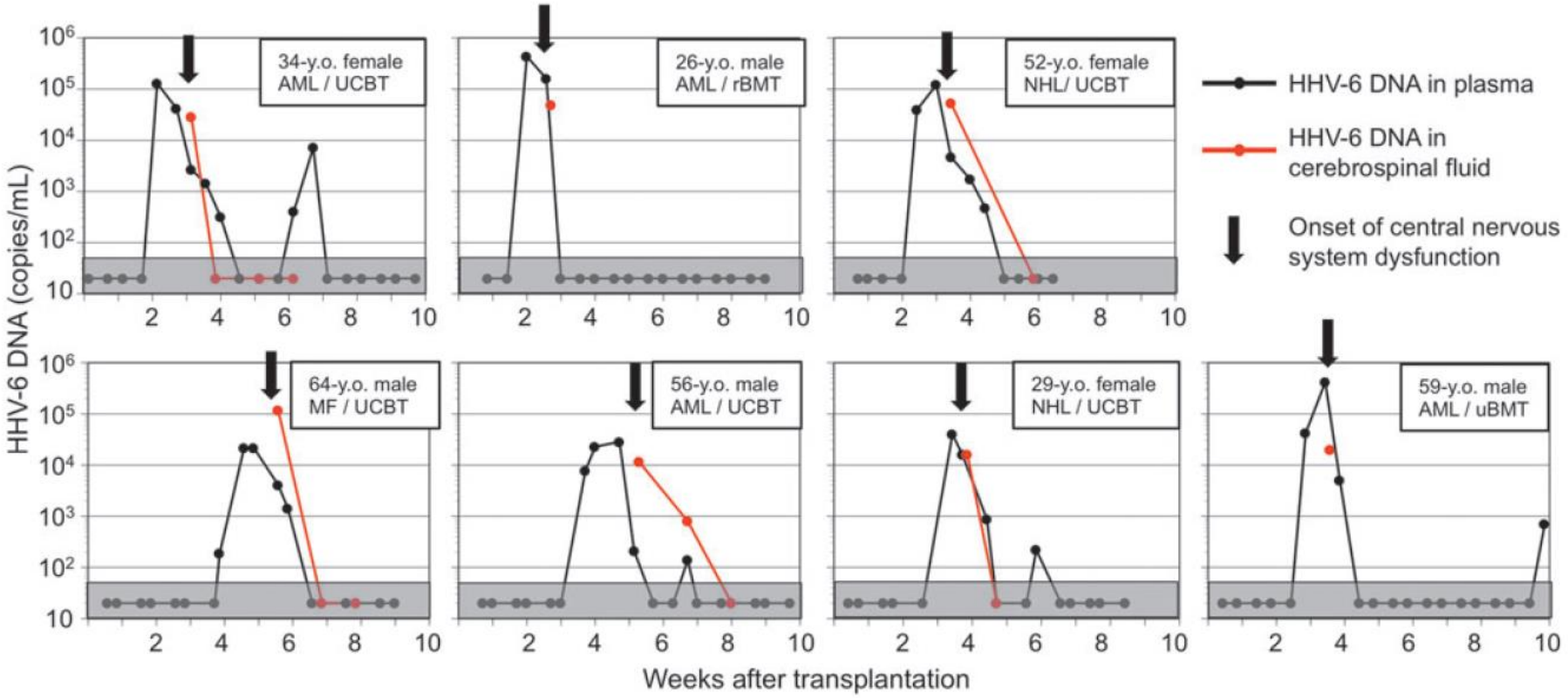


Figure 2. Cumulative incidence curves for patients who received umbilical cord blood transplantation (red line) versus bone marrow transplantation or peripheral blood stem cell transplantation (black line). *A*, First detection of positive human herpesvirus 6 (HHV-6) DNA. *B*, First detection of plasma HHV-6 DNA $\geq 10^4$ copies/mL. *C*, HHV-6 encephalitis. Abbreviations: BMT/PBSCT, bone marrow transplantation or peripheral blood stem cell transplantation; HHV-6, human herpesvirus 6; UCBT, umbilical cord blood transplantation.

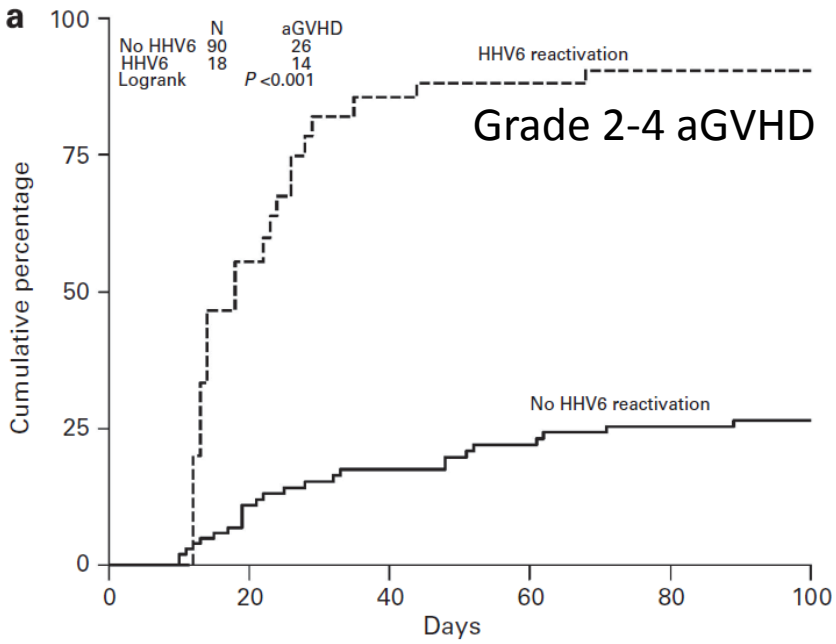
Kinetics of HHV6 DNA in patients who developed encephalitis



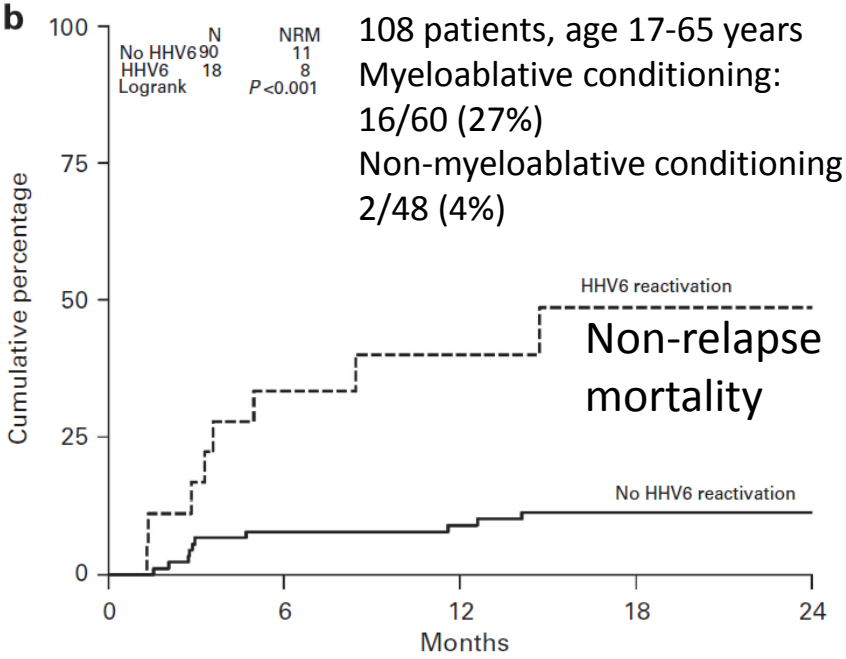
Human herpes virus 6 reactivation: important predictor for poor outcome after myeloablative, but not non-myeloablative allo-SCT

PJA de Pagter[1], R Schuurman[2], L Keukens[1], M Schutten[3], JJ Cornelissen[4], D van Baarle[1,5], E Fries[2], EAM Sanders[1], MC Minnema[6], BR van der Holt[7], E Meijer[8] and JJ Boelens[1]

Bone Marrow Transplantation (2013) **48,** 1460–1464



Grade 2-4 aGVHD



108 patients, age 17-65 years
Myeloablative conditioning: 16/60 (27%)
Non-myeloablative conditioning: 2/48 (4%)

Non-relapse mortality

HHV6 reactivation, mostly variant B, occurs in 40-60% of transplant recipients, and is associated with:

- Myelosuppression and graft failure
- Graft-versus-host disease
- Interstitial pneumonitis
- Encephalitis
- Hepatitis
- increased transplant-related mortality

Summary

- CMV, Adenovirus and EBV are important causes of viral reactivation in paediatric allo-HSCT recipients
- Immune reconstitution is integral to risk stratification of viral reactivation, disease and prognosis
- Donor, recipient and type of stem cell graft should be taken into consideration when designing a viral surveillance schema and pre-emptive treatment strategy