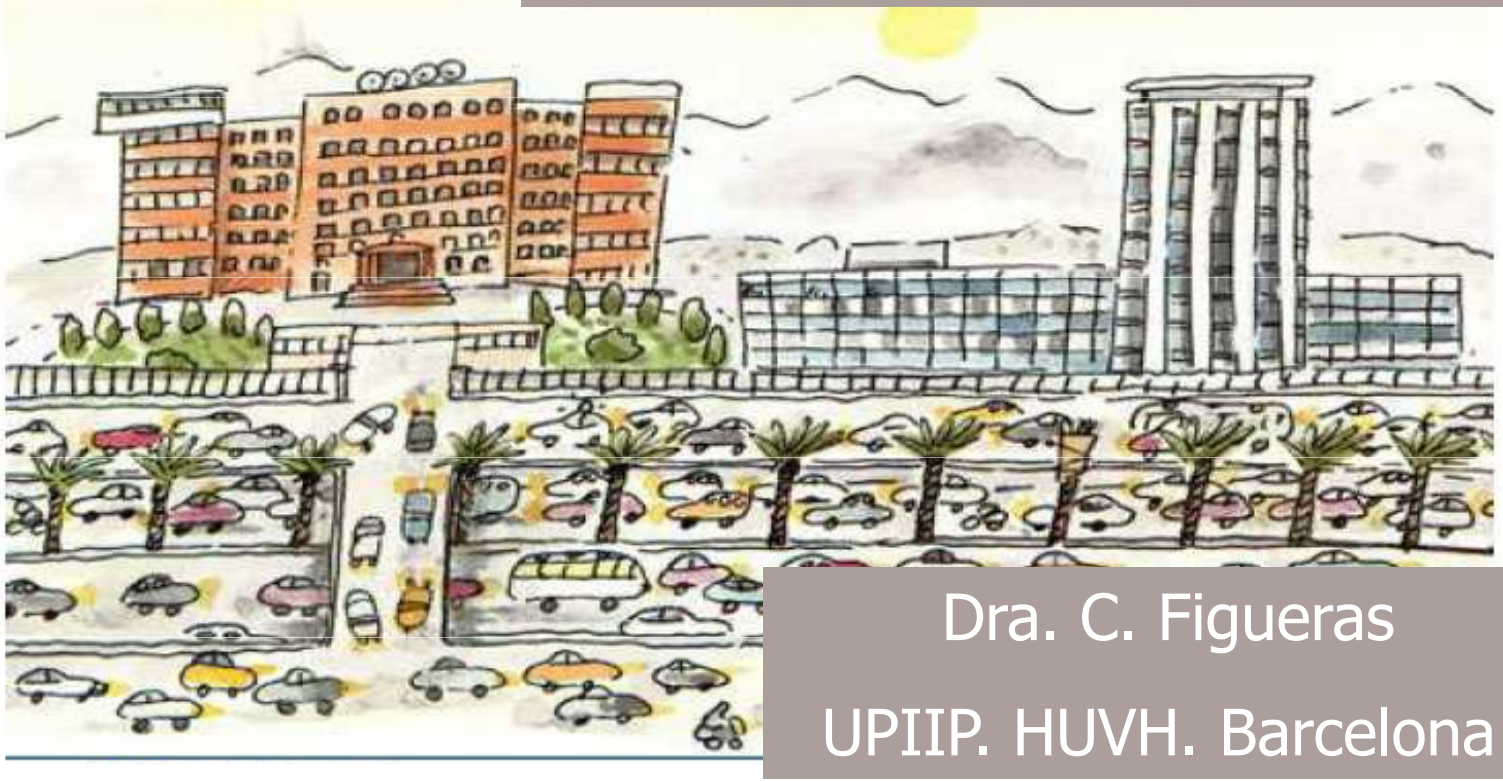
Infección Viral en el Paciente con Cáncer

Vall d'Hebron
Hospital

Barcelona, 15 noviembre 2013



Dra. C. Figueras

UPIIP. HUVH. Barcelona

Introducción: Infección y cáncer

La epidemiología de las complicaciones infecciosas en el tratamiento del cáncer, evoluciona paralelamente a las estrategias y procedimientos utilizados en el tratamiento.

Factores determinantes de la infección:

- Tipo y grado de inmunosupresión
- Situación clínica paciente. Comorbilidades
- Epidemiología infecciosa propia y del entorno

Inmunosupresión: Fc. determinantes

- Tto antineoplásico:
  QT citotóxica
  QT citostática
  Agentes biológicos: Deplecionadores linfoc T/B
  Inhibidores TNFa
- RDT/Corticoides/Esplenectomía
- Procedimientos invasivos diagnóstico-terapéuticos

+

- Determinantes genéticos
- Situación clínica/estadio enfermedad
- Comorbilidades.
- Inmunosupresión previa

Calendario: Infecciones virales en TPH

0-30d	Neutropenia prolongada Mucositis Accesos vasculares	Infecc bacterianas Infecc. Por Candida VHS
30-100 d	Deterioro inmunidad celular	CMV *P. jirovecii* *Aspergillus*
> 100d	Deterioro inmunidad celular y humoral Alteración sistema retículoendotelial	CMV, VVZ, VEB, AdV Virus respiratorios Bacterias encapsuladas

Infección viral:
Etiopatogenia y presentación clínica

- Primoinfección/reinfección (v. comunitarios)
- Reactivación (v. endógenos)

⬇

- Viremia//replicación epitelios (resp, urotel...)
  ↓
- Afectación sistémica//afect. local

⬇

Enfermedad: ef. citopático+respuesta inflamat
+ sobreinfección bacteriana → Fibrosis

Control de la infección: Niveles de actuación

- Profilaxis 1ª: evitar viremia a partir de la colonización/invasión de epitelios (p. entrada)
- Profilaxis 2ª: evitar viremia a partir de los reservorios
- Tto. Anticipado: tratar la viremia antes de que ocurra afectación orgánica
- Tto. Dirigido: tratar la enfermedad o afect. orgánica

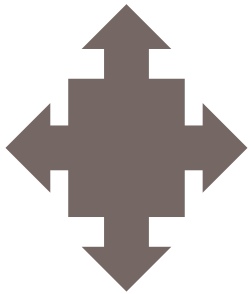
Condicionantes evolución infecc. viral

Situación clínico-inmunológica del paciente

+

Características inmunológicas del donante de TPH

(Arginina en posición 245 en la proteina KIR2DL1 de cel NK: ↓ 60% mortalidad)
Leung W 2012, J Clin Oncology



Características infección viral

Tratamiento antiviral:
- estrategia terapéutica
- eficacia
- R
- toxicidad

10 puntos/temas/aspectos a destacar...

1. Control infección CMV: Profilaxis y Tto. anticipado

- Tto. prolongado: - peor reconstitución CMV-CTLs
  - inducción R

⬇ *Meijer E, Clin Microb Review 2003*

Profilaxis prolongada (3-4m) en sero+:
- Disminución infecc y enf. temprana (<100d)
- Incremento infecc. y enf. tardía por CMV

⬇

Tratamiento anticipado de corta duración (14 d): mejor estrategia para prevenir enferm. CMV

Hasta cuando mantener esta estrategia?:
Utilidad MTZ respuesta celular T- CMV especifica?

2. Valoración riesgo replicación CMV en TPH: Quantiferon- CMV

- Medición respuesta celular T CMV- específica a partir INF-G producido por cel CD8+ CMV-específicas. (>0,1-0,2 IU/ml)

  ⬇ *Clari MA 2012, Clin Vaccine Immunol, 19: 791-796*

- Predicción riesgo de clearence vs progresión de la replicación viral.

  ⬇ *Lisboa LF. 2012.Transplantation93(2):195-200*
  Fleming T. 2010. J.Med.Virol.82:433-440

- Optimización selección estrategia terapéutica: > eficiencia y < toxicidad

3.Tto. anticipado CMV: papel de Valganciclovir

Table 1: Studies on VGC in the preemptive setting after alloHSCT.

Author year [ref.]	Design	*N* patients	VGC dose	VGC efficacy	Toxicity reported
van der Heiden et al. 2006 [5]	Retrospective VGC/GCV	34	1800 mg/d	80%	None
Ayala et al. 2006 [6]	Retrospective VGC mono	18	1800 mg/d × 14, → 900 mg/d × ≥7	93%	None
Busca et al. 2007 [7]	Retrospective VGC mono	15	1800 mg/d × 14, → 900 mg/d × 14	73%	27% severe hematotoxicity
Candoni et al. 2008 [8]	Retrospective VGC mono	30	1800 mg/d versus 900 mg/d	93% 87%	≤WHO °II
de la Cruz-Vicente et al. 2008 [9]	Prospective VGC/GCV	11	1800 mg/d × 14, → 900 mg/d × 14	100%	None
Wang et al. 2008 [10]	Retrospective VGC mono	19	1800 mg/d × 14, → 900 mg/d × 14	95%	None
Takenaka et al. 2009 [11]	Retrospective VGC mono	10	1800 mg/d × 21	90%	10% severe neutropenias
Saleh et al. 2010 [12]	Retrospective VGC mono	47	1800 mg/d × ≥7, → 900 mg/d × ≥7	97%	17% severe neutropenias
Palladino et al. 2010 [13]	Retrospective VGC mono	34	1800 mg/d versus 900 mg/d	100% 83%	None
Liu et al. 2010 [14]	Prospective VGC mono	54	1800 mg/d × 14, → 900 mg/d × 14	89%	None
Ruiz-Camps et al. 2011 [15]	Prospective VGC/GCV	166		91%	5% adverse events

Tto. anticipado CMV: papel de Valganciclovir

Table 2: Patient cohorts of preemptive therapy for CMV viremias.

	Cohort 1 (1996–2006)			Cohort 2 (2007–2011)		
	VGC	Non-VGC	*P*	VGC	Non-VGC	*P*
N patients	79	90	–	48	70	–
N viremias	165	147	–	67	135	–

Bone Marrow Research
Volume 2012, Article ID 874601, 5 pages
doi:10.1155/2012/874601

Clinical Study

Improving Safety of Preemptive Therapy with Oral Valganciclovir for Cytomegalovirus Infection after Allogeneic Hematopoietic Stem Cell Transplantation

Corinna Barkam, Haytham Kamal, Elke Dammann, Helmut Diedrich, Stefanie Buchholz, Matthias Eder, Jürgen Krauter, Arnold Ganser, and Michael Stadler

Department of Hematology, Hemostasis, Oncology, and Stem Cell Transplantation, Hannover Medical School, 30625 Hannover, Germany

Cohorte 1: retrospectivo
Cohorte 2: prospectivo N:287

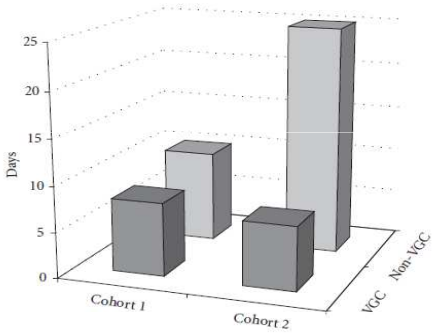


Figure 1: Mean total hospitalization for treatment of CMV viremia plus complications.

- Clearence CMV : > para VGC en c1 y sin diferencias en c2
- <hospitaliz en c1(> rehospitaliz x neutropenia) y < en c2 (nueva estrategia de vigilancia)
- > mielotoxic con VGC en c1 y < en c2

Tto anticipado ambulatorio con VGC es una buena opción requiriendo MTZ neutrófilos

4. CMV y Resistencia a antivirales (GCV,CDV, PFA)

Mutaciones inductoras de R:

- UL-97 (fosfotransferasa): GCV-R /> incidencia.
- UL-54 (DNA-polimerasa): GCV, CDV, PFA-R

Fischer L. Antiviral Res oct 2013

YJ.Kim Transplant Infect Dis 2012:14:611-617

Fc de riesgo:

- Exposición prolongada a antivirales
- Dosis/niveles inadecuados

Opciones terapéuticas:

- MTZ/TDM GCV: *Rigo-Bonnin R, Clin Chim Acta oct 2013*
- GCV a dosis altas: 7,5- 10 mg/kg/12h IV

Gracia-Ahufinger, Transplantation Apr 2013

5) Control infecc VHS y VVZ: Resistencia a Aciclovir

- ACV, GCV: Requieren activación TK- viral
- Foscarnet y Cidofovir: No requieren activación

Mecanismos de R:

- 95%: Mutación TK viral (pérdida actividad):ACV-R ↑nivel
- 5%:Mutación DNA-polimerasa viral:foscarnet-R ↓nivel
- Mutaciones en ambas enzimas: (ACV+Foscarnet)-R

- VVZ: persistencia en 59%: - 50% complicaciones
  - 27% ACV-R

Van der Beek M, CID 2013; 56(3):335-43

- VHS: 4- 10,9% (hasta 36%) ACV-R

6) Inmunoterapia adoptiva con cel T citotóxicas específicas

- Infusión de cel T CD4+ y CD8+ viro-específicas: ~10M/M2
- METODOLOGÍA:

  - Extracción in vivo del donante: no siempre disponible y inmunidad específica no asegurada.

  - Obtención de banco de cel de donantes inmunes con polimorfismos HLA comunes: inmunidad no asegurada y riesgo de EICH

  - Obtención de banco de líneas celulares con polimorfismos HLA comunes en las que se ha generado inmunidad in vitro: riesgo de EICH

Terapia celular T (multi)virus-específica

TRANSPLANTATION BLOOD, 5 NOVEMBER 2009 VOLUME 114, NUMBER 19

Cytotoxic T lymphocyte therapy with donor T cells prevents and treats adenovirus and Epstein-Barr virus infections after haploidentical and matched unrelated stem cell transplantation

Ann M. Leen,[1] Anne Christin,[1] Gary D. Myers,[1] Hao Liu,[1] Conrad R. Cruz,[1] Patrick J. Hanley,[1] Alana A. Kennedy-Nasser,[1] Kathryn S. Leung,[1] Adrian P. Gee,[1] Robert A. Krance,[1] Malcolm K. Brenner,[1] Helen E. Heslop,[1] Cliona M. Rooney,[1] and Catherine M. Bollard[1]

[1]Center for Cell and Gene Therapy and Departments of Pediatrics, Immunology, Medicine, and Virology, Baylor College of Medicine, Texas Children's Hospital and the Methodist Hospital, Houston

Eficacia en profilaxis lineas cel inmunes a Adv y VEB

Plenary Paper BLOOD, 27 JUNE 2013 • VOLUME 121, NUMBER 26

CLINICAL TRIALS AND OBSERVATIONS

Multicenter study of banked third-party virus-specific T cells to treat severe viral infections after hematopoietic stem cell transplantation

Ann M. Leen,[1] Catherine M. Bollard,[1] Adam M. Mendizabal,[2] Elizabeth J. Shpall,[3] Paul Szabolcs,[4] Joseph H. Antin,[5] Neena Kapoor,[6] Sung-Yun Pai,[5,7] Scott D. Rowley,[8] Partow Kebriaei,[2] Bimalangshu R. Dey,[9] Bambi J. Grilley,[1] Adrian P. Gee,[1,10] Malcolm K. Brenner,[1] Cliona M. Rooney,[1,10] and Helen E. Heslop[1]

[1]Center for Cell and Gene Therapy, Baylor College of Medicine, Texas Children's Hospital, The Methodist Hospital, Houston, TX; [2]The EMMES Corporation, Rockville, MD; [3]MD Anderson Cancer Center, Houston, TX; [4]Duke University Medical Center, Durham, NC; [5]Dana-Farber Cancer Institute, Boston, MA; [6]Children's Hospital of Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, CA; [7]Boston Children's Hospital, Boston, MA; [8]John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ; [9]Massachusetts General Hospital, Boston, MA; and [10]Production Assistance for Cell Therapy Center at Baylor College of Medicine, Houston, TX

- Estudio multicéntrico
- 50 pts (seleccionados)
- Tto infec. refract (CMV,VEB,Adv)
- VSTs generadas in vitro de pull de donantes de banco con polimorfismos HLA parcialmente (5-8 de 10) comunes e inmunes a los 3 v
- Eficacia >70%
- Ausencia de EICH por alo-reactividad

blood

2013 121: 5108-5109
doi:10.1182/blood-2013-05-500082

Antiviral cell therapy: is this the future?

Juan C. Gea-Banacloche

Eficacia en pts con > inmunosupresión?

7) Infección por virus BK

- Adquisición (v. respiratoria): Primoinfección

- Latencia: cel.epit. escam. cervicales, cel. uroteliales, gland salivales y prostática, leucocitos...

- Reactivación y replicación: cistitis hemorragica, encefalitis, pneumonitis, retinitis, vasculopatia...

Transplant Infectious Disease, ISSN 1398-2273

Case report

Fatal BK virus pneumonia following stem cell transplantation

Y. Akazawa, Y. Terada, T. Yamane, S. Tanaka, M. Aimoto, H. Koh, T. Nakane, K-R. Koh, H. Nakamae, M. Ohsawa, K. Wakasa, M. Hino. Fatal BK virus pneumonia following stem cell transplantation. Transpl Infect Dis 2012: 14: E142–E146. All rights reserved

Y. Akazawa[1], Y. Terada[1], T. Yamane[1], S. Tanaka[2], M. Aimoto[1], H. Koh[1], T. Nakane[1], K.-R. Koh[1], H. Nakamae[1], M. Ohsawa[2], K. Wakasa[2], M. Hino[1]

- Replicación anómala/oncogénesis: próstata, vejiga, SNC, hueso, páncreas...

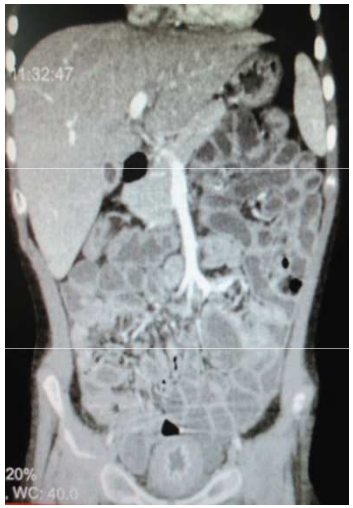
Virus BK, cistitis hemorrágica y Tto

Patogenesis CH:

- Lesión citopática
- Resp inflamatoria/
- Reconst. autoinmun

⬇

CH y nefropatía obstr.



Ciprofloxacin Decreased Polyoma BK Virus Load in Patients Who Underwent Allogeneic Hematopoietic Stem Cell Transplantation

Anskar Y. H. Leung,[1] Maggie T. L. Chan,[1] Kwok-Yung Yuen,[2] Vincent C. C. Cheng,[2] Kwok-Hung Chan,[2] Chris L. P. Wong,[2] Raymond Liang,[1] Albert K. W. Lie,[1] and Yok-Lam Kwong[1]

Ciprofloxacin Decreased BKV Reactivation • CID 2005:40 (15 February)

Table 1. *Therapeutic interventions targeting BKV*

Intervention	Applicability		Proposed mechanism of action	Reported adverse events	Effectiveness	References
	BKVN	HC				
Tapering of immune suppression	Yes	No	Reconstitution of immune responses directed against BKV	Rejection of the allograft kidney	Effective	[74;92;94; 104;106; 108-110]
Cidofovir	Yes	Yes	Inhibitor of viral replication, mechanism unknown	Severe anterior uveitis, potentially nephrotoxic	Doubtful	[118-121]
Leflunomide	Yes	Yes	Pyrimidine depletion, tyrosine kinase inhibition	Thrombocytopenia, (haemolytic) anaemia and thrombotic microangiopathy	Doubtful	[125-129]
IVIg	Yes	Yes	Antibody-mediated neutralisation	Paradoxical increase in viral load	Doubtful	[122-124]
Fluorochinolones	Yes	Yes	Inhibition of large T antigen helicase activity	None	Doubtful	[130-132]
Statins	Yes	Yes	Prevention of caveolae-mediated endocytosis	None	Very doubtful	[133]

Van Aalderen, et al. BK virus infection in transplant recipients.

MAY 2012, VOL. 70, NO 4

8. Infección por V. Respiratorios Comunitarios: HRV, HCoV

Table 2. Prevalence and clinical diagnosis of respiratory virus

Respiratory virus	Number (%)		
	Virus-positive	Clinical diagnosis	
		URI	LRTI
Rhinovirus	25 (28.1)	19 (76.0)	6 (24.0)
Parainfluenza virus 3	16 (18.0)	10 (62.5)	6 (37.5)
Respiratory syncytial virus A	13 (14.6)	6 (46.2)	7 (53.8)
Adenovirus	12 (13.5)	4 (33.3)	8 (66.7)*
Human coronavirus	10 (11.2)	9 (90.0)	1 (10.0)
Respiratory syncytial virus B	10 (11.2)	5 (50.0)	5 (50.0)
Parainfluenza virus 2	4 (4.5)	2 (50.0)	2 (50.0)
Influenza virus B	3 (3.4)	3 (100.0)	0 (0)
Parainfluenza virus 1	2 (2.2)	0 (0)	2 (100.0)
Influenza virus A	1 (1.1)	1 (100.0)	0 (0)
Human metapneumovirus	1 (1.1)	1 (100.0)	0 (0)
Total†		60	37

*$P < 0.05$; †More than 2 viruses were co-detected in 8 patients. URI, upper respiratory infection; LRTI, lower respiratory tract infection.

Choi JH, et al. • Respiratory Viral Infections in Pediatric HSCT Patients

Human rhinovirus and coronavirus detection among allogeneic hematopoietic stem cell transplantation recipients

*Filippo Milano,[1,2] *Angela P. Campbell,[1,3,4] Katherine A. Guthrie,[1] Jane Kuypers,[1,3] Janet A. Englund,[1,3,4] Lawrence Corey,[1,3] and Michael Boeckh[2,3]

[1]Fred Hutchinson Cancer Research Center, Seattle, WA; [2]University La Sapienza, Rome, Italy; [3]University of Washington, Seattle; and [4]Seattle Children's Hospital, WA

BLOOD, 11 MARCH 2010 • VOLUME 115, NUMBER 10

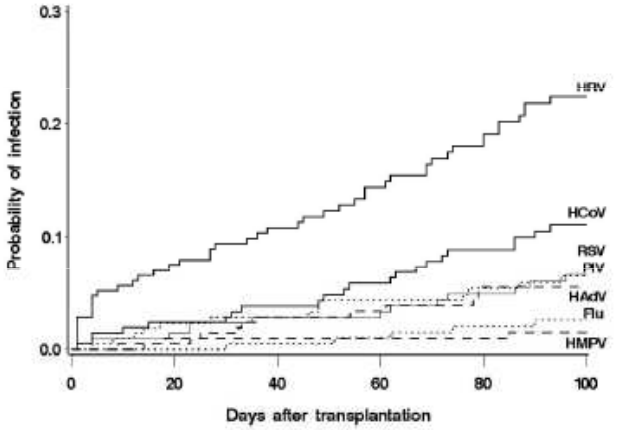


Figure 1. Cumulative incidence of first infection episodes of HRV, HCoV, and other respiratory viruses (RSV, PIV, HMPV, influenza, adenovirus) after transplantation in 215 HCT recipients.

- HRV + HCoV:Incidencia acumulada 33% en +100 d TPH
- 4% LRTID graves (ag únicos/coinfección)
- Coinfecciones frecuentes
- Replicación/eliminación viral prolongada (>3 sem)
- Ausencia tratamiento específico

Infección por V. Resp. Comunitarios
Tratamiento VRS y HPIV

Table 5. Recommendations for Community-Acquired Respiratory Virus Treatment in Hematopoietic Stem Cell Transplantation and Leukemia Patients

- Deferral of conditioning therapy should be considered for patients with CARV RTID planned for allogeneic HSCT (***BII***)
- Deferral of conditioning/chemotherapy could be considered for patients with CARV RTID scheduled for chemotherapy of hemato-oncological diseases (***BIII***)
- Patients with RSV URTID undergoing allogeneic HSCT or recipients of allogeneic HSCT with risk factors for progression to RSV LRTID and death should be treated with aerosolized or systemic ribavirin and IVIG (***BII***)
- For allogeneic HSCT patients with HPIV LRTID, treatment with aerosolized or systemic ribavirin and IVIG may be considered (***BIII***)
- For allogeneic HSCT patients with CARV URTID or CARV LRTID other than RSV or HPIV, aerosolized or systemic ribavirin and IVIG treatment cannot be recommended (***CIII***)

CID 2013:56 (15 January)

Fourth European Conference on Infections in Leukaemia (ECIL-4): Guidelines for Diagnosis and Treatment of Human Respiratory Syncytial Virus, Parainfluenza Virus, Metapneumovirus, Rhinovirus, and Coronavirus

Hans H. Hirsch,[1,2] Rodrigo Martino,[3] Katherine N. Ward,[4] Michael Boeckh,[5] Hermann Einsele,[6] and Per Ljungman[7,8]

Table 7. Use of Systemic Ribavirin for Respiratory Syncytial Virus or Human Parainfluenza Virus Respiratory Tract Infectious Diseases[a]

Oral or intravenous ribavirin maximal dosing 10 mg/kg body weight every 8 h for adults	
Day 1: Start with 600 mg loading dose, then 200 mg every 8 h	
Day 2: 400 mg every 8 h	
Day 3: Increase the dose to a maximum of 10 mg/kg body weight every 8 h	
In case of adverse events:	Decrease dose or discontinue ribavirin
Creatinine clearance:	Oral or intravenous administration
30–50 mL/min	Maximal 200 mg every 8 h
10–30 mL/ min	No recommendation can be given[b]

[a] Modified after [14].

[b] Some experts use 200 mg once daily under close clinical and laboratory monitoring.

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Transplant Infectious Disease, ISSN 1398-2273

Review article

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

S. Matthes-Martin[1], T. Feuchtinger[2], P.J. Shaw[3], D. Engelhard[4], H.H. Hirsch[5], C. Cordonnier[6], P. Ljungman[7], on behalf of the fourth European Conference on Infections in Leukemia

[1]Department of Pediatrics, Stem Cell Transplantation Unit, St Anna Children's Hospital, Medical University, Vienna, Austria, [2]Department of Pediatrics, University Hospital, Tübingen, Germany, [3]Oncology Unit, The Children's Hospital at Westmead, Sydney, Australia, [4]Department of Pediatrics, Hadassah University Hospital, Jerusalem, Israel, [5]Department of Virology, University Hospital, Basel, Switzerland, [6]Department of Hematology, Hôpital Henri Mondor, Assistance Publique-Hôpitaux de Paris, and Université Paris-Est Créteil, Creteil, France, [7]Department of Hematology, Karolinska University Hospital, and Department of Medicine Huddinge, Section of Hematology, Karolinska Institutet, Stockholm, Sweden

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.

9) Infección por adenovirus

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.

Infección por adenovirus: Tratamiento

Prophylaxis and therapy of adenovirus (AdV) infections

Prophylactic and preemptive treatment

- Prophylactic antiviral therapy with currently available antiviral drugs is not recommended (BIII)
- Patients with viremia and at least 1 risk factor should receive preemptive antiviral treatment with cidofovir 3–5 mg/kg/week for 2–3 weeks; thereafter, every other week* (BII)

Treatment of proven or probable AdV disease

- Immunosuppressive therapy should be reduced or withdrawn whenever possible (AII)
- Patients with probable or proven human AdV (HAdV) disease should be treated with intravenous cidofovir (either 5 mg/kg weekly for 2–3 weeks; thereafter, every other week) (BIII)
- At day of cidofovir administration, protective measures should be taken such as hyperhydration, oral probenicid (BIII) and, if possible, other nephrotoxic drugs should be avoided (BIII)
- Ribavirin is not recommended for AdV disease (CIII)
- Therapy with donor-derived HAdV-specific T cells should be reserved for patients who do not respond to antiviral therapy and should be performed in the context of clinical trials in experienced centers (BIII)

*An alternative schedule of 1 mg/kg 3 times/week has been described.

- CMX001:derivado cidofovir de administración VO

Matthes-Martin S, Expert Rev Anti Infect Ther 2013, 11(10):1017-28.

- Ribavirina: serotipo C
- GGIV

10) Infección por Norovirus
Infección emergente?

MECHANISMS OF DISEASE

Norovirus Gastroenteritis in Immunocompromised Patients

Karin Bok, Ph.D., and Kim Y. Green, Ph.D.

N Engl J Med 2012;367:2126-32.

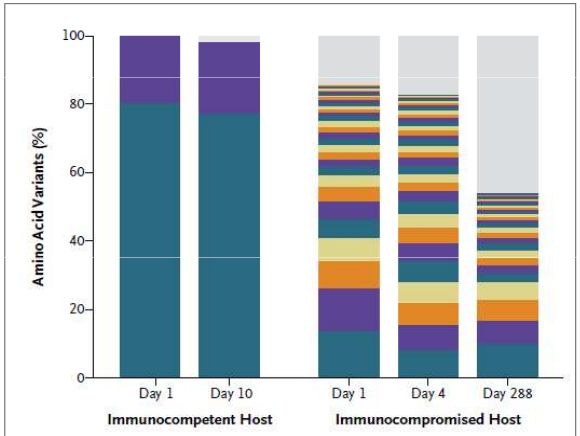

Figure 2. Distributions of Norovirus Variants in Representative Immunocompetent and Immunocompromised Hosts.

The bar graph shows the frequency distribution of VP1 norovirus variants, identified through next-generation sequencing, in an immunocompetent host and an immunocompromised host. Each unique variant is represented by a different color. Given the limited color palette, repeated colors represent distinct variants. Low-frequency variants, with an estimated frequency of occurrence below the detection threshold (2%), are shown in gray. Only two variants were detected in the immunocompetent host, and they remained stable throughout the 10 days of infection. No predominant variant was observed in the immunocompromised host. Instead, numerous low-frequency variants coexisted, and their prevalences varied over the course of the infection. Adapted from Bull et al.[34]

Table 2. Characteristics of Norovirus Gastroenteritis in Immunocompetent versus Immunocompromised Hosts.

Characteristic	Immunocompetent Hosts	Immunocompromised Hosts
Prevalence	Leading cause of gastroenteritis worldwide	Not established; estimated at about 17 to 18%
Seasonality	Peak in winter months	Year-round
Clinical features	Acute onset, duration of 24 to 48 hr	Acute onset, indefinite duration
Viral shedding	20 to 40 days	Weeks to years
Level of virus	10^8 to 10^9 genome copies per gram of stool	10^5 to 10^8 genome copies per gram of stool, depending on level of immunosuppressive therapy
Evolution of virus in host	Small number of stable variants	Markedly diverse variants
Tissue tropism	Small intestine	Small intestine
Complications	Dehydration	Dehydration, malnutrition, dysfunction of intestinal barrier
Treatment	Infection is usually self-limiting; rehydration, if needed	No virus-specific treatment is available; supportive care, adjustment of immunosuppressive therapy
Prognosis	Usually excellent, but the infection can be life-threatening	Poor to excellent; chronic infection is common

Infección crónica en ID

⬇

Población viral diversa: se generan múltiples variantes

Tto: IG duodenal/nitazoxanida/ribavirina

Tratamiento individualizado: Importancia

- Escenarios diferentes y complejos
- Consideraciones farmacológicas y del paciente
- Comorbilidad importante y variable

Maximizar eficacia del tratamiento

Disminuir la toxicidad

Diseñar terapias perfiladas

Atender a las necesidades del paciente

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Gracias !

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