Infection et immunodépression

Keyvan Razazi

Médecine Intensive Réanimation

Hôpital Henri Mondor, Créteil

« Groupe Infection et immunodépression G2I »

MEDECINE INTENSIVE REANIMATION
HOPITAL HENRI MONDOR

Liens d’intérêt

- Shionogi lecture fees
- MSD lecture fees
- Pfizer travel grant

Composition du groupe

23 membres:

- Infectiologues
- Hématologues
- Greffeurs (rein, poumon, moelle)
- Réanimateur

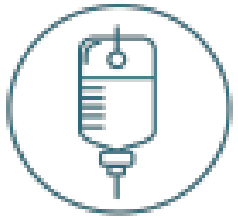
Pneumococcal and influenza vaccination coverage among at-risk adults: A 5-year French national observational study

Benjamin Wyplosz [a,*], Jérôme Fernandes [b], Ariane Sultan [c], Nicolas Roche [d], François Roubille [e], Paul Loubet [f], Bertrand Fougère [g], Bruno Moulin [h], Didier Duhot [i], Alexandre Vainchtock [j], Fanny Raguideau [j], Joannie Lortet-Tieulent [j], Emmanuelle Blanc [k], Jennifer Moïsi [k], Gwenaël Goussiaume [k]

Year	2014	2015	2016	2017	2018
Immunocompromised patients, n	490,556	513,137	536,645	562,134	570,035
Vaccination coverage, n (%)	50,298 (10.3%)	53,132 (10.4%)	57,130 (10.7%)	77,405 (13.8%)	106,977 (18.8%)
Chronic autoimmune or inflammatory disease treated by immunosuppressive or biologic drugs, n	147,832	161,199	174,258	187,521	191,527
Vaccination coverage, n (%)	20,499 (13.9%)	21,836 (13.6%)	25,597 (14.7%)	36,967 (19.7%)	50,825 (26.5%)
Chemotherapy-treated solid cancer or hematologic malignancy, n	143,371	144,566	147,076	150,157	152,255
Vaccination coverage, n (%)	7794 (5.4%)	7075 (4.9%)	6945 (4.7%)	9192 (6.1%)	14,422 (9.5%)
HIV, n	95,196	98,026	100,841	104,226	100,604
Vaccination coverage, n (%)	12,450 (13.1%)	15,462 (15.8%)	16,776 (16.6%)	19,882 (19.1%)	23,714 (23.6%)
Solid organ transplant, n	46,068	47,751	49,640	51,721	53,971
Vaccination coverage, n (%)	3796 (8.2%)	4518 (9.5%)	5200 (10.5%)	7203 (13.9%)	10,362 (19.2%)
Hereditary immune deficits, n	27,697	28,914	31,203	33,316	34,999
Vaccination coverage, n (%)	2307 (8.3%)	2129 (7.4%)	2143 (6.9%)	2988 (9.0%)	4744 (13.6%)
Asplenia or hyposplenia, n	29,511	30,458	31,336	32,508	33,429
Vaccination coverage, n (%)	4737 (16.1%)	3573 (11.7%)	2404 (7.7%)	3416 (10.5%)	5529 (16.5%)
Nephrotic syndrome, n	15,059	15,875	16,703	17,567	18,648
Vaccination coverage, n (%)	870 (5.8%)	930 (5.9%)	1066 (6.4%)	1570 (8.9%)	2468 (13.2%)
Hematopoietic stem cell transplant[a], n	9771	9970	10,378	10,866	11,381
Vaccination coverage, n (%)	1608 (16.5%)	1044 (10.5%)	512 (4.9%)	683 (6.3%)	1393 (12.2%)

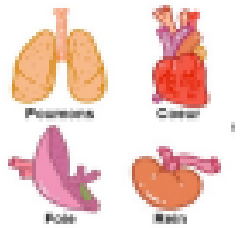
Patients immunodéprimés

Maladies inflammatoires chroniques traitées
~ 700 000 personnes



Néoplasies sous chimiothérapie
~ 400 000 personnes

Infection par le VIH
~ 170 000 personnes



Transplantation d'organe
~ 70 000 personnes

Données non publiées

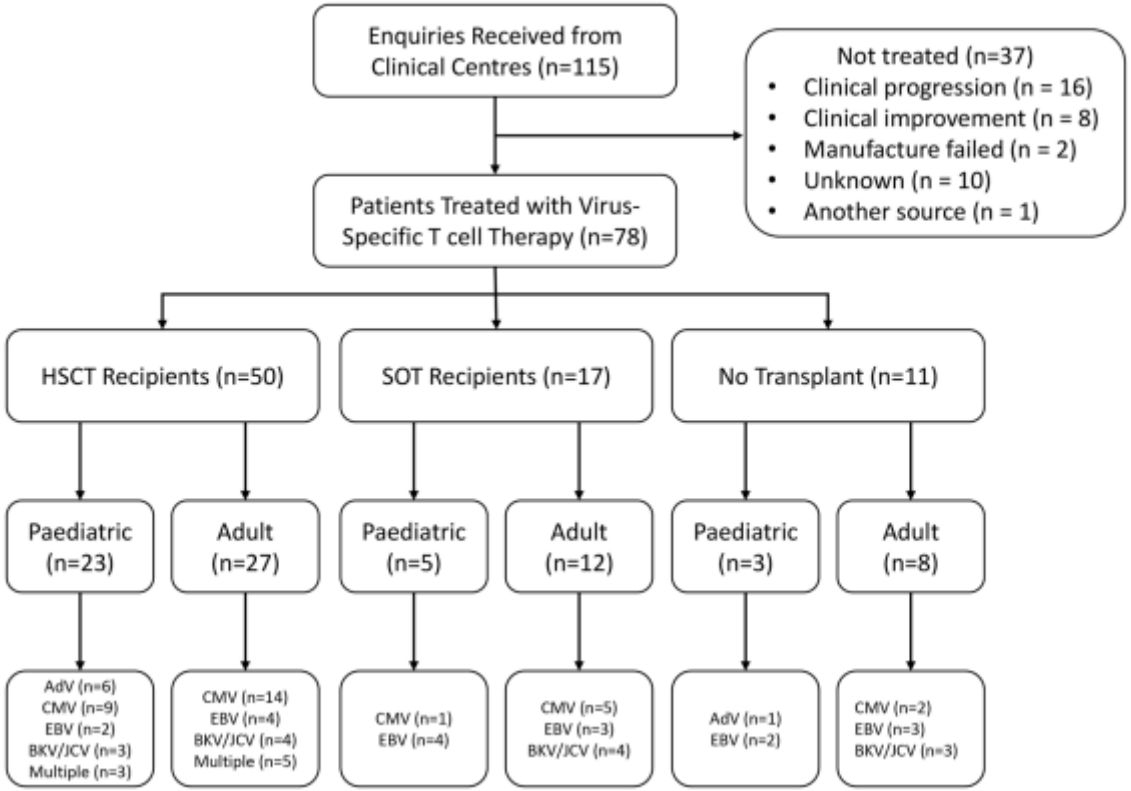
Les études marquantes

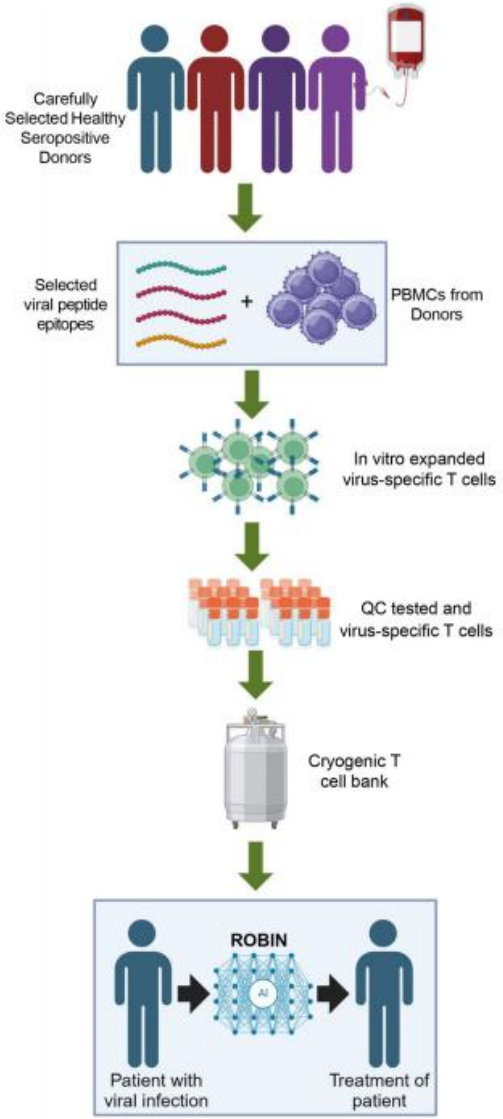
nature communications

Article

https://doi.org/10.1038/s41467-024-54595-2

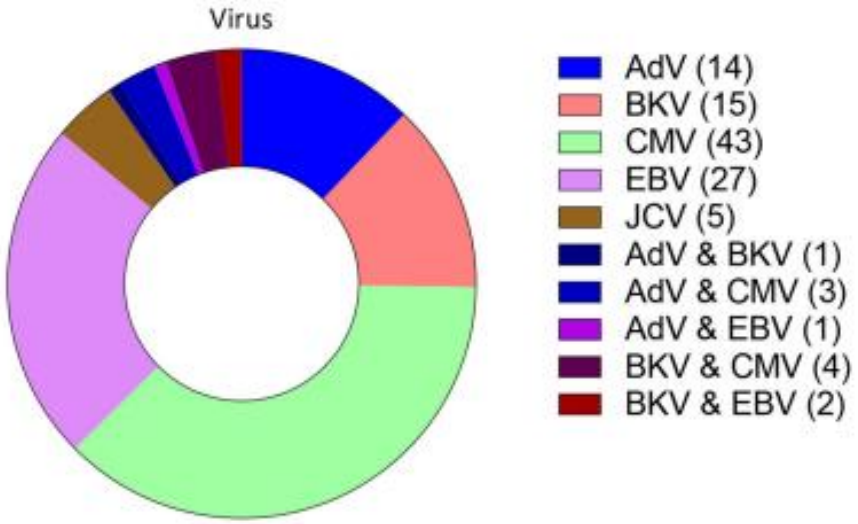
Compassionate access to virus-specific T cells for adoptive immunotherapy over 15 years

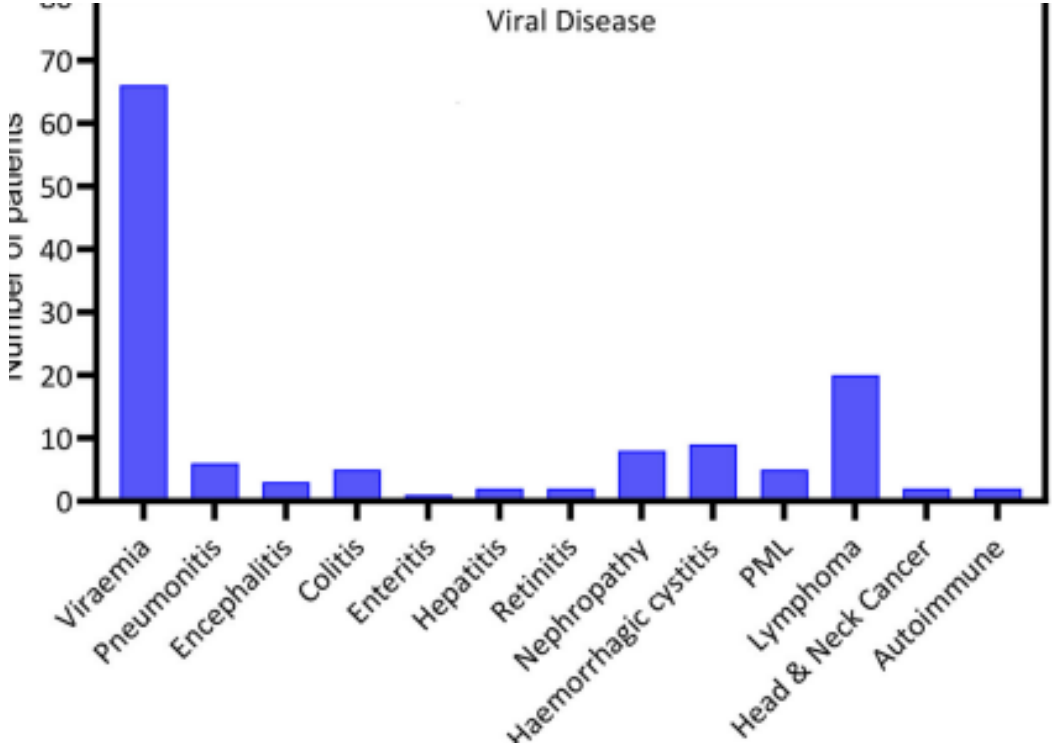




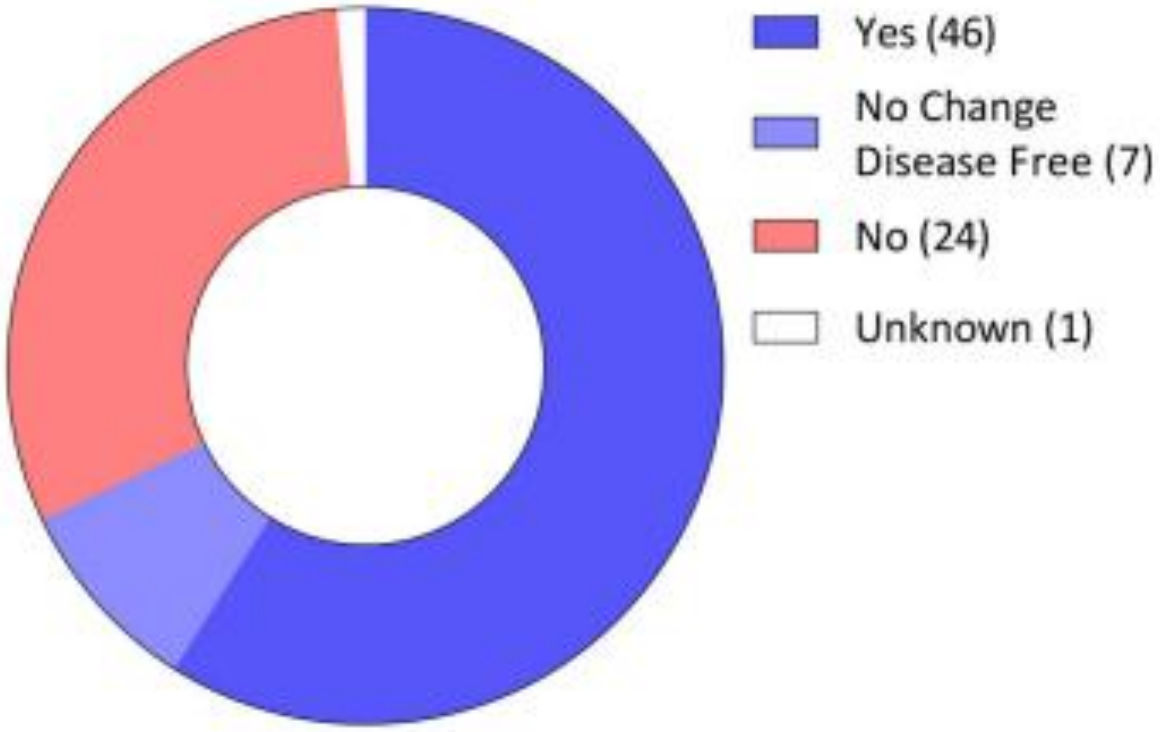
Robin is a propriety algorithm which facilitates exact matching of allogeneic T cell therapy with patient

Caractéristiques des infections





Amélioration clinique

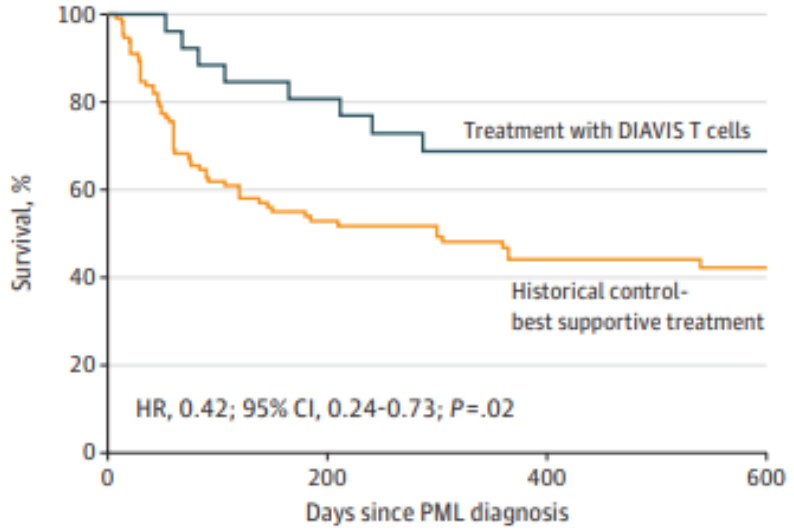


JAMA Neurology | Original Investigation

Directly Isolated Allogeneic Virus-Specific T Cells in Progressive Multifocal Leukoencephalopathy

Nora Möhn, MD; Lea Grote-Levi, MD; Mike P. Wattjes, MD, PhD; Agnes Bonifacius, PhD; Dennis Holzwart, MS; Franziska Hopfner, MD; Sandra Nay, MD; Sabine Tischer-Zimmermann, PhD; Mieke Luise Saßmann; Philipp Schwenkenbecher, MD; Kurt-Wolfram Sühs, MD; Nima Mahmoudi, MD; Clemens Warnke, MD; Julian Zimmermann, MD; David Hagin, MD, PhD; Lilia Goudeva, MD; Rainer Blasczyk, MD; Armin Koch, PhD; Britta Maecker-Kolhoff, MD; Britta Eiz-Vesper, PhD; Günter Höglinger, MD; Thomas Skripuletz, MD

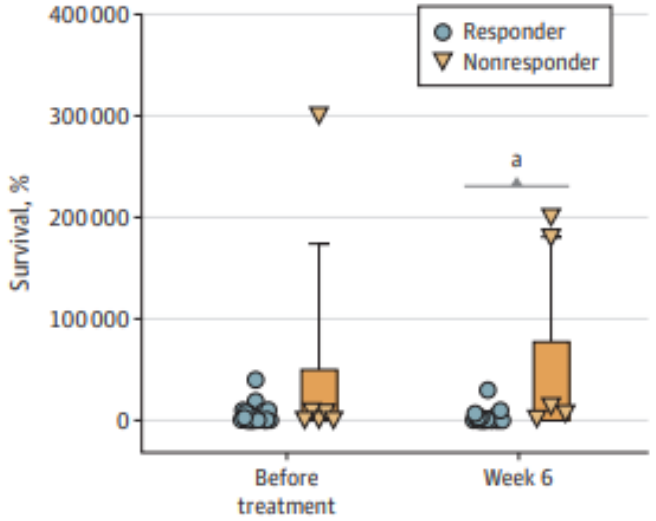
Survie



No. at risk

DIAVIS T cells	26	21	12	5
BST controls	113	47	25	22

Charge virale

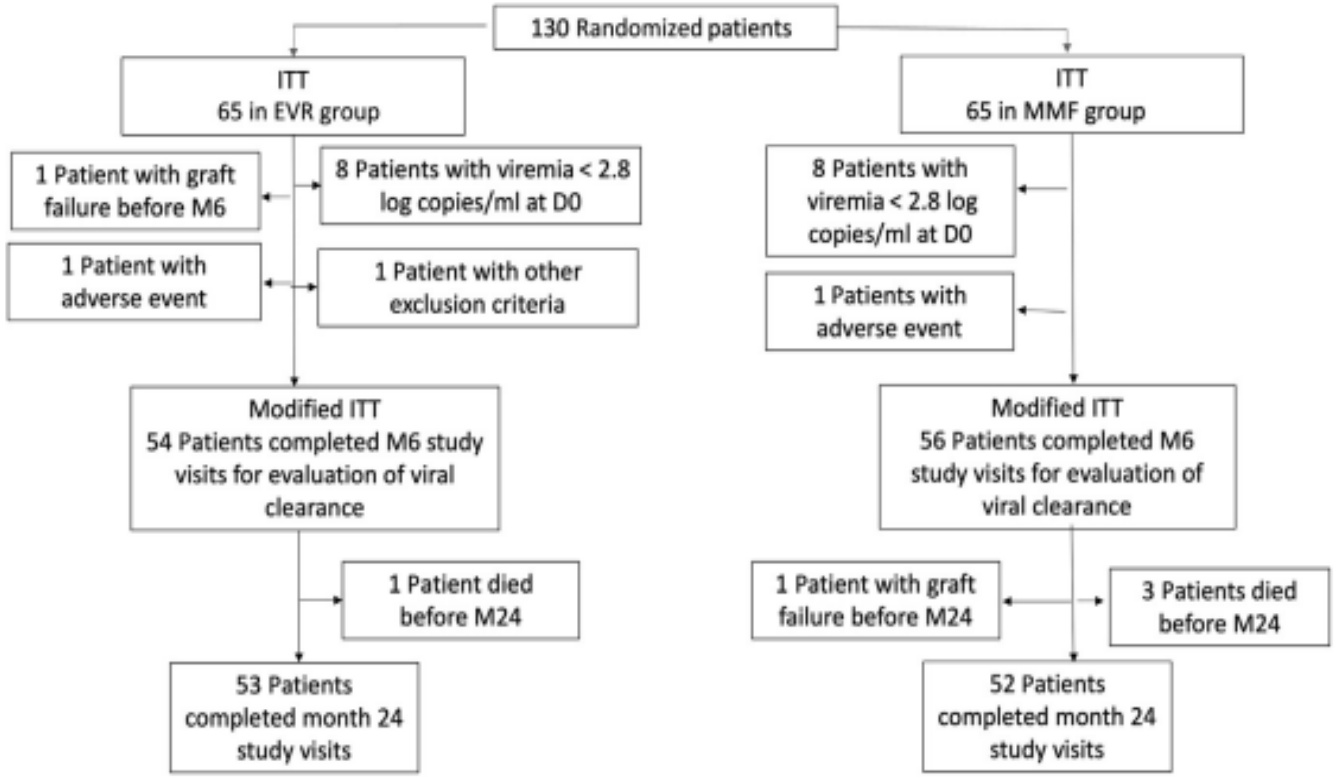


clinical trial www.kidney-international.org

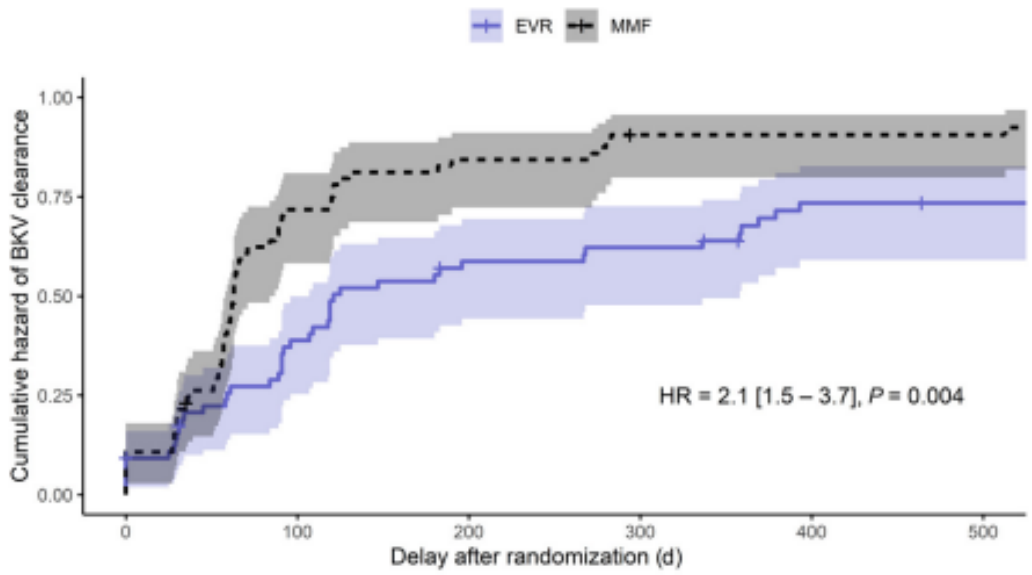
Insights from the BKEVER Trial comparing everolimus versus mycophenolate mofetil for BK Polyomavirus infection in kidney transplant recipients

see commentary on page 230

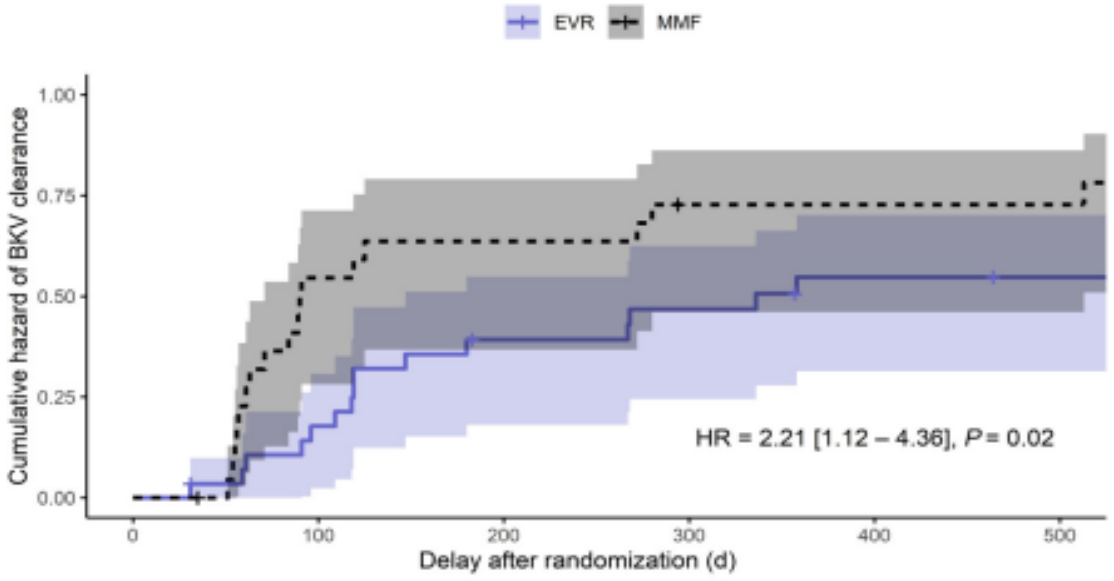
Sophie Caillard[1], Nicolas Meyer[2], Morgane Solis[3], Dominique Bertrand[4], Maite Jaureguy[5], Dany Anglicheau[6], Laure Ecotiere[7], Matthias Buchler[8], Nicolas Bouvier[9], Betoul Schvartz[10], Jean Philippe Rerolle[11], Anne Elisabeth Heng[12], Lionel Couzi[13], Agnes Duveau[14], Emmanuel Morelon[15], Yann LeMeur[16], Léonard Golbin[17], Eric Thervet[18], Ilies Benotmane[1] and Samira Fafi-Kremer[3]



Clairance BK virus



Clairance BK virus (BK virémie>4log)



10th EUROPEAN CONFERENCE on INFECTIONS in LEUKAEMIA

Bacterial: febrile neutropenia – duration of therapy - new drugs

Dina Averbuch (Israel), Manuela Aguilar Guisado (Spain), Murat Akova (Turkey), Francesco Baccelli (Italy), Nicole Blijlevens (The Netherlands), Catherine Cordonnier (France), Carol Garcia Vidal (Spain), Malgorzata Mikulska (Italy), Patricia Muñoz (Spain), Dionysos Neofytos (Switzerland), Yuri Vanbiervliet (Belgium), Thierry Calandra (Switzerland)

Final slide set
Post meeting

From September 19th to 21st, 2024

- **Golden Tulip Sophia Antipolis**
  Nice, France

Revision of recommendations for empirical antibiotic therapy: escalation approach

	Escalation approach ECIL 4	Escalation approach ECIL 10
Indication **B-II for all**	1) Uncomplicated presentation; 2) No known colonization with resistant bacteria; 3) No previous infection with resistant bacteria; 4) In centers where infections due to resistant pathogens are rarely seen at the onset of febrile neutropenia	**No change**
Options for initial antibiotic therapy	1) Anti-pseudomonal cephalosporin (cefepime*, ceftazidime*) **AI** 2) Piperacillin-tazobactam **AI** 3) Other possible options include: • Ticarcillin-clavulanate • Cefoperazone-sulbactam • Piperacillin + gentamicin	1) Anti-pseudomonal cephalosporin (cefepime*, ceftazidime*) **AI** 2) Piperacillin-tazobactam **AI** 3) Other possible options include: • Cefoperazone-sulbactam • Piperacillin + gentamicin

*** Avoid if ESBLs are prevalent**

**** AI for efficacy, but should be avoided in uncomplicated patients lacking risk factors for resistant bacteria, to preserve activity for seriously-ill patients**

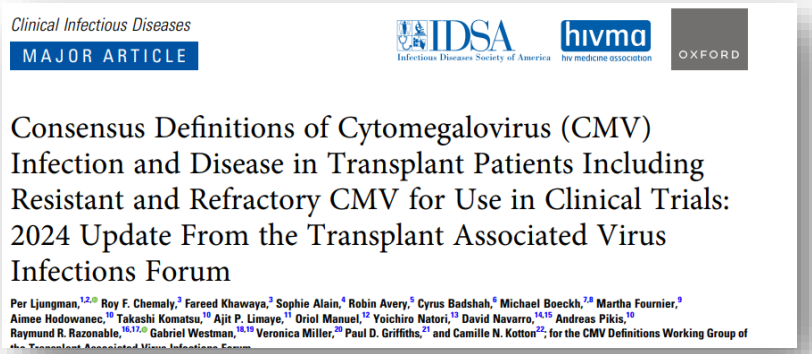
Revision of recommendations for empirical antibiotic therapy: de-escalation approach (in red changes vs ECIL4)

	De-escalation approach ECIL 4	De-escalation approach ECIL 10
Indication	1) Complicated presentations **BII** 2) Known colonization with resistant bacteria **BII** 3) Previous infection with resistant bacteria **BII** 4) In centers where resistant pathogens are regularly seen at the onset of febrile neutropenia **BII**	1) Sepsis/Septic shock 2) Known colonization with resistant bacteria; 3) Previous infection with resistant bacteria; 4) In centers where resistant pathogens are regularly seen at the onset of febrile neutropenia.
Options for initial antibiotic therapy	1) Carbapenem monotherapy **BII** 2) Combination of anti-pseudomonal beta-lactam + aminoglycoside or quinolone (with carbapenem as the beta- lactam in seriously ill-patients) **BIII** 3) Colistin + beta-lactam +/- rifampicin (for PsA, AB, SM) **BIII** 4) Early coverage of resistant-Gram-positives with a glycopeptide or newer agent (If risk factors for Gram-positives present) **CIII**	1) Carbapenem monotherapy 2) Combination of anti-pseudomonal beta-lactam + aminoglycoside 3) Beta lactam targeting the suspected colonizing pathogen based on susceptibility testing 4) Early coverage of resistant-Gram-positives with a glycopeptide or newer agent if risk factors for Gram-positives present

Autres recommandations ECIL-10

- CMV
- COVID 19
- Virus respiratoire communautaire
- Clostridium

Définition Infection à CMV



Revised Definitions of Refractory CMV Infection/Disease for Use in Clinical Trials

Refractory CMV infection: augmentation charge virale ou baisse de moins d'1 log après 2 semaine de ttt bien conduit

Refractory CMV end-organ disease: pas d'amélioration ou aggravation signe cliniqueaprès 2 semaines de ttt bien conduit

Definition of CMV Antiviral Drug Resistance for Use in Clinical Trials

Refractory CMV Infection avec une alteration du genome qui confère une diminutionn de sensibilité à 1 ou plusieurs antiviraux

En réanimation

- 1/3 des patients
- Moins d'acquisition de BMR chez les immunodéprimés, moins de PAVM?

Kreitmann L ICM 2023, CCM 2025

- Aide de la métagénomique sur le diagnostic microbiologique des pneumonies

Zhao respiratoru resarch 2024
Azar Chest 2021
Peng Journal of infection 2021

Les études du groupe

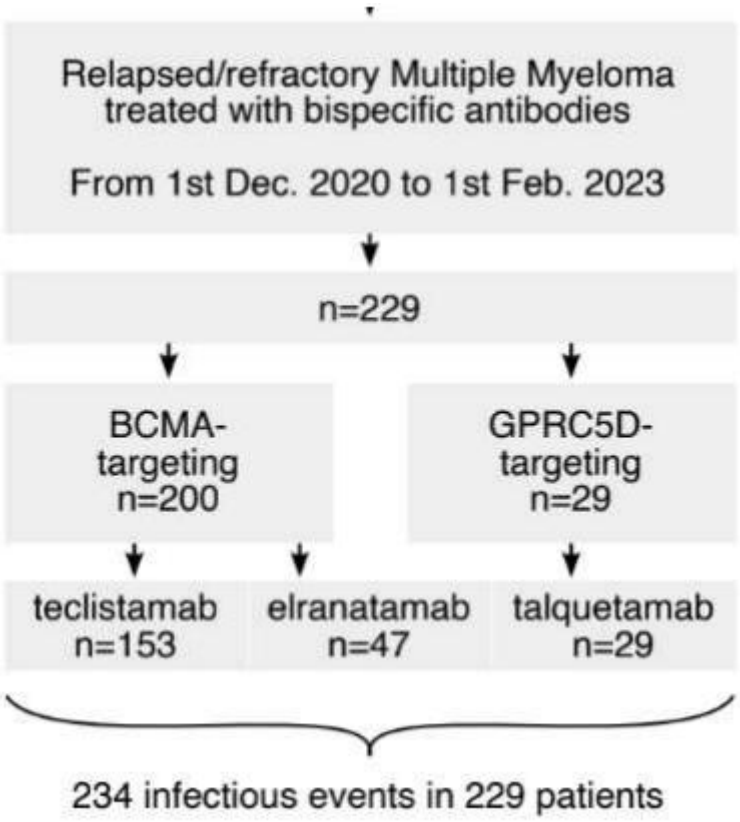
Incidence des infections après traitement par Bispécifique chez les myélomes

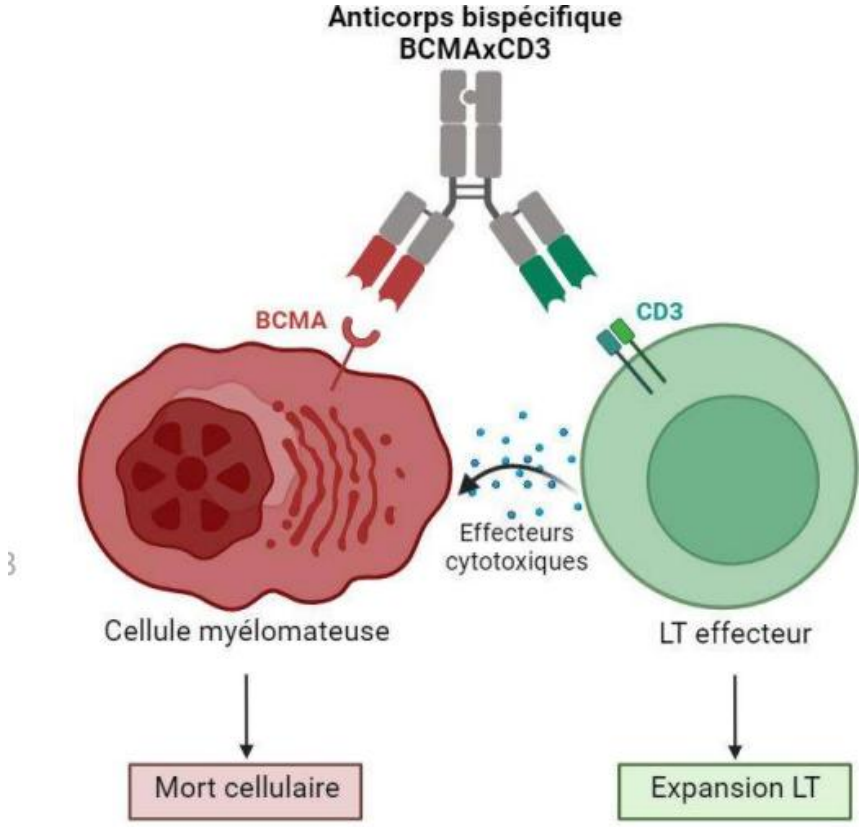
Original article

Characteristics and incidence of infections in patients with multip myeloma treated by bispecific antibodies: a national retrospective study

Aurélie Jourdes [1], Elise Cellerin [2], Cyrille Touzeau [3], Stéphanie Harel [4], Blandine Deni Guillaume Escure [6], Emmanuel Faure [6, 7], Simon Jamard [8], Francois Danion [9, 10], Cécile Sonntag [11], Florence Ader [12, 13], Lionel Karlin [14], Sarah Soueges [12], Clarisse Cazelles [15, 16], Clémentine de La Porte des Vaux [17], Laurent Frenzel [15, 18], Fanny Lanternier [17, 19], Xavier Brousse [20], Titouan Cazaubiel [21, 22], Pierre Berger [23], Aude Collignon [24], Mathieu Blot [25, 26, 27], Andrea Pieragostini [28], Morgane Charles [29], Carine Chaleteix [30], Alexis Redor [31], Virginie Roland [32], Tom Cartau [33], Margaret Macro [34], Thomas Chalopin [2], Nicolas Vallet [2, 35], Aurore Perrot [20, 36], Guillaume Martin-Blondel [1, 37, *], on behalf of the G2I and the IFM networks

CMI CLINICAL MICROBIOLOGY AND INFECTION
ESCMID

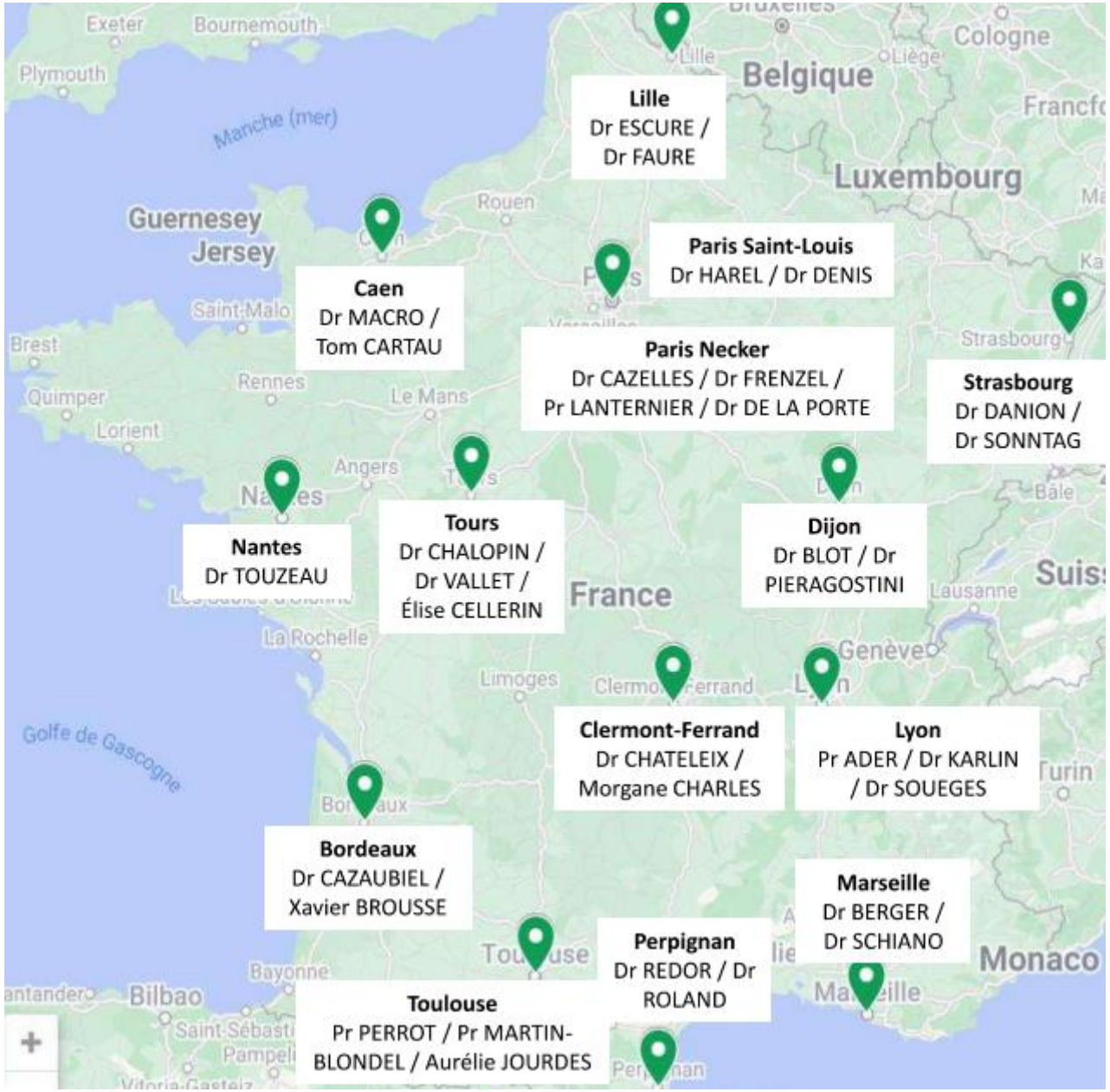




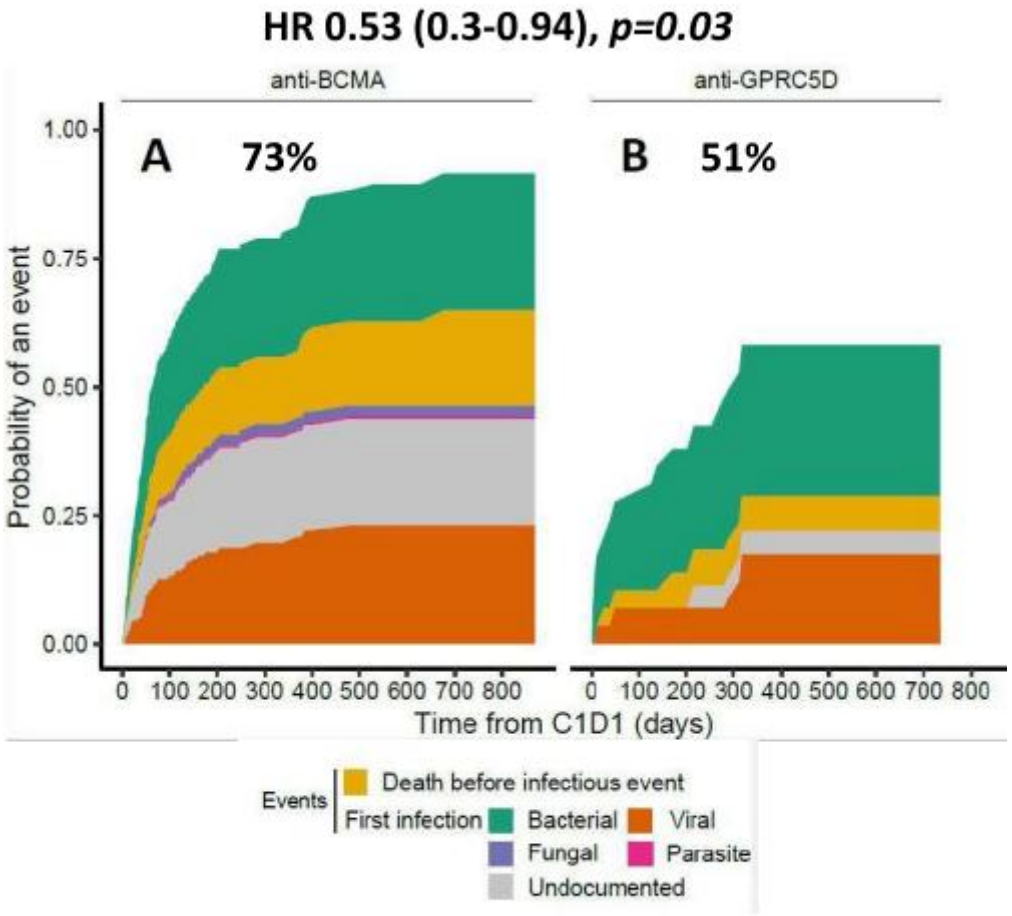
[1]Moreau *et al.* 2022 ; [2]Lesokhin *et al.* 2022 ; [3]Chari *et al.* 2022.

14 centres

Collaboration hémato/ infectiologues



Incidence plus élevée avec anti-BCMA



- Survenue d'au moins un épisode infectieux : **142 patients (62%)**

- **234 épisodes infectieux** au total :

- 131 (56%) ayant nécessité une hospitalisation dont 30 (13%) en réanimation

- 20 (9%) décès

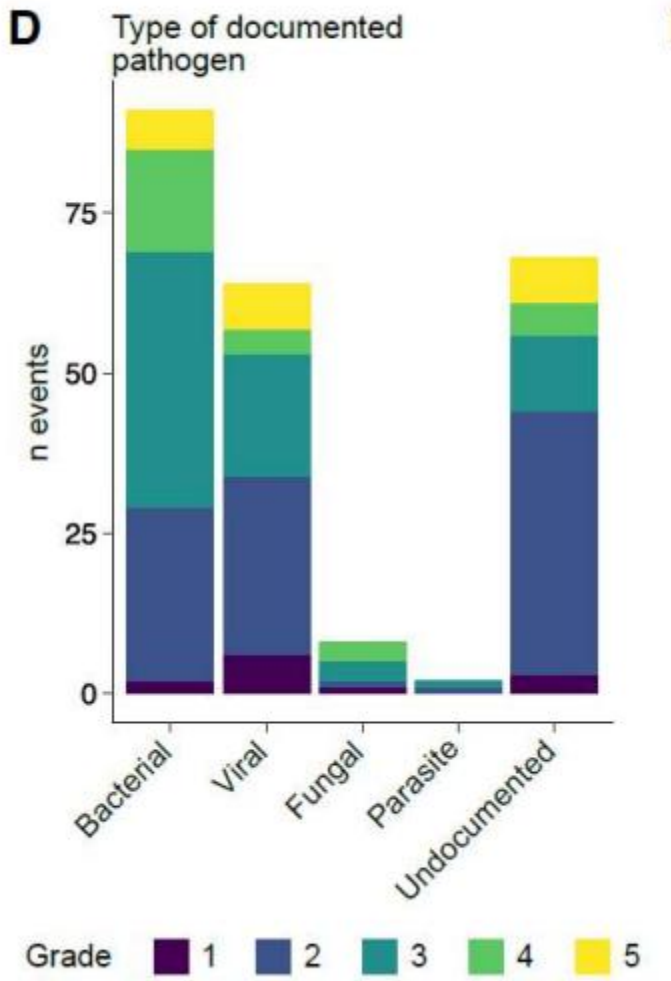
- 70 (30%) ayant conduit à une pause du traitement ; 31 (13%) à un arrêt du traitement par BsAb.

- Incidence cumulative globale du 1er épisode infectieux : **70%**

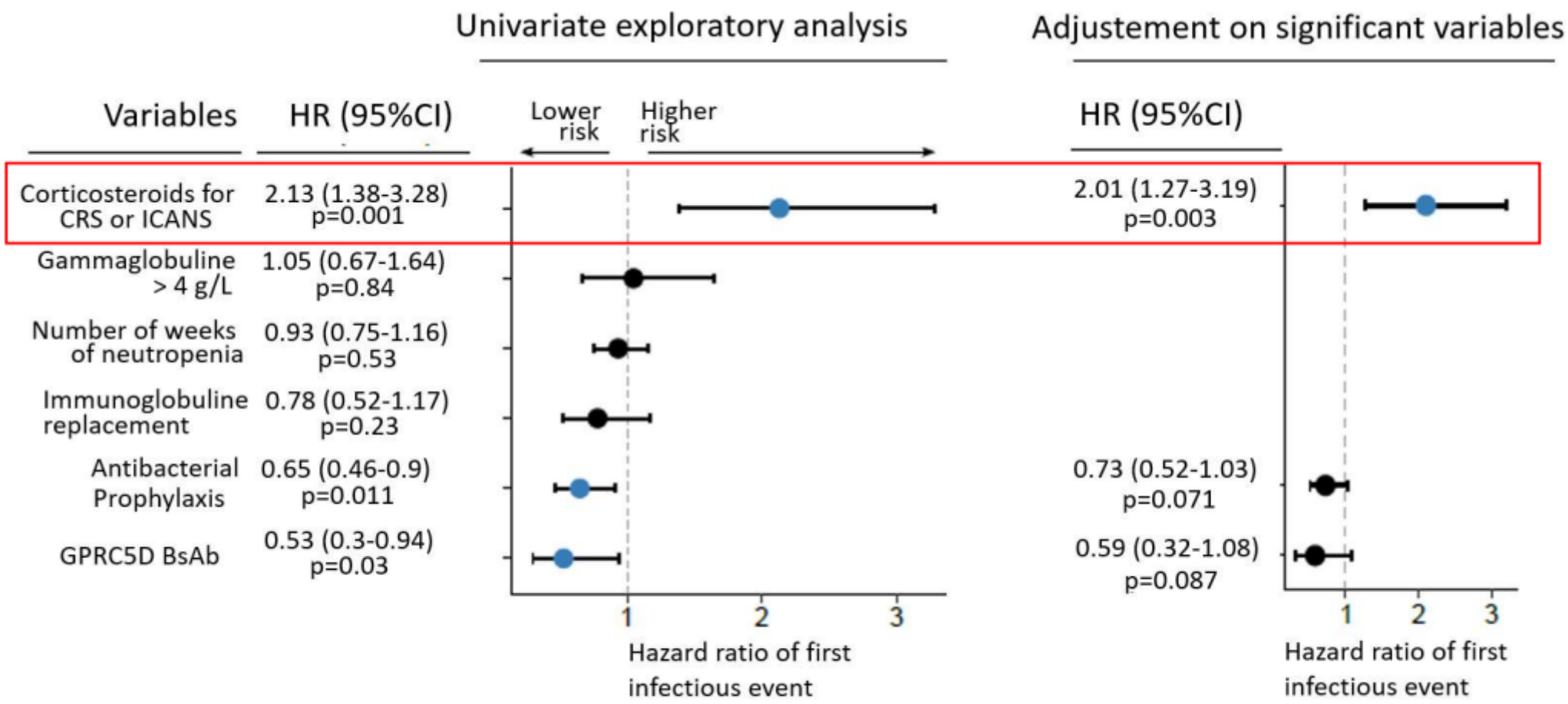
  - 73% dans le groupe anti-BCMA
  - 51% dans le groupe anti-GPRC5D

Caractéristiques des infections

Variables	Total (n=234)
Site of infection, *n*(%)	
Systemic	52 (22)
Upper respiratory tract	19 (8)
Lower respiratory tract	97 (41)
Gastrointestinal tract	23 (10)
Genitourinary tract	23 (10)
Skin and soft tissue	11 (5)
CNS	2 (1)
Pathogens isolated *, *n*(%)	**n=165**
Bacterial	**92/165 (56)**
Enterobacteriaceae	48/165 (29)
Pseudomonas aeruginosa and other non-fermentative Gram-negative bacteria	13/165 (7)
Anaerobic bacteria	11/165 (6)
Enterococci	6/165 (4)
Staphylococci	5/165 (3)
Streptococci [a]	4/165 (2)
Haemophilus influenzae	4/165 (2)
Neisseria	1/165 (1)
Viral	**63/165 (38)**
Respiratory viruses [b]	40/165 (24)
CMV	8/165 (5)
Enterovirus	3/165 (2)
HSV	2/165 (1)
VZV	2/165 (1)
Parvovirus B19	2/165 (1)
HBV	2/165 (1)
JC virus	2/165 (1)
Sapovirus	1/165 (1)
Adenovirus	1/165 (1)
Fungi	**8/165 (5)**
Aspergillus spp.	6/165 (4)
Scedosporium spp.	1/165 (1)
Pneumocystis jirovecii	1/165 (1)
Parasites	**2/165 (1)**
Toxoplasmosis	1/165 (1)
Giardiasis	1/165 (1)



Facteur de risque d'infection



Utilisation en vie réelle du Céfidérocol chez les patients immunodéprimés

Infectious Disease Practice

Real-world multicentre study of cefiderocol treatment of immunocompromised patients with infections caused by multidrug-resistant Gram-negative bacteria: CEFI-ID

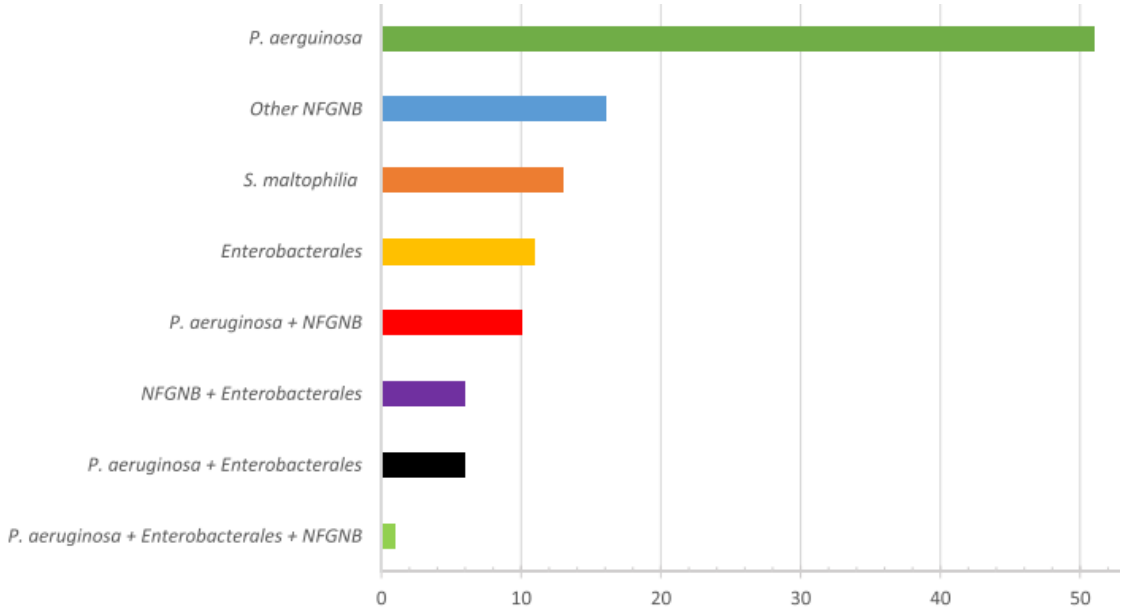
Sarah Soueges [a,*], Emmanuel Faure [b], Perrine Parize [c], Fanny Lanternier-Dessap [c], Hervé Lecuyer [d], Anne Huynh [e], Guillaume Martin-Blondel [f,g], Benjamin Gaborit [h], Mathieu Blot [i], Arnaud Magallon [j], Elodie Blanchard [k], Xavier Brousse [l], Marin Lahouati [m,n], Anne-Sophie Brunel [o], Eloise Le Banner [p], François Camelena [q], Romaric Larcher [r], Alix Pantel [s], Giovanna Melica [t], Keyvan Razazi [u], François Danion [v], Frederic Schramm [w], Oana Dumitrescu [x], Baptiste Hoellinger [v], Florence Ader [a,y], On behalf of the G2I (Groupe Immunodepression et Infections) network [1]

n=114		
Demographics		
Age (year)		60 [50–67.7]
Sex ratio (M/F)		2.6
Underlying conditions		
Charlson comorbidity index		4.5
SOT		40 (35%)
	Lung	17 (42.5%)
	Kidney	10 (25%)
	Liver	11 (27.5%)
	Heart	2 (5%)
Hematological malignancy		44 (38.5%)
	Myeloid	27 (61.3%)
	Lymphoid	17 (38.7%)
HSCT		19 (16.6%)
	Allo HSCT	13 (68.4%)
	Auto HSCT	6 (31.6%)
Active solid neoplasia		28 (24.5%)
	Digestive/biliary/pancreas	19 (67.8%)
	Lung	4 (14.2%)
	ENT	4 (14.2%)
	Urinary tract/kidney	1 (3.8%)
Interstitial lung disease		4 (3.5%)

Caractéristiques des infections

Characteristics of infections and patient's outcome.

Site of infection	
Respiratory tract infection	55 (48.2%)
Urinary tract infection	16 (14%)
Intra-abdominal infection	11 (9.6%)
Venous catheter related infection	10 (8.7%)
Skin and soft tissue infection	8 (7%)
Central nervous system infection	3 (2.6%)
Associated bloodstream infection	42 (38.8%)
Complications of infections	
ICU admission	67 (58.7%)
Mechanical ventilation	47 (70%)
Vasopressive support	43 (64.1%)
Day 28 outcomes	
Infection cure	61 (53.3%)
Overall mortality	43 (37.7%)
Attributable mortality	29 (25.4%)
Day 90 outcomes	
Overall mortality	58 (52.2%)
Attributable mortality	39 (35.1%)
Lost to follow up	3 (2.6%)



Enterobacterales antibiotic susceptibility, (n=24)	
Ceftazidime/avibactam	26.6% (n=4/15)
Imipenem-cilastatin/relebactam	25% (n=2/8)
Meropenem/vaborbactam	71.4% (n=5/7)
Colistine	26.6% (n=4/15)
***P. aeruginosa* antibiotic susceptibility, (n=68)**	
Ceftolozane/tazobactam	21.6% (n=13/60)
Ceftazidime/avibactam	21.3% (n=13/61)
Imipenem-cilastatin/relebactam	23.8% (n=10/42)
Colistine	96.1% (n=50/52)

rechute

Relapses and resistance acquisition	
Day 28 relapses	20 (17.5%)
Day 28 resistance acquisition	2 (10%)
Day 90 relapses	7 (9.8% of alive patients at day 28)
Day 90 resistance acquisition	1 (14.2%)

Data are presented as n (%) for dichotomous variables and median [IQR] for continuous variables. Abbreviations: IQR, interquartile range; NFGNB, non-fermentative Gram-negative bacilli.

Revue du groupe

MISE AU POINT PRATIQUE

Actualisation sur les stratégies de prise en charge antibiotique de la neutropénie fébrile en hématologie

Updating Febrile Neutropenia Antibiotic Management Strategies in Haematology

Raphaël Paret[a], Jean-Philippe Talarmin [b], Guillaume Martin-Blondel[c], Benjamin Gaborit [d,e,*], le groupe de travail G2I [#]

REVUE GÉNÉRALE DE LA LITTÉRATURE

Complications infectieuses des nouvelles immunothérapies et thérapies ciblées

Infectious complications of new immunotherapies and targeted therapies

Anne-Sophie Brunel[a,*], Florence Ader[b], au nom du groupe Immunodépression et Infections (G2I) [#]

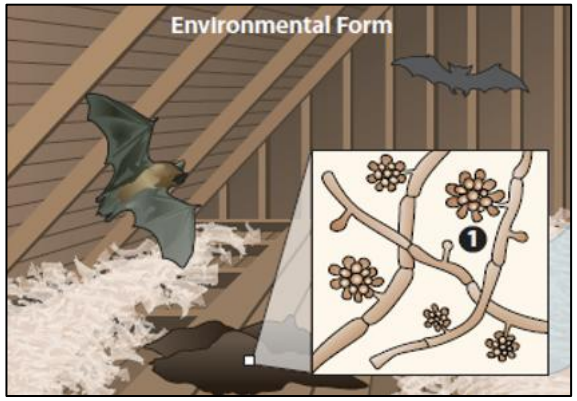
[a] *Service de Maladies Infectieuses et Tropicales, Centre hospitalier universitaire de Besançon, France*
[b] *Service de Maladies Infectieuses et Tropicales, Hospices Civils de Lyon, France*

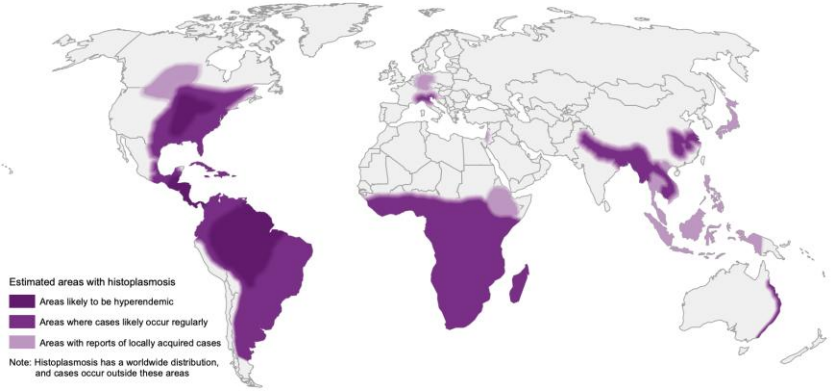
Etudes en cours de soumission

- HISTO: Histoplasmose en réanimation

- CEFI-BURN Cefiderocol chez les brulés

HISTOREA: histoplasmose admis en réanimation



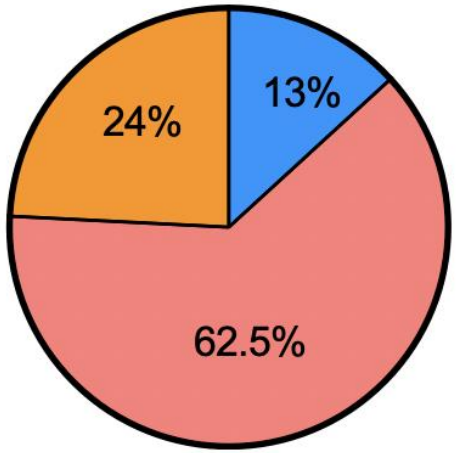


- rétrospective
- 2013-2023

Screening dans 60 centres	Au moins 1 cas dans 20 centres	**91 patients inclus**

Les patients éligibles

- > 18 ans
- Hospitalisé en réanimation
- Avec un diagnostic d'histoplasmose établi **avant ou pendant l'hospitalisation**



68% Antilles/Guyane

32% Métropole

PVVIH

Immunocompétents

Autres ID

->Mortalité en réanimation **47%**

Merci de votre attention

- maillage du réseau sur toute la France
- Partenariat notamment avec la néphrologie, l'hématologie
- Possibilité de recherche phase 2, 3 ou 4