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Meta-Analysis

Risk factors for mortality from pneumocystis carinii pneumonia (PCP) in non-HIV patients: a meta-analysis

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Keywords: *non-HIV, pneumocystis pneumonia, risk factor, mortality, meta-analysis*

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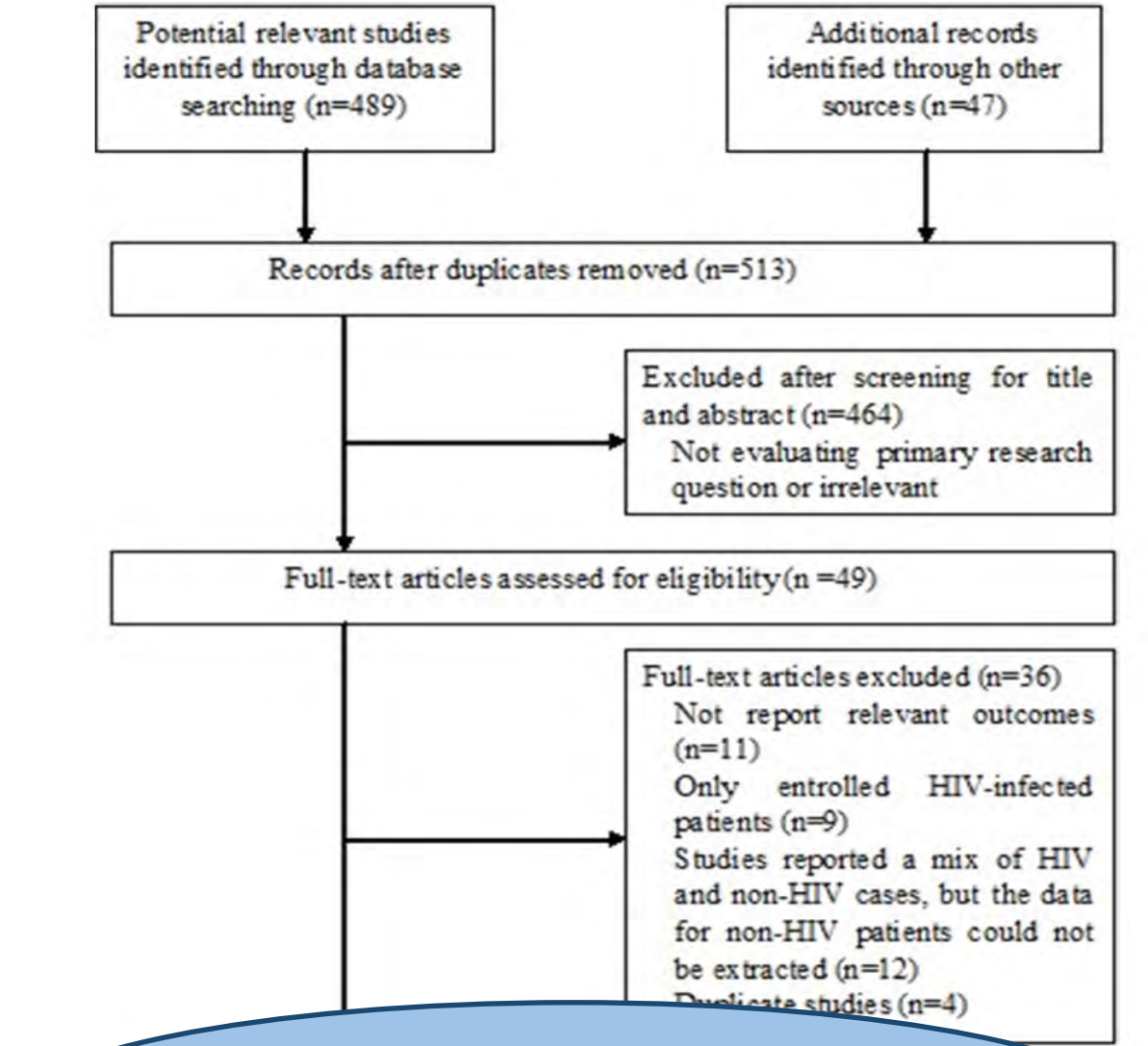
RESULTS



13 études

Table 1: Characteristics of selected studies

Author	Year	Country	Sample size	Mean age,y	Male, (%)	Diagnosis of PCP	PCP prophylaxis	Steroid use before PCP diagnosis	Antimicrobial agents		Adjunctive steroids	Outcome
									TMP-SMX	Others		
Hardak [11]	2012	Israel	58	56	30 (52%)	PCR	NA	NA	58 (100%)	0 (0%)	44 (76%)	in-hospital mortality
Kofteridis [10]	2014	Greece	62	65	43 (70%)	Sputum or BAL,	21 (34%)	NA	62 (100%)	0 (0%)	50 (81%)	in-hospital mortality
Mansharamani [1]	2000	US	22	58	22 (67%)	Sputum, BAL, or lung biopsy	0 (0%)	30 (91%)	NA	NA	NA	in-hospital and 1-year mortality
Li [12]	2014	Taiwan	20	50	9 (45%)	PCR	0 (0%)	NA	20 (100%)	0 (0%)	20 (100%)	in-hospital mortality
Kim [13]	2014	Korea	173	56	116 (67%)	PCR, sputum or BAL	6 (3.5%)					
Chen [8]	2015	China	69	39	25 (36%)	PCR, suptum, BAL ,or lung tissue	NA	NA	59(86%)	Clindamycin or primaquine, 10%	58(84%)	in-hospital mortality
Zahar [9]	2002	France	39	52	20(51%)	BAL	5 (13%)	NA	39(100%)	NA	33(85%)	30-day mortality
Asai [14]	2012	Japan	23	71	13(57%)	PCR, sputum or BAL	1 (4.3%)	NA	23(100%)	NA	100%	NA
Matsumura [15]	2011	Japan	82	64	51 (62%)	PCR	3 (4%)	65(79%)	77(94%)	Pentamidine, 6%	60(73%)	30-day mortality.
Tamai [16]	2013	Japan	29	59	14 (48%)	PCR or BAL	1 (3%)	NA	28 (97%)	Pentamidine, 3%	29 (100%)	in-hospital mortality
Roblot [17]	2002	Japan	103	57	61 (59%)	BAL	4 (4%)	57 (55%)	96 (93%)	Atovaquone, 1%; dapsone, 1%	58 (56%)	30-day mortality
Lemiale [18]	2013	France	139	48	79(57%)	BAL	5 (3.6%)	NA	NA	NA	NA	ICU mortality
Ko [19]	2014	Korea	48	53	33(69%)	BAL or lung tissue	14 (29%)	47 (98%)	47 (98%)	Pentamidine, 1%	47 (98%)	in-hospital mortality

PCP, pneumocystis carinii pneumonia; PCR, polymerase chain reaction; NA, not available; BAL, bronchoalveolar lavage; TMP-SMZ trimethoprim sulphamethoxazole. ICU, Intensive Care Unit; TMP-SMX, Trimethoprim/sulfamethoxazole.

n=6 identifications microbiologiques

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n= 4 PCR + microbiologie +

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Traitement numéro 1 = Bactrim

Table 2: The underlying immunosuppressive conditions in HIV-negative patients with PCP

Condition	No of patients (%)	Proportion (%)
Hematological malignancies, n (%)	252	29.1
Acute myeloblastic leukaemia	37	4.3
Acute lympoblastic leukaemia	25	2.9
Chronic lympocytic leukaemia	40	4.6
Chronic myeloblastic leukaemia	7	0.81
Lymphoma	98	11.3
Multiple myeloma	19	2.2
Others	26	3.0
Solid tumors	52	6.0
Lung cancer	29	3.3
Breast cancer	11	1.3
Stomach cancer	1	0.12
Colon cancer	5	0.58
Cervical cancer	1	0.12
Others	5	0.58
Autoimmune disease/ chronic inflammatory disease, n (%)	174	20.1
Systemic lupus erythematosus	51	5.9
Wegener's granulomatosis	1	0.12
Reumatoid arthritis	53	6.1
Sarcoidosis	3	0.35
dermatomyositis	20	2.3
Chronic kidney disease	0	0
Autoimmune hepatitis	2	0.23
Others	43	5.0
Organ or bone marrow Transplantation	121	14.0
Type of immunosuppressive treatment	484	55.8
Chemotherapy alone	152	17.5
Steroids + chemotherapy	188	21.7
Steroids	144	16.6

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Table 3: Synthesis of the main results from this systematic review

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Demographic factors	Age	Age (years) mean ± SD	9	657	6.33 (3.45–9.21)	< 0.0001	0
	Gender	Female vs Male	11	1531	1.43 (1.12–1.83)	0.004	0
	Respiratory failure	Yes vs No	4	203	6.16 (2.57–14.77)	< 0.0001	0
	ICU admission	Yes vs No	2	82	4.85 (1.28–18.38)	0.02	0
	Smoker	Yes vs No	3	1066	0.97 (0.69–1.38)	0.88	0
	Time from onset of symptoms to diagnosis	Time (days), mean ± SD	4	16	3.53 (0.73–6.33)	0.01	0
Underlying diseases	Haematological malignancy	Yes vs No	7	541	0.64 (0.44–0.92)	0.02	32
	Solid tumor	Yes vs No	6	548	2.66 (1.72–4.13)	< 0.0001	0
	Autoimmune disease	Yes vs No	6	411	1.07 (0.67–1.69)	0.78	67
	Organ transplantations	Yes vs No	5	369	0.38 (0.20–0.74)	0.004	39
Symptom	Fever	Yes vs No	4	1152	0.91 (0.63–1.33)	0.64	0
	Dyspnea	Yes vs No	3	1070	1.50 (1.10–2.04)	0.01	0
	Cough	Yes vs No	2	235	0.68 (0.39–1.18)	0.17	0
Laboratory findings	LDH	LDH (U/L) mean ± SD	9	754	151 (90–212)	< 0.0001	7
	Neutropenia (< 1500/mL)	Yes vs No	2	120	1.43 (0.56–3.66)	0.45	0
	Albumin	Albumin g/L, mean ± SD	6	463	-0.39 (-0.49 - -0.28)	< 0.0001	52
Presence of co-infection	Bacterium	Yes vs No	7	574	2.17 (1.34–3.51)	0.002	25
	Cytomegalovirus	Yes vs No	4	199	2.33 (1.15–4.71)	0.02	40
	Aspergillus	Yes vs No	2	151	10.45 (2.79–40.45)	0.0007	0
Treatment	PCP prophylaxis	Yes vs No	5	1196	0.97 (0.69–1.34)	0.83	0
	Adjunctive steroids	Yes vs No	6	445	1.15 (0.72–1.82)	0.55	0
	Previous Corticosteroid	Yes vs No	3	254	1.05 (0.54–2.03)	0.88	0
	Mechanical ventilation	Yes vs No	7	558	23.46 (14.02–39.28)	< 0.0001	35

OR, Odds Ratio; WMD, weighted mean difference; ICU, Intensive Care Unit; PCP, pneumocystis carinii pneumonia; LDH, lactate dehydrogenase.

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Pas d'impact des corticoïdes

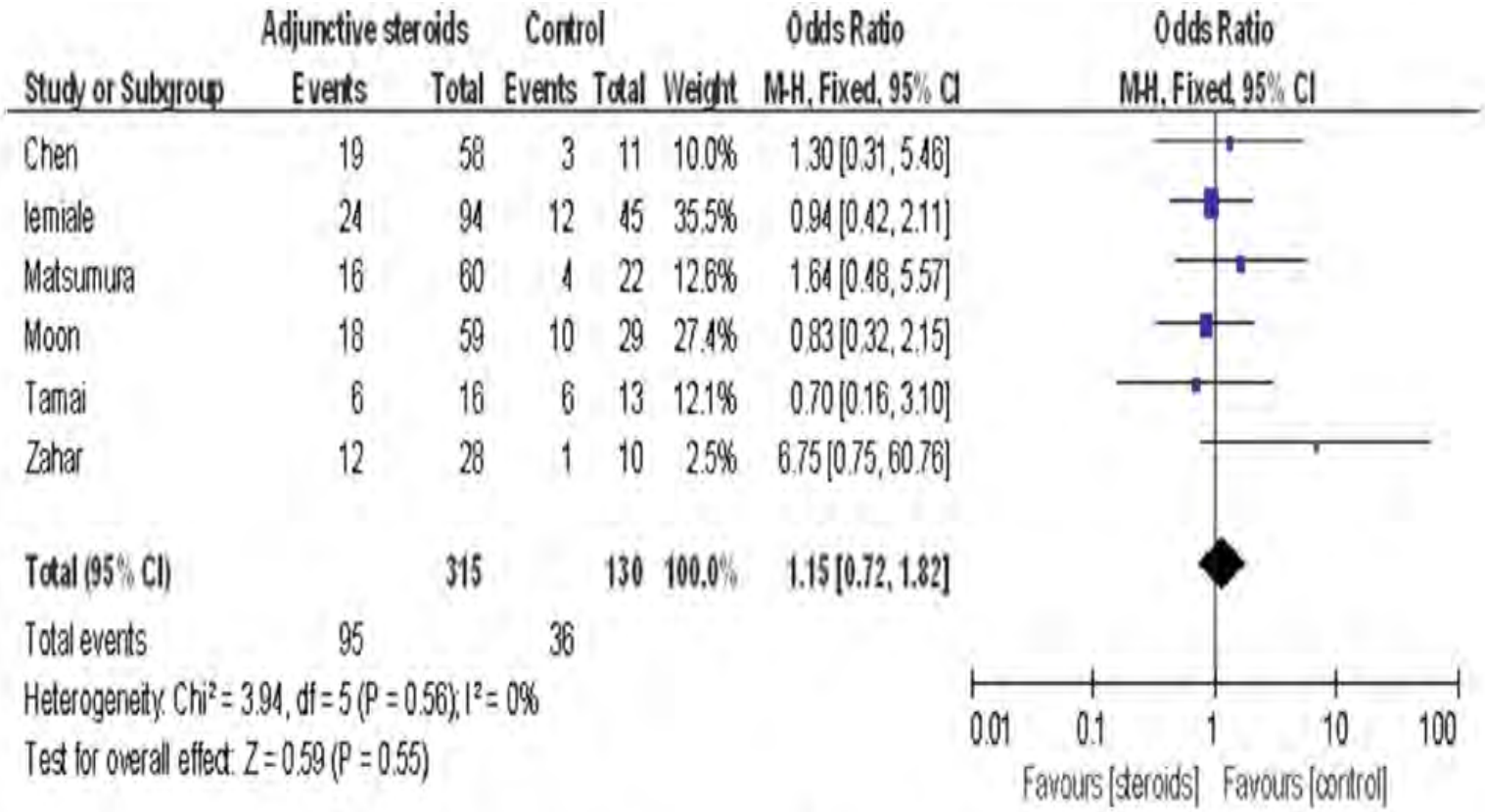

Figure 3: Association between adjuvant steroids and mortality.

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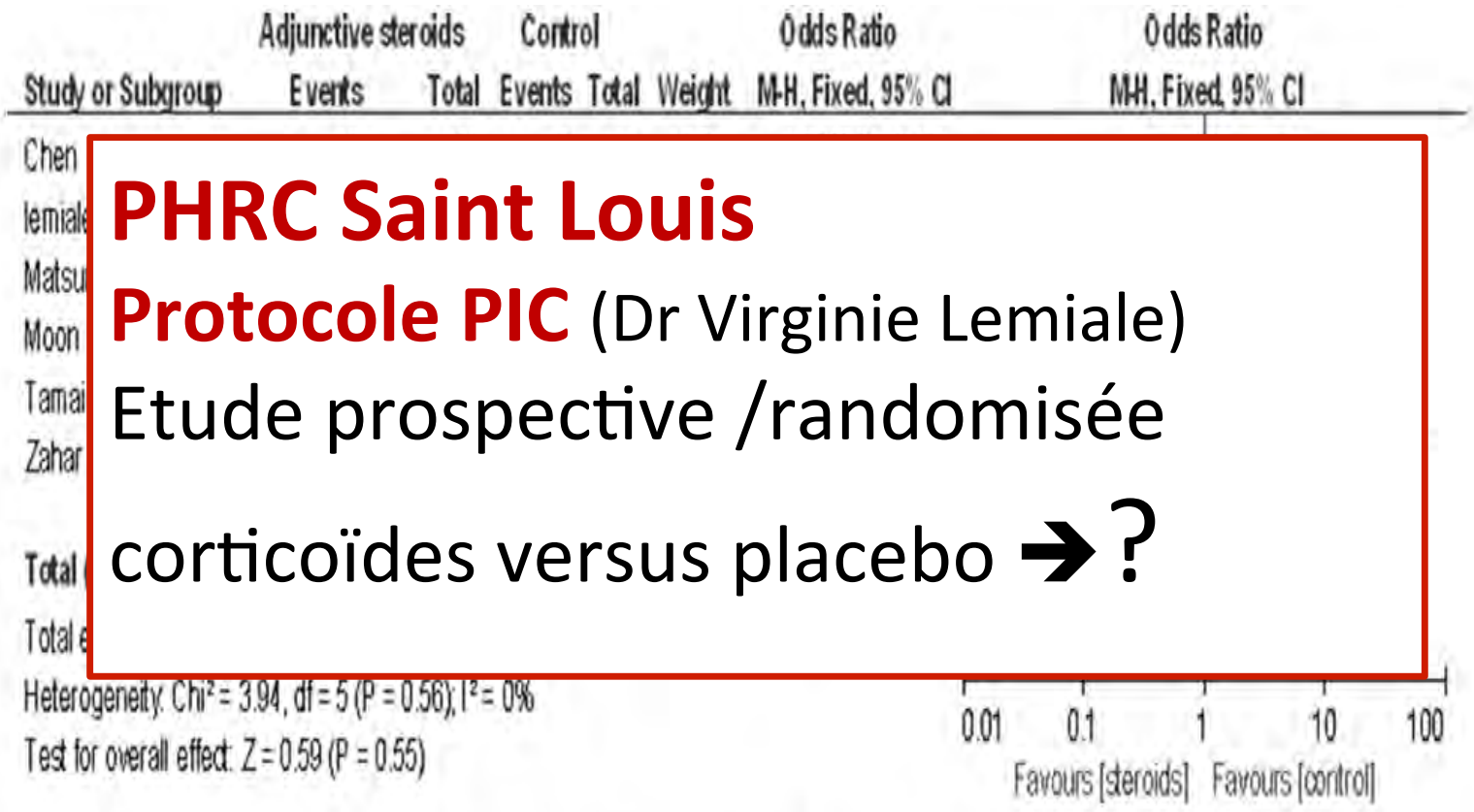

PHRC Saint Louis

Protocole PIC (Dr Virginie Lemiale)

Etude prospective /randomisée

corticoïdes versus placebo ➔ ?

Figure 3: Association between adjuvant steroids and mortality.

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 42), pp: 71946-71953

Research Paper

Diagnosis of *Pneumocystis jirovecii* pneumonia with serum cell-free DNA in non-HIV-infected immunocompromised patients

Dong Wang[1,*], Yang Hu[1,*], Ting Li[1], Heng-Mo Rong[1] and Zhao-Hui Tong[1]

[1]Department of Respiratory Medicine and Critical Care Medicine, Beijing Institute of Respiratory Medicine and Beijing Chao-Yang Hospital, Capital Medical University, Beijing, 100020, China

[*]These authors contributed equally to this work

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Keywords: *cell-free DNA, immunocompromised patients, Pneumocystis jirovecii, polymerase chain reaction, serum*

Received: *March 29, 2017* ***Accepted:*** *May 08, 2017* ***Published:*** *May 20, 2017*

72 patients (35 PCP/36 non PCP)

Détection cfADN (cell free ADN) dans le sérum

Sensibilité = **68.3%**

Spé = 97.2%

VPP = 96%

VPN = 76%

Infections fongiques

Résistance

Changes in in vitro susceptibility patterns of *Aspergillus* to triazoles and correlation with aspergillosis outcome in a tertiary care cancer center (1999-2015)

IDSA Infectious Diseases Society of America *2017*

Sang Taek Heo#,[1, 7] Alexander M. Tatara#,[1, 5] Cristina Jiménez-Ortigosa,[6] Ying Jiang,[1] Russell E Lewis,[1*], Jeffrey Tarrand,[2] Frank Tverdek,[3] Nathaniel D. Albert,[1] Paul E. Verweij,[4] Jacques F Meis,[4] Antonios G. Mikos,[5] David S. Perlin,[6] Dimitrios P. Kontoyiannis[1]

Recueil souche aspergillus (prélèvements respiratoires)
Objectifs = Evaluation modification de résistance entre 1999-2002 (**avant vorico et posa**) et 2003-2015
Retrospective (cas =Aspergillus souche résistante **/ témoin** = A. souche sauvage)

➔ **Corrélation mortalité à J42**
➔ **FDR de résistance**

Aspergillus

Résistance

Changes in in vitro susceptibility patterns of *Aspergillus* to triazoles and correlation with aspergillosis outcome in a tertiary care cancer center (1999-2015)

Résultats

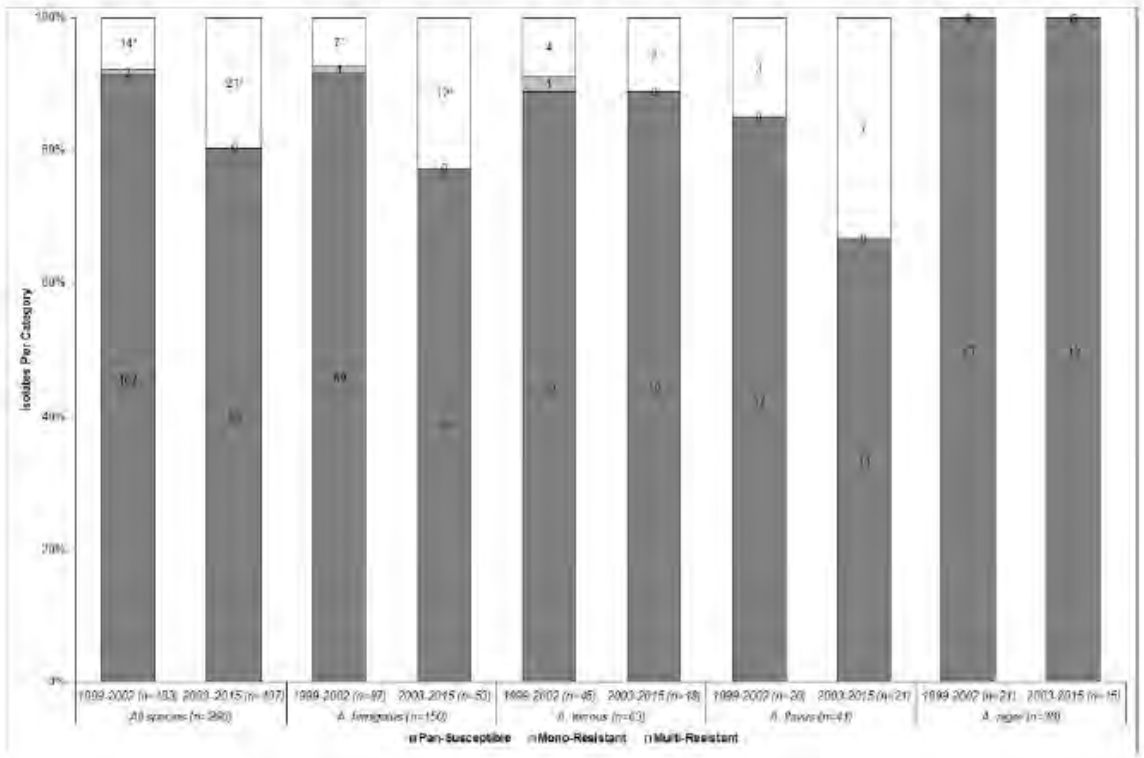
290 échantillons aspergillus
37 (13%) résistant

Bas niveau de résistance
(CMI<8mg/L)

Taux de résistance + élevé dans la deuxième période

Pas de polymorphisme des gènes cyp51A erg3C erg1

Figure 1



Aspergillus

Résistance

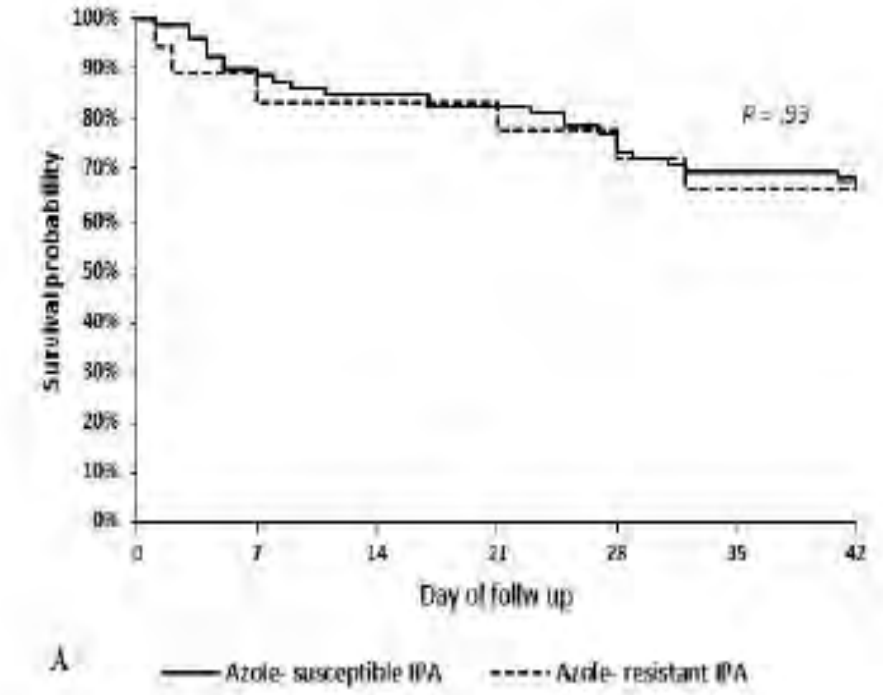
Changes in in vitro susceptibility patterns of *Aspergillus* to triazoles and correlation with aspergillosis outcome in a tertiary care cancer center (1999-2015)

Résultats

Pas de corrélation

entre mortalité à J42 et la résistance

Figure 2



Aspergillus

Résistance

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Résultats → FDR de résistance

Table 3. Independent risk factors for invasive pulmonary aspergillosis caused by aspergilli with a non-wild type azole MIC

Predictor	OR (95% CI)	*P* value
Asian race	20.9 (2.5 – 173.5)	.0048
Culture specimen -BAL fluid	4.4 (1.03 – 18.6)	.046
Previous azole exposure history[a]	9.6 (1.9 – 48.5)	.0063

Aspergillus

Résistance

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Infections fongiques

Traitement

ECIL-6 guidelines for the treatment of invasive candidiasis, aspergillosis and mucormycosis in leukemia and hematopoietic stem cell transplant patients

Frederic Tissot,[1] Samir Agrawal,[2] Livio Pagano,[3] Georgios Petrikkos,[4] Andreas H. Groll,[5] Anna Skiada,[6] Cornelia Lass-Flörl,[7] Thierry Calandra,[1] Claudio Viscoli[8] and Raoul Herbrecht[9]

Haematologica 2017
Volume 102(3):433-444

ECIL 6 guidelines 1ère ligne API

Isavuconazole

Table 7. ECIL-6 recommendations for first-line treatment of invasive aspergillosis.

	Grade	Comments
Voriconazole[a]	A I	Daily dose: 2x6 mg/kg on day 1 then 2x4 mg/kg (initiation with oral therapy: C III)
Isavuconazole	A I	As effective as voriconazole and better tolerated
Liposomal amphotericin B	B I	Daily dose: 3 mg/kg
Amphotericin B lipid complex	B II	Daily dose: 5 mg/kg
Amphotericin B colloidal dispersion	C I	Not more effective than d-AmB but less nephrotoxic
Caspofungin	C II	
Itraconazole	C III	
Combination voriconazole[a] + anidulafungin	C I	
Other combinations	C III	
Recommendation against use Amphotericin B deoxycholate	A I	Less effective and more toxic

[a]Monitoring of serum levels is indicated. In the absence of sufficient data for first-line monotherapy, anidulafungin, micafungin and posaconazole have not been graded.

Infections fongiques

Clinical Infectious Diseases

MAJOR ARTICLE

Pharmacodynamics of Isavuconazole for Invasive Mold Disease: Role of Galactomannan for Real-Time Monitoring of Therapeutic Response

Laura L. Kovanda,[1,2] Ruwanthi Kolamunnage-Dona,[3] Michael Neely,[4] Johan Maertens,[5] Misun Lee,[2] and William W. Hope[1]

[1]Antimicrobial Pharmacodynamics and Therapeutics, Department of Molecular and Clinical Pharmacology, Institute of Translational Medicine, University of Liverpool, United Kingdom; [2]Astellas Pharma Global Development, Inc, Northbrook, Illinois; [3]Department of Biostatistics, Institute of Translational Medicine, University of Liverpool, United Kingdom; [4]Laboratory of Applied Pharmacokinetics and Bioinformatics, Saban Research Institute, and Division of Pediatric Infectious Diseases, Children's Hospital Los Angeles, University of Southern California; and [5]Universitaire Ziekenhuizen, Leuven, Belgium

78 patients sous Isavuconazole analyses pharmacologiques

A J 7 augmentation de> 0,25 unités Ag augmentait significativement le risque de décès (HR, **9,766,** intervalle de confiance à 95% [IC], 4,356-21,9, p <0,0001)

Infections fongiques

Imagerie

The Reversed Halo Sign: Pathognomonic Pattern of Pulmonary Mucormycosis in Leukemic Patients With Neutropenia?

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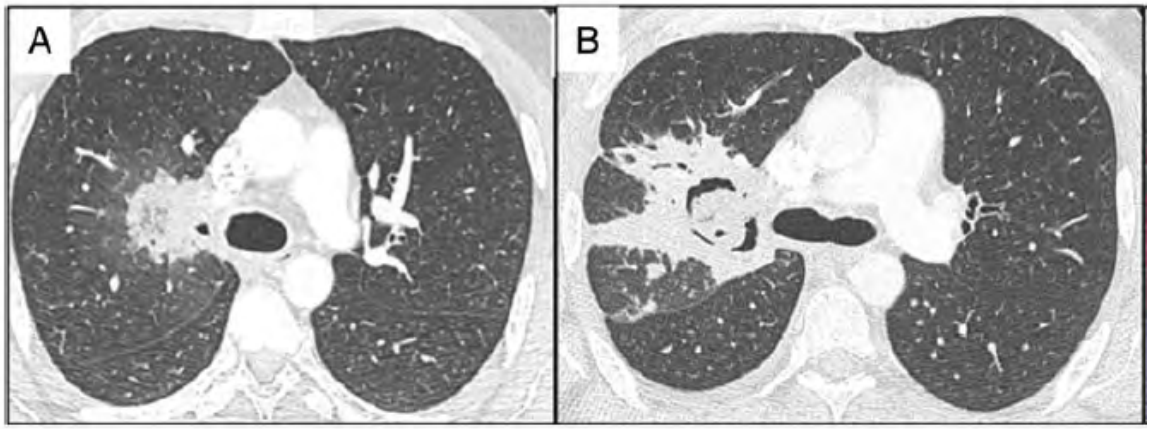
Clinical Infectious Diseases 2014



➔ Leucémie + **neutropénie**
Signe halo inversé
très évocateur mucormycose

➔ Traitement

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ORIGINAL ARTICLE

Prevalence of the reversed halo sign in neutropenic patients compared with non-neutropenic patients: Data from a single-centre study involving 27 patients with pulmonary mucormycosis (2003-2016)

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Mycoses. 2017;1–8.

Etude rétrospective
N=27 patients

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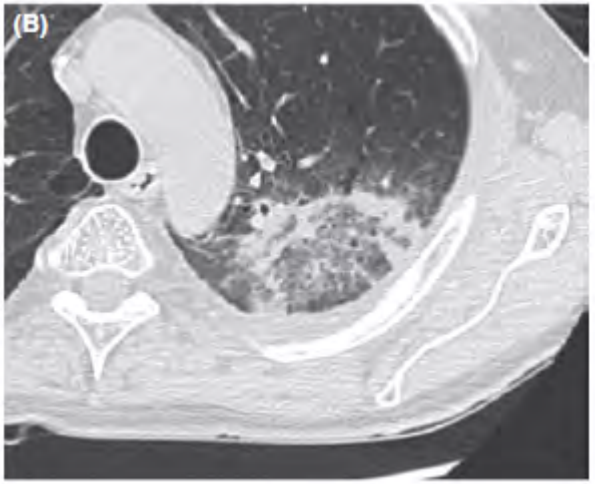
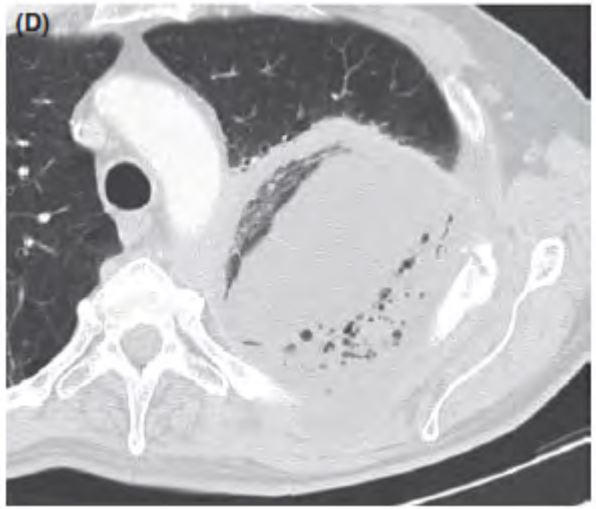
TABLE 3 Radiologic findings

Radiologic findings	Group 1 (neutropenic) (n=patients)	Group 2 (not neutropenic) (n=patients)	*P* value
Number	14	13	NA
Reversed halo sign (RHS)	11 **79%**	4 **31%**	.021
Reticulations inside ground-glass opacity (in case of RHS)	10	3	.476
Halo sign	2	3	.648
Consolidation	5	4	1
Ground-glass opacity	7	5	.704
Cavitation	4	3	1
Pleural effusion	5	5	1
Nodules	7	9	.44
Micronodules	2	4	.385
Bronchial syndrome	5	2	.385
Parietal location	2	1	.481
Extrathoracic locations	8	5	.449





CHEST

Serial assessment of pulmonary lesion volume by computed tomography allows survival prediction in invasive pulmonary aspergillosis

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12 January 2017

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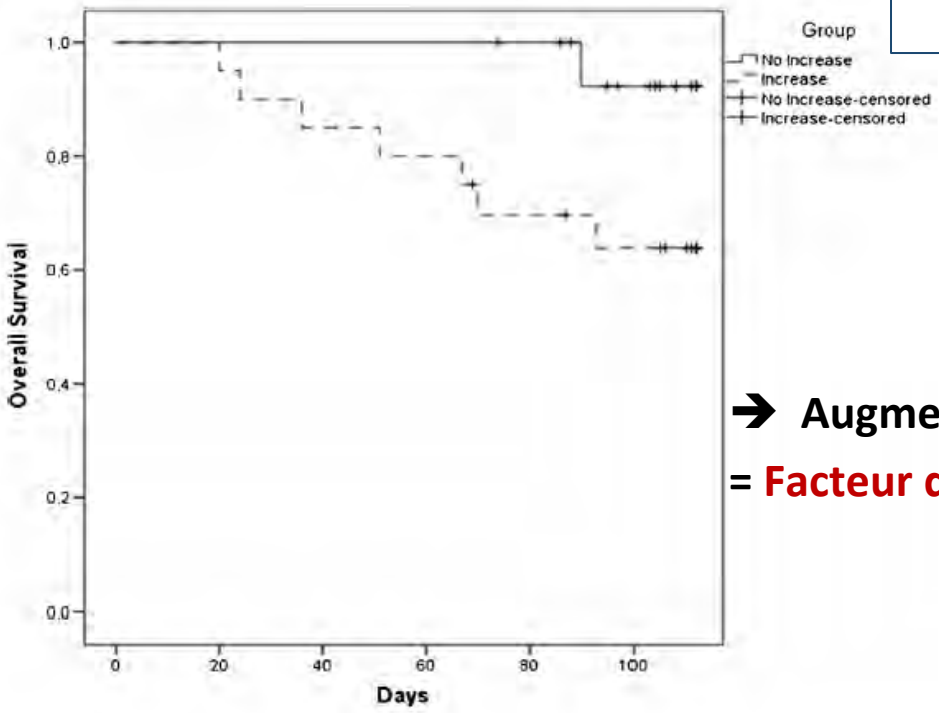
Fig. 2 Overall survival using any increase of lesion volume after day 7 as cut-off ($p = 0{,}039$, log-rank test)



➔ **Augmentation volume entre J7- J 14**

= Facteur de mauvais pronostic

Infections virales

Clinical Significance of Human Coronavirus in Bronchoalveolar Lavage Samples from Hematopoietic Cell Transplantation Recipients and Patients with Hematologic Malignancies

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IDSA Infectious Diseases Society of America

2017

Etude rétrospective

➔ Décrire **caractéristiques cliniques/pronostiques** des patients avec une **PCR + coronavirus dans le LBA**

➔ **Evaluer les différences de taux de mortalité entre différents virus**

Clinical Significance of Human Coronavirus in Bronchoalveolar Lavage Samples from Hematopoietic Cell Transplantation Recipients and Patients with Hematologic Malignancies

Résultats 2006-2016

35 patients (37 épisodes) avec infection respiratoire basse à coronavirus

- **60% (n=21) nécessitaient de l'O2 au diagnostic**
- **54% (n=19) DCD dans les 90 jours du diagnostic**
- Co pathogène 57% des cas (12 virus 10 fongique 8 bactéries)

Clinical Significance of Human Coronavirus in Bronchoalveolar Lavage Samples from Hematopoietic Cell Transplantation Recipients and Patients with Hematologic Malignancies

IDSA Infectious Diseases Society of America

Table 6. Multivariable Cox Regression Analysis for Overall Mortality by Day 90 after Diagnosis of Lower Respiratory Tract Disease (n = 286)

Covariates	Categories	Adjusted hazard ratio (95% CI)	P-value
Respiratory virus	Respiratory syncytial virus	1	
	Parainfluenza	1.13 (0.77-1.67)	0.52
	Influenza	0.88 (0.47-1.66)	0.70
	Human coronavirus	1.34 (0.66-2.71)	0.41

➔**La mortalité associée aux infections basses à coronavirus était similaire à celle du VRS**

Infections virales

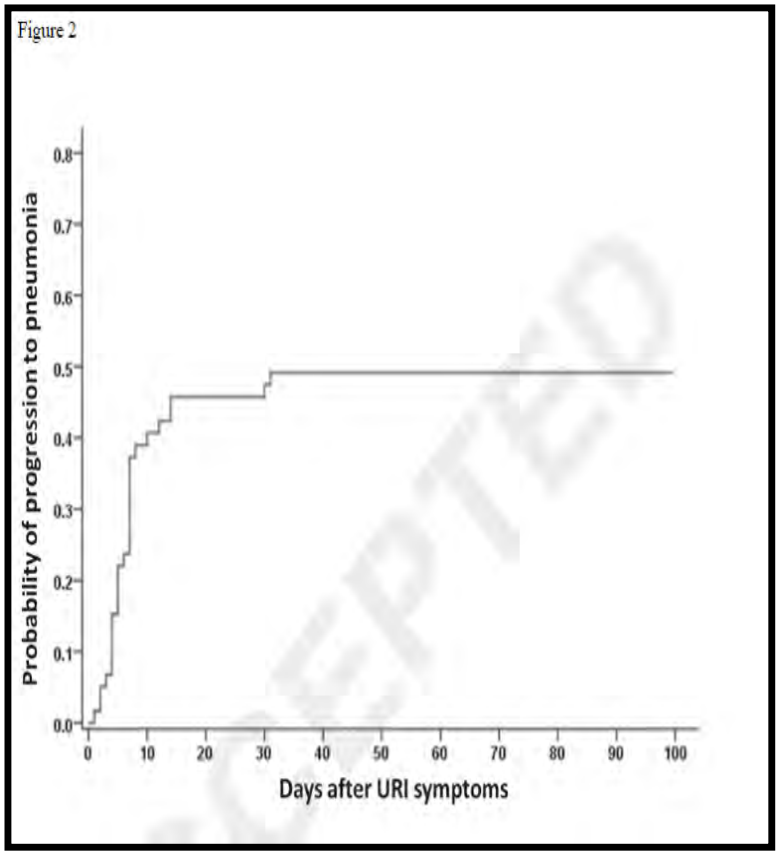
Human Metapneumovirus Infection: Pneumonia Risk Factors in Solid Organ Transplantation Patients and CT findings

Hyun Jung Koo, MD, PhD[1], Han Na Lee, MD[2], Sang Ho Choi, MD, PhD[3], Heungsup Sung, MD, PhD[4], Sang Young Oh, MD, PhD[1], So Youn Shin, MD, PhD[5], Hwa Jung Kim, MD, PhD[6] and Kyung-Hyun Do, MD, PhD[1*]

Transplantation Publish Ahead of Print
DOI: 10.1097/TP.0000000000001965

Etude rétrospective 01/2010 et 02/2016
Caractéristiques cliniques scanographiques et les FDR de pneumonie à métapneumovirus

Human Metapneumovirus Infection: Pneumonia Risk Factors in Solid Organ Transplantation Patients and CT findings



Résultats

59 transplantés

30 (50,8%) infections hautes

29 **(49,2%) progression vers une infection basse**

Co infection 39% (23/59)

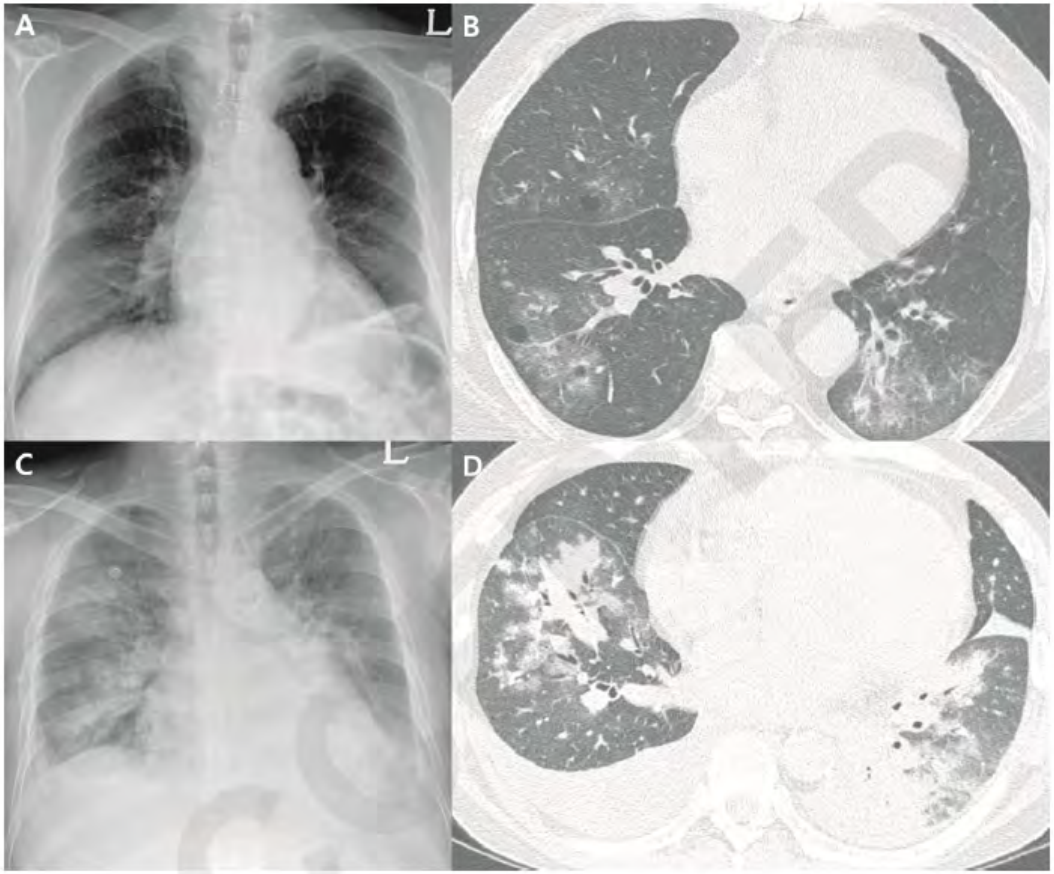
Human Metapneumovirus Infection: Pneumonia Risk Factors in Solid Organ Transplantation Patients and CT findings

Table 4. Bivariate analysis of risk factors for human metapneumovirus pneumonia in patients with solid organ transplantation (n = 59)

Variables	HR	95% CI	*P* value
Initial CRP at admission			
0–3 mg/dL	1.00		
>3 mg/dL	1.93	0.75–1.97	0.18
>10 mg/dL	2.93	1.19–7.21	0.02
Lymphocyte count at diagnosis			
>0.7 × 10^3/μL	1.00		
≤0.7 × 10^3/μL	2.24	1.04–4.85	0.04

Pas de caractéristique clinique

Human Metapneumovirus Infection: Pneumonia Risk Factors in Solid Organ Transplantation Patients and CT findings



86% atteinte bilatérale

Les lésions + fréquentes

- Micronodules centrolobulaires 83%

- Condensation alvéolaire 55%

- Verre dépoli 75%

ECIL 7 prophylaxie CMV allogreffe

Infections virales

Drug	Grading	References	Comment
Aciclovir	CI	Prentice, *Lancet* 1994 Milano, *Blood 2011*	Less efficient than valaciclovir
Valaciclovir	BI	Ljungman, *Blood* 2002 Winston *CID* 2003 Milano, Blood 2011	Association with preemptive strategy
Ganciclovir/ valganciclovir	CI CIIh	Winston, *Ann Intern Med* 1993 Goodrich , *Ann Intern Med* 1993 Montesinos, *BBMT 2009*	 Cord blood SCT
Foscarnet	DIIu	Ordemann, *Ann Hematol* 2000 Bregante et al, *BMT* 2000	
Letermovir	AI (provisional)	Ljungman, *EBMT 2017*	

Infection/inflammation

JAMA | Original Investigation

Effect of Azithromycin on Airflow Decline–Free Survival After Allogeneic Hematopoietic Stem Cell Transplant
The ALLOZITHRO Randomized Clinical Trial

Anne Bergeron, MD, PhD; Sylvie Chevret, MD, PhD; Angela Granata, MD; Patrice Chevallier, MD, PhD; Laure Vincent, MD; Anne Huynh, MD; Reza Tabrizi, MD; Hélène Labussiere-Wallet, MD; Marc Bernard, MD; Sylvain Chantepie, MD; Jacques-Olivier Bay, MD, PhD; Anne Thiebaut-Bertrand, MD; Sylvain Thepot, MD, PhD; Nathalie Contentin, MD; Luc-Matthieu Fornecker, MD, PhD; Natacha Maillard, MD; Karine Risso, MD; Ana Berceanu, MD, PhD; Didier Blaise, MD, PhD; Regis Peffault de La Tour, MD, PhD; Jason W. Chien, MD, MSc; Valérie Coiteux, MD; Gérard Socié, MD, PhD; for the ALLOZITHRO Study Investigators

JAMA. 2017;318(6):557-566.

Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomised, double-blind, placebo-controlled trial

Peter G Gibson, Ian A Yang, John W Upham, Paul N Reynolds, Sandra Hodge, Alan L James, Christine Jenkins, Matthew J Peters, Guy B Marks, Melissa Baraket, Heather Powell, Steven L Taylor, Lex E X Leong, Geraint B Rogers, Jodie L Simpson

Lancet 2017; 390: 659–68

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Merci pour votre attention

Pas impact prophylaxie

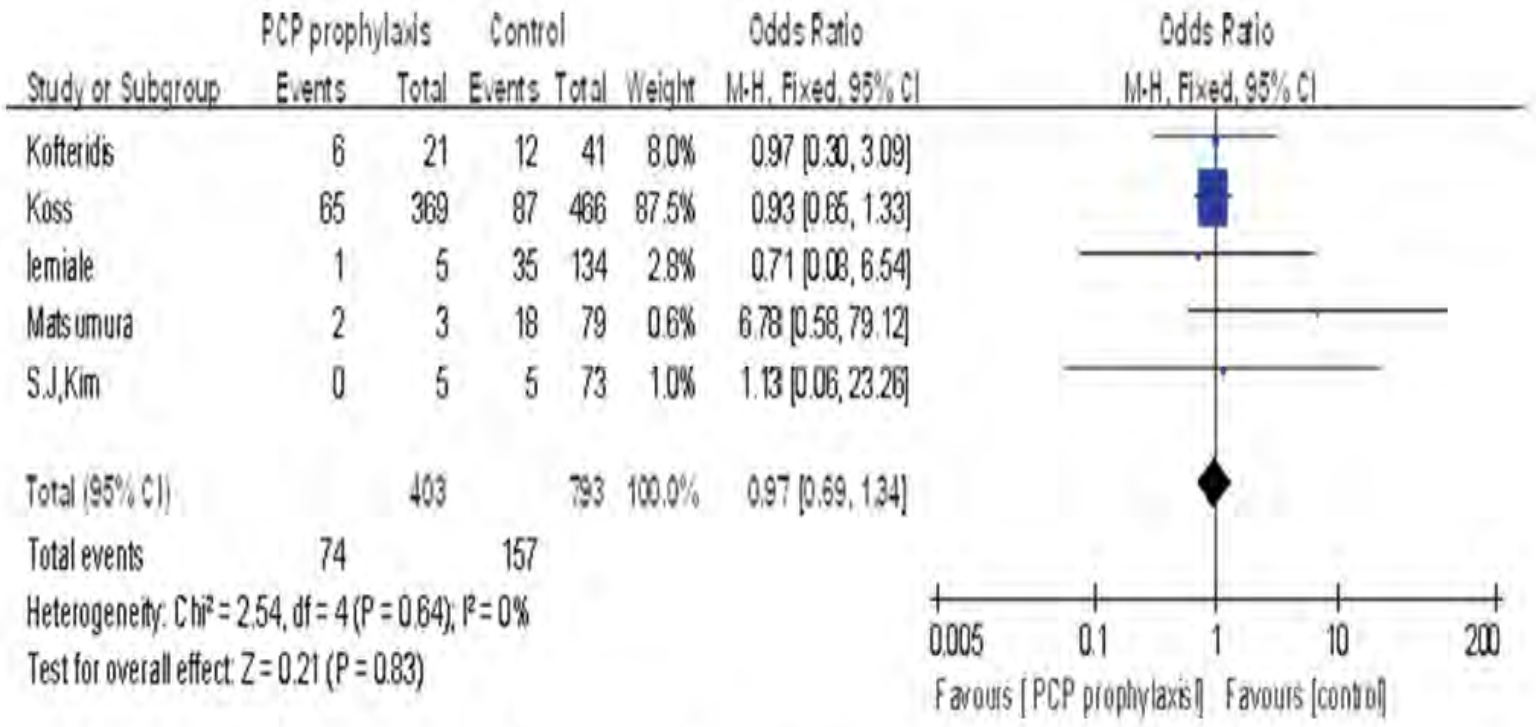

Figure 2: Association between PCP prophylaxis and mortality.