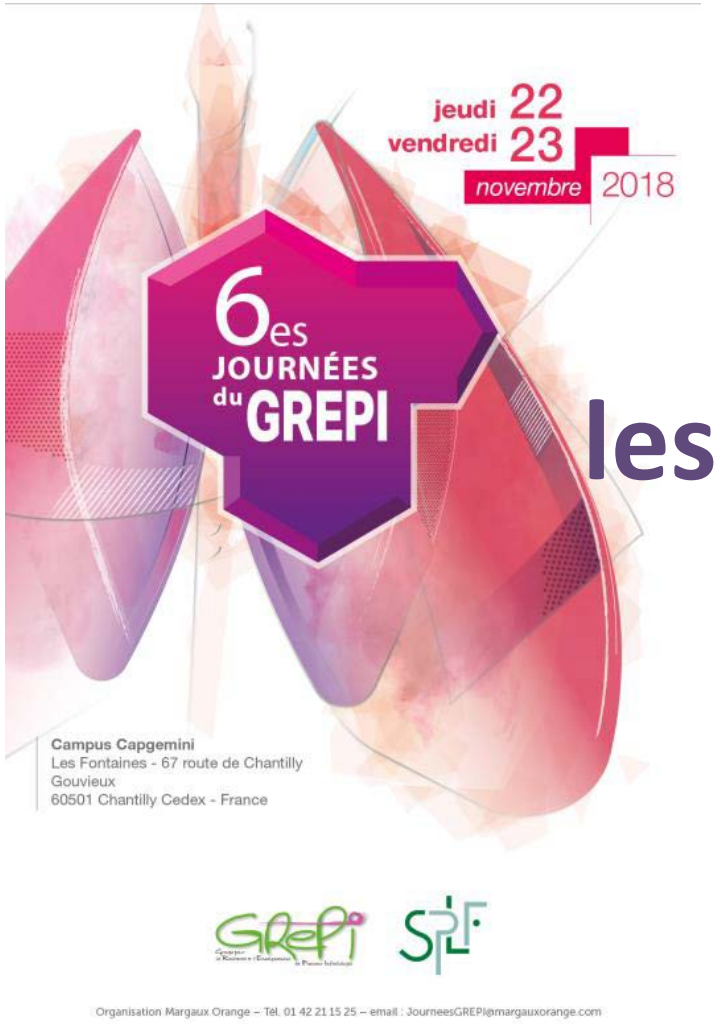


Immunodéprimés les nouveautés de l'année

Dr Adrien Tissot

Service de Pneumologie, CHU Nantes

Prednisone for the Prevention of Paradoxical Tuberculosis-Associated IRIS

Meintjes et al

Délai court entre TTT antituberculeux et ARV / Tx CD4+ bas **= risque de SRI**

mais

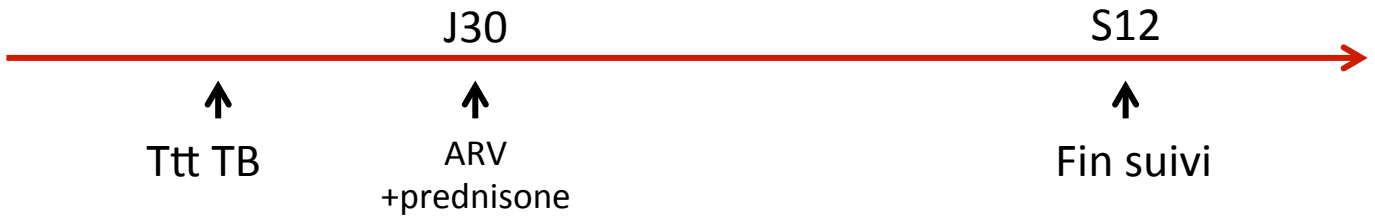
Début ARV précoce (2S) >> début tardif (8S)

Randomisée, double aveugle, contrôlée contre placebo, monocentrique

Inclusions:

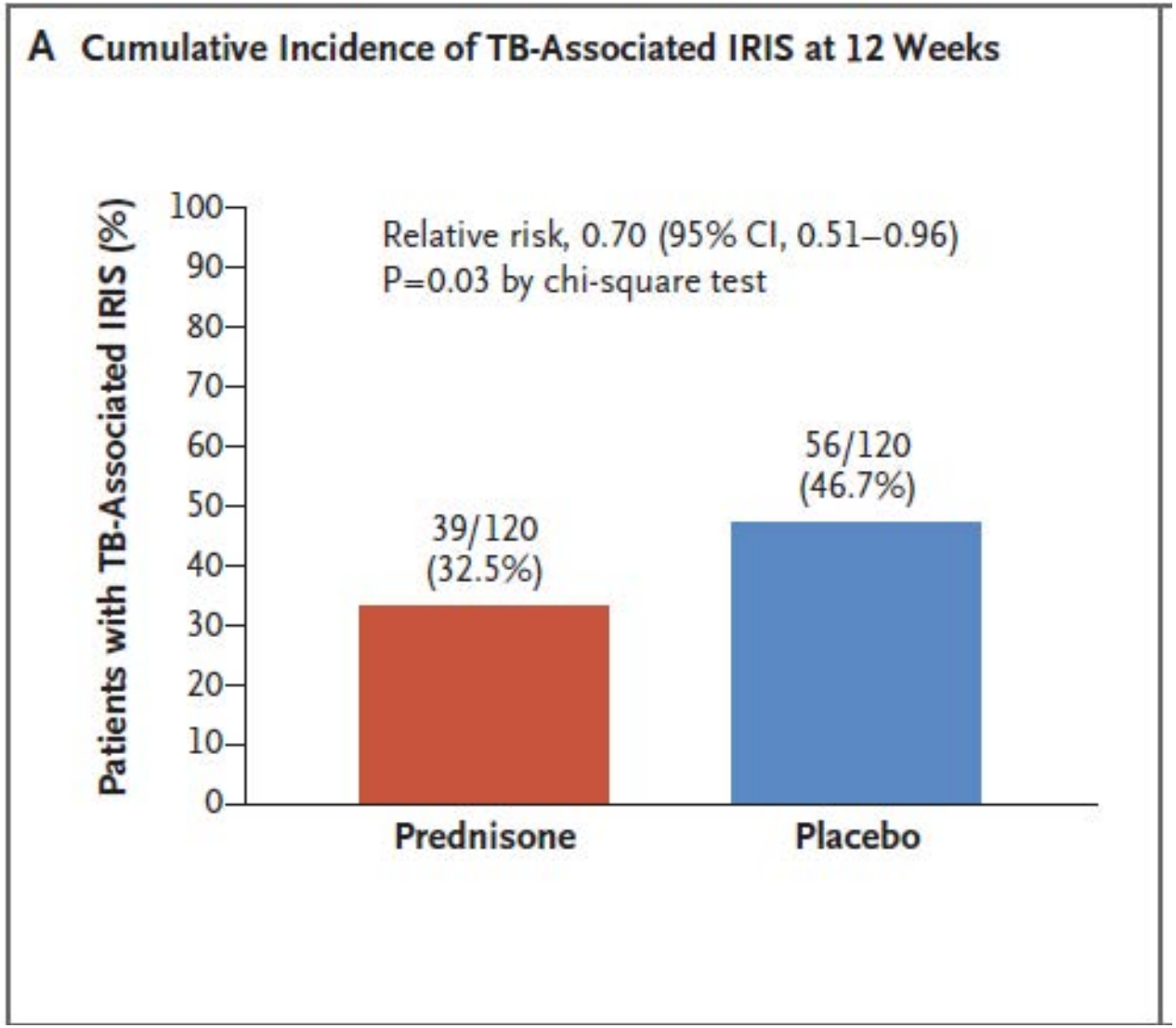
- VIH+ naïf ARV
- CD4 < 100 C/ml
- Tuberculose confirmée, traitement débuté < 30 jours

Prednisone: 40 mg pdt 14 jrs puis 20 mg pdt 14 jrs



Prednisone for the Prevention of Paradoxical Tuberculosis-Associated IRIS

Meintjes et al



Subgroup	Prednisone Group (N=120)	Placebo Group (N=120)	Relative Risk (95% CI)
	no./total no. (%)		
CD4 count at screening			
≤50 cells/μl	28/60 (46.7)	37/62 (59.7)	0.78 (0.56–1.10)
>50 cells/μl	11/60 (18.3)	19/58 (32.8)	0.56 (0.29–1.07)
HIV-1 RNA viral load at screening			
>100,000 copies/ml	36/102 (35.3)	50/99 (50.5)	0.70 (0.50–0.97)
≤100,000 copies/ml	3/17 (17.6)	5/20 (25.0)	0.71 (0.20–2.53)
Microbiologically confirmed TB†	33/86 (38.4)	43/89 (48.3)	0.79 (0.56–1.12)
No rifampin-resistant TB diagnosed after enrollment‡	39/118 (33.1)	55/119 (46.2)	0.72 (0.52–0.99)

Pas de risque augmenté de K ou d'infection sévère

THE LANCET

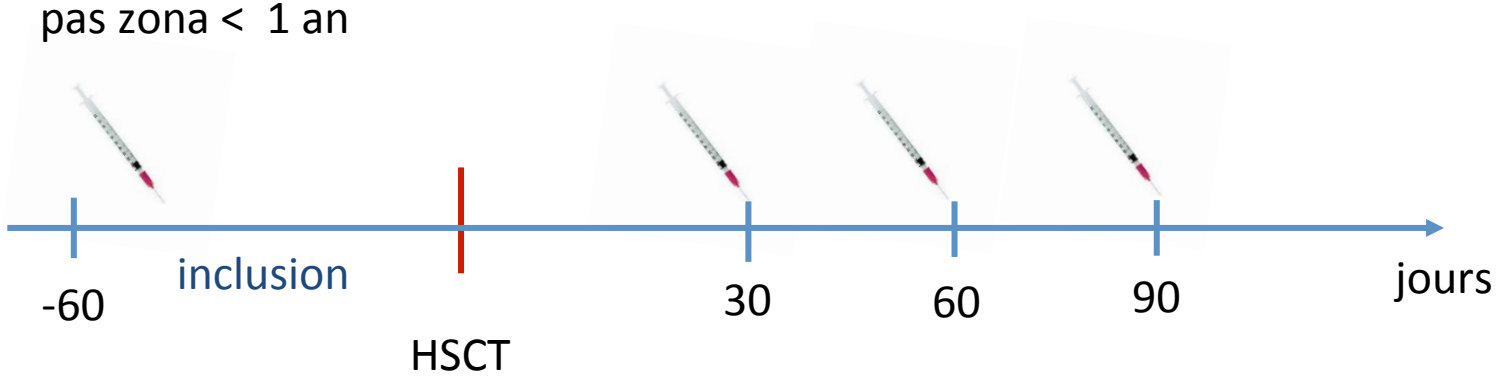
Inactivated varicella zoster vaccine in autologous HSTC recipients: an international, multicentre, randomised, double-blind, placebo-controlled trial

Critères d'inclusions:

> 18 ans

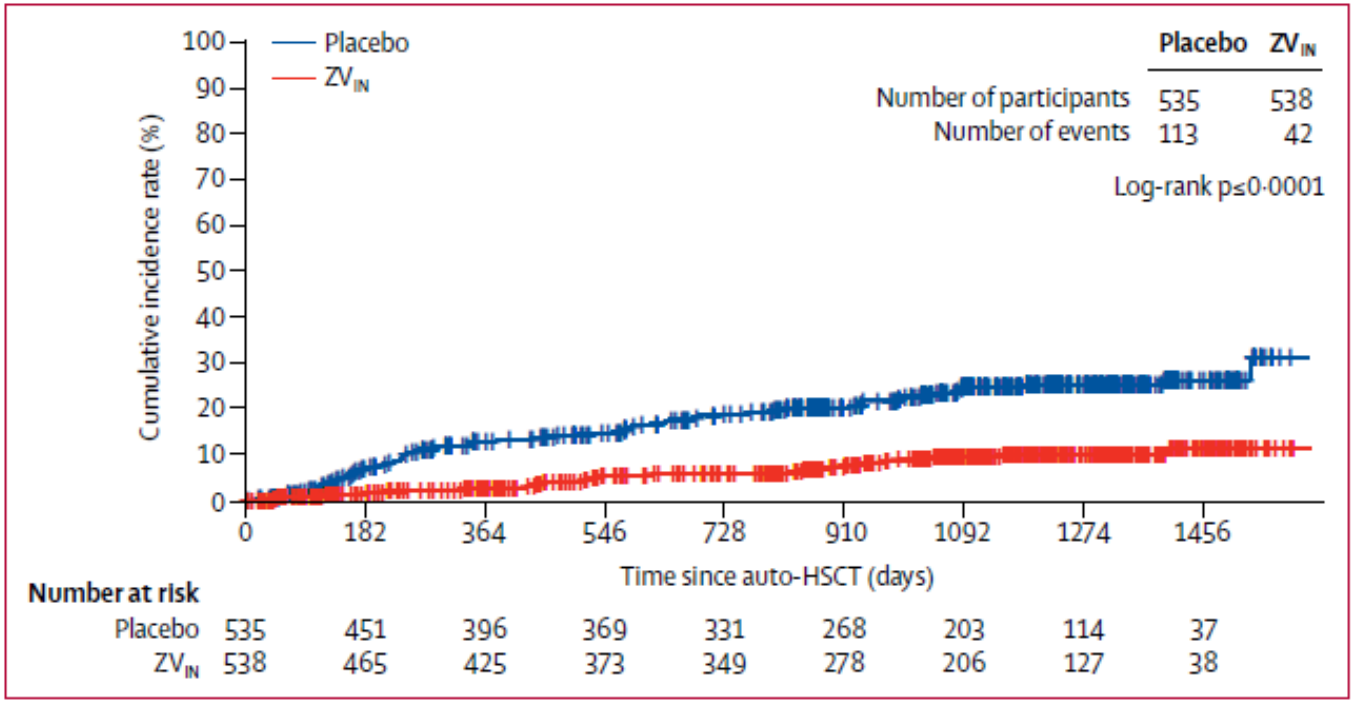
ATCD varicelle ou VZV séro+

pas zona < 1 an



1257 patients randomisés,
726 patients analysés

	Inactivated varicella zoster virus vaccine consistency lot group (n=538)			Placebo group (n=535)			Estimated vaccine efficacy (%; 95% CI)*
	Confirmed participants	Follow-up (person-years)	Incidence (per 1000 person-years)	Confirmed participants	Follow-up (person-years)	Incidence (per 1000 person-years)	
Herpes zoster disease	42 (8%)	1277	32·9	113 (21%)	1230	91·9	63·8% (48·4–74·6)
Moderated-to-severe herpes zoster-associated pain†	19 (4%)	1277	14·9	61 (11%)	1230	49·6	69·5% (49·0–81·8)
Herpes zoster-related complications†	12 (2%)	1277	9·4	44 (8%)	1230	35·8	73·5% (49·8–86·0)
Post-herpetic neuralgia‡	3 (1%)	1277	2·3	18 (3%)	1230	14·6	83·7% (44·6–95·2)



	Inactivated varicella zoster virus vaccine consistency lot		Placebo	
	Participants at each timepoint	Observed response (90% CI)	Participants at each timepoint	Observed response (90% CI)
Interferon-γ ELISPOT				
Baseline				
GMC	128	30·9 (23·7–40·2)	129	33·6 (26·5–42·7)
28 days after fourth dose				
GMC	102	62·8 (45·8–86·2)	116	10·4 (7·9–13·7)
GMFR	98	2·95 (2·11–4·12)	114	0·52 (0·39–0·70)
1 year after fourth dose				
GMC	84	73·5 (50·9–106·3)	89	20·2 (14·9–27·4)
GMFR	81	3·91 (2·71–5·65)	87	0·95 (0·66–1·36)
2 years after fourth dose				
GMC	58	102·0 (64·6–161·2)	70	33·5 (22·7–49·4)
GMFR	53	6·12 (3·67–10·20)	70	1·80 (1·14–2·85)

Vaccination en Transplantation

A Double-Blind, Randomized Trial of High-Dose vs Standard-Dose Influenza Vaccine in Adult Solid-Organ Transplant Recipients

Vaccins inactivés standard-dose: 15µg de 3 HG des 3-4 souches circulantes
Vaccins high-dose: 60µg

172 patients randomisés, saison 2016-2017
A/California/7/2009(H1N1)pdm09, A/Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008

Analyse:
- 84 patients HD
- 77 patients SD

Type of transplant (%)	
Kidney	67 (39.0)
Liver	38 (22.1)
Lung	25 (14.5)
Heart	23 (13.3)
Combined	19 (11.0)

Table 2. Seroconversion to High-Dose vs Standard-Dose Influenza Vaccine, per-protocol Population

	Standard Dose (n = 77)	High Dose (n=84)	*P* Value
Seroconversion (%)			
A/H1N1	16 (20.8)	34 (40.5)	.007
A/H3N2	25 (32.5)	48 (57.1)	.002
B/Brisbane	32 (41.6)	49 (58.3)	.033
B/Phuket[a]	11 (14.3)	28 (33.3)	.005
Seroprotection post-vaccine (%)			
A/H1N1	64 (83.1)	70 (83.3)	.97
A/H3N2	57 (74.0)	67 (79.8)	.39
B/Brisbane	70 (90.9)	79 (94.0)	.55
B/Phuket[a]	51 (66.2)	67 (79.8)	.053

- Facteurs affectant la séroconversion:
  vaccin HD
  ttt MMF < 2gr/jr

Vaccination en Transplantation

A 5-Year Prospective Multicenter Evaluation of Influenza Infection in Transplant Recipients

Kumar et al

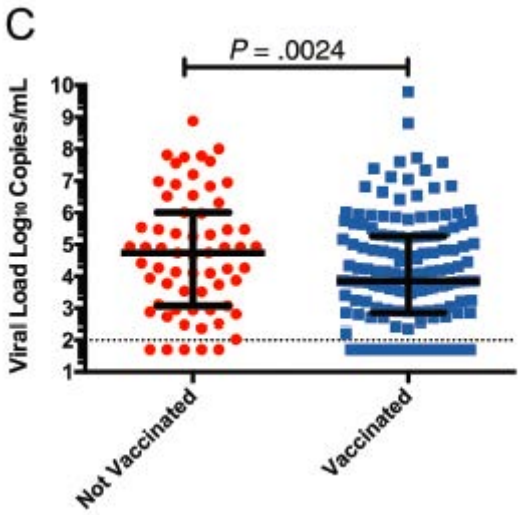
- Etude multicentrique prospective observationnelle, saisons 2010-2015
- SOT et HSCT
- Dg confirmé par prélèvement nasopharyngé ou LBA

Type of transplant	
SOT	477 (77.4)
Kidney	207 (33.6)
Liver	63 (10.2)
Heart	57 (9.3)
Lung	116 (18.8)
Combined	34 (5.5)
HSCT	139 (22.6)
Allogeneic	91 (14.8)
Autologous	48 (7.8)

Table 2. Outcomes of Patients With Influenza

Outcome	All Patients (N = 616)
LRTI	134/606 (22.1)
Hospitalization[a]	373/561 (66.5)
Admission to ICU	68/616 (11.0)
Mechanical ventilation	49/616 (8.0)
Death (all cause at 30 d)	18/615 (2.9)
Death (all cause at 180 d)	42/615 (6.8)

Vaccination dans la saison
+
Ttt antiviral précoce
=
Facteurs protecteurs pour pneumopathie et Admission USI



CMV

Letermovir Prophylaxis for Cytomegalovirus in Hematopoietic Cell Transplantation

Marty et al

Essai phase III, randomisé, double aveugle
CMV séropositif/virémie -
Letermovir/Placebo, IV/PO

480 mg / jr (ou 240 mg/jr si ciclo) pdt 3 mois

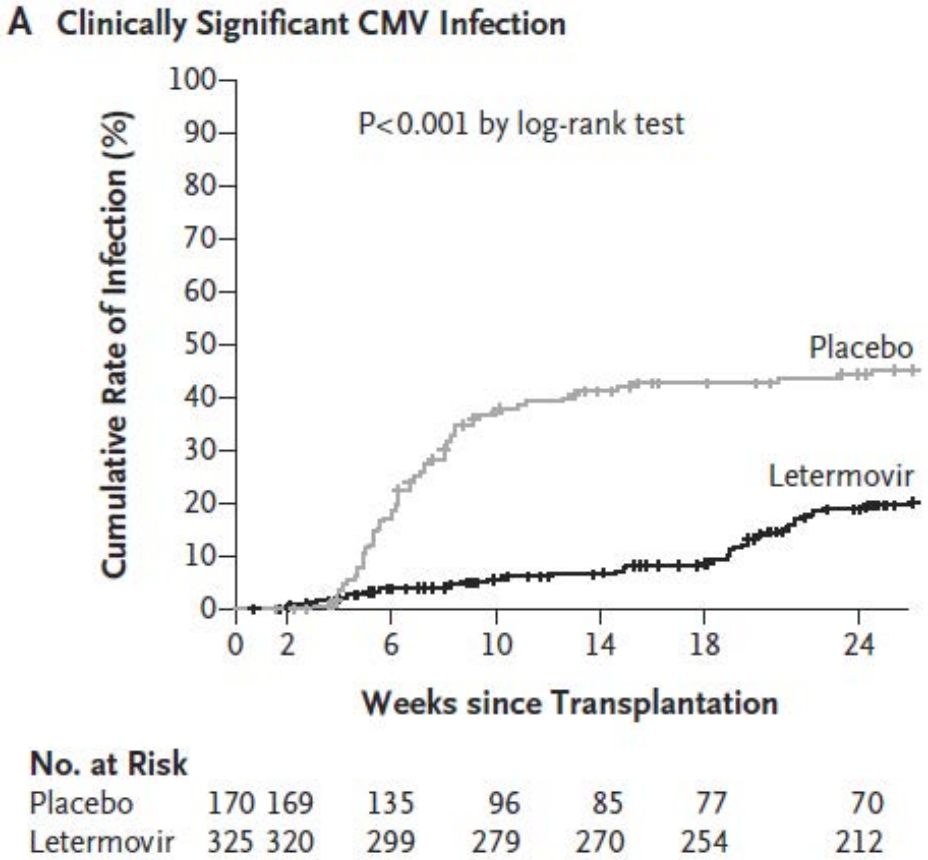
Surveillance PCR CMV, si positif → ttt selon pratique locale

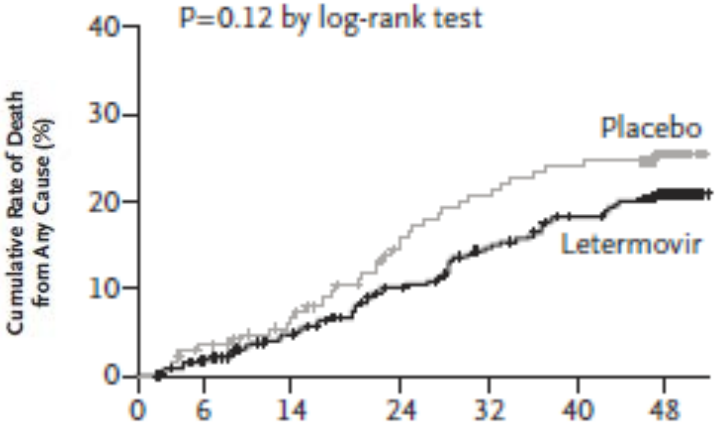
Critère d'évaluation principal:

% patients avec infection CMV cliniquement significative à 6 mois

Letermovir Prophylaxis for Cytomegalovirus in Hematopoietic Cell Transplantation

Marty et al

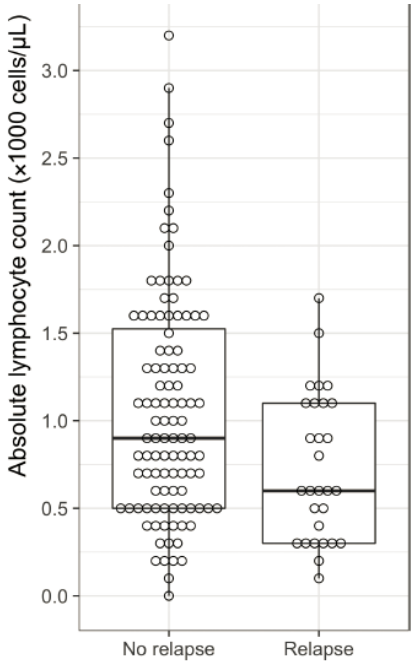


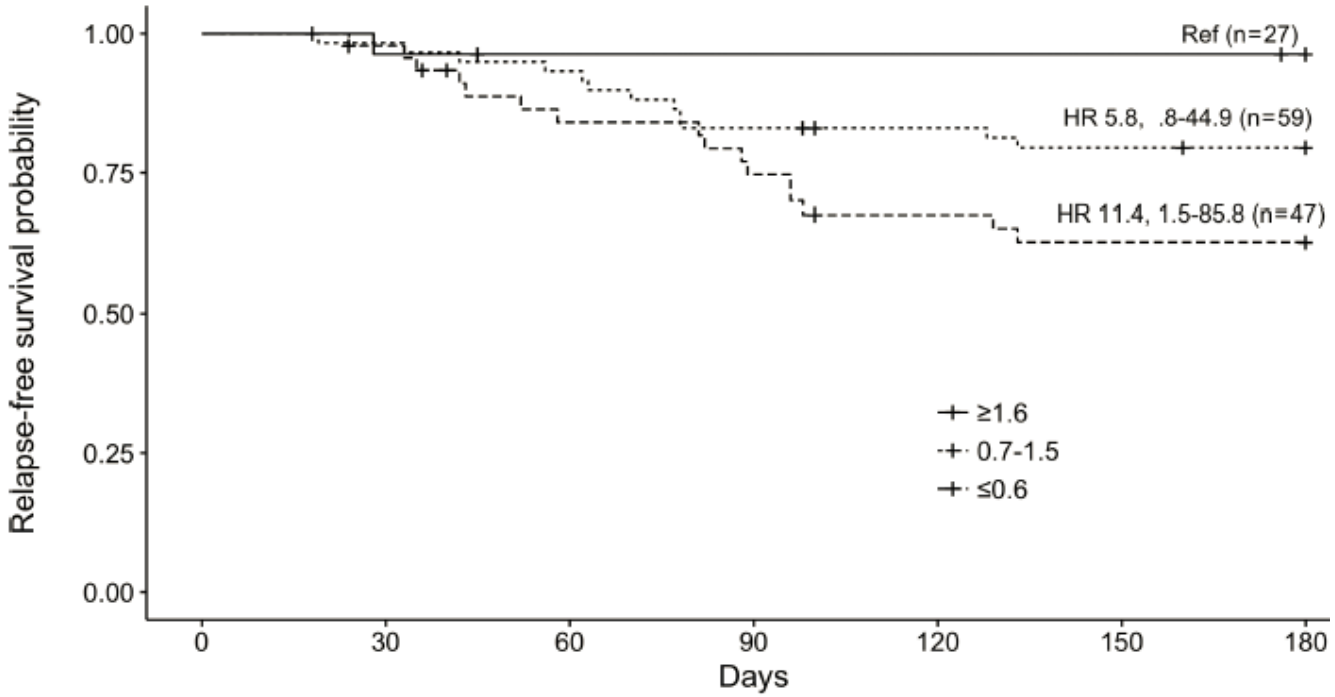


CMV

Absolute Lymphocyte Count: A Predictor of Recurrent CMV Disease in SOT

Gardiner et al





CMV

IDSA
Infectious Diseases Society of America

Absolute Lymphocyte Count:
A Predictor of Recurrent CMV Disease in SOT

Gardiner et al

Table 2. Results of Multivariable Analysis Demonstrating Adjusted Hazard Ratios for Relapse of Cytomegalovirus Infection

Variable	Adjusted HR (95% CI)	*P* Value
Antilymphocyte therapy	2.51 (1.21–5.20)	.01
Recipient CMV seronegative	1.89 (.89–4.01)	.10
High peak viral load	2.67 (1.21–5.89)	.02
Decrease in ALC (per 100 cells/μL increment)	1.11 (1.03–1.20)	.009

Risque Aspergillaire en transplantation pulmonaire

The Journal of Heart and Lung Transplantation
The Official Publication of the International Society for Heart and Lung Transplantation

Clinical risk factors for invasive Aspergillosis in LTRs

Aguilar et al

- Etude multicentrique rétrospective internationale
- 900 patients
- Suivi 4 ans

471 patients avec prophylaxie universelle

412 patients avec prophylaxie préemptive/ciblée

Vorico (38%), Itraco (26%), Ampho B inh (36%), …

79 patients ont présenté une aspergillose invasive

115 épisodes

Apparition à 7,7 mois

Clinical risk factors for invasive in LTRs

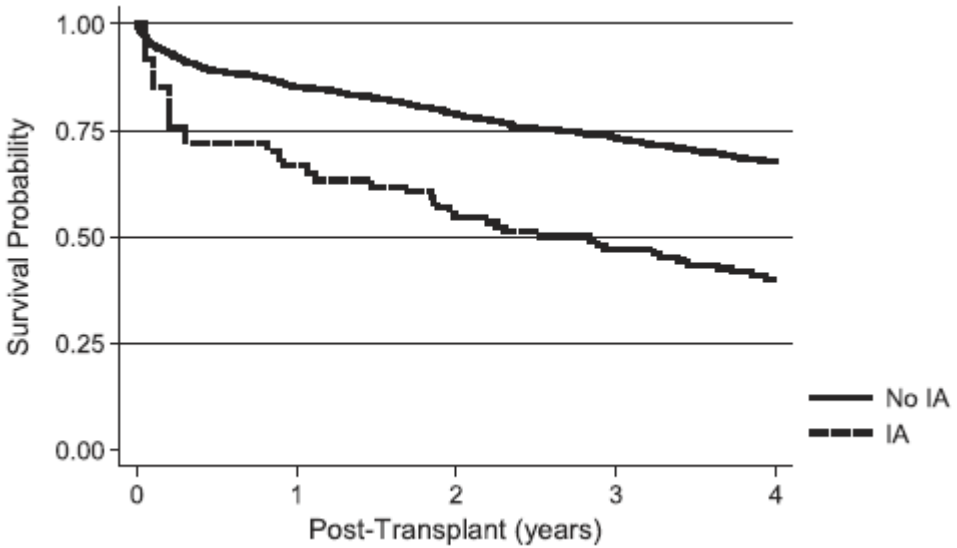
The Journal of Heart and Lung Transplantation
The Official Publication of the International Society for Heart and Lung Transplantation

Analyse univariée:

- T monopulmonaire et fibrose pulmonaire idiopathique
- > 2 épisodes surdosages CNI
- > 4 épisodes rejet aigu cellulaire
- colonisation aspergillaire post T pulmonaire ≤ 1 an

Analyse multivariée:

- T monopulmonaire
- colonisation aspergillaire post TP ≤ 1 an



Risque Aspergillaire en transplantation pulmonaire

The Journal of Heart and Lung Transplantation
The Official Publication of the International Society for Heart and Lung Transplantation

A strategy for prevention of fungal infections in lung transplantation: Role of bronchoalveolar lavage fluid galactomannan and fungal culture

Husain et al

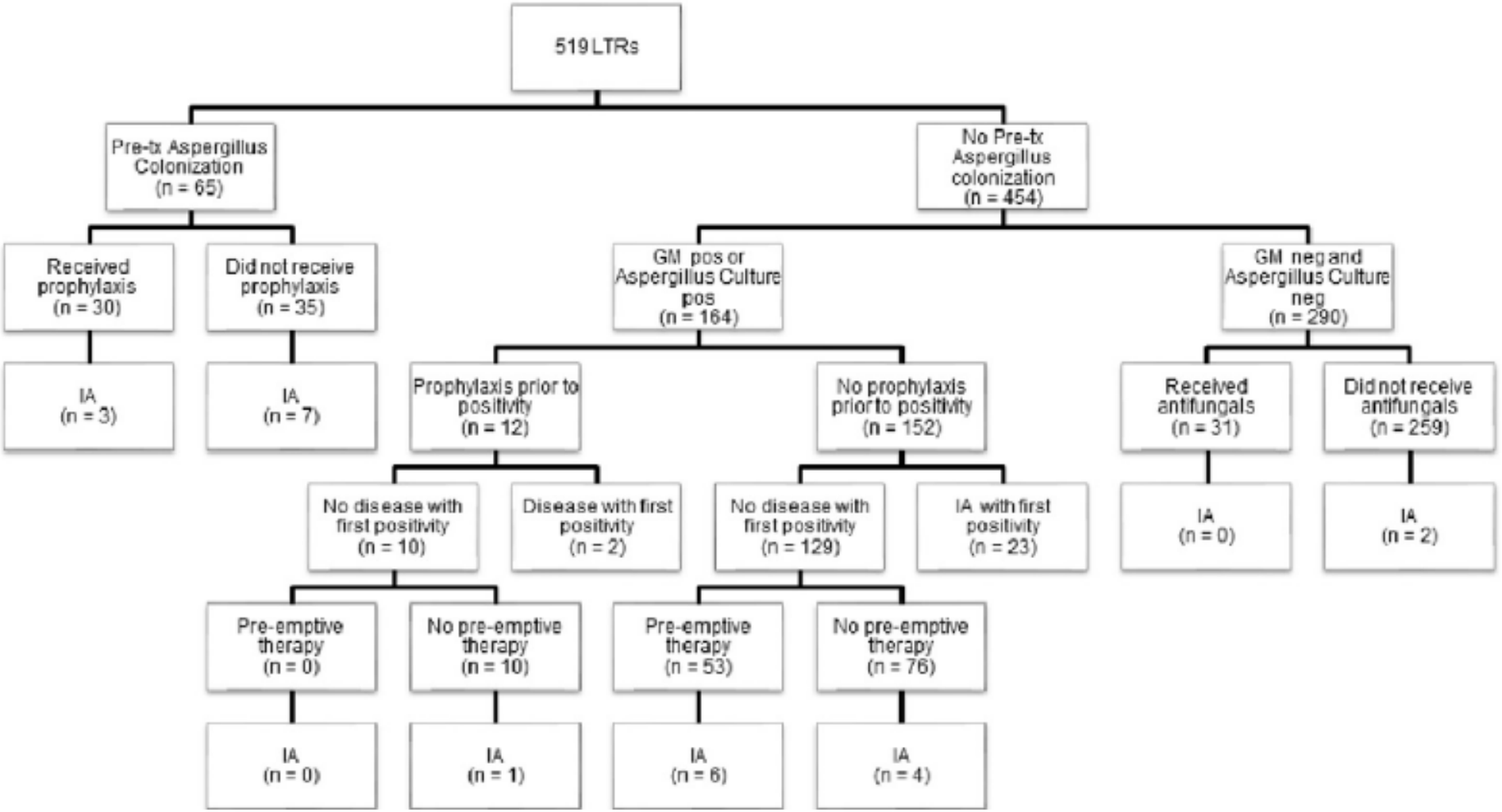
- Etude monocentrique rétrospective (Toronto)
- 519 patients analysés/3077 fibroscopies
- Suivi 1 an

Stratégie de traitement fongique:

Si Asp+ pré greffe -> Traitement Vorico/Ampho B inh
Arrêt ttt à 6S si GM et cultures –

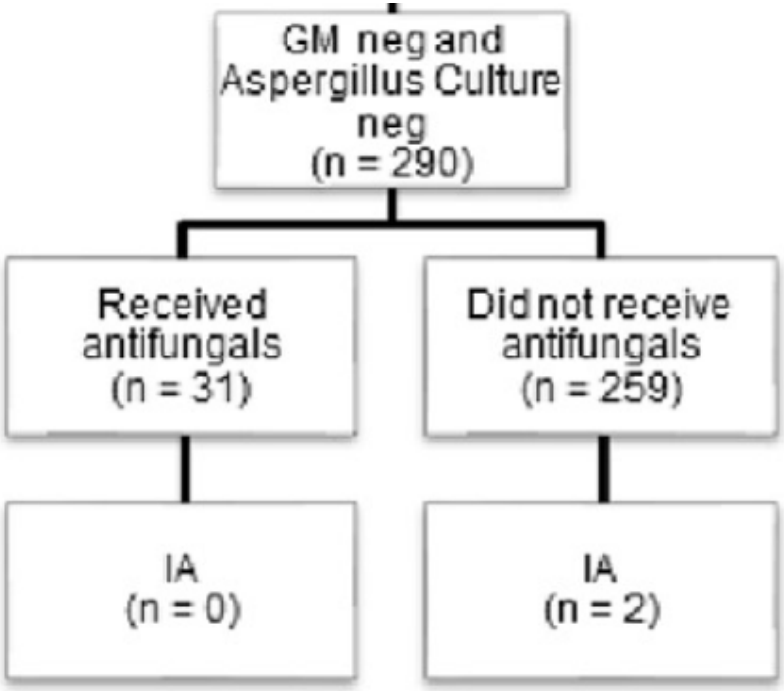
Si Asp+ (GM ou culture) post greffe -> Vorico

47 aspergilloses invasives



47 aspergilloses invasives

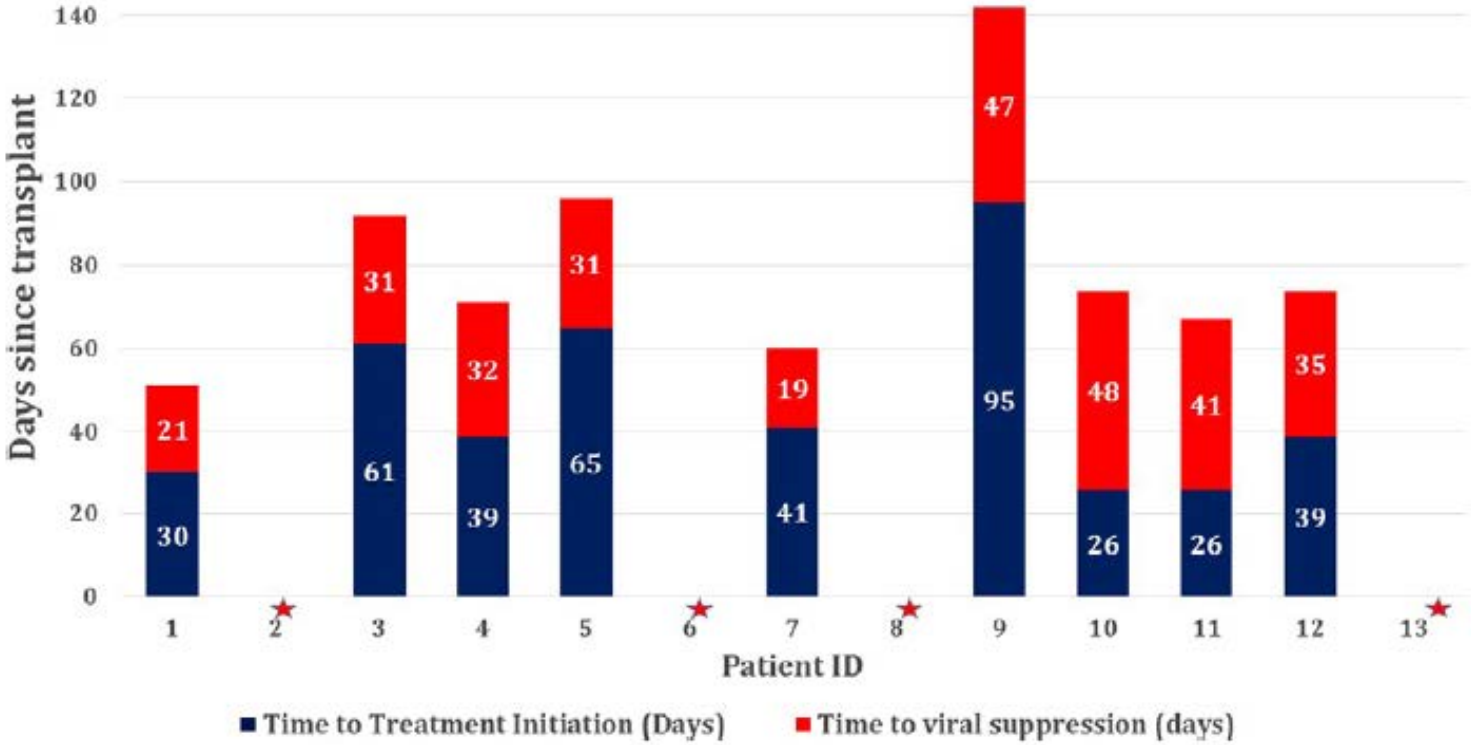
Réduction de moitié du ttt préventif



The Journal of
Heart and Lung Transplantation
The Official Publication of the International Society for Heart and Lung Transplantation

Early outcomes using hepatitis C–positive donors for cardiac transplantation in the era of effective direct-acting anti-viral therapies

Schlendorf et al



Messages pour la maison

1. Co-infection TB-VIH: début précoce ARV + prednisone
2. Vaccin inactivé VZV
3. Importance de vaccination antigrippale en transplantation
4. Letermovir- CMV, un nouvel ami ?
5. Difficulté PEC risque aspergillaire en transplantation pulmonaire

Table 3. Adverse Events (Safety Population).*

Event	Letermovir Group (N=373)	Placebo Group (N=192)	Difference (95% CI)	P Value
	number of patients with event (percent)		*percentage points*	
Any adverse event	365 (97.9)	192 (100)	−2.1 (−4.2 to −0.2)	0.07
GVHD	146 (39.1)	74 (38.5)	0.6 (−8.0 to 8.9)	0.96
Diarrhea	97 (26.0)	47 (24.5)	1.5 (−6.3 to 8.8)	0.77
Nausea	99 (26.5)	45 (23.4)	3.1 (−4.6 to 10.3)	0.49
Fever	77 (20.6)	43 (22.4)	−1.8 (−9.2 to 5.2)	0.70
Rash	76 (20.4)	41 (21.4)	−1.0 (−8.4 to 5.9)	0.87
Vomiting	69 (18.5)	26 (13.5)	5.0 (−1.7 to 11.0)	0.17
Cough	53 (14.2)	20 (10.4)	3.8 (−2.2 to 9.2)	0.25
Peripheral edema	54 (14.5)	18 (9.4)	5.1 (−0.8 to 10.4)	0.11
Fatigue	50 (13.4)	21 (10.9)	2.5 (−3.6 to 7.8)	0.49
Mucosal inflammation	46 (12.3)	24 (12.5)	−0.2 (−6.4 to 5.3)	0.99
Headache	52 (13.9)	18 (9.4)	4.6 (−1.3 to 9.8)	0.15
Abdominal pain	44 (11.8)	18 (9.4)	2.4 (−3.3 to 7.5)	0.47
Acute kidney injury	36 (9.7)	25 (13.0)	−3.4 (−9.5 to 1.9)	0.28
Decreased appetite	38 (10.2)	22 (11.5)	−1.3 (−7.2 to 3.9)	0.74
Hypertension	31 (8.3)	21 (10.9)	−2.6 (−8.4 to 2.3)	0.38
Constipation	27 (7.2)	20 (10.4)	−3.2 (−8.8 to 1.5)	0.26