Généralités sur la TRANSPLANTATION HÉPATIQUE

Partie 3

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GHPS

Complications infectieuses liées au traitement immunosuppresseur

- Ne sont pas toujours parlantes
  - Cliniquement (Fievre)
  - Biologiquement (GB, PCT,…)

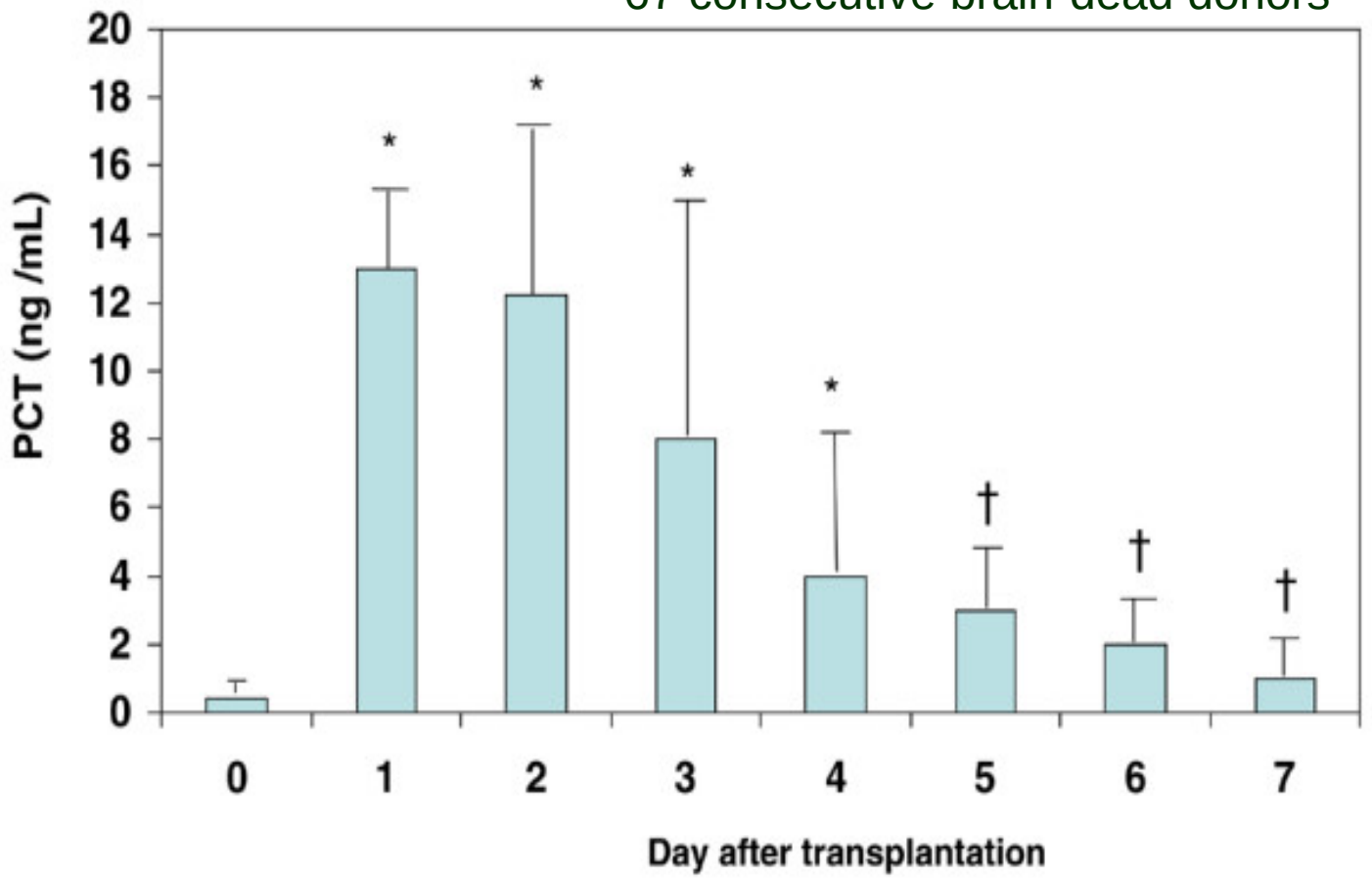
  => risque de retard diagnostic

- Intérêt des prélèvements «faciles»

Time course of procalcitonine (PCT) in the recipient before liver transplantation and during the first week after liver transplantation

D. Eyraud et al Crit Care. 2008; 12(4)

67 consecutive brain-dead donors



Results are expressed as mean ± standard deviation.

*$P < 0.05$ (versus D0), †$P < 0.05$ (versus D1).

Multivariate analysis of predictive factors of concentration of procalcitonin in recipients and donors

D Eyraud et al Crit Care. 2008; 12(4)

Variable	*P* univariate	*P* multivariate
Days in intensive care unit of donor	0.52	
Age of donor	0.5	
Heart retrieval	0.16	
Infection in donor	0.75	
Cardiac arrest in donor	0.0001	0.003
Epinephrine or norepinephrine doses in donor	0.002	0.046

Donors

Variable	*P* univariate	*P* multivariate
Age of recipient	0.7	NS
Cold ischemia	0.97	NS
Warm ischemia	0.18	NS
Veno-venous bypass	0.34	NS
Liver vascular exclusion tolerance	0.01	NS
Transfusion of recipient	0.22	NS
Procalcitonin donor concentration	0.005	NS
Pre-liver transplantation procalcitonin concentration	0.37	NS
Severe portal hypertension	0.07	NS
Epinephrine or norepinephrine doses in donor	0.07	NS
Days in intensive care unit of donor	0.03	NS
Age of donor	0.5	NS
Heart retrieval	0.16	NS
Cardiac arrest in donor	<0.0001	0.001
Infection in donor	<0.0001	0.0039

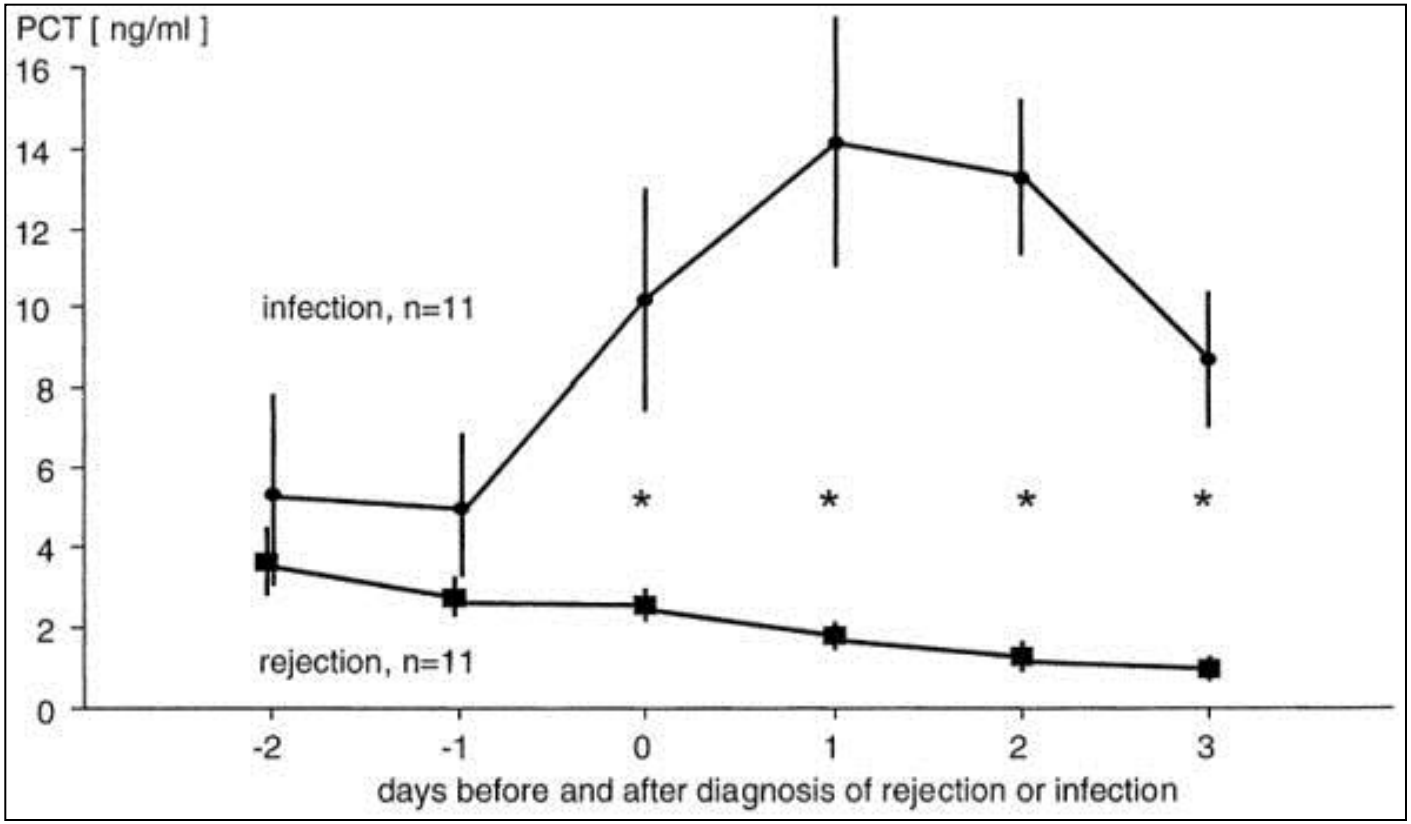
Recipients

Procalcitonin in fever of unknown origin after liver transplantation: A variable to differentiate acute rejection from infection.

Kuse, Ernst-R; Langefeld, Iris; Jaeger, Karsten; Kulpmann, Wolf-R

Critical Care Medicine. 28(2):555-559, February 2000.

F Procalcitonin (PCT) plasma concentrations in infection and rejection (n = 11, except day 3 because one patient died on day 2; mean and SEM from the time-courses of Figures 2 and 3; *p < .05). Day 0, day the diagnosis was made.



Infections post-greffe

- **Transmises par le greffon**

  - rares, mais de tous types

- **Acquises de « novo »**

  - bactériennes (70%)

  - virales (20%)

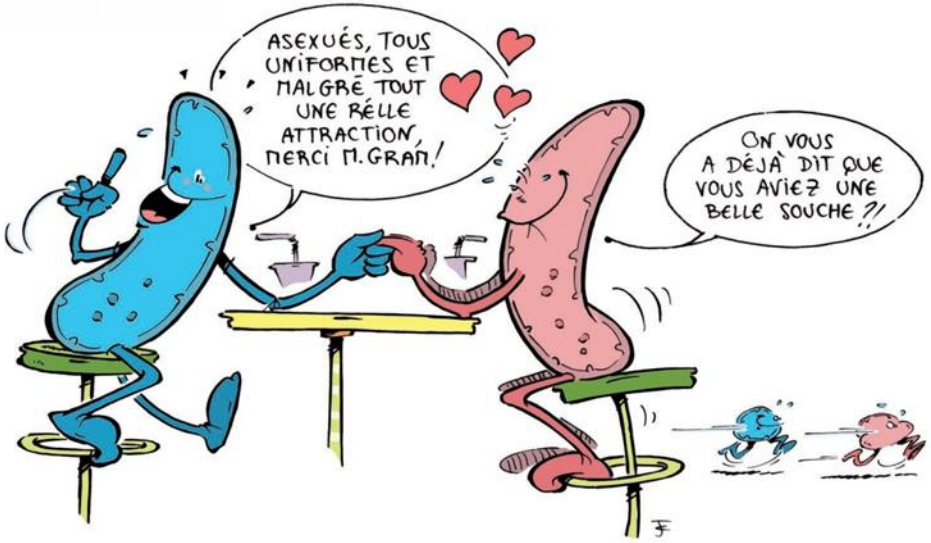
  - myco-parasitaires (candidose,aspergillose,…) (10%)

- **Reactivation d'infections latentes**

  - virales (CMV, EBV, …) +++

  - BK

Types d'infections après transplantation d'organes



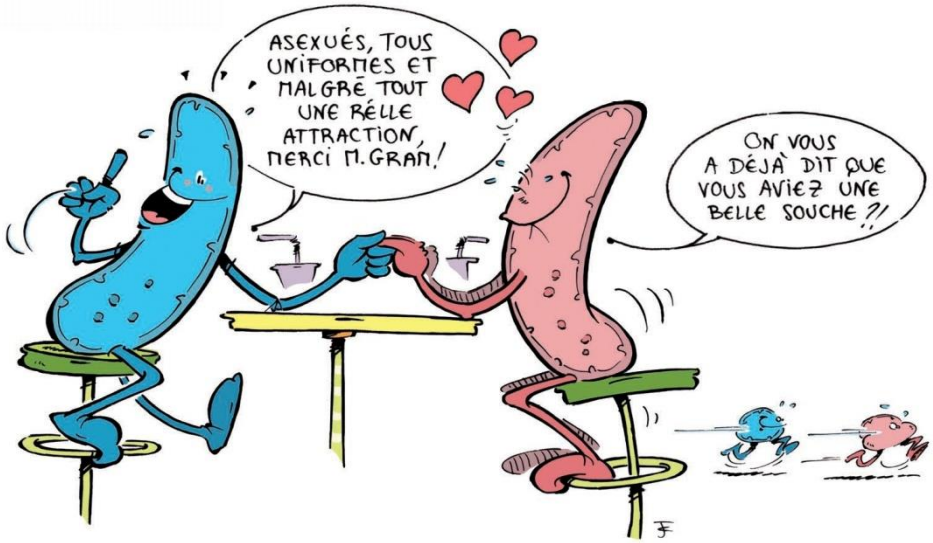
Guidés par
1-Délai post op
2-Degré Quantitatif et Cumulatif d'IS

D'après Fishman JA. Infection in solid-organ transplant recipients. NEJM 2007; 357 (25): 2601-14

Facteurs de Risques Infectieux

- Facteurs PreTH
  - UNOS
  - MELD
  - Etat Nutritionnel (sarcopénie ?)
- Liées procédures chirurgicales
  - Ischemie reperfusion
  - Transfusions
  - Stéatose
  - PNF
  - Complications vasculaires, biliaires
- Post TH
  - Intensification IS (rejet, …)

Complications infectieuses liées au traitement IS



Bactériennes

- 1° mois +++

- Infections respiratoires, urinaires, pariétales, bactériémies …

- Bactéries Nosocomiales (hospit antérieures)

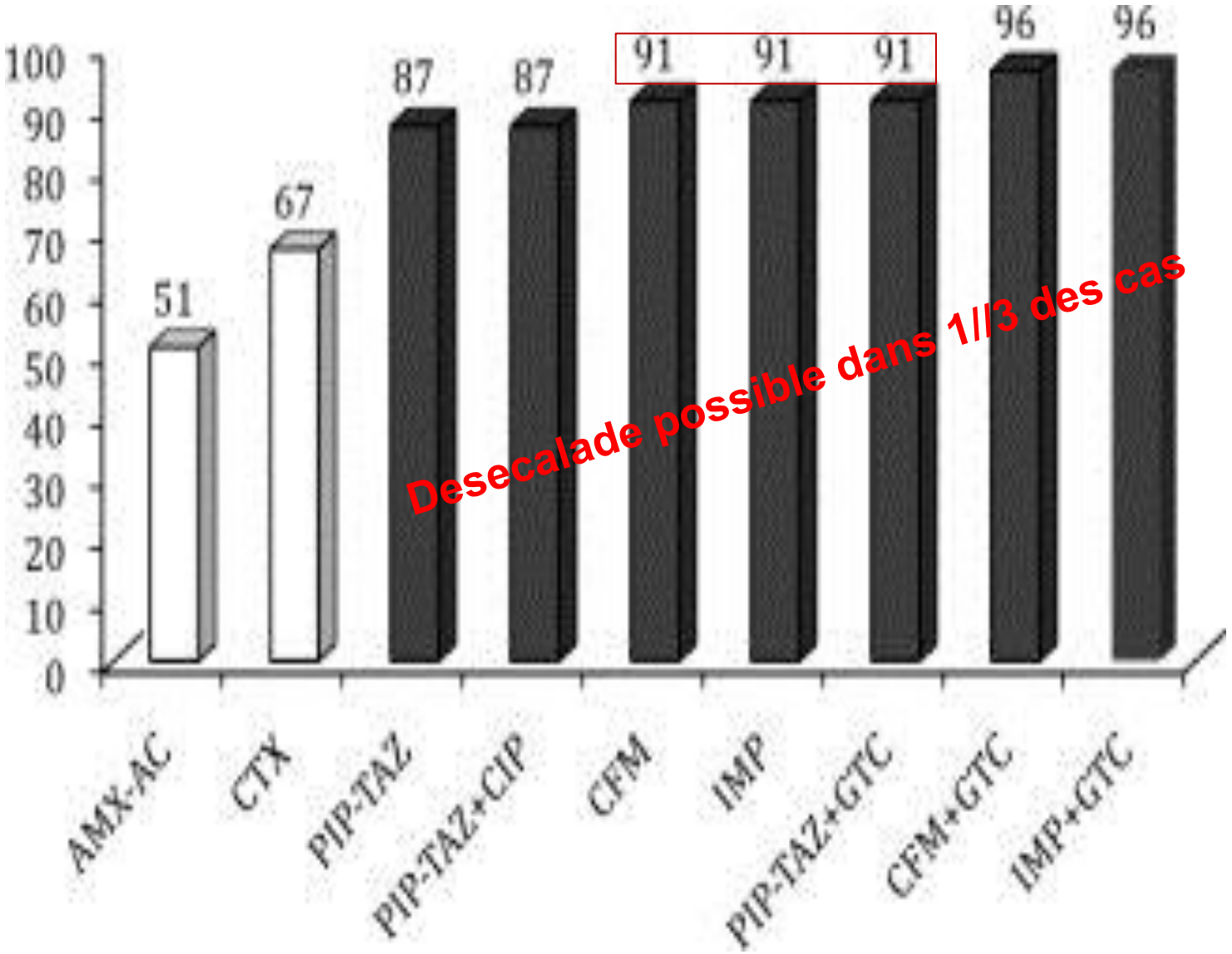
Weiss E.
LIVER TRANSPLANTATION 16, 2010

Microorganism	n (%)
Gram-negative bacilli	**22 (61.1)**
Acinetobacter baumannii	1 (2.8)
Citrobacter freundii	1 (2.8)
Enterobacter sp.	2 (5.6)
Escherichia coli	3 (8.3)
Haemophilus influenzae	7 (19.4)
Hafnia alvei	1 (2.8)
Klebsiella oxytoca	1 (2.8)
Proteus vulgaris	1 (2.8)
Pseudomonas aeruginosa	4 (11.1)
Serratia marcescens	1 (2.8)
Gram-positive cocci	**14 (38.9)**
Streptococcus pneumoniae	3 (8.3)
Other *Streptococcus* species	3 (8.3)
MSSA	7 (19.4)
MRSA	1 (2.8)
Total pathogens	36

Results expressed as numbers and percentages of total causative pathogens for E-HAP.

single-center
cohort prospective
148 LT
Incidence E-HAP 15,5%
dans les 6° jours
documentation bacterio
PDP ou aspi tracheale

Early-onset pneumonia after liver transplantation: Microbiological findings and therapeutic consequences



Liver Transplantation Volume 16, Issue 10, pages 1178-1185, 16 JUL 2010

Early-Onset Pneumonia After Liver Transplantation: Microbiological Findings and Therapeutic Consequences

E. Weiss

LIVER TRANSPLANTATION 16, 2010

Characteristic	All Patients (n = 148)	Patients with E-HAP (n = 23)	Patients without E-HAP (n = 125)	*P* Value
	Results are expressed as medians and ranges or as numbers and percentages.			
Total duration of mechanical ventilation (days)	2 (0-53)	9 (0-45)	2 (0-53)	<0.01
Length of stay in ICU (days)	8 (2-78)	17 (5-78)	7 (2-65)	<0.01
ICU mortality [n (%)]	16 (10.8)	4 (17.4)	12 (9.6)	0.27
Seven-day mortality [n (%)]	6 (4.1)	2 (8.7)	4 (3.2)	0.23
One-month mortality [n (%)]	12 (8.1)	3 (13)	9 (7.2)	0.4
One-year mortality [n (%)]	22 (14.9)	5 (21.7)	17 (13.6)	0.34

Complications infectieuses fungiques

- Candida +++, Aspergillus
- Pronostic extrement grave
- Intérêt d'un diagnostic rapide, avant les signes cliniques
- Place du suivi des antigénémies Candida Aspergillaire?

Proportion of Aspergillus and Candida infections among invasive fungal infections in different groups of organ transplant recipients

Type of organ transplant	Invasive fungal infections, %	*Aspergillus*, %	*Candida*, %
Heart	5–21	77–91	8–23
Lung and heart-lung	15–35	25–50	43–72
Liver	7–42	9–34	35–91
Kidney	1.4–14	0–10	90–95
Pancreas	18–38	0–3	97–100
Small bowel	40–59	0–3.6	97–100

Adapted with permission [35].

Singh N: Antifungal prophylaxis for solid organ transplant recipients: seeking clarity amidst controversy.
Clin Infect Dis 2000, 31:545–553

Facteurs de Risques Infections Fungiques Profondes post Transplantation

Antibiotherapie Prophylactique ou Curative pre ou post TH
Epuration Rénale
Re Transplantation

Transplantation. **2003**;75:2023–2029.

Complications chirurgicales +/- reprise chir
Durée d'intervention
Transfusions
Durée de séjour en réa

Colonisation à Candida
Infections à CMV +++

Clin Infect Dis. **2001**;33:S47–S52.

Risk factors for invasive candidiasis in OLT

Liver **High-risk liver transplant recipients:**

Major:
MELD score >30
Re-transplantation, fulminant hepatic failure,
Renal failure requiring replacement therapy,

Minor:
MELD score 20–30,
split, living-donor
>40 transfusion blood products,
choledochojejunostomy (Roux-en-Y)
Renal failure not requiring replacement therapy (CrCl <50 mL/min)
Early re-intervention,
multifocal colonization/infection by *Candida* spp.

Galvada J Clin Microbiol Infect September **2014** Volume 20, Issue Supplement s7

Analysis of Risk Factors for Invasive Fungal Infections Ok Atilgan Exp Clin Transplant 2014 Mar; 12 suppl 1 :110-6

Variable	Invasive Fungal Infection Group 1	No Invasive Fungal Infection Group 2	*P* Value
Patients	10	295	
OLTx	11	297	
Re-OLTx	1	2	*P* < .05
Transplant age (y)	38.6 ± 18.93 (6 month-63 year)	25.28 ± 20.59 (2 months-65 year)	*P* < .05
Sex (M/F)	8/2	193/102	NS
Donor type (leaving/deceased)	7/3	237/58	NS
Donor age (y)	35.2 ± 16.83 (7-56)	33.5 ± 11.78 (9 month-72 year)	NS
Surgery time (h)	9.9 ± 2.28 (7-14)	8.87 ± 2.11 (4-20)	NS
Total length of stay hospital (mean days postorthotopic liver transplant)	41.4 ± 31.21 (14-97)	21.49 ± 16.56 (3-154)	*P* < .01
Duration of stay surgical intensive care unit (mean days)	11.7 ± 14.14 (1-46)	2.36 ± 3.5 (1-43)	*P* < .001
Diabetes mellitus	6	18	*P* < .001
Cytomegalovirus	3	21	*P* < .01
Preoperative creatine	1.18 ± 0.82 (0.3-2.7)	0.8 ± 2.3 (0.1-40)	*P* < .05
Preoperative albumin	3.08 ± 0.71 (2.1-4.4)	3.24 ± 0.7 (0.9-5.4)	NS
Preoperative bilirubin	10.35 ± 13.72 (0.7-37.10)	13.69 ± 15.24 (0.3-75)	NS
Preoperative prothrombin time	18.6 ± 3.2 (13-24)	23.15 ± 12.7 (1.8-141)	NS
Postoperative hepatitis	1	23	NS
Status (alive/dead)	1/9	228/67	*P* < .001

Abbreviations: NS, not significant ($P \geq .05$); OLT, orthotopic liver transplant

Traitement Anti Fungique?

Prophylactique en l'absence d'Infection chez des patients à haut risque d'IFI

Empirique en l'absence de documentation mycologique

Pre Emptif IFI probable ou possible

Curatif des IFI prouvées

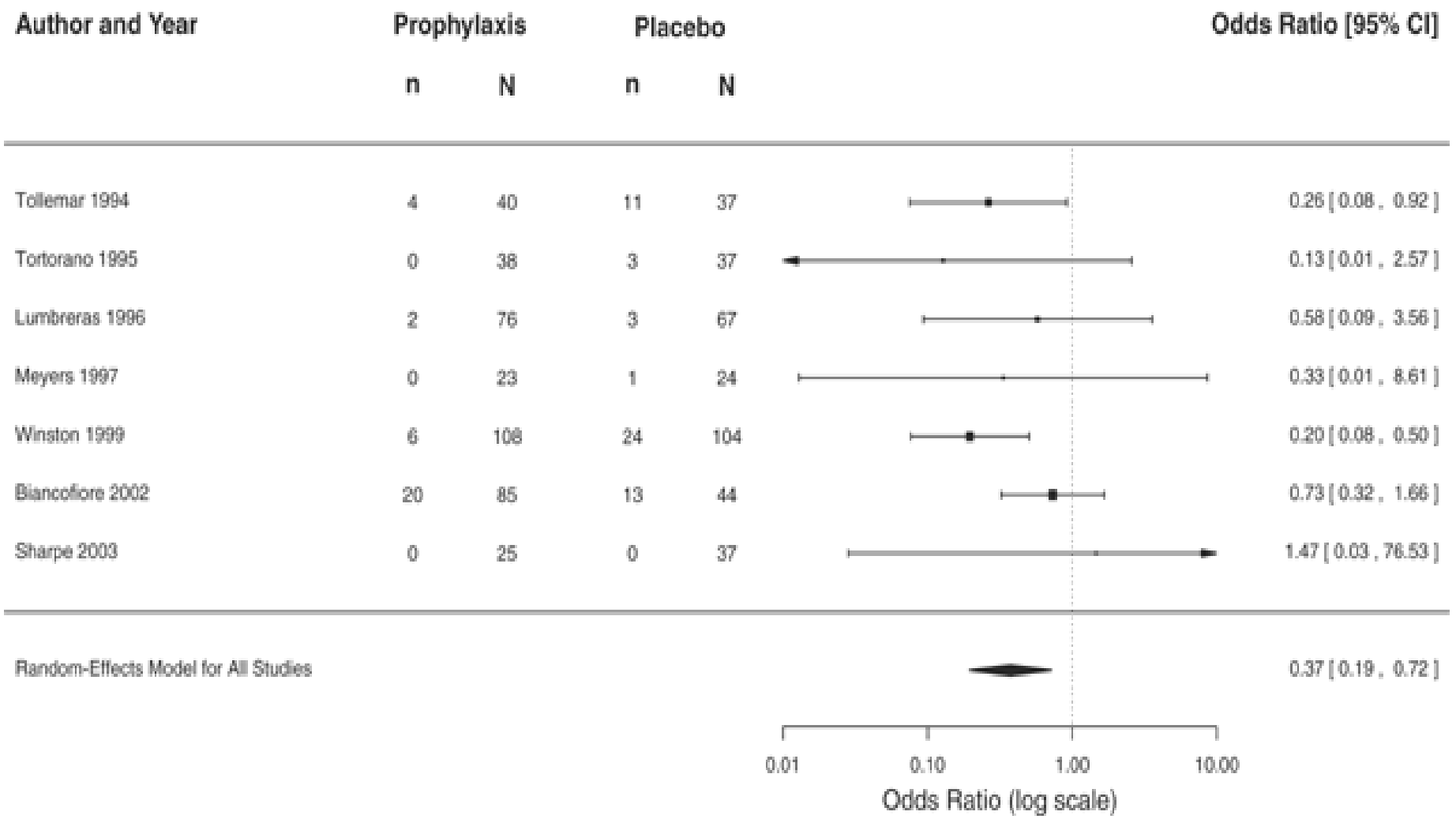
Risque de modifier

- l'écologie au profit des Candida non albicans
- le profil de Resistance (R Fluco)

=> Systématique vs Chez patients à risques?

Antifungal Prophylaxis in Liver Transplantation: A Systematic Review and Network Meta-Analysis

American Journal of Transplantation Volume 14, Issue 12, p 2765-2776,NOV 2014



ANTIFUNGAL PROPHYLAXIS IN LIVER TRANSPLANT RECIPIENTS - 2009 RECOMMENDATIONS AND CONCLUSIONS

AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

AASLD

balancing the line

between prophylaxis in appropriate patients

and overuse,

which may ultimately lead to worse outcomes

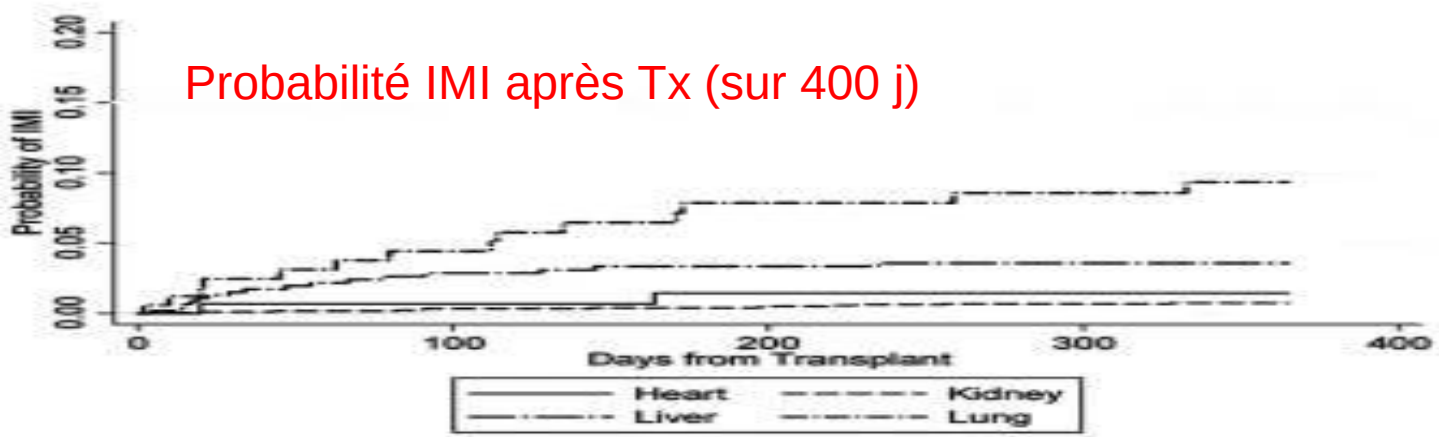
3 methods may be considered:

- targeting of highest-risk patients,
- appropriate dosing,
- and a limited duration of therapy

Epidemiology, outcomes, and mortality predictors of invasive mold infections(IMI) among transplant recipients: a 10-year, single-center experience

D. Neofytos Transpl Infect Dis. 2013 June ; 15(3): 233–242

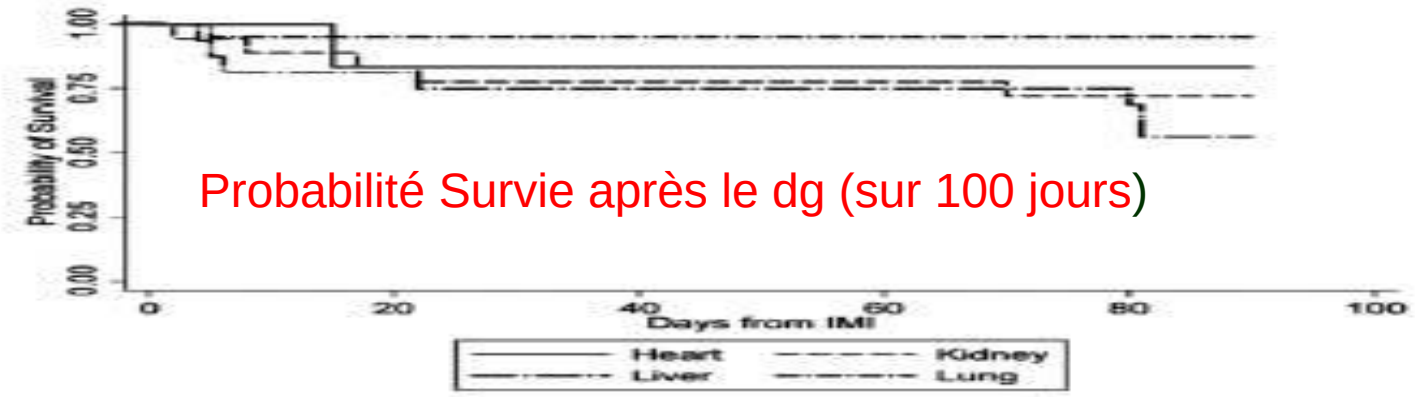
(a)



Probabilité IMI après Tx (sur 400 j)

Lung
Liver
Heart
Kidney

(b)



Probabilité Survie après le dg (sur 100 jours)

Lung
Heart
Kidney
Liver

ANTIFUNGAL PROPHYLAXIS IN LIVER TRANSPLANT RECIPIENTS - 2009 RECOMMENDATIONS AND CONCLUSIONS

AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

AASLD

- The use of SDD as universal prophylaxis cannot be recommended
- The incidence and timing of post-transplantation infections at one's own institution should be analyzed.

  Populations with rates of infection 10% should be considered for prophylaxis
- Recent data suggest that modern surgical and medical practices have dramatically reduced the risk of candidiasis (1.7%, from Singh and colleagues).This data suggests that because the general liver transplant population has a low risk of infection, prophylactic antifungals should only be utilized in those patients at highest risk

Antifungal prophylaxis in SOT

Liver

High-Risk Liver Recipients :

Major:
Retransplantation,
fulminant hepatic failure,
MELD ≥30
Renal failure requiring
replacement therapy

Minor:
MELD score 20–30,
Split, Living-donor,
Choledochojejunostomy (Roux-en-Y),
High transfusion requirement (≥40
units of cellular blood products),
Renal failure not requiring
replacement therapy (CrCl
<50 mL/min),
Early reintervention,
multifocal colonization/infection
by *Candida*spp.

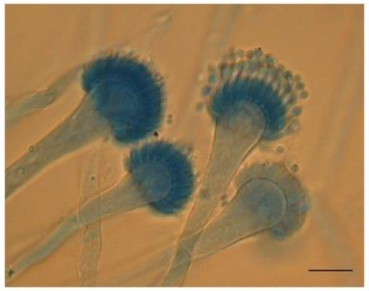
If 1 major or 2 minor criteria :

Micafungin (A–II)
Caspofungin (A–II)
Lip-AB IV (A–II)
AB lipid complex IV (A–II)
Anidulafungin (B–III)

2–4 weeks
or until resolution of risk
factors

Galvada J Clin Microbiol Infect
September 2014 Volume 20, Issue S7

Aspergillose post Tx



2° Infection fongique la + fqte en post TH
= 25% des infections fongiques invasives
Inhalation spores ubiquitaires
Puis processus angio invasion avec lésions infarcissements
Et dissémination extrapulmonaire (SNC, ..)

Diagnostic difficile Interet de l'ex direct du LBA en cas de culture +
Biologie place des PCR sériques(faux +) et LBA? Galactomanane?
Intéret de la radiologie / des biopsies

Délai d'apparition Précoce (médiane de diagnostic 2,5 semaines post TH)
but 55% of *Aspergillus* infections occur 90 days after transplantation,
with 25% occurring after 1 year of transplant

92% de mortalité

Singh N, Transplantation.1997;64:716–720
Singh N, Clin Infect Dis 2003;36:46-52.

Facteurs de Risque
Ins Rénale +/- EER, reTH, infection CMV, séjour preTH en ICU, infections bactériennes répétées, corticoides preTH, Hépatite Fulminante, OKT3, Agemie Asp +

Fortun J, Liver Transpl.2002;8:1065–1070.

Incidence et mortalité de l'aspergillose après transplantation

Type de transplantation	Incidence (% pts) Asp. Invasive	Mortalité (% pts) Asp. Invasive
Möelle	6.4	92
Poumon	8.4	74
Foie	1.7	87
Cœur	6.2	78
Rein	0.7	75
Pancréas	1.3	100

Paterson DL, Singh N. Medecine 1999, 78:123-138

Risk factors for invasive aspergillosis

Liver transplant	Re-transplantation	More than 6 g of accumulative prednisone in the third month after transplantation
	Kidney failure, especially post-transplant Haemodialysis	Post-transplant renal failure Post-transplant haemodialysis
	Fulminant hepatic failure	Leukopenia (<500/mm^3)
	Complicated surgery or reoperation	Chronic graft dysfunction

Galvada J Clin Microbiol Infect September 2014 Volume 20, Issue Supplement s7

ANTIFUNGAL PROPHYLAXIS IN LIVER TRANSPLANT RECIPIENTS - 2009 RECOMMENDATIONS AND CONCLUSIONS

AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

AASLD

If *Aspergillus* is a target pathogen (based on local epidemiology), either caspofungin or amphotericin B should be used for prophylaxis

2 historical cohort trials which utilized standard dose lipid amphotericin B products is as follows:

3/261(1%) in the intervention arms developed aspergillosis vs 10/80 (13%) in the preintervention arms
and overall 1-year mortality rates were 41/261 (16%) and 17/80 (21%), respectively

Hellinger WC, LiverTranspl 2005;11:656-662
Singh, Transplantation 2001;71:910-913.

Surgery criteria for invasive *Aspergillosis* in SOT

Organ involvement	Recommendation
Injuries close to **large vessels**	Resection of the lesion
Pericardium involvement	Pericardiectomy
Chest wall invasion by lung injury	Chest injury and chest wall resection is needed (possible later reconstruction)
Empyema	Chest tube drainage is required or even surgical drainage and thoracotomy (whether organized or infiltrative)
Haemoptysis secondary to a pulmonary lesion	Cavity resection vs. embolization
Skin and soft tissue involvement	Debridement and resection with wide margins
Endocarditis	Remove all devices Vegetation and infected valve resection is required
Osteomyelitis	Debridement and cleaning of the affected tissue, with subsequent possibility of reconstruction is required (musculoskeletal grafts or bone grafts)
Central nervous system involvement	Resection and withdrawal of affected tissue and space-occupying lesions is required
Endophthalmitis/panophthalmitis	Vitrectomy, evisceration or enucleation, as required

Complications infectieuses virales post Tx

A la phase aigue

a) CMV (= HHV5) +++

b) Autres virus de la famille des Herpes

c) Parvovirus B19

d) HVE

Plus tard

e) Recidive de la maladie initiale (HCV, HBV, …)

f) EBV

g) HHV8

CMV disease vs infection

- Infection :

  detection virale asymptomatique

- Maladie :

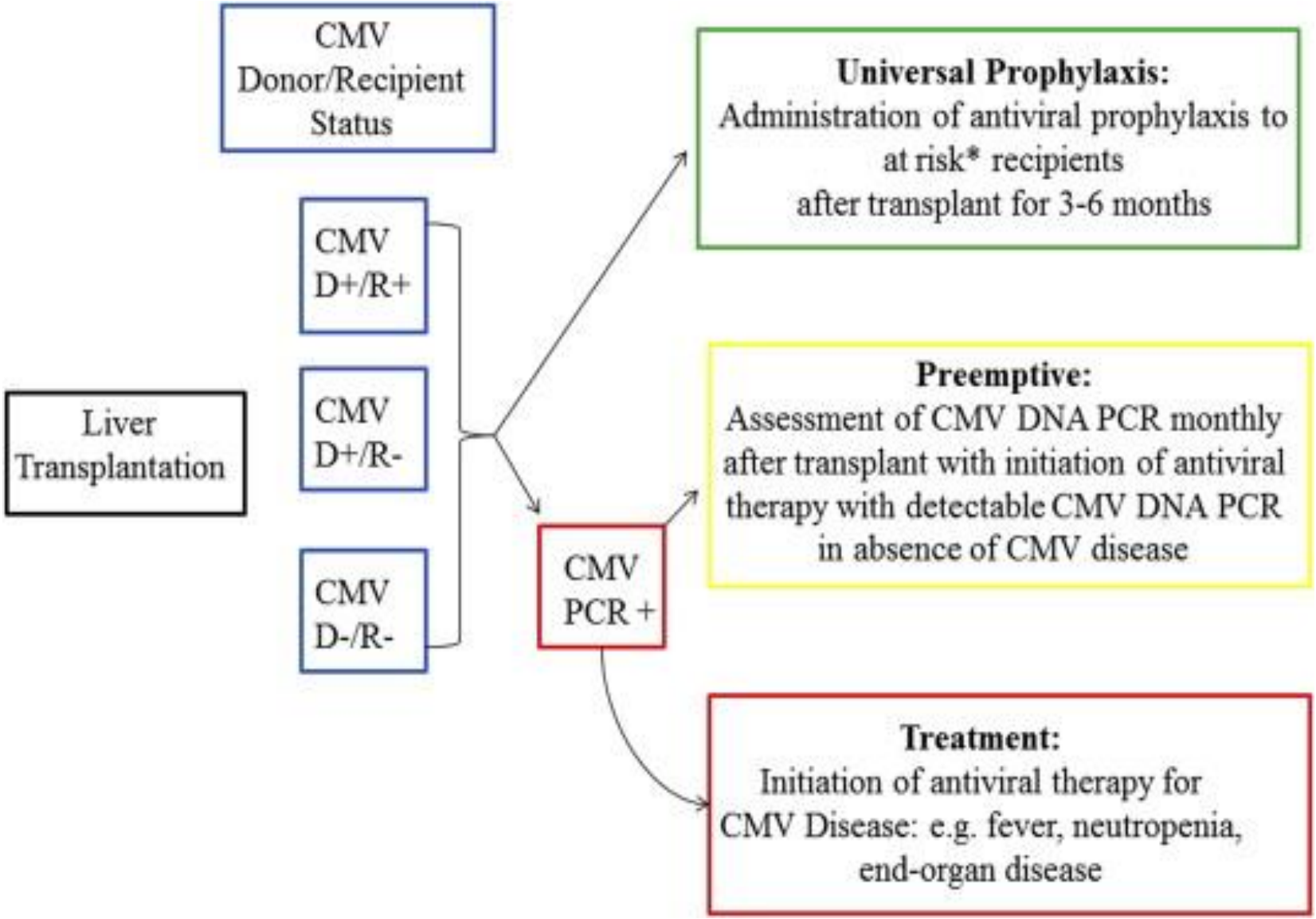
  detection virale avec symptomes cliniques

Estimated incidence of CMV disease during the first 12 month after liver transplantation

Bruminhent J et al . CMV after liver transplantation 2014|Volume 6|Issue 6|

	Use of anti-CMV prophylaxis for 3-6 month	
	No	**Yes**
CMV D+/R-	44%-65%	12%-30%
CMV D+/R+	18.20%	2.70%
CMV D-/R+	7.90%	3.90%
CMV D-/R-	1%-2%	0%
All patients	18%-29%	4.80%

CMV management after liver transplant



Comparison of antiviral prophylaxis and pre-emptive strategies for CMV prevention in OLT

Prevention characteristics	Prophylaxis strategy	Pre-emptive strategy
CMV disease	Very effective at preventing CMV infection and disease	Effective to prevent CMV disease; does not prevent CMV infection
Late-onset CMV disease	Higher risk of late and very-late onset CMV disease	Reduces incidence of late onset CMV disease
Ideal treatment population	CMV D+R- are highest risk patients	CMV R+ patients
Logistics of strategy	Logistically more feasible, but still requires frequent monitoring of adverse effects	Requires weekly viral load testing; standardized viral load thresholds still being investigated
Cost	Higher drug costs (1441 € / mois) ; lower laboratory/monitoring costs (81€ / PCR CMV)	Higher laboratory/monitoring costs; lower drug costs
Safety/adverse effects	More frequent adverse effects such as myelosuppression due to longer treatment periods	Shorter treatment periods; fewer toxicities
Indirect CMV effects	Better evidence showing reduction of graft rejection, improved graft survival, opportunistic infections	Limited evidence overall, but may not reduce indirect effects
Effect on mortality	Reduces mortality from CMV disease	Limited evidence regarding mortality reduction
CMV resistance	More common compared to pre-emptive strategy	Some evidence regarding effect on resistance but overall uncommon

Complications infectieuses virales CMV, incidence et facteurs de Risque

En l'absence de prophylaxie

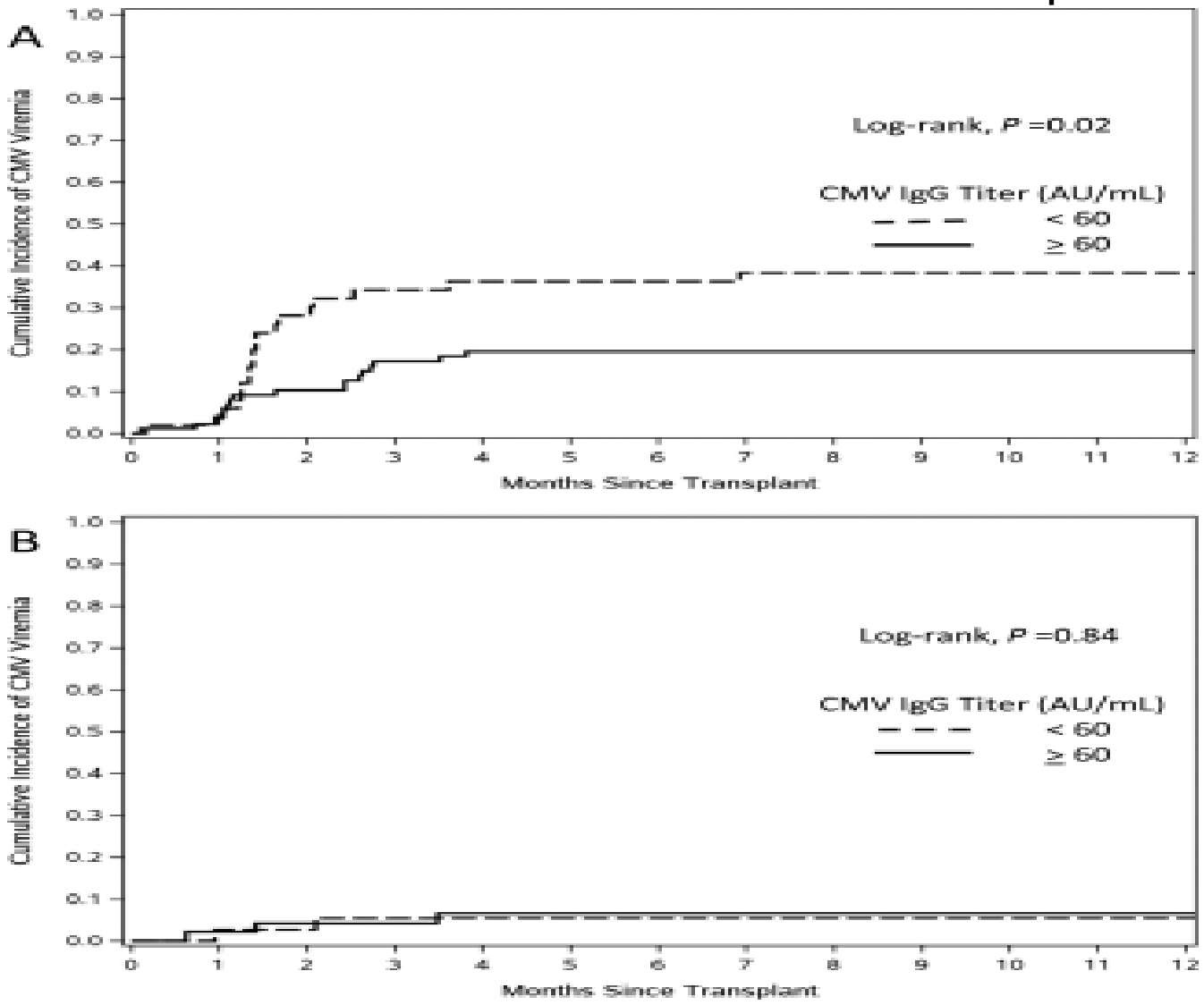
Incidence globale 20 à 30 % et jusqu'à 65% si D+/R-

- Risque corrélé aux statuts virologiques du donneur et du receveur (D+ / R-)
- Hépatite fulminante
- Retransplantation
- Infection bactérienne grave
- Utilisation de SAL ou OKT3

- Interets des produits sanguins CMV neg ?

Risk factors for cytomegalovirus reactivation after liver transplantation: Can pre-transplant cytomegalovirus antibody titers predict outcome?

Bruminhent Liver Transplantation 21 (4) 539-546, MAR 2015



(A) donor CMV +

pre-transplant CMV IgG titers of <60 versus ≥60 AU/mL

(B) donor CMV -

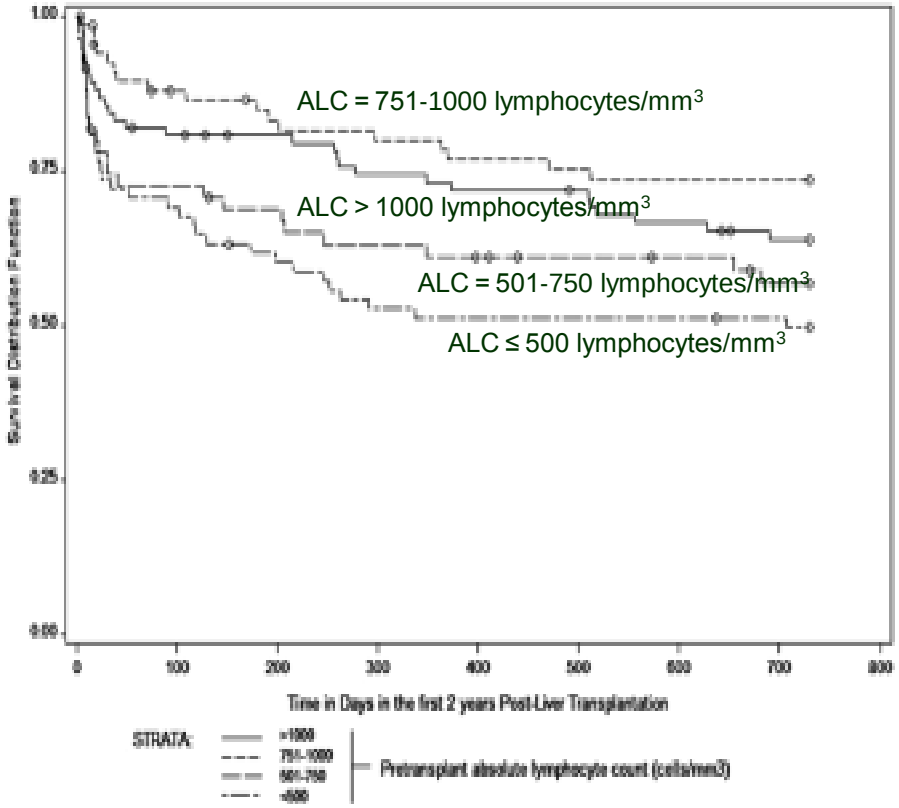
Pretransplant lymphopenia is a novel prognostic factor in cytomegalovirus and noncytomegalovirus invasive infections after liver transplantation

Nierenberg Liver Transplantation 20 (12) 1497-1507, 2014

A

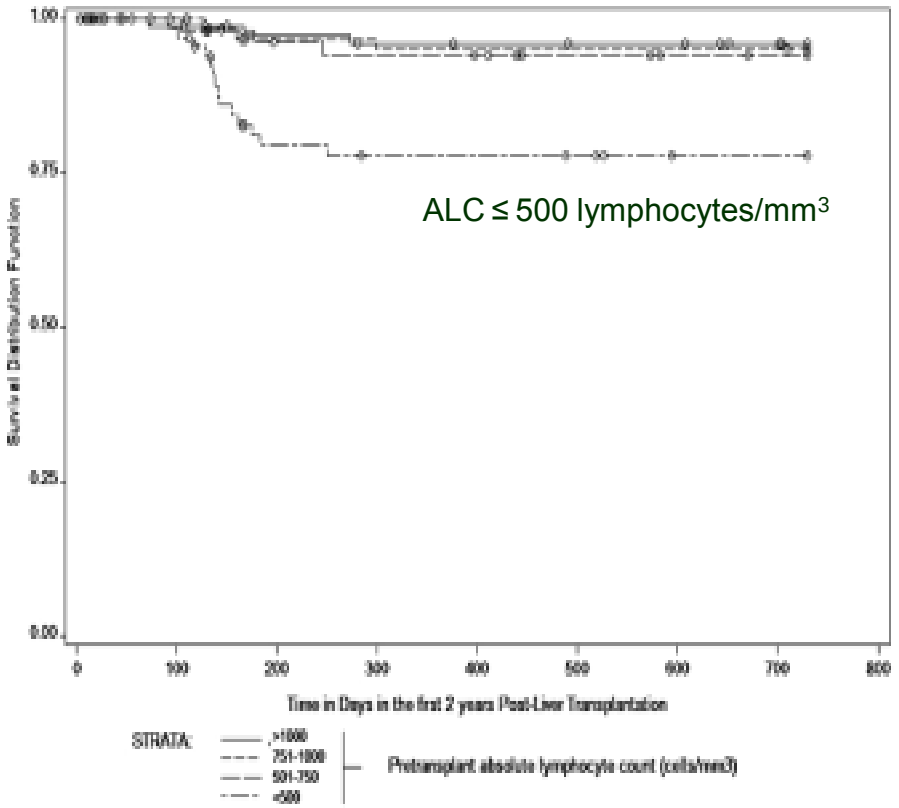
Survival free of non-CMV infection in the entire cohort, n=276: by grades of pretransplant lymphopenia

in the first 2 years after LT



B

Survival free of CMV disease in the entire cohort, n = 276: by grades of pretransplant lymphopenia



Currently available antiviral drugs for cytomegalovirus prophylaxis and treatment in liver transplant recipients

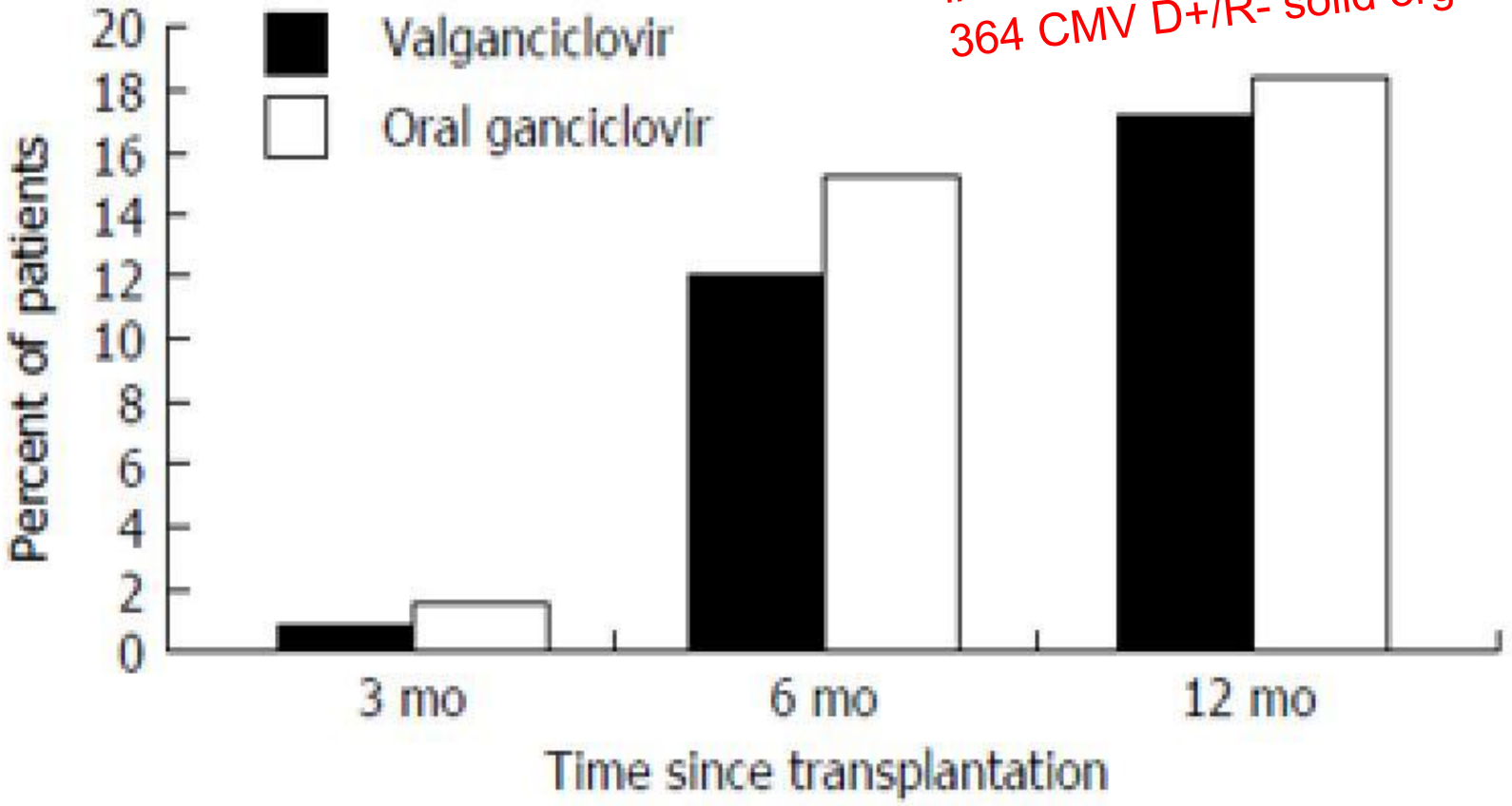
Bruminhent J et al . CMV after liver transplantation 2014 Volume 6, Issue 6

Drug	Route	Usual adult prophylaxis dose	Usual adult treatment dose	Comments on use and major toxicity
Ganciclovir	IV	5 mg/kg once daily	5 mg/kg twice daily	Intravenous access; leukopenia
Ganciclovir	Oral	1 g three times daily	Not applicable	Low oral bioavailability; high pill burden
Valganciclovir	Oral	900 mg once daily	900 mg twice daily	Ease of administration; leukopenia
Foscarnet	IV	Not recommended	60 mg/kg every 8 h (or 90 mg/kg every 12 h)	Second-line drug Intravenous access; nephrotoxicity
Cidofovir	IV	Not recommended	5 mg/kg once weekly × 2 then every 2 wk thereafter	Third-line drug Intravenous access; nephrotoxicity

Time to the onset of cytomegalovirus disease in solid organ transplant recipients who received three month of oral ganciclovir or valganciclovir prophylaxis

Paya C, Am J Transplant. 2004;**4**:611-620

multicenter randomized non-inferiority clinical trial
364 CMV D+/R- solid organ



Diagnostic des Infections à CMV

- Virémies, viruries en au moins 48 heures…
- Peu d'interet des sérologies si IGg CMV +
- Intérêt des PCR Quantitatives (Cout 81 €)
- Biopsies avec immunomarquage

Direct and indirect clinical effects of cytomegalovirus in transplant recipients

Direct clinical effects	**Indirect clinical effects**	
CMV syndrome	Acute allograft rejection	
Fever > 38 °C for 2/4 d	Chronic allograft rejection	
Malaise	Allograft failure	
Myelosuppression	Vanishing duct syndrome/ductopenia	
Tissue-invasive CMV disease[1] Gastrointestinal disease (entire gastrointestinal tract can be affected)	Allograft hepatitis and fibrosis	
	Vascular thrombosis	
	Opportunistic and other infections	Fungal (Asperg, PNCC)
	Hepatitis	
Pneumonitis	Bacterial (Nocardia)	
Retinitis	Viral (HHV-6, HHV-7, EBV)	
CNS disease	Hepatitis C virus recurrence	
Carditis	EBV associated PTLD	
Mortality	Mortality	

The Role of Secondary Cytomegalovirus Prophylaxis for Kidney and Liver Transplant Recipients.

2001-2010
Secondary prophylaxis used at the discretion of each clinician
22 KT and 20 LT

	Kidney transplant recipients		Liver transplant recipients	
	Secondary PPX (n=16)	No Secondary PPX (n=6)	Secondary PPX (n=2)	No Secondary PPX (n=18)
Mean years of follow-up (range)	3.2 (1.7-6.8)	5.0 (0.2-9.1)	1.9 (0.9-2.8)	4.2 (0.8-8.2)
CMV relapse	4 (25%)	2 (33%)	0	2 (11%)
Type of relapse				
Disease	3	2	0	0
Infection	1	0	0	2
Mean days to relapse[b] (range)	275 (15-735)	328 (10-645)	N/A	30 (7-52)
Graft loss	3 (19%)	2 (33%)	2 (100%)	3 (17%)
Alive at last follow-up	16 (100%)	6 (100%)	0	11 (61%)

[a] There were no statistically significant differences in outcomes within the kidney and liver transplant groups.
[b] Days from the cessation of CMV treatment.
PPX, prophylaxis; CMV, cytomegalovirus.

Sullivan, T Transplantation. 99(4):855-859, April 2015.

Recommendations for the treatment of CMV disease in solid organ transplant recipients 2014

ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

Valganciclovir or intravenous ganciclovir
are recommended as first-line treatment. Grade: AI.

Valganciclovir is preferred except in cases of life-threatening disease and in situations where oral intake may not be appropriate. Grade: AII.(60 cps = 1 mois =1441 €)

Sequential therapy (starting with IV ganciclovir followed by valganciclovir) may be an alternative strategy. Grade: BII.

Antiviral dose adjustment should be performed based on renal function by Cockroft-Gault formula. Grade: AI.

Dose reduction of valganciclovir and ganciclovir due to adverse events should be avoided due to risk of resistance. Grade: AIII.

The addition of G-CSF should be considered before cessation of antiviral therapy in cases of severe leukopenia. Grade: BIII.

Laboratory monitoring of CMV should be performed weekly during the treatment phase to monitor response. Grade: AII. (PCR CMV = 81 €)

Recommendations for the treatment of CMV disease in solid organ transplant recipients 2014

ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

Treatment should be continued until viral eradication is achieved at least on one assay after a minimum of 2 weeks. Grade: AII. *souvent 2 PCR CMV neg a 1 semaine d'intervalle*

Secondary prophylaxis is not routinely recommended. Grade: CIII.

Dose reduction of immunosuppressive therapy should be considered in severe CMV disease, in non-responding patients, in patients with high viral loads and those with leukopenia. Grade: AIII.

Intravenous immunoglobulin may be considered for severe forms of CMV disease such as pneumonitis. Grade: BII.

Ganciclovir resistance should be suspected when persistence of or increase in viral load or clinical progression of CMV disease is detected despite adequate exposure to the drug after 3 weeks. Grade: AII.

Foscarnet is the empirical alternative antiviral treatment in the presence of serious CMV disease and suspected ganciclovir resistance provided no genotypic study is available. Grade: AII.

Anti – CMV à venir

Objectif

efficacité similaire ou meilleure

avec meilleure tolérance

le letermovir et le brincidofovir, entrent actuellement dans leur dernière phase de développement clinique

Compartimentalisation et Archivage des CMV résistants aux antiviraux

- **La compartimentalisation** signifie une différence entre le génotype de résistance des souches virales retrouvées au niveau de la circulation sanguine et celui des virus présents au niveau des organes touchés par la maladie.

  Cela a été particulièrement décrit chez des patients atteints de rétinite ou d'encéphalite à CMV, chez qui des souches sauvages étaient isolées au niveau de l'humeur aqueuse ou du liquide céphalorachidien, tandis que des variants résistants étaient retrouvés au niveau du sang périphérique.

  Une discordance inverse a également été décrite, mais de façon moins fréquente.

- **Le phénomène d'« archivage »** désigne la persistance au long cours des CMV résistant aux antiviraux dans l'organisme, avec un risque de réactivation ultérieure de ces virus mutants au cours d'un nouvel épisode d'infection/maladie.

Complications infectieuses liées au traitement IS

b) les autres virus du groupe Herpes:

- HSV
- HHV6 / HHV8
- Zona
- HHV6 / HHV8

c) Parvovirus B19

d) Hépatite Virale E

Infections à Parvovirus B19

- Principal représentant des Erythrovirus, est un petit virus non enveloppé dont le tropisme cellulaire est restreint.
- Virus ubiquitaire, responsable du mégalérythème épidémique ou 5 ème maladie, de manifestations articulaires, d'atteintes hématologiques et d'infections materno-fœtales
- Pénètre par voie respiratoire, puis gagne la circulation sanguine ce qui lui permet d'atteindre les cellules cibles, les précurseurs érythroïdes, et ainsi de se répliquer
- Entre le 2ème et le 12ème jour après le contact, une virémie et de façon concomitante une réticulopénie qui chez les sujets sains est sans conséquence clinique et ne s'accompagne pas d'anémie. En revanche, lorsque la durée de vie des érythrocytes est raccourcie et qu'il existe une érythroblastopénie chronique, on observe des crises d'érythroblastopénie aiguës et transitoires avec une anémie brutale et profonde.
- La réponse immune permet de contrôler rapidement la réplication et la virémie disparaît lorsque les AC IgM puis IgG sont synthétisés. Apparaissent alors le rash et les manifestations articulaires liés au dépôt de complexes immuns
- Dans le contexte de la greffe, se manifeste cliniquement essentiellement par des cytopénies, l'atteinte des trois lignées est possible

Complications infectieuses virales : Hépatite Virale E

4 génotypes

1-2 : pays en voie de developpement (eau)

3-4 : zoonose en pays industrialisés (cochon)

-in immunocompetent patients

HEV may generally cause subclinical or self-limiting illness

-in immunocompromised patients

Chronic HEV infection has been recently reported occasionally leading to significant hepatic injury or advanced fibrosis and cirrhosis

Hépatite Virale E post OLT

In Germany,

- 4% of OLT recipients (226 patients) were positive for HEV antibodies compared with
- 3% of patients with chronic liver diseases
- and 1% of healthy controls.

Pischke S, Liver Transpl. 2010;16:74–82.

HEV infection can lead to chronic hepatitis in OLT recipients,which can progress into a spectrum of hepatic injury, including graft loss.

Evaluation for chronic HEV infection should be considered in liver recipients

Récidive de la maladie virale initiale
Récidive Virale B

- **Réinfection du greffon**

  dans 80% des cas, en l'absence de prophylaxie (réplication favorisée par l'IS)

- **Prophylaxie à vie**

  Lamivudine (Zeffix°) ou Adefovir (Hepsera®)

  et Ig anti-HbS / 3 - 4 mois

=> Suivi PCR B Quantitative et AC anti HbS

Récidive de la maladie virale initiale
Récidive Virale C :

En cas de replication pre-TH

La réinfection est quasi constante après TH

avec une hépatite Chronique dans 50 à 80 % des cas

+/- recidive cirrhogene rapide

Quand (re)-traiter?

Comment traiter?

-IFN	taux de réponse faile
	expose au rejet chronique (effet I.stimulant)
-Ribavirine	pas d'effet sur la replication virale
-IFN + Riba	taux elevé de réponse sans rejet
-Antiprotéases	

http://www.dondorganes.fr/

CARTE DE DONNEUR

JE DÉCIDE DE FAIRE DON, après ma mort, d'éléments de mon corps (organes, tissus) en vue d'une greffe. Je témoigne de cette décision en portant cette carte sur moi.

NOM

PRÉNOM DATE

SIGNATURE

trans-forme.org dondorganes.fr