’Best of’ Infectiologie 2024

Prof. Pierre Tattevin

Maladies Infectieuses et Réanimation Médicale

Hôpital Pontchaillou, CHU Rennes

Liens d’intérêt: conseils scientifiques (2019-2024)

- Pfizer
- Advanz
- Gilead
- Biomérieux
- Basiléa
- Takéda
- Abbott

Tri sélectif

1. Publications majeures depuis le ‘Best of’ du 32ème congrès STPI (Mai 2023)
2. Impact sur nos pratiques (diagnostiques/thérapeutiques)
3. D’intérêt pour infectiologues & microbiologistes

Best of STPI/SPILF 2024

1. Antibiotiques / Antifongiques
2. Tuberculose
3. IST / VIH
4. COVID
5. Vaccins / prévention

Best of STPI/SPILF 2024

1. Antibiotiques / Antifongiques
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Antimicrobial for 7 or 14 Days for Febrile Urinary Tract Infection in Men: A Multicenter Noninferiority Double-Blind, Placebo-Controlled, Randomized Clinical Trial

Matthieu Lafaurie,[1] Sylvie Chevret,[2] Jean-Paul Fontaine,[3] Pierre Mongiat-Artus,[4] Victoire de Lastours,[5,6] Lélia Escaut,[7] Stéphane Jaureguiberry,[7] Louis Bernard,[8] Franck Bruyere,[9] Caroline Gatey,[10] Sophie Abgrall,[11] Milagros Ferreyra,[12] Hugues Aumaitre,[12] Caroline Aparicio,[13] Valérie Garrait,[14] Vanina Meyssonnier,[15] Anne Bourgarit-Durand,[16] Amélie Chabrol,[17] Emilie Piet,[18] Jean-Philippe Talarmin,[19] Marine Morrier,[20] Etienne Canoui,[21] Caroline Charlier,[21,22] Manuel Etienne,[23] Jerome Pacanowski,[24] Nathalie Grall,[6,25] Kristell Desseaux,[26] Florence Empana-Barat,[27] Isabelle Madeleine,[28] Béatrice Bercot,[6,29] Jean-Michel Molina,[30,a] and Agnès Lefort,[5,6,a]; for the PROSTASHORT Study Group[b]

Prostashort: peut-on traiter 7 jours l'IU masculine fébrile ?

- **Etude randomisée multicentrique double aveugle**
- Homme, **IU fébrile** sensible aux FQ
- Traitement empirique C3G ou FQ
- **Critère principal S6:**
  - ***Guérison clinique + microbiologique***
  - ***Sans nécessité de nouvel ATB***
- **Critères secondaires**
  - Rechute IU entre S6 et S12
  - Portage fécal *Enterobacterales* MDR

Lafaurie M et al. Clin Infect Dis 2023

Antimicrobial for 7 or 14 Days for Febrile Urinary Tract Infection in Men: A Multicenter Noninferiority Double-Blind, Placebo-Controlled, Randomized Clinical Trial

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Prostashort: peut-on traiter 7 jours l'IU masculine fébrile ?

Analysis	7-Day Therapy No. of Participants With Event/Total No. (%)	14-Day Therapy	*P* Value
Intention-to-treat	(n = 115)	(n = 125)	
Main analysis[a]	64 (55.7)	97 (77.6)	
Microbiological success[b]	91 (79.1)	117 (93.6)	.001
Clinical success[c]	110 (95.6)	125 (100)	.02
No new antibiotic after the end of treatment	93 (80.9)	116 (92.8)	.007
Per-protocol	(n = 108)	(n = 117)	
Main analysis[a]	64 (59.3)	96 (82.1)	

Lafaurie M et al. Clin Infect Dis 2023

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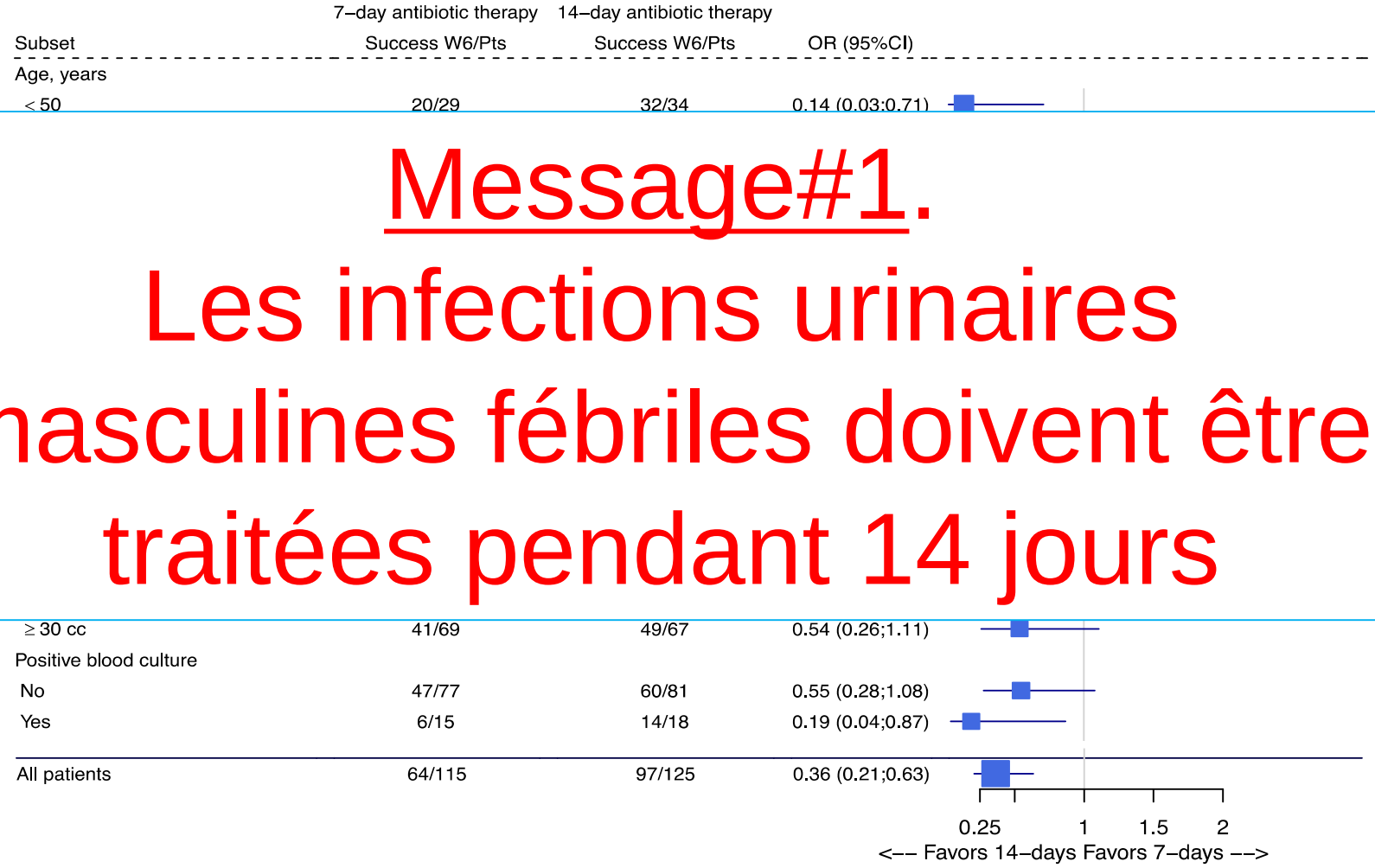

Message#1.

Les infections urinaires masculines fébriles doivent être traitées pendant 14 jours

Lafaurie M et al. Clin Infect Dis 2023

Efficacy and safety of an early oral switch in low-risk *Staphylococcus aureus* bloodstream infection (SABATO): an international, open-label, parallel-group, randomised, controlled, non-inferiority trial

*Achim J Kaasch, Luis Eduardo López-Cortés, Jesús Rodríguez-Baño, José Miguel Cisneros, M Dolores Navarro, Gerd Fätkenheuer, Norma Jung, Siegbert Rieg, Raphaël Lepeule, Laetitia Coutte, Louis Bernard, Adrien Lemaignen, Katrin Kösters, Colin R MacKenzie, Alex Soriano, Stefan Hagel, Bruno Fantin, Matthieu Lafaurie, Jean-Philippe Talarmin, Aurélien Dinh, Thomas Guimard, David Boutoille, Tobias Welte, Stefan Reuter, Jan Kluytmans, Maria Luisa Martin, Emmanuel Forestier, Hartmut Stocker, Virginie Vitrat, Pierre Tattevin, Anna Rommerskirchen, Marion Noret, Anne Adams, Winfried V Kern, Martin Hellmich, Harald Seifert, for the SABATO study group**

Relais per os pour les bactériémies à *S. aureus* (BSA) non compliquées

- **Etude randomisée internationale en ouvert**
- **BSA non compliquées (SASM ou SARM):**
  - Pas de foyer profond (endocardite, etc.)
  - Hémoc H72 traitement **négative**
  - Pas de matériel intra-vasculaire conservé
- **Essai stratégique = randomisation après 5-7 j IV** => modalités Tt jusqu'à J14
  - Relais per os (cotrimoxazole, clindamycine ou linézolide)
  - Vs. poursuite IV (jusqu'à J14)
- **Critère principal J90, par comité d'adjudication 'en aveugle' du traitement**
  - **EI lié à la BSA** *(rechute, foyer secondaire, décès)*

Kaasch A et al. Lancet Infect Dis 2024

	Intention-to-treat population		
	Oral switch group (n=108)	Intravenous group (n=105)	Percentage-point difference (95% CI)
Primary endpoint			
SAB-related complication within 90 days	14 (13%)	13 (12%)	0·7 (–7·8 to 9·1)
Any complication	9 (9%); 11	17 (17%); 5	–7·9 (–17·6 to 1·9)

Message#2.

On peut effectuer un relais *per os* à J5-J7 pour les bactériémies à *S. aureus* non compliquées

Kaasch A et al. Lancet Infect Dis 2024

Cefepime–Taniborbactam in Complicated Urinary Tract Infection

Florian M. Wagenlehner, M.D., Leanne B. Gasink, M.D., Paul C. McGovern, M.D., Greg Moeck, Ph.D., Patrick McLeroth, M.D., MaryBeth Dorr, Ph.D., Aaron Dane, M.Sc., and Tim Henkel, M.D., Ph.D., for the CERTAIN-1 Study Team*

Une nouvelle association beta-lactamine-inhibiteur beta-lactamase

- **Etude randomisée internationale double aveugle**
- **IU ‘compliquées’ (40% pyélonéphrite) à BGN MDR**
  - Céfépime-taniborbactam (2 g/0,5 g) x 3/j (perf. 2 h)
  - Mérpoénème 1 g x 3/j (perf 30’)
- **Critère principal J21, guérison clinique et microbio**

Characteristic	Cefepime–Taniborbactam (N = 293)	Meropenem (N = 143)
Gram-negative pathogen — no. (%)	293 (100)	143 (100)
Enterobacterales species		
Any	281 (95.9)	137 (95.8)
Cefepime-resistant	66 (22.5)	30 (21.0)
ESBL-producing‖	76 (25.9)	40 (28.0)
Multidrug-resistant**	100 (34.1)	55 (38.5)

Wagenlehner F et al. N Engl J Med 2024

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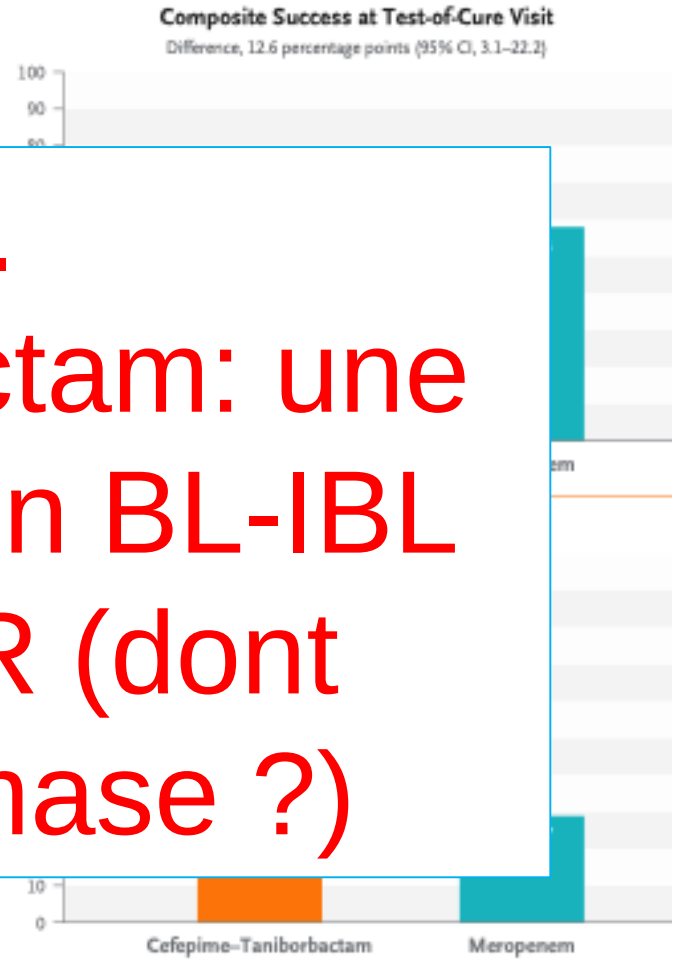

Message#3.

Céfépime-taniborbactam: une nouvelle combinaison BL-IBL pour les BGN XDR (dont métallo-bêtalactamase ?)

Wagenlehner F et al. N Engl J Med 2024

Efficacy and safety of rezafungin and caspofungin in candidaemia and invasive candidiasis: pooled data from two prospective randomised controlled trials

George R Thompson III, Alex Soriano, Patrick M Honore, Matteo Bassetti, Oliver A Cornely, Marin Kollef, Bart Jan Kullberg, John Pullman, Maya Hites, Jesús Fortún, Juan P Horcajada, Anastasia Kotanidou, Anita F Das, Taylor Sandison, Jalal A Aram, Jose A Vazquez, Peter G Pappas

Une échinocandine à longue durée d'action (1/semaine)

- **Etude randomisée internationale double aveugle**
  - Rezafungine IV 1/semaine (400 mg J0 puis 200 mg/semaine)
  - Caspofungine IV 1/j (70 mg J0 puis 50 mg/j)

- **Infections invasives à *Candida* sp.**
  - 73% candidémie
  - *C. albicans* (43%), *C. glabrata* (25%), *C. tropicalis* (17%), *C. parapsilosis* (14%)

- **Critère principal = Mortalité à J30**

Thompson GR et al. Lancet Infect Dis 2024

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	Rezafungin (n=139)	Caspofungin (n=155)	Treatment difference (95% CI)
Primary pooled efficacy endpoint: day 30 all-cause mortality			
Deceased or unknown survival status	26 (19%)	30 (19%)	..
Known deceased	21 (15%)	25 (16%)	..
Unknown survival status	5 (4%)	5 (3%)	..
Alive	113 (81%)	125 (81%)	..
Death rate*	..	..	−1·5% (−10·7 to 7·7)
Exploratory efficacy endpoints			
Patients with negative blood culture†‡			
At 24 h	63/105 (60%)	57/116 (49%)	..
At 48 h	80/103 (78%)	73/115 (64%)	..

Thompson GR et al. Lancet Infect Dis 2024

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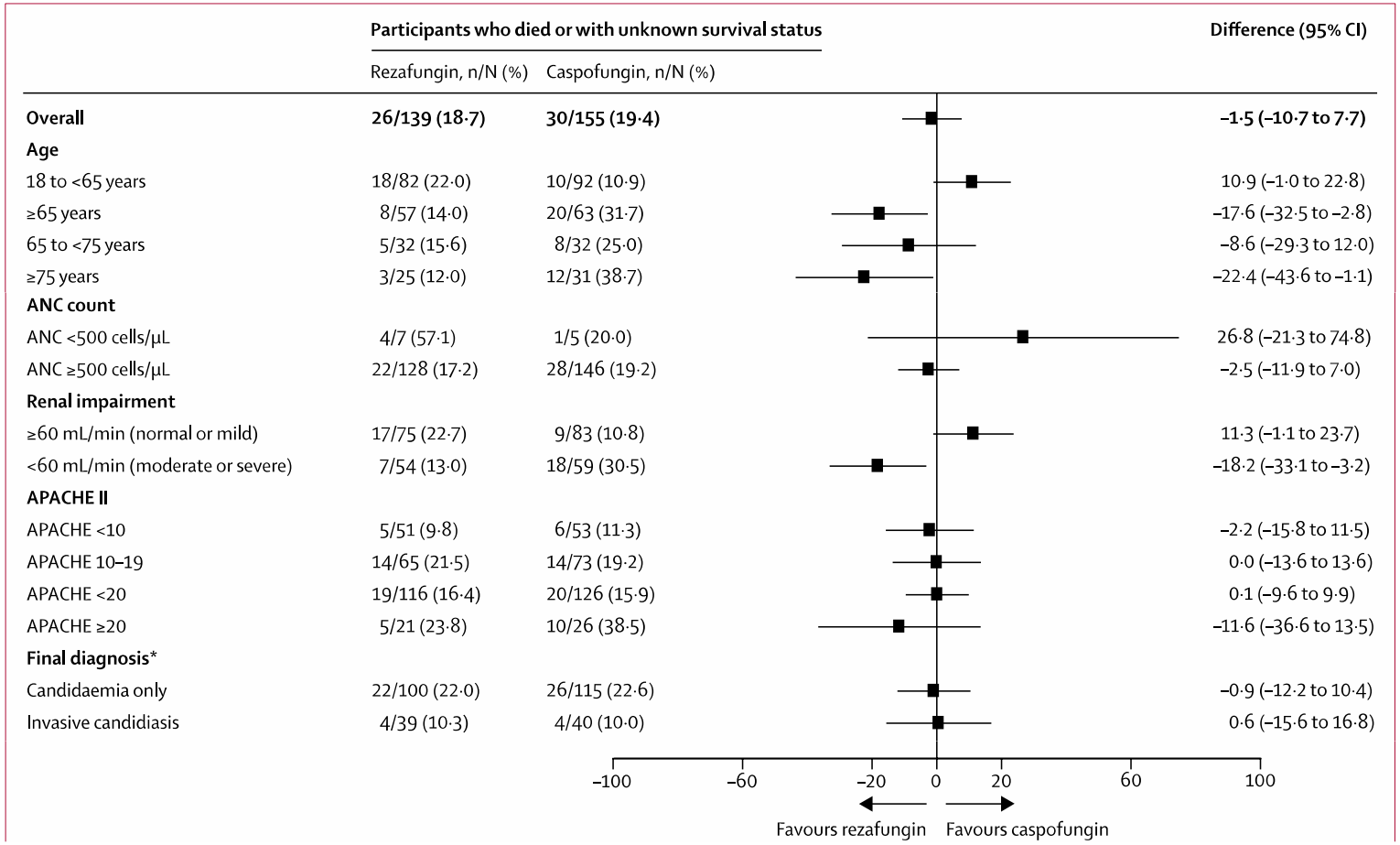

Thompson GR et al. Lancet Infect Dis 2024

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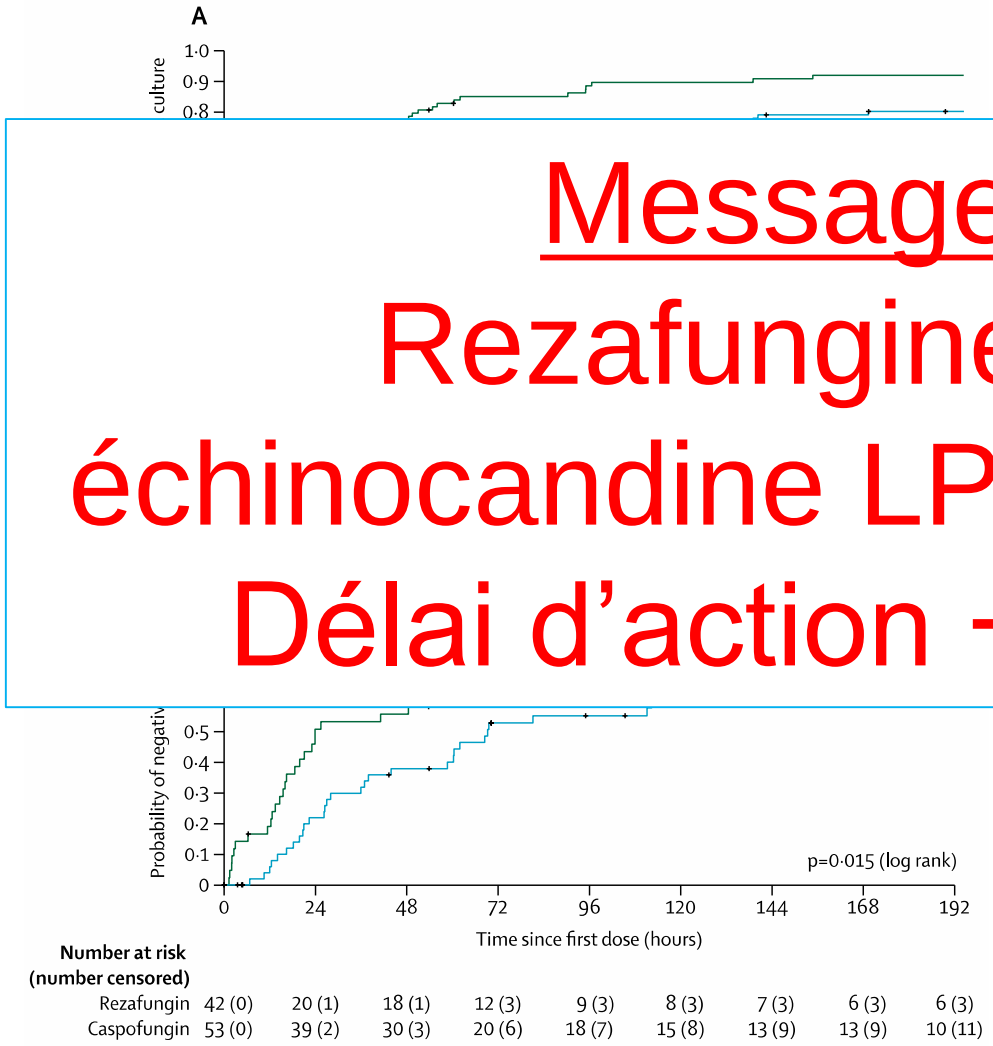


Message#4.

Rezafungine = 1ère échinocandine LP (1/semaine)

Délai d'action + rapide ?

Thompson GR et al. Lancet Infect Dis 2024

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Effectiveness and safety of dalbavancin in France: a prospective, multicentre cohort study

Johan Courjon[a,*], Eric Senneville[b], Hajnal-Gabriela Illes[c,1], Patricia Pavese[d], David Boutoille[e], Frederic C. Daoud[f], Nathalie Dunkel[g], Pierre Tattevin[h]

Dalbavancine: demi-vie = 14 jours => Vancomycine 'LP'
Posologie variable: ex. 1500 mg J1, puis 1000 mg J14, puis J42…
NB. 1500 € le gramme !!

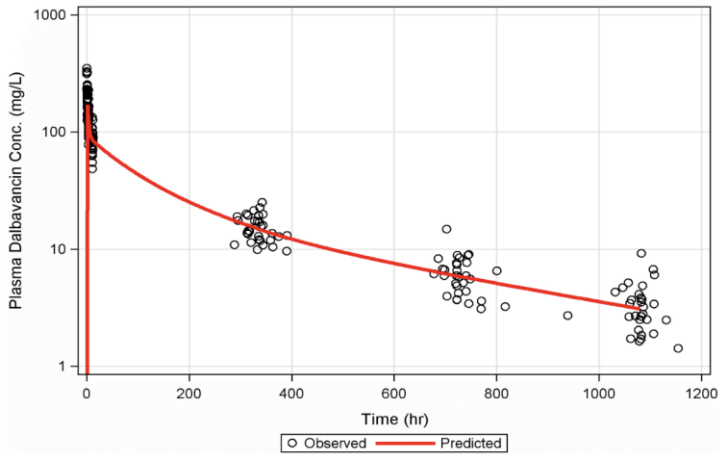


FIG 3 Linear plot of the population mean predicted amount of dalbavancin in serum versus time, overlaid upon the observed data.

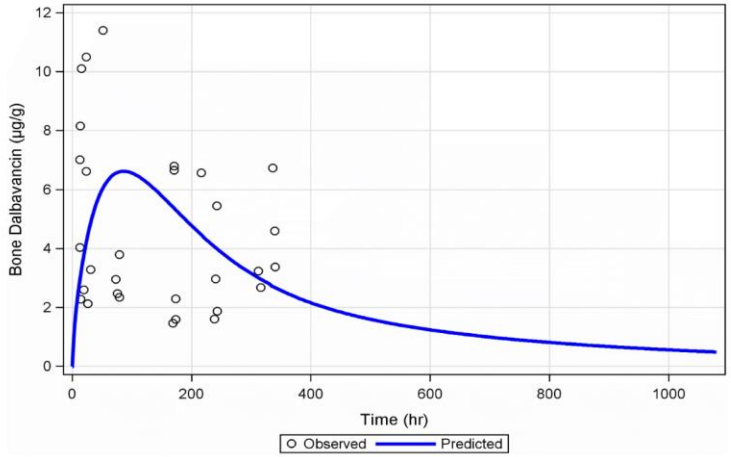


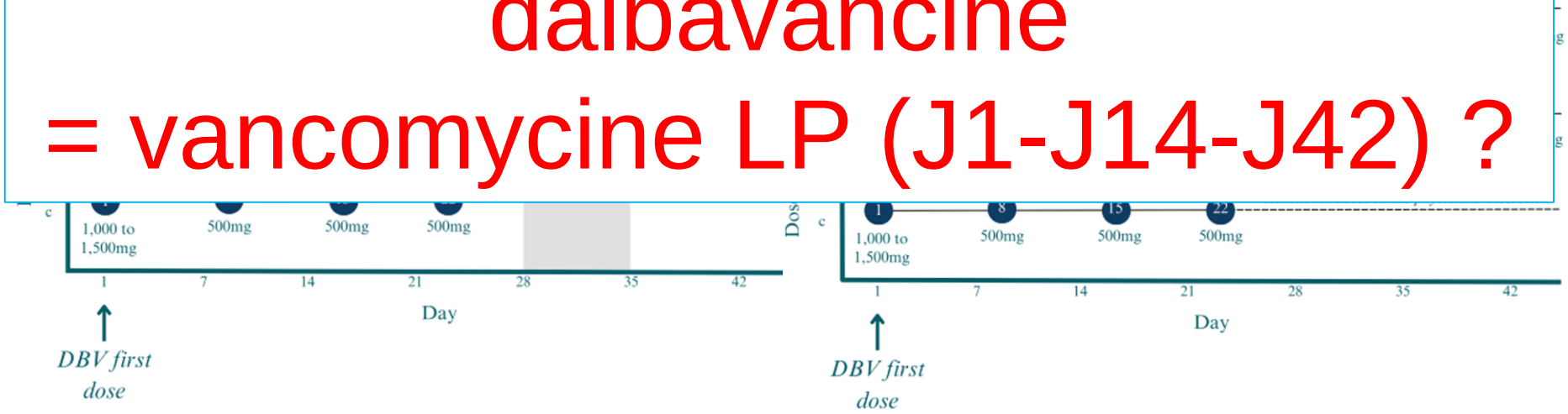
FIG 4 Linear plot of the population mean predicted amount of dalbavancin in bone versus time, overlaid upon the observed data.

Courjon J et al. Intern J Antimicrob Agents 2023

Expert Opinion on Dose Regimen and Therapeutic Drug Monitoring for Long-Term Use of Dalbavancin: Expert Review Panel

Eric Senneville[a,*], Guillermo Cuervo[b], Matthieu Gregoire[c,d], Carmen Hidalgo-Tenorio[e,f], François Jehl[g], Jose M. Miro[b,h], Andrew Seaton[i], Bo Söderquist[j,k], Alex Soriano[l,h], Florian Thalhammer[m], Federico Pea[n,o]

Message#5.
dalbavancine
= vancomycine LP (J1-J14-J42) ?



Senneville E et al. Intern J Antimicrob Agents 2023

Best of STPI/SPILF 2024

1. Antibiotiques / Antifongiques
2. Tuberculose
3. IST / VIH
4. COVID
5. Vaccins / prévention

Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults

Joseph Donovan, Ph.D., Nguyen D. Bang, Ph.D., Darma Imran, M.D., Ho D.T. Nghia, Ph.D., Erlina Burhan, Ph.D., Dau T.T. Huong, M.Sc., Nguyen T.T. Hiep, M.D., Lam H.B. Ngoc, B.Sc., Dang V. Thanh, M.D., Nguyen T. Thanh, M.D., Anna L.S. Wardhani, B.Sc., Kartika Maharani, M.D., Cakra P. Gasmara, M.D., Nguyen H.H. Hanh, M.D., Pham K.N. Oanh, M.D., Riwanti Estiasari, Ph.D., Do D.A. Thu, B.Sc., Ardiana Kusumaningrum, M.D., Le T. Dung, M.D., Do C. Giang, Ph.D., Dang T.M. Ha, Ph.D., Nguyen H. Lan, M.D., Nguyen V.V. Chau, Ph.D., Nguyen T.M. Nguyet, B.Sc., Ronald B. Geskus, Ph.D., Nguyen T.T. Thuong, Ph.D., Evelyne Kestelyn, M.P.H., Raph L. Hamers, Ph.D., Nguyen H. Phu, Ph.D., and Guy E. Thwaites, F.R.C.P., for the ACT HIV Investigators*

La dexaméthasone est-elle bénéfique au cours des TB neuro-méningées des PVVIH ?

- **Etude randomisée multicentrique double aveugle**
- **Vietnam, n = 520**
  - *Jamais reçu d'ARV = 50%*
  - *CD4 < 50/mm^3 = 50%*
- **Dexaméthasone, 6-8 semaines**
- **Critère principal: Survie à M12**

Donovan J et al. N Engl J Med 2023

Rappel: étude pivot Thwaites et al. 2004

TABLE 1. British Medical Research Council clinical criteria for the severity of TBM[a]

Stage/grade	Classic criterion[b]	Contemporary criterion[c]
I	Fully conscious and no focal deficits	Alert and oriented without focal neurological deficits
II	Conscious but with inattention, confusion, lethargy, and focal neurological signs	Glasgow coma score of 14-11 or 15 with focal neurological deficits
III	Stuporous or comatose, multiple cranial nerve palsies, or complete hemiparesis or paralysis	Glasgow coma score of 10 or less, with or without focal neurological deficits

Outcome and Group	Dexamethasone	Placebo	Relative Risk (95% CI)	P Value
	no./total no. (%)			
Death				
All patients	87/274 (31.8)	112/271 (41.3)	0.69 (0.52–0.92)	0.01
Grade				
I	15/90 (16.7)	26/86 (30.2)	0.47 (0.25–0.90)	0.02
II	38/122 (31.1)	50/125 (40.0)	0.71 (0.46–1.1)	0.11
III	34/62 (54.8)	36/60 (60.0)	0.81 (0.51–1.29)	0.38
Relative risk of death stratified according to grade†			0.68 (0.52–0.91)	0.007
HIV status				
Negative	57/227 (25.1)	67/209 (32.1)	0.72 (0.51–1.02)	0.07
Positive	27/44 (61.4)	37/54 (68.5)	0.86 (0.52–1.41)	0.55

Thwaites et al, NEJM 2004

Dexamethasone in TB meningitis

Week	Dose Dexamethasone IV
3	0.2
4	0.1
Taper as oral Dexamethasone 4mg/day, 3mg/day, 2mg/day & 1mg/day each for 1 week	

Thwaites et al, NEJM 2004

Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults

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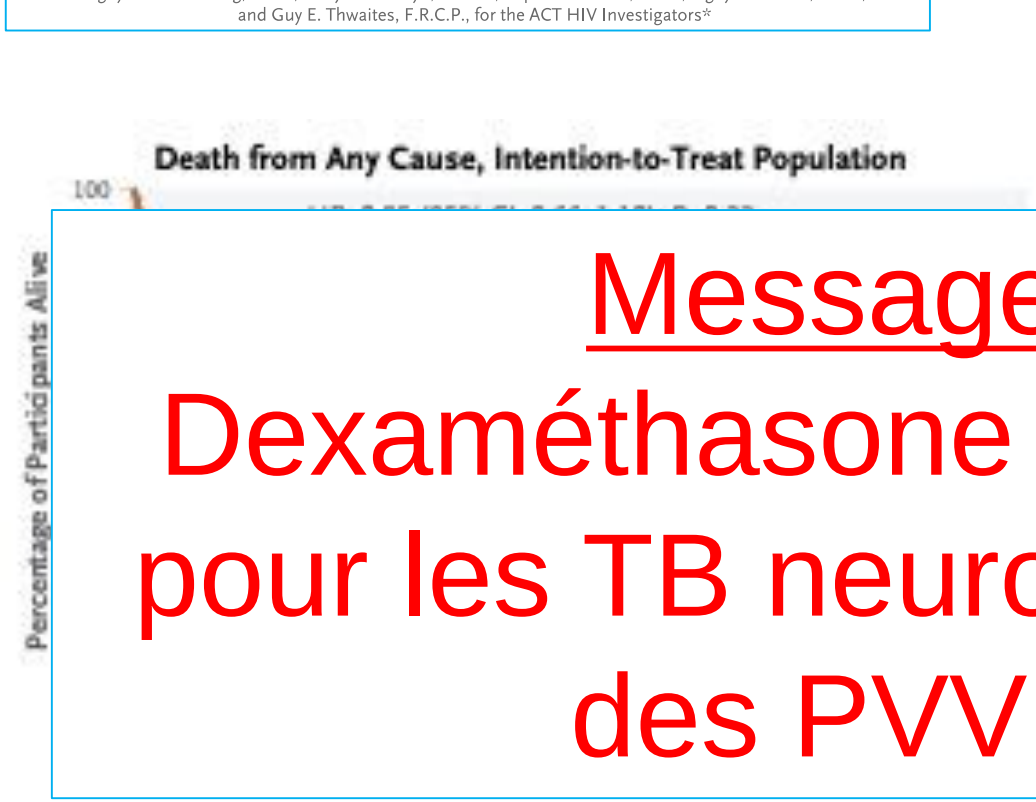

Message#6.

Dexaméthasone sans intérêt pour les TB neuro-méningées des PVVIH ?

Donovan J et al. N Engl J Med 2023

Best of STPI/SPILF 2024

1. Antibiotiques / Antifongiques
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Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

Anne F. Luetkemeyer, M.D., Deborah Donnell, Ph.D., Julia C. Dombrowski, M.D., M.P.H., Stephanie Cohen, M.D., M.P.H., Cole Grabow, M.P.H., Clare E. Brown, Ph.D., Cheryl Malinski, B.S., Rodney Perkins, R.N., M.P.H., Melody Nasser, B.A., Carolina Lopez, B.A., Eric Vittinghoff, Ph.D., Susan P. Buchbinder, M.D., Hyman Scott, M.D., M.P.H., Edwin D. Charlebois, Ph.D., M.P.H., Diane V. Havlir, M.D., Olusegun O. Soge, Ph.D., and Connie Celum, M.D., M.P.H., for the DoxyPEP Study Team*

Rappel Best of '2023'

Etude randomisée en ouvert, population à haut risque IST

1. Prepeurs
2. PVVIH ayant présenté ≥ 1 IST bactérienne au cours des 12 derniers mois

⇒ **Doxycycline, 200 mg dose unique dans les 24h (max 72h) après rapport non protégé**

Critère principal = incidence IST bactérienne (*Chlamydia* / Gono / Syphilis)

Critère secondaire = émergence résistance doxy + colonisation *S. aureus*

Luetkemeyer A et al. N Engl J Med 2023

Postexposure Doxycycline to Prevent

Eri
Edv

Rappel Best of '2023'

s

PLWH cohort 30/119

Hazard ratio for PrEP cohort, 0.34 (95% CI, 0.23–0.51)

Hazard ratio for PLWH cohort, 0.48 (95% CI, 0.28–0.83)

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

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RR Doxy-PEP

- Gono 0,45
- Chlamydia 0,12
- Syphilis 0,13

A PrEP Cohort

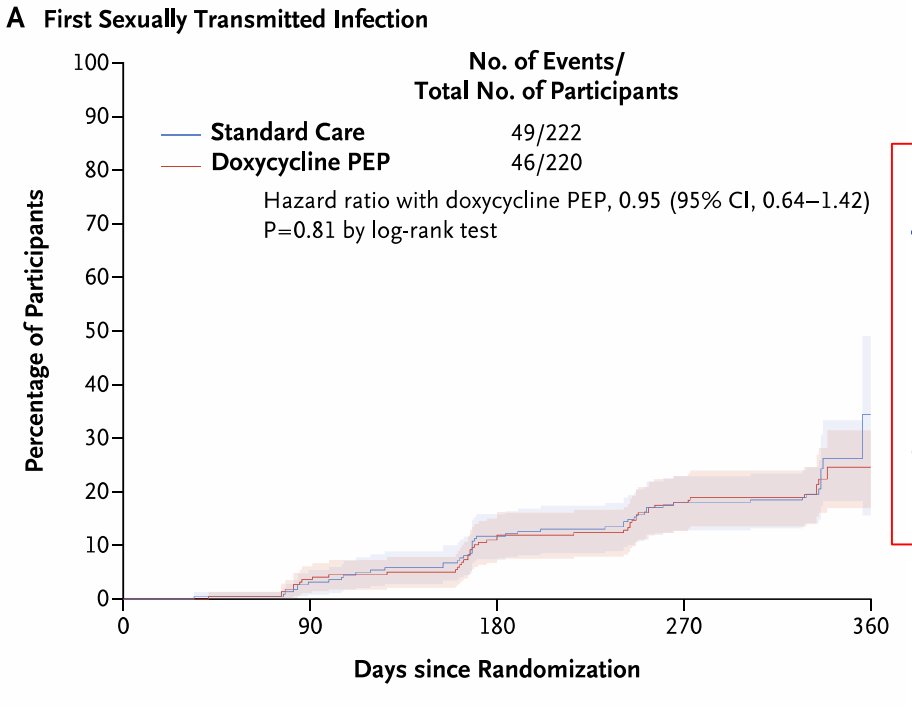
Analyses	Doxycycline	Standard Care	Relative Risk (95% CI)
	no. of quarterly visits with event /total no. of visits (%)		
Primary analysis			
Any STI	61/570 (10.7)	82/257 (31.9)	0.34 (0.24–0.46)
Secondary analysis			
Any gonorrhea	52/570 (9.1)	52/257 (20.2)	0.45 (0.32–0.65)
Urethral	5/570 (0.9)	12/257 (4.7)	0.19 (0.06–0.55)
Pharyngeal	38/570 (6.7)	34/257 (13.2)	0.50 (0.32–0.78)
Rectal	25/570 (4.4)	29/257 (11.3)	0.40 (0.23–0.69)
Any chlamydia	8/570 (1.4)	31/257 (12.1)	0.12 (0.05–0.25)
Urethral	1/570 (0.2)	6/257 (2.3)	0.07 (0.01–0.59)
Pharyngeal	2/570 (0.4)	4/257 (1.6)	0.22 (0.04–1.14)
Rectal	7/570 (1.2)	23/257 (8.9)	0.14 (0.06–0.32)
Any early syphilis	2/570 (0.4)	7/257 (2.7)	0.13 (0.03–0.59)

Rappel Best of '2023'

Luetkemeyer A et al. N Engl J Med 2023

Doxycycline Prophylaxis to Prevent Sexually Transmitted Infections in Women

Jenell Stewart, D.O., M.P.H., Kevin Oware, M.A., Deborah Donnell, Ph.D., Lauren R. Violette, M.P.H., Josephine Odoyo, R.N., M.P.H., Olusegun O. Soge, Ph.D., Caitlin W. Scoville, M.P.H., Victor Omollo, M.B., Ch.B., M.P.H., Felix O. Mogaka, M.B., Ch.B., Fredericka A. Sesay, M.B., Ch.B., M.P.H., R. Scott McClelland, M.D., M.P.H., Matthew Spinelli, M.D., M.P.H., Monica Gandhi, M.D., M.P.H., Elizabeth A. Bukusi, M.B., Ch.B., M.Med., M.P.H., Ph.D., and Jared M. Baeten, M.D., Ph.D., for the dPEP Kenya Study Team*



Message#7:

1. Stratégie inefficace dans cette population
2. Incidence IST relativement basse
3. Gonocoque 100% doxy-R
4. Observance estimée à 30%

(dosage doxy racine du cheveu)

Stewart J et al. N Engl J Med 2023

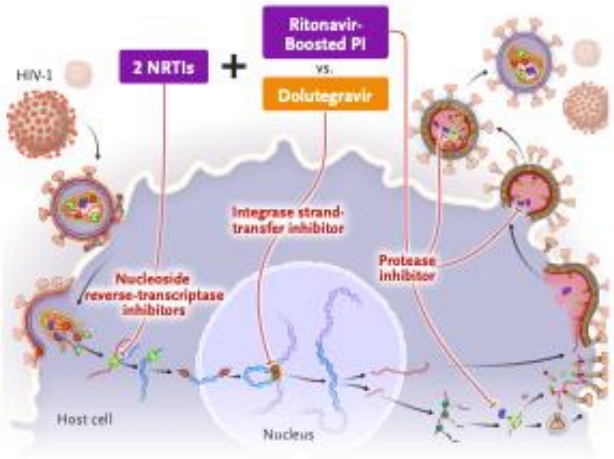
Second-Line Switch to Dolutegravir for Treatment of HIV Infection

Loice A. Ombajo, M.B., Ch.B., M.Med., Jeremy Penner, M.D., Joseph Nkuranga, M.B., Ch.B., Jared Mecha, M.B., Ch.B., M.Med., Margaret Mburu, M.P.H., Collins Odhiambo, Ph.D., Florentius Ndinya, M.B., Ch.B., M.Med., Rukia Aksam, M.B., Ch.B., Richard Njenga, B.Sc., Simon Wahome, M.Pharm., Peter Muiruri, M.B., Ch.B., Sheila Eshiwani, M.B., Ch.B., Maureen Kimani, M.B., Ch.B., Catherine Ngugi, M.B., Ch.B., and Anton Pozniak, M.B., Ch.B., M.D.

PVVIH en succès sous seconde ligne ARV (IP boostés): Peut-on passer au dolutegravir sans test résistance ?

- **Etude randomisée multicentrique en ouvert (Kenya)**
  - 795 PVVIH avec CV < 50 copies/mL sous IP boosté
  - Poursuite ARV idem vs switch dolutegravir

- **Critère principal: VIH indétectable à 12 mois**



Ombajo L et al. N Engl J Med 2023

Second-Line Switch to Dolutegravir for Treatment of HIV Infection

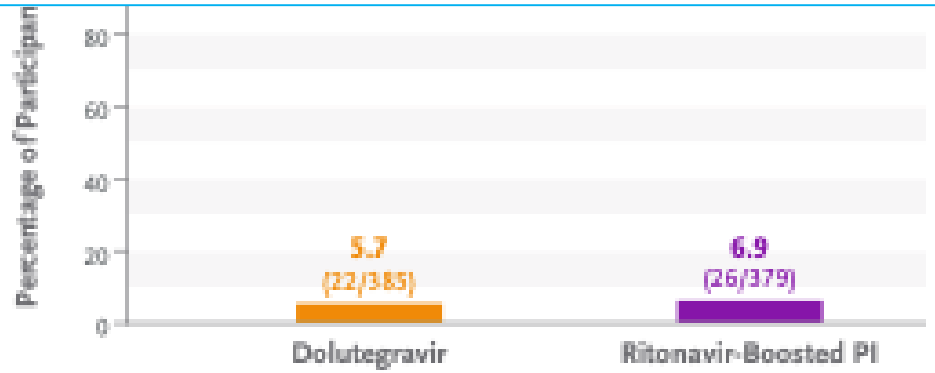
Loice A. Ombajo, M.B., Ch.B., M.Med., Jeremy Penner, M.D., Joseph Nkuranga, M.B., Ch.B., Jared Mecha, M.B., Ch.B., M.Med., Margaret Mburu, M.P.H., Collins Odhiambo, Ph.D., Florentius Ndinya, M.B., Ch.B., M.Med., Rukia Aksam, M.B., Ch.B., Richard Njenga, B.Sc., Simon Wahome, M.Pharm., Peter Muiruri, M.B., Ch.B., Sheila Eshiwani, M.B., Ch.B., Maureen Kimani, M.B., Ch.B., Catherine Ngugi, M.B., Ch.B., and Anton Pozniak, M.B., Ch.B., M.D.

Virologic Failure at Week 48

Message#8.

PVVIH bien contrôlé sous traitement 2nde ligne (IP/r)

=> Relais dolu sans hésiter !



Ombajo L et al. N Engl J Med 2023

Essai REPRIEVE : pitavastatine chez les PVVIH (1)

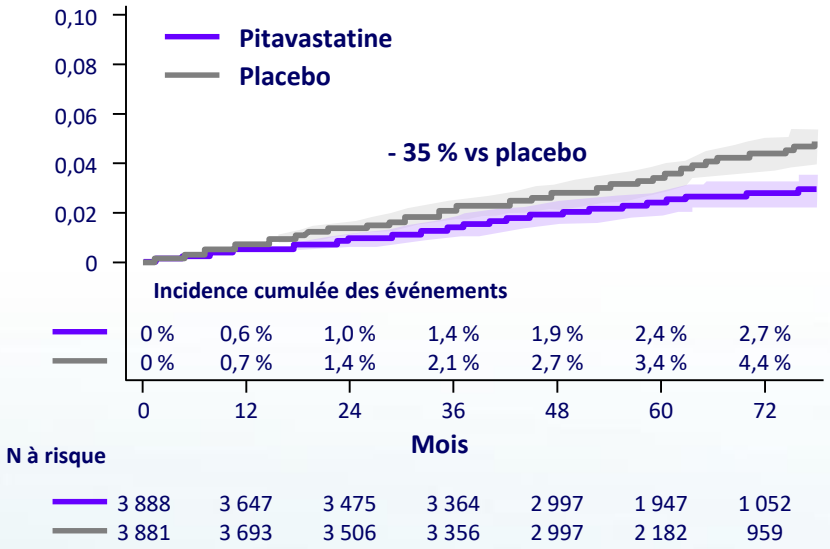
- **Critères d'inclusion**
  - **PVVIH CD4 > 100/mm³, âge 40 à 75 ans, pas de maladie cardiovasculaire**
  - **Score de risque de maladie cardiovasculaire athérosclérotique (MCVA) faible ou modéré** :
    - < 7,5 % et LDL-cholestérol < 1,9 g/L
    - 7,5 à 10 % et LDL-cholestérol < 1,6 g/L
    - > 10 % et ≤ 15 % et LDL-cholestérol < 1,3 g/L
-
- **Critère de jugement principal : événement cardiovasculaire majeur**
  - Décès de cause cardiovasculaire
  - Infarctus du myocarde
  - Angor instable
  - AIT ou AVC
  - Revascularisation artérielle
  - AOMI

Grinspoon S. NEJM 2023;389(8):687-699

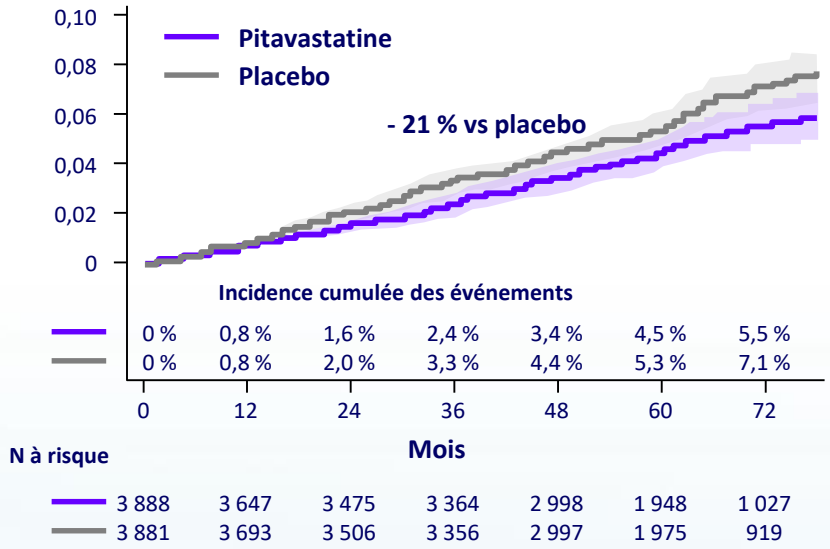
Essai REPRIEVE : pitavastatine chez les PVVIH (1)

- **Arrêt prématuré de l'essai en raison d'une efficacité démontrée**

Délai de survenue du 1er événement CV majeur



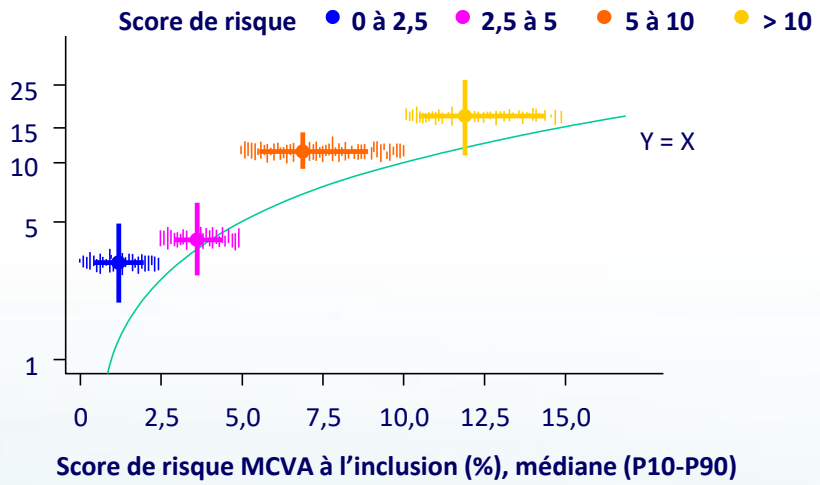
Délai de survenue du 1er événement CV majeur ou décès



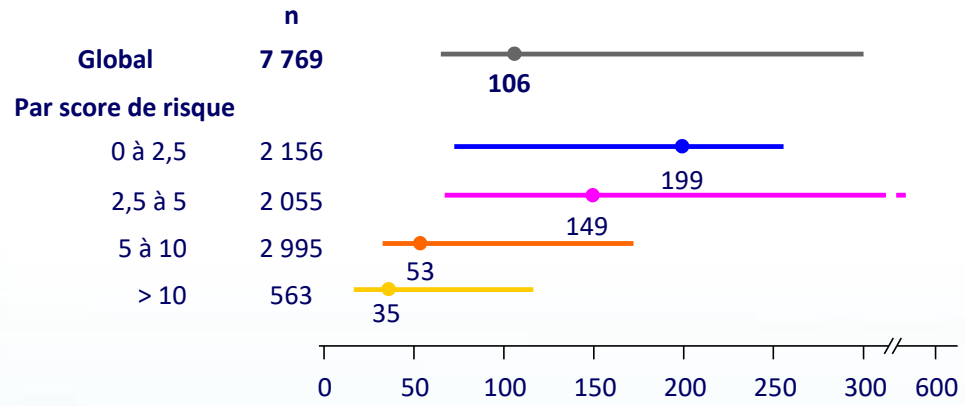
Grinspoon S. NEJM 2023;389(8):687-699

Essai REPRIEVE : pitavastatine chez les patients VIH+ (1)

Incidence estimée des événements cardiovasculaires majeurs/1 000 p-a (IC 95 %) dans le groupe placebo



Nombre (IC 95 %) devant être traités pendant 5 ans pour prévenir 1 événement cardiovasculaire majeur



Grinspoon S. NEJM 2023;389(8):687-699

Essai REPRIEVE : pitavastatine chez les patients VIH+ (1)

- **Réduction du LDL-cholestérol**
  - 30 % dans le groupe pitavastatine, durable
  - Impact clinique (35 % de réduction des événements CV majeurs) plus élevé que anticipé (17 %) sur la seule réduction du LDL-cholestérol : autres mécanismes potentiels du bénéfice (anti-inflammatoire ?)

- **Evénements indésirables**
  - Evénements indésirables graves de même fréquence dans les 2 groupes
  - Symptômes d'ordre musculaire plus élevés dans le groupe pitavastatine, mais le plus souvent modérés (arrêt de pitavastatine : environ 1 %)
  - Incidence de survenue de diabète 5,3 % dans le groupe pitavastatine vs 4,0 % dans le groupe placebo
  - Pas d'effet sur la survenue de grade 3 d'élévation des ALAT ou de rhabdomyolyse

- **Conclusion : pitavastatine 4 mg x 1/jour prévient les événements cardiovasculaires majeurs chez les PVVIH avec risque CV faible ou modéré et LDL-cholestérol normal**

Grinspoon S. NEJM 2023;389(8):687-699

Statines chez les PVVIH

- Suite aux ré
  - BHIVA rap / (Novembre 2023)
    - ***We rec CVD irrespective of lipid pr***
    - *We rec rade 2A)*
    - *We sug*

Message#9.

Statines pour tous les PVVIH >40 ans ?

Best of STPI/SPILF 2024

1. Antibiotiques / Antifongiques
2. Tuberculose
3. IST / VIH
4. COVID
5. Vaccins / prévention

RESEARCH SUMMARY

Randomized Trial of BCG Vaccine to Protect against Covid-19 in Health Care Workers

Pittet LF et al. DOI: 10.1056/NEJMoa2212616

Message#10.

En médecine, quand on essaie un traitement ‘au hasard’, ça ne marche pas !

Pittet LF et al. N Engl J Med 2023

Oral Simnotrelvir for Adult Patients with Mild-to-Moderate Covid-19

Bin Cao, M.D., Yeming Wang, M.D., Hongzhou Lu, M.D., Chaolin Huang, M.D., Yumei Yang, M.D., Ph.D., Lianhan Shang, M.D., Zhu Chen, M.D., Rongmeng Jiang, M.D., Yihe Liu, M.D., Ling Lin, M.D., Ping Peng, M.D., Fuxiang Wang, M.D., Fengyun Gong, M.D., Honglin Hu, M.S., Cong Cheng, M.D., Xiangyang Yao, M.D., Xianwei Ye, M.D., Hourong Zhou, M.D., Yinzhong Shen, M.D., Chenfan Liu, M.D., Chunying Wang, M.D., Zhennan Yi, M.D., Bijie Hu, M.D., Jiuyang Xu, M.D., Xiaoying Gu, Ph.D., Jingshan Shen, Ph.D., Yechun Xu, Ph.D., Leike Zhang, Ph.D., Jia Fan, M.D., Renhong Tang, Ph.D., and Chen Wang, M.D.

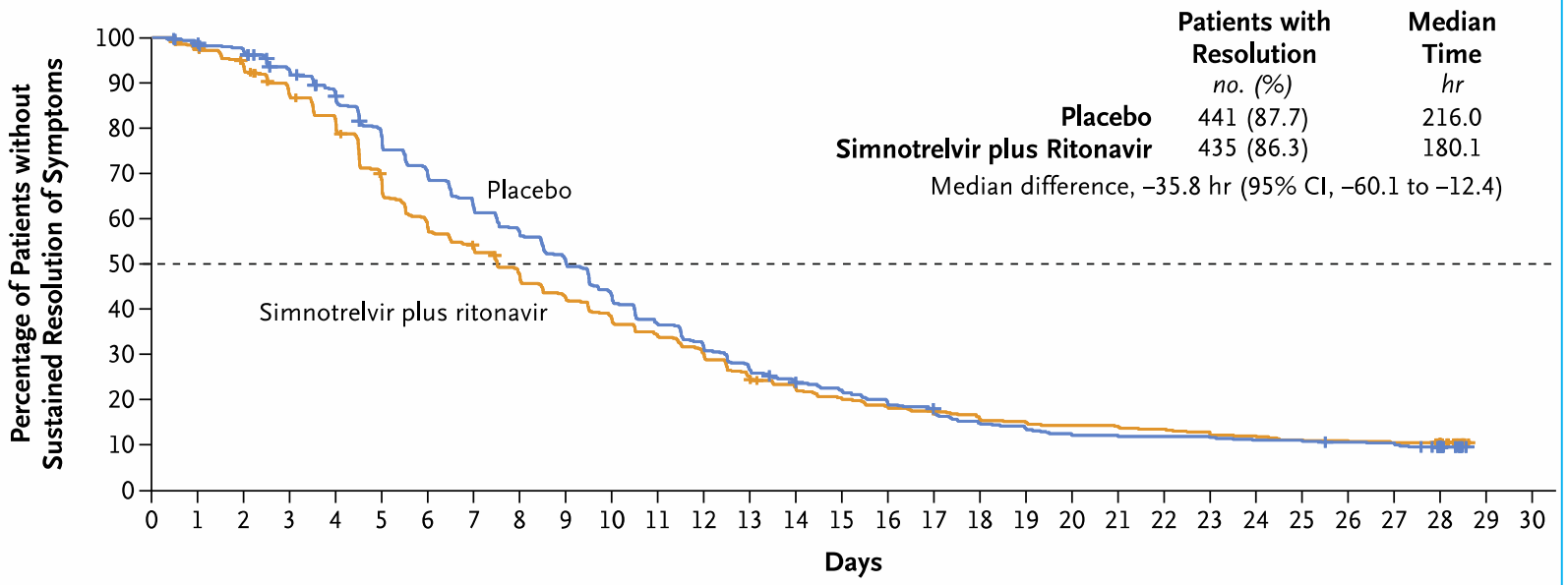
COVID: changement de paradigme

- **Etude randomisée multicentrique double aveugle (Chine)**
  - Période ‘Omicron’ (2022)
  - COVID non grave, symptomes < 72 h
- **Critère principal**
  - **Délai avant disparition des symptomes**
- **Critère secondaire**
  - Excrétion virale J5

Cao B et al. N Engl J Med 2023

Oral Simnotrelvir for Adult Patients with Mild-to-Moderate Covid-19

A Time to Sustained Resolution of Covid-19 Symptoms



	Patients with Resolution *no. (%)*	Median Time *hr*
Placebo	441 (87.7)	216.0
Simnotrelvir plus Ritonavir	435 (86.3)	180.1

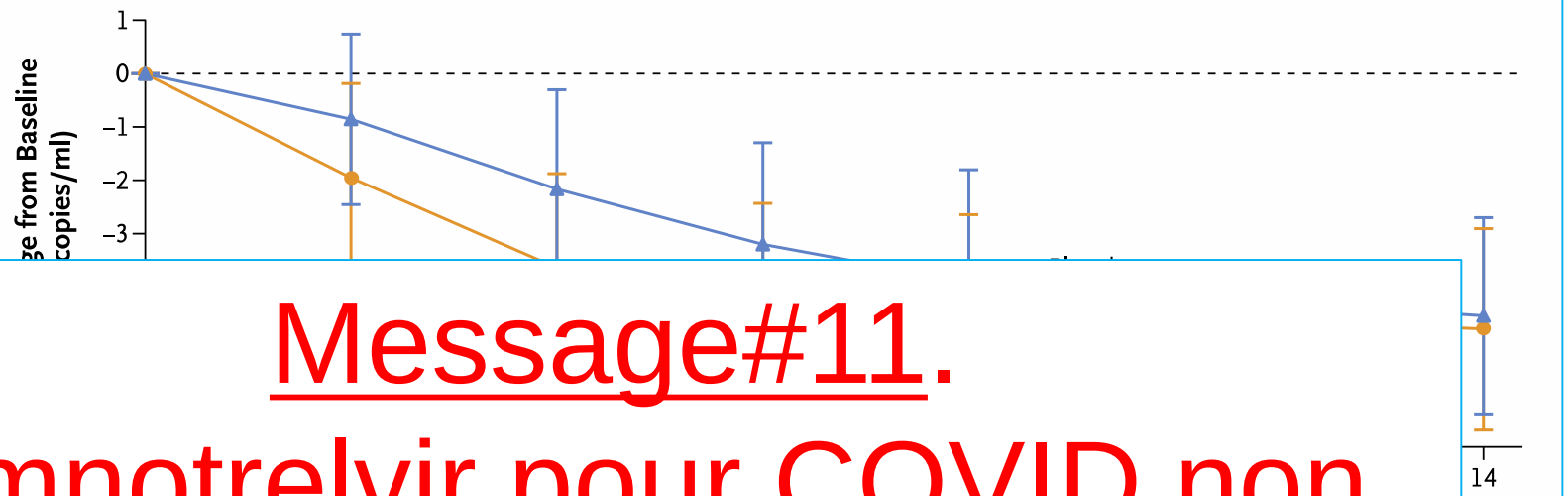
Median difference, −35.8 hr (95% CI, −60.1 to −12.4)

No. at Risk

Placebo	503	495	484	457	425	379	337	304	274	244	207	179	152	129	114	106	91	85	70	63	57	56	56	55	52	52	49	48	38	0
Simnotrelvir plus ritonavir	504	489	463	429	394	329	281	258	227	205	182	164	145	119	106	95	87	82	73	70	67	66	63	57	56	52	51	49	45	0

Cao B et al. N Engl J Med 2023

Oral Simnotrelvir for Adult Patients with Mild-to-Moderate Covid-19



Message#11.

Simnotrelvir pour COVID non grave c/o immunocompétent

⇒guérison en 7,5 j vs 9 j

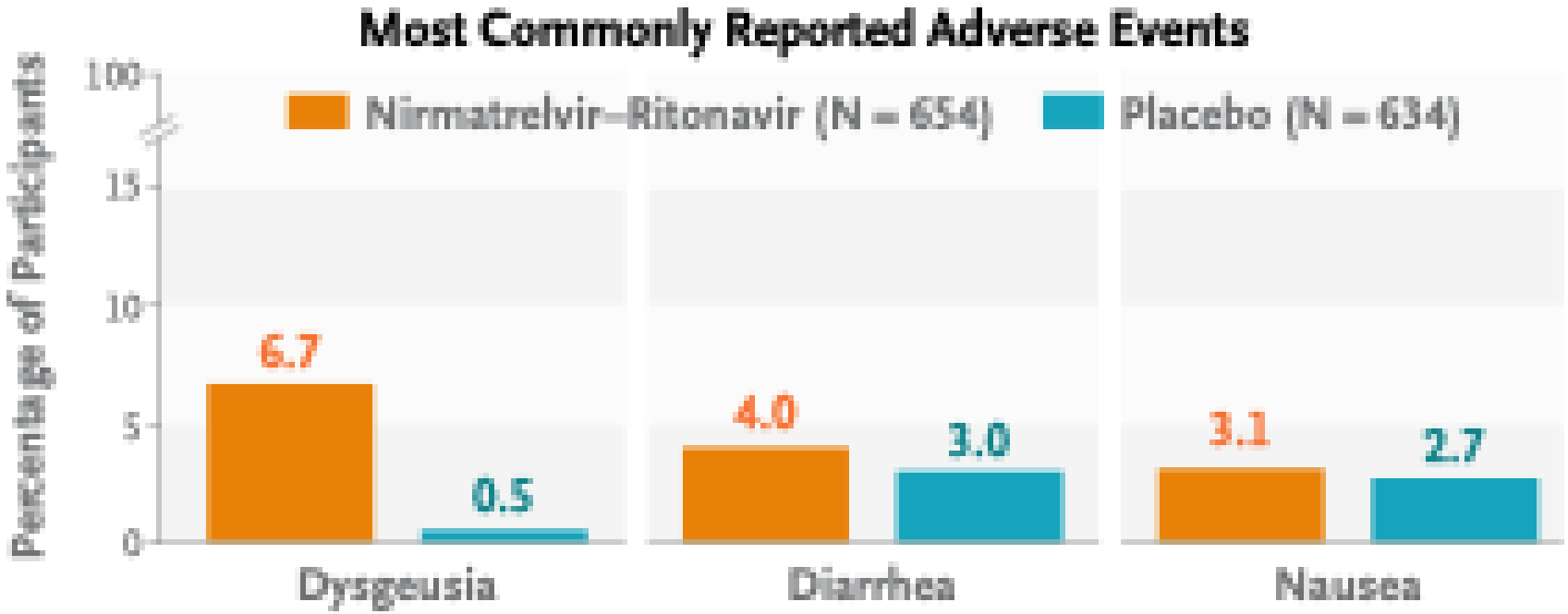
- Intérêt pour COVID long ?
- Intérêt pour contagiosité ?

Cao B et al. N Engl J Med 2023

RESEARCH SUMMARY

Nirmatrelvir for Vaccinated or Unvaccinated Adult Outpatients with Covid-19

Hammond J et al. DOI: 10.1056/NEJMoa2309003



Hammond J et al. N Engl J Med 2024

Convalescent Plasma for Covid-19–Induced ARDS in Mechanically Ventilated Patients

Benoît Misset, M.D., Michael Piagnerelli, M.D., Ph.D., Eric Hoste, M.D., Ph.D., Nadia Dardenne, M.Sc., David Grimaldi, M.D., Ph.D., Isabelle Michaux, M.D., Ph.D., Elisabeth De Waele, M.D., Ph.D., Alexander Dumoulin, M.D., Philippe G. Jorens, M.D., Ph.D., Emmanuel van der Hauwaert, M.D., Frédéric Vallot, M.D., Stoffel Lamote, M.D., Walter Swinnen, M.D., Nicolas De Schryver, M.D., Vincent Fraipont, M.D., Nathalie de Mey, M.D., Nicolas Dauby, M.D., Ph.D., Nathalie Layios, M.D., Jean-Baptiste Mesland, M.D., Ph.D., Geert Meyfroidt, M.D., Ph.D., Michel Moutschen, M.D., Ph.D., Veerle Compernolle, M.D., Ph.D., André Gothot, M.D., Ph.D., Daniel Desmecht, D.V.M., Ph.D., Maria I. Taveira da Silva Pereira, M.D., Ph.D., Mutien Garigliany, D.V.M., Ph.D., Tome Najdovski, Ph.D., Axelle Bertrand, M.Sc., Anne-Françoise Donneau, Ph.D., and Pierre-François Laterre, M.D.

- **Etude randomisée multicentrique ouvert (Belgique)**
- **COVID grave (intubé < 5 j)**

=> Plasma de convalescent hyper-immun

- **Critère principal**
  - **Mortalité à J28**

Misset B et al. N Engl J Med 2023

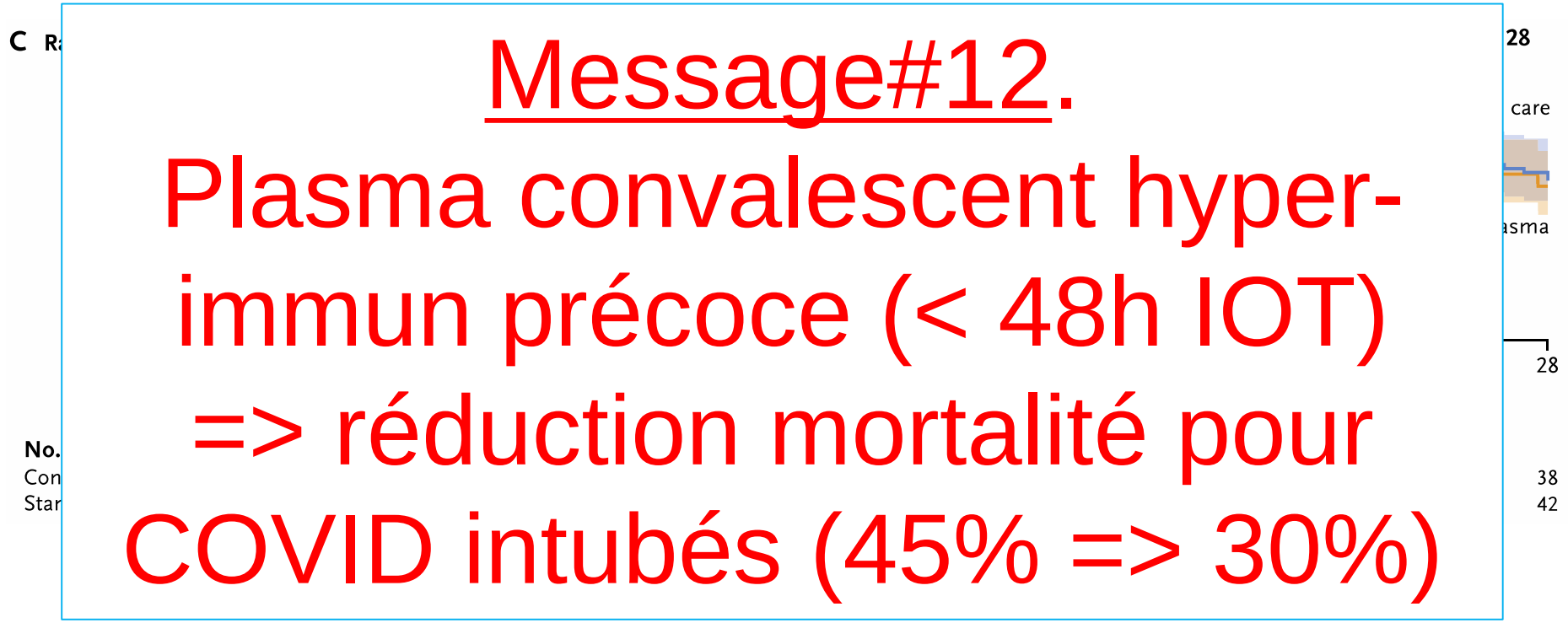
Convalescent Plasma for Covid-19–Induced ARDS in Mechanically Ventilated Patients

Table 2. Mortality at Day 28.*

Population	Convalescent Plasma	Standard Care	P Value
	no. of deaths/no. of patients (%)		
Total	84/237 (35.4)	107/238 (45.0)	0.03†
Randomization stratum			
≤48 Hr after IMV initiation	56/171 (32.7)	80/171 (46.8)	
>48 Hr after IMV initiation	28/66 (42.4)	27/67 (40.3)	

Misset B et al. N Engl J Med 2023

Convalescent Plasma for Covid-19–Induced ARDS in Mechanically Ventilated Patients



Message#12.

Plasma convalescent hyper-immun précoce (< 48h IOT) => réduction mortalité pour COVID intubés (45% => 30%)

Misset B et al. N Engl J Med 2023

A synbiotic preparation (SIM01) for post-acute COVID-19 syndrome in Hong Kong (RECOVERY): a randomised, double-blind, placebo-controlled trial

Raphaela I Lau, Qi Su*, Ivan S F Lau, Jessica Y L Ching, Martin C S Wong, Louis H S Lau, Hein M Tun, Chris K P Mok, Steven W H Chau, Yee Kit Tse, Chun Pan Cheung, Moses K T Li, Giann T Y Yeung, Pui Kuan Cheong, Francis K L Chan†, Siew C Ng†*

- **Post-COVID documentés, adultes (n=463)**
  - Pré-/probiotiques (*Bifidobacterium sp.* & oligosachharides)
  - PO, 2/j x 6 mois, vs placebo
  - **Critère principal = amelioration symptoms PACS à M6**
    (post-acute COVID-19 symptoms, CDC)
  - Critères secondaires
    - Qualité de vie
    - Activité physique
    - Tolérance
    - Analyse qualitative microbiote fécal

Lau RI et al. Lancet Infect Dis 2023

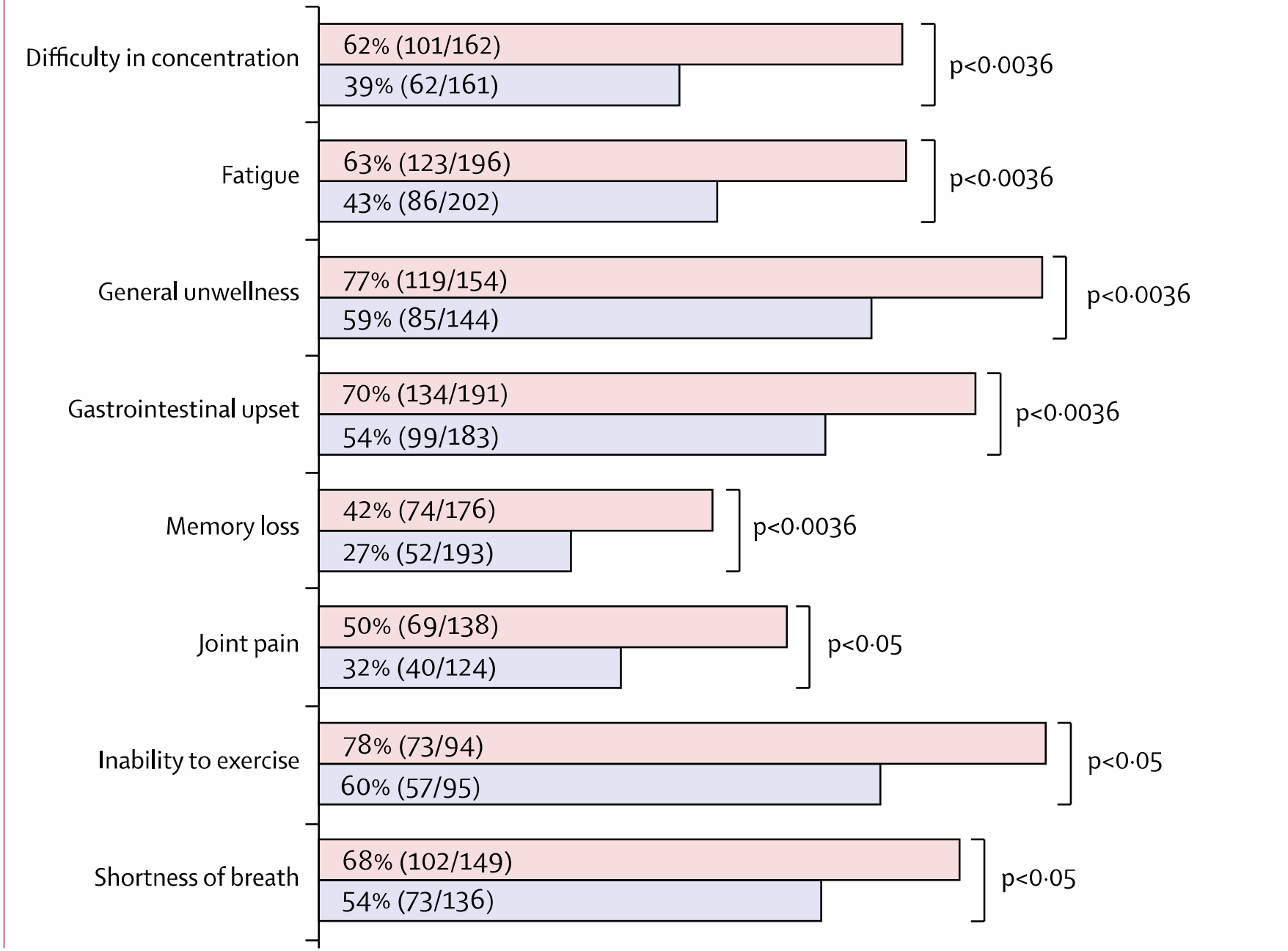


Figure 2: **Proportion of PACS symptoms alleviation by 6 months**

Lau RI et al. Lancet Infect Dis 2023

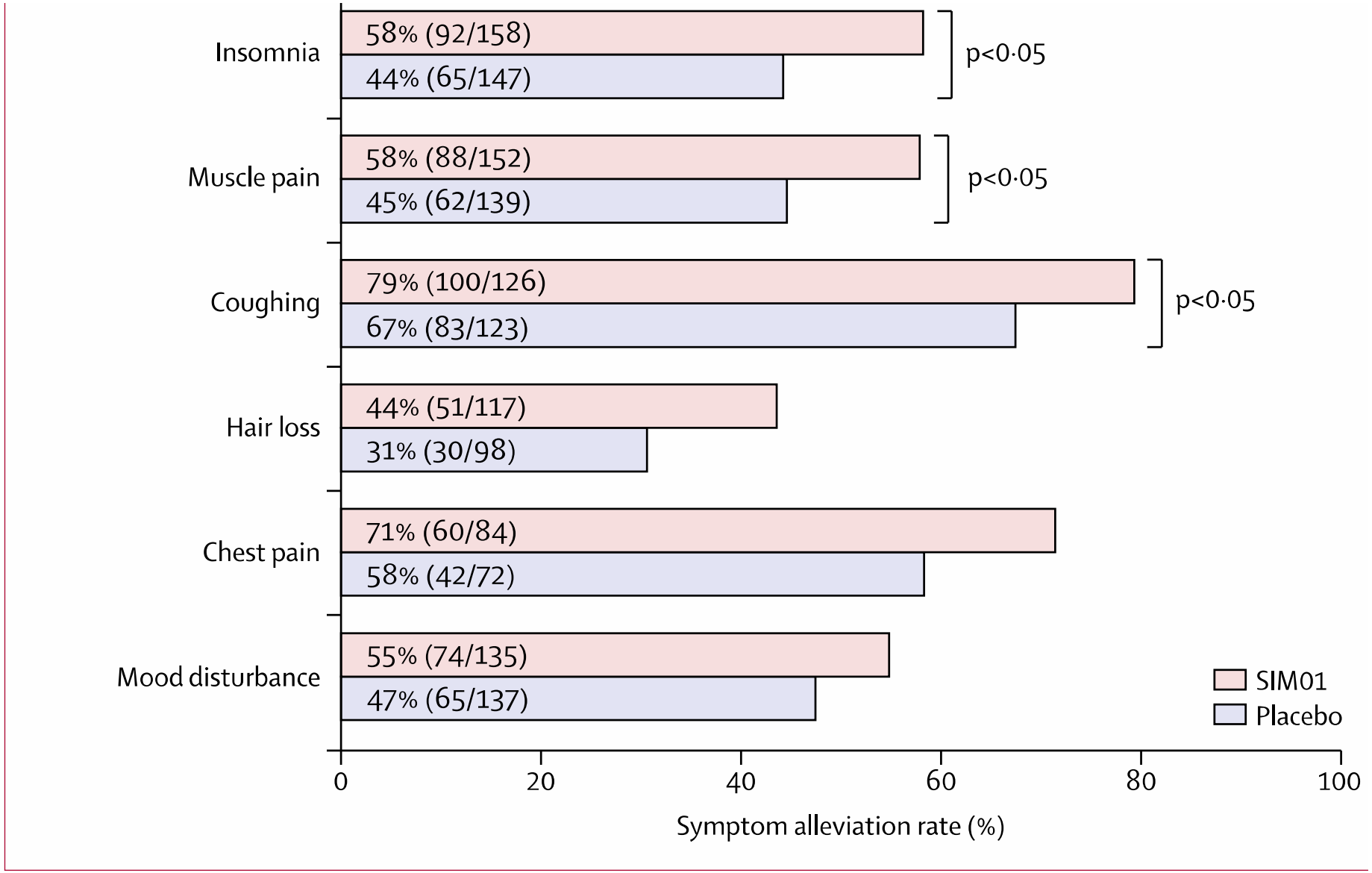


Figure 2: **Proportion of PACS symptoms alleviation by 6 months**

Lau RI et al. Lancet Infect Dis 2023

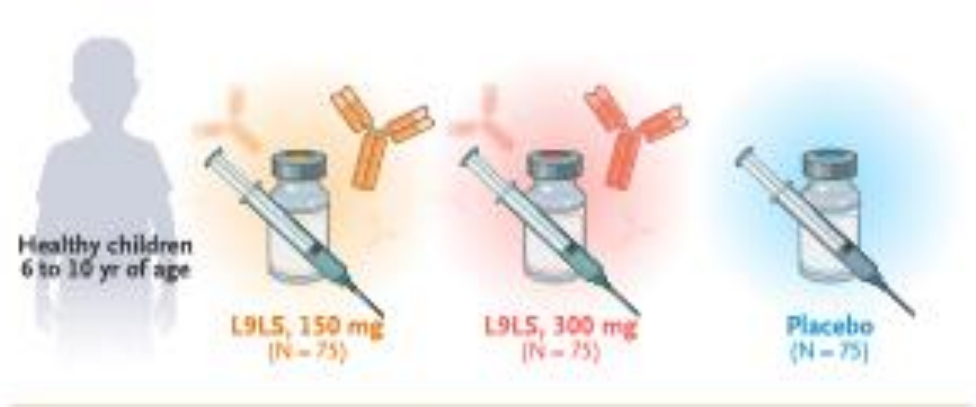
Best of STPI/SPILF 2024

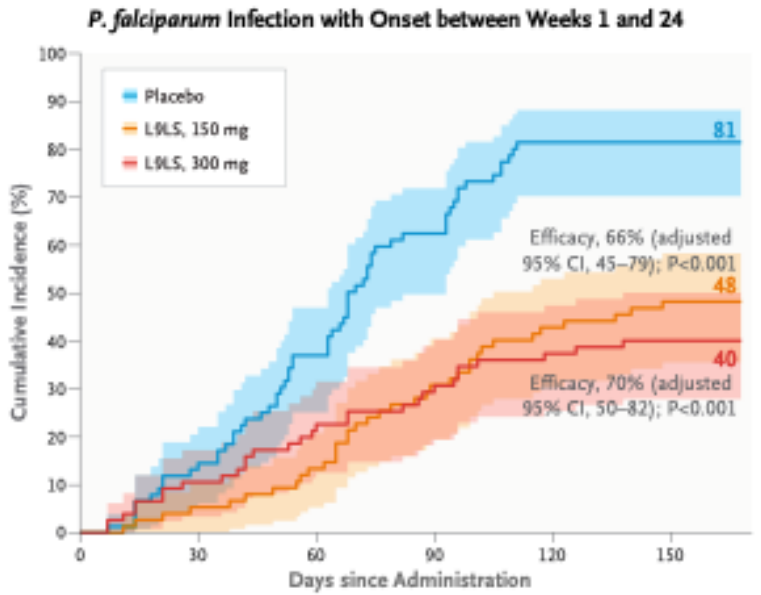
1. Antibiotiques / Antifongiques
2. Tuberculose
3. IST / VIH
4. COVID
5. Vaccins / prévention

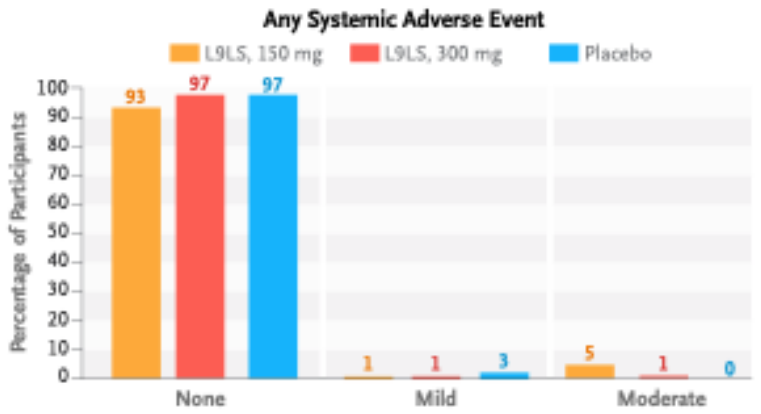
RESEARCH SUMMARY

Subcutaneous Administration of a Monoclonal Antibody to Prevent Malaria

Kayentao K et al. DOI: 10.1056/NEJMoa2312775





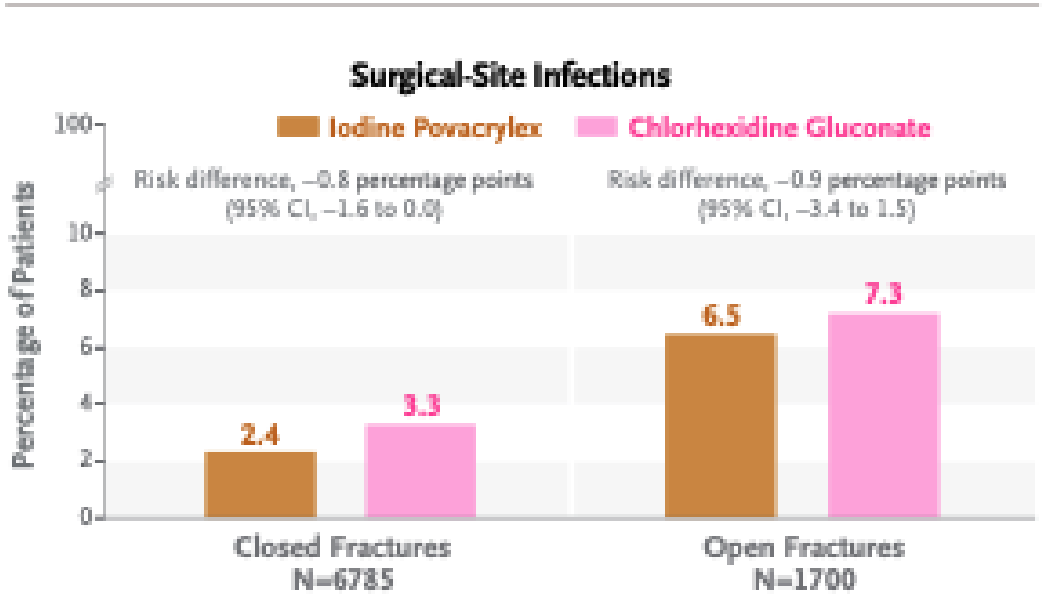


Kayentao K et al. N Engl J Med 2024

RESEARCH SUMMARY

Skin Antisepsis before Surgical Fixation of Extremity Fractures

The PREP-IT Investigators DOI: 10.1056/NEJMoa2307679



The PREP-IT investigators. N Engl J Med 2024

ORIGINAL ARTICLE

RSV Prefusion F Protein–Based Maternal Vaccine — Preterm Birth and Other Outcomes

Ilse Dieussaert, I.R., Joon Hyung Kim, M.D., Sabine Luik, M.D., Claudia Seidl, M.Sc., Wenji Pu, Ph.D., Jens-Ulrich Stegmann, M.D., Geeta K. Swamy, M.D., Peggy Webster, M.D., and Philip R. Dormitzer, M.D., Ph.D.

Table 2. Vaccine Efficacy against Medically Assessed RSV-Associated Lower Respiratory Tract Disease in Infants up to 6 Months of Age.*

Outcome	RSVPreF3-Mat Group (N=3426)		Placebo Group (N=1711)		Vaccine Efficacy (95% Credible Interval)
	Events	Incidence	Events	Incidence	
	no.	*no. of events/ 1000 person-yr*	*no.*	*no. of events/ 1000 person-yr*	%
Any medically assessed RSV-associated lower respiratory tract disease	16	9.7	24	29.2	65.5 (37.5–82.0)
Severe medically assessed RSV-associated lower respiratory tract disease	8	4.8	14	17.0	69.0 (33.0–87.6)

Dieussaert I et al. N Engl J Med 2024

ORIGINAL ARTICLE

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Ilse Dieussaert, I.R., Joon Hyung Kim, M.D., Sabine Luik, M.D., Claudia Seidl, M.Sc., Wenji Pu, Ph.D., Jens-Ulrich Stegmann, M.D., Geeta K. Swamy, M.D., Peggy Webster, M.D., and Philip R. Dormitzer, M.D., Ph.D.

Table 4. Post Hoc Analysis of the Risk of Preterm Birth among Infants According to Risk Factor.*

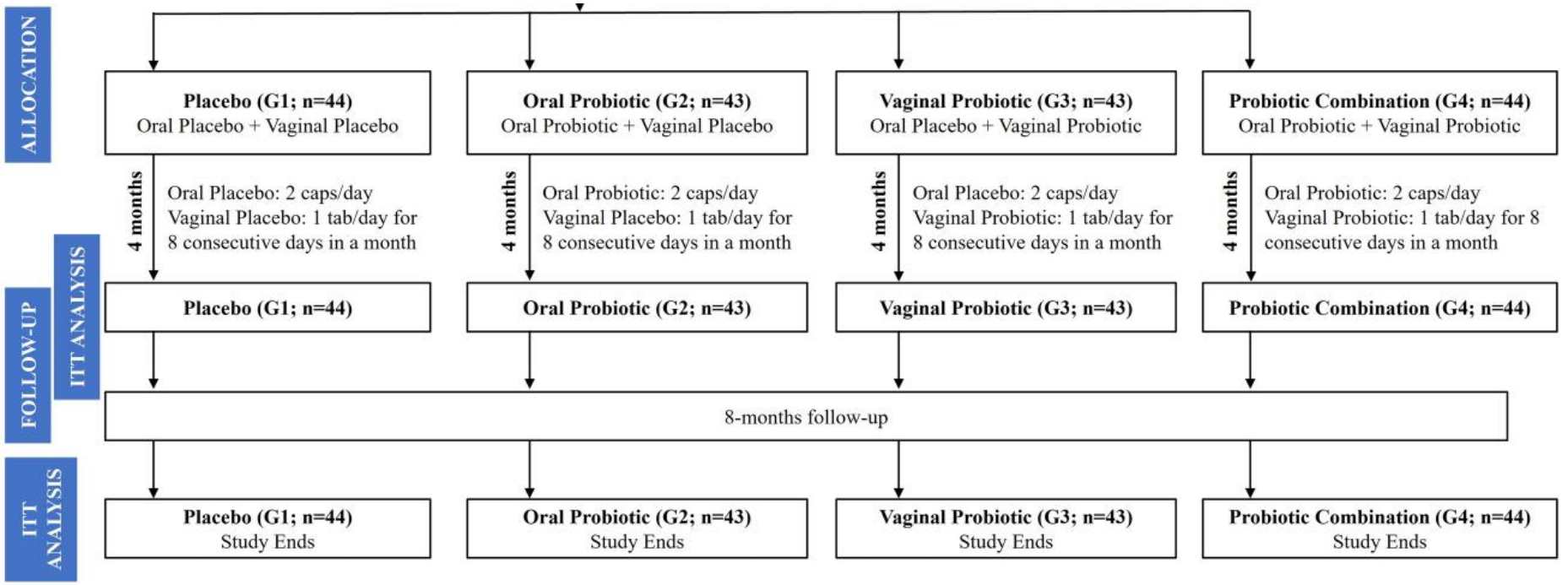
Variable	RSVPreF3-Mat Group		Placebo Group		Relative Risk (95% CI)
	Infants	Incidence (95% CI)	Infants	Incidence (95% CI)	
	no. of preterm births/total no.	%	*no. of preterm births/total no.*	%	
Preterm birth†					
Overall	237/3494	6.8 (6.0–7.7)	86/1739	4.9 (4.0–6.1)	1.37 (1.08–1.74)
Moderate-to-late preterm	224/3494	6.4 (5.6–7.3)	84/1739	4.8 (3.9–5.9)	1.33 (1.04–1.69)
Very preterm	11/3494	0.3 (0.2–0.6)	2/1739	0.1 (0.0–0.4)	2.74 (0.61–12.34)

Dieussaert I et al. N Engl J Med 2024

Effectiveness of Prophylactic Oral and/or Vaginal Probiotic Supplementation in the Prevention of Recurrent Urinary Tract Infections: A Randomized, Double-Blind, Placebo-Controlled Trial

Varsha Gupta,[1] Paola Mastromarino,[2] and Ritu Garg[3]

- **Femmes pré-ménopausées, IU récidivantes (n=174)**



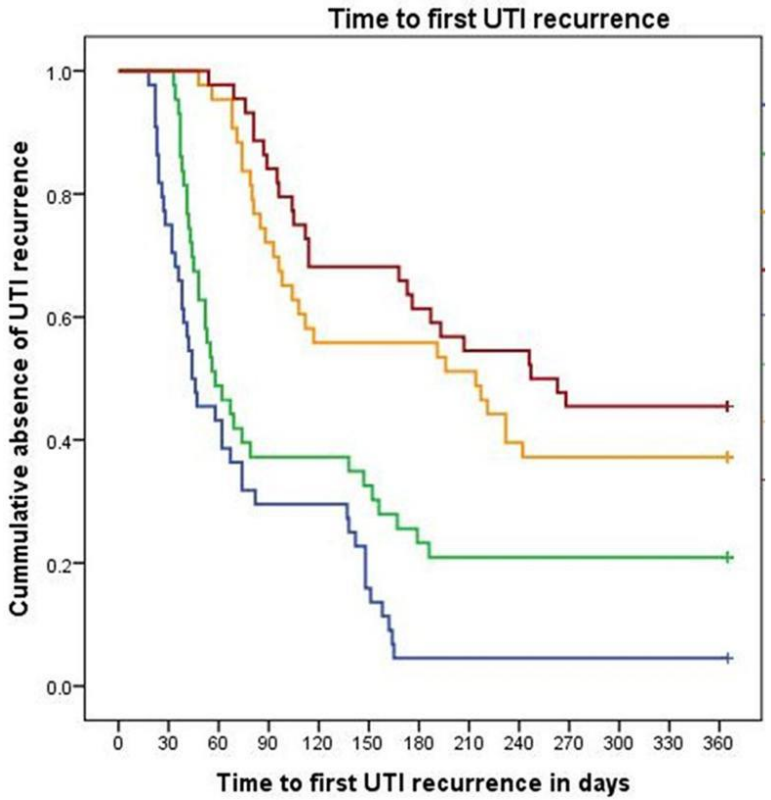
Gupta V et al. Clin Infect Dis 2024

Effectiveness of Prophylactic Oral and/or Vaginal Probiotic Supplementation in the Prevention of Recurrent Urinary Tract Infections: A Randomized, Double-Blind, Placebo-Controlled Trial

Varsha Gupta,[1] Paola Mastromarino,[2] and Ritu Garg[3]

Table 2. Number of Symptomatic Urinary Tract Infection Recurrences at 4 Months and 12 Months in the Treatment Groups

Parameter	Group[a]	Number of UTI Recurrences	Mean UTI Recurrences	*F*-value	*P* Value
Number of symptomatic UTI recurrences at 4 mo	G1	31	2.10 ± 0.97	15.6	<.001
	G2	27	1.63 ± 0.85[b]		
	G3	18	1.06 ± 0.74[b,c]		
	G4	14	1.07 ± 0.79[b,c]		
Number of symptomatic UTI recurrences at 12 mo	G1	42	3.83 ± 1.12	27.3	<.001
	G2	34	3.38 ± 0.92		
	G3	27	2.18 ± 0.74[b,c]		
	G4	24	2.04 ± 0.62[b,c]		



Gupta V et al. Clin Infect Dis 2024

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Varsha Gupta,[1] Paola Mastromarino,[2] and Ritu Garg[3]

Table 5. Vaginal Microbiota Pre- and Post-Treatment as Assessed by Quantitative Reverse Transcription Polymerase Chain Reaction in the Treatment Groups

Vaginal Microbiota (Relative Quantification)		G1[a]	G2[a]	G3[a]	G4[a]	*P* Value (Between Groups)
Escherichia coli	Pre	3.37 ± 1.3	6.61 ± 7.2	4.63 ± 3.01	4.86 ± 2.8	.404
	Post	4.55 ± 1.4[b]	1.70 ± 2.1[c]	0.96 ± 1.03[c,d]	1.01 ± 0.96[c,d]	<.001
Klebsiella pneumoniae	Pre	1.77 ± 0.7	3.75 ± 4.2	4.01 ± 2.2	3.48 ± 2.1	.242
	Post	2.67 ± 1.8	1.61 ± 1.3	1.34 ± 1.03[d]	1.13 ± 0.9[d]	.73
Proteus mirabilis	Pre	2.83 ± 1.6	3.51 ± 2.9	4.18 ± 1.0	4.84 ± 3.2	.29
	Post	3.07 ± 2.6	4.17 ± 2.5	2.54 ± 1.1[d]	1.60 ± 0.8[b,d]	.046
Bifidobacterium	Pre	1.67 ± 1.6	2.52 ± 3.2	2.02 ± 1.4	2.64 ± 2.8	.788
	Post	2.20 ± 2.8	5.73 ± 4.6	4.09 ± 3.04	5.97 ± 2.7[d]	.065
Lactobacillus	Pre	0.68 ± 0.5	2.65 ± 3.4	1.32 ± 1.5	0.73 ± 0.6	.94
	Post	1.12 ± 0.6	1.31 ± 0.8	3.71 ± 3.02[d]	4.16 ± 3.4[c,d]	0.008

Abbreviation: G, group.

[a]G1 used oral placebo + vaginal placebo; G2 used oral probiotic + vaginal placebo; G3 used oral placebo + vaginal probiotic; and G4 used oral probiotic + vaginal probiotic.

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Table 6. Global Assessment of Improvement in Patient's Condition at 4 Months in the Treatment Groups

Treatment Group[a]/Improvement Compared to Baseline	Very Much Improved	Much Improved	Minimally Improved	No Change	Minimally Worse	Much Worse
G1	0 (0%)	4 (9.1%)	5 (11.4%)	22 (50.0%)	13 (29.5%)	0 (0%)
G2	0 (0%)	1 (2.3%)	9 (20.9%)	25 (58.1%)	8 (18.6%)	0 (0%)
G3	11 (25.6%)	19 (44.2%)	10 (23.3%)	2 (4.7%)	1 (2.3%)	0 (0%)
G4	9 (20.5%)	24 (54.5%)	10 (22.7%)	1 (2.3%)	0 (0%)	0 (0%)

[a]G1 used oral placebo + vaginal placebo; G2 used oral probiotic + vaginal placebo; G3 used oral placebo + vaginal probiotic; and G4 used oral probiotic + vaginal probiotic.

Gupta V et al. Clin Infect Dis 2024

Les 10 messages à ramener à la maison:

1. **14 j pour IU masculines fébriles**
2. **Relais per os à J5-J7 pour bactériémies *S. aureus* non compliquées**
3. **Céfépime-taniborbactam pour BGN XDR (dont metallo-betalactamase)**
4. **Rezafungine = échinocandine LP (1/semaine)**
5. **Dalbavancine = vancomycine LP (J0 J14 J42… ?)**
6. **Dexaméthasone sans intérêt pour TB neuro-méningée des PVVIH**
7. **Doxycycline post-exposition IST décevante chez les femmes**
8. **Relais dolutegravir pour PVVIH sous ARV 2nde ligne (IP boostés)**
9. **Statine pour tous les PVVIH >40 ans**
10. **Plasma convalescent hyperimmun précoce pour COVID intubé**

Longue vie à la STPI & la STPI junior !

& Choukrane aux ami-e-s Tunisien-ne-s !