PLACE DU QUANTIFERON MONITOR EN NEPHROLOGIE

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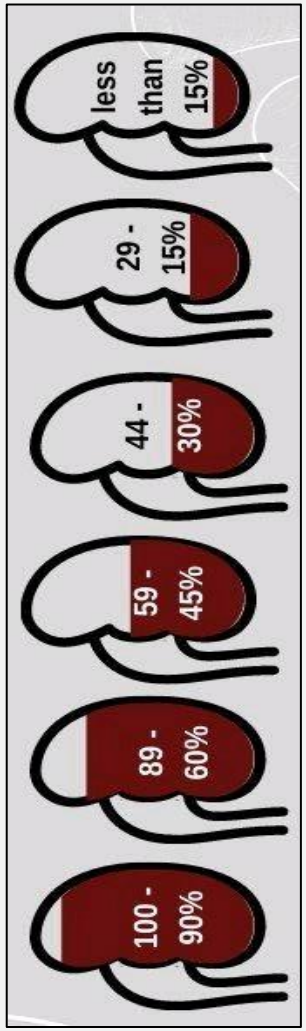
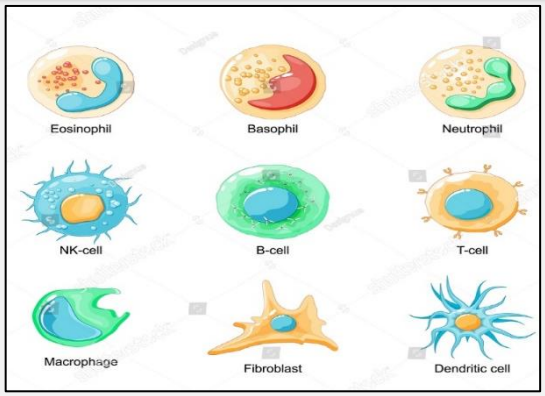
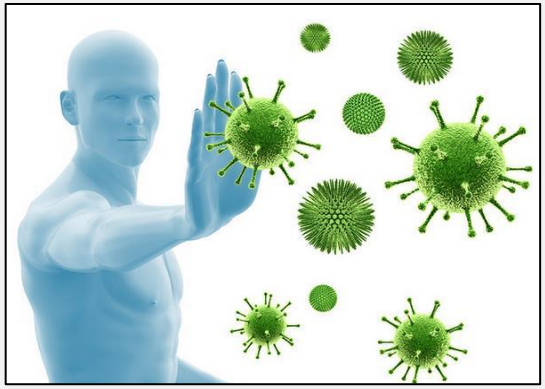
Quantiféron Monitor en Néphrologie, Introduction

Maladie Rénale Chronique





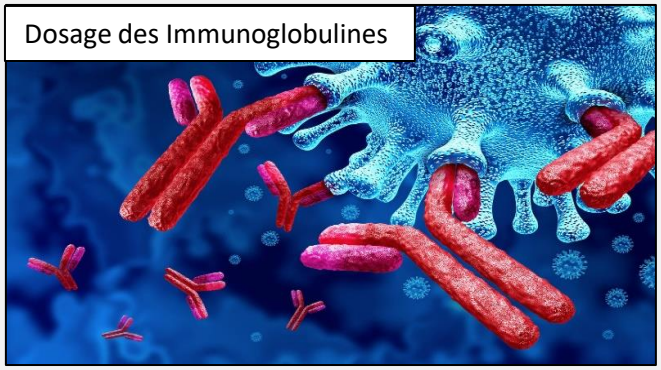
Immunité

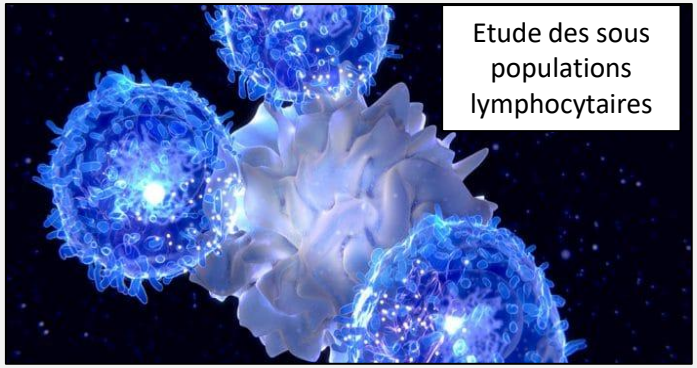


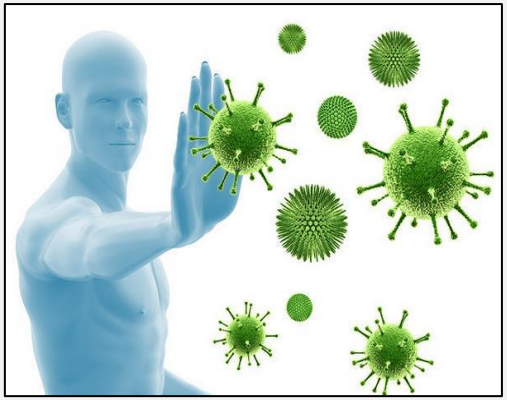
Risque infectieux

Groupe à risque ?

Quantiféron Monitor en Néphrologie, MRC & Risque Infectieux - Marqueurs ?





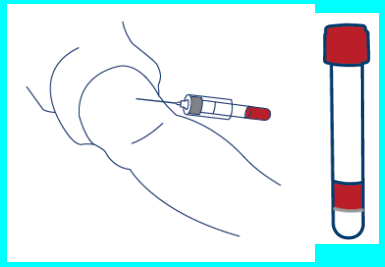


Functional immune assay using interferon-gamma could predict infectious events in end-stage kidney disease.

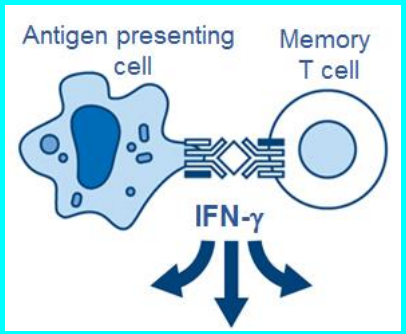
Boyer-Suavet S, Cremoni M, Dupeyrat T, Zorzi K, Brglez V, Benzaken S, Esnault V, Seitz-Polski B.

Clin Chim Acta. 2020 Mar;502:287-292. doi: 10.1016/j.cca.2019.11.018. Epub 2019 Nov 30.

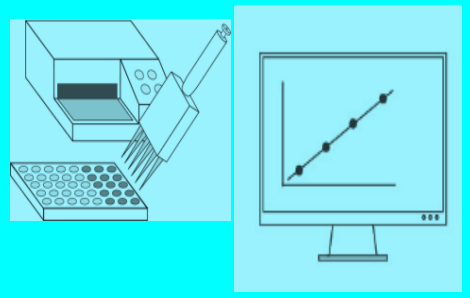
Quantiféron Monitor en Néphrologie, Technique



1. **Whole blood collection and exposure to immune-stimulants**



2. Stimulant recognition and production of interferon-gamma (IFN-γ)



3. Quantification of IFN-γ by ELISA

- **QFM utilise une combinaison de stimulants, ciblant spécifiquement différents types de cellules impliquées dans le système immunitaire:**
  - **inné : agonistes TLR.**
  - **adaptatif: stimulation TCR.**
- **Technique ELISA**
- **Test IGRA: ''Interferon Gamma Released Assay 'ou Test de relargage de l'interféron gamma, mesure la production d'interféron gamma suite à cette stimulation .**
- **Test non spécifique d'un pathogène,**
- **Test qualitatif et quantitatif.**
- **Test valide, fiable, reproductible, rapide , simple et peu couteux?**

Quantiféron Monitor en Néphrologie, Quantiféron Monitor - Interprétation

- ☞ Les résultats du **QFM** sont disponibles en 24 heures.
- ☞ La double stimulation avec des ligands innés et adaptatifs: avantage significatif par rapport aux dosages à un seul stimulant.
- ☞ Interprétation:

QFM IFN-γ (IU/ml)	Classification	Interpretation
<15	Faible	Réponse faible IFN-γ aux stimulants immunitaires innés et adaptatifs
15-1000	Moderée	Réponse IFN-γ modérée aux stimulants immunitaires innés et adaptatifs
>1000	Elevée	Réponse IFN-γ élevée aux stimulants immunitaires innés et adaptatifs

1) Sood, S.et al. (2014) Transplantation, **97**,

Quantiféron Monitor en Néphrologie, Transplantation Rénale

- La transplantation rénale (TR) est la meilleure option pour les patients atteints d'insuffisance rénale chronique terminale . Pour éviter le rejet de l'organe greffé, les receveurs de greffe renale reçoivent un traitement immunosuppresseur à vie.
- La thérapie immunosuppressive, cependant, est une arme à double tranchant:

  *Une immunosuppression excessive peut précipiter des cancers et des infections.

  *Tandis que la sous-immunosuppression augmente le risque de rejet de greffe.
- Ainsi, il est important de surveiller la fonction du système immunitaire chez les receveurs et de guider le dosage des immunosuppresseurs et des agents anti-infectieux .

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (1-1)

2020 ; 99(27):e21010

Medicine®

Observational Study

OPEN

Evaluation of cell-mediated immune response by QuantiFERON Monitor Assay in kidney transplant recipients presenting with infective complications

Ivan Margeta, MD[a], Ivana Marekovic, MD, PhD[b,d], Ana Pešut, MD[b], Marina Zelenika, MD[c], Marija Dorotić[a], Ivana Mrnjec[a], Mladen Knotek, MD, PhD[a,d,*]

Abstract

The net level of immunosuppression in kidney transplant recipients is difficult to assess. QuantiFERON Monitor (QFM) is an in vitro diagnostic test that detects interferon-γ (IFN-γ) release in peripheral blood. The aim of our study was to compare QFM testing results in stable kidney transplant recipients and kidney transplant recipients with infection, in a single-centre cohort.

We enrolled 71 kidney transplant recipients from our transplantation centre. They were divided into 2 groups according to clinical presentation (Stable kidney transplant recipients or Infection).

There were no significant differences in interferon-γ release between the 2 groups (Stable kidney transplant recipients 140.59 ± 215.28 IU/ml, Infection group 78.37 ± 197.03 IU/ml, $P = .24$). A further analysis revealed that kidney transplant recipients presenting with bacterial infection had significantly lower IFN-γ release when compared to stable kidney transplant recipients (26.52 ± 42.46 IU/ml vs 140.59 ± 215.28 IU/ml, $P = .04$).

Kidney transplant recipients presenting with bacterial infection had lower IFN-γ release when compared to stable kidney transplant recipients. The QFM test may be useful as a tool to help guide immunosuppression dosing in kidney transplant recipients, but further studies are required to confirm its diagnostic value.

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (1-2)

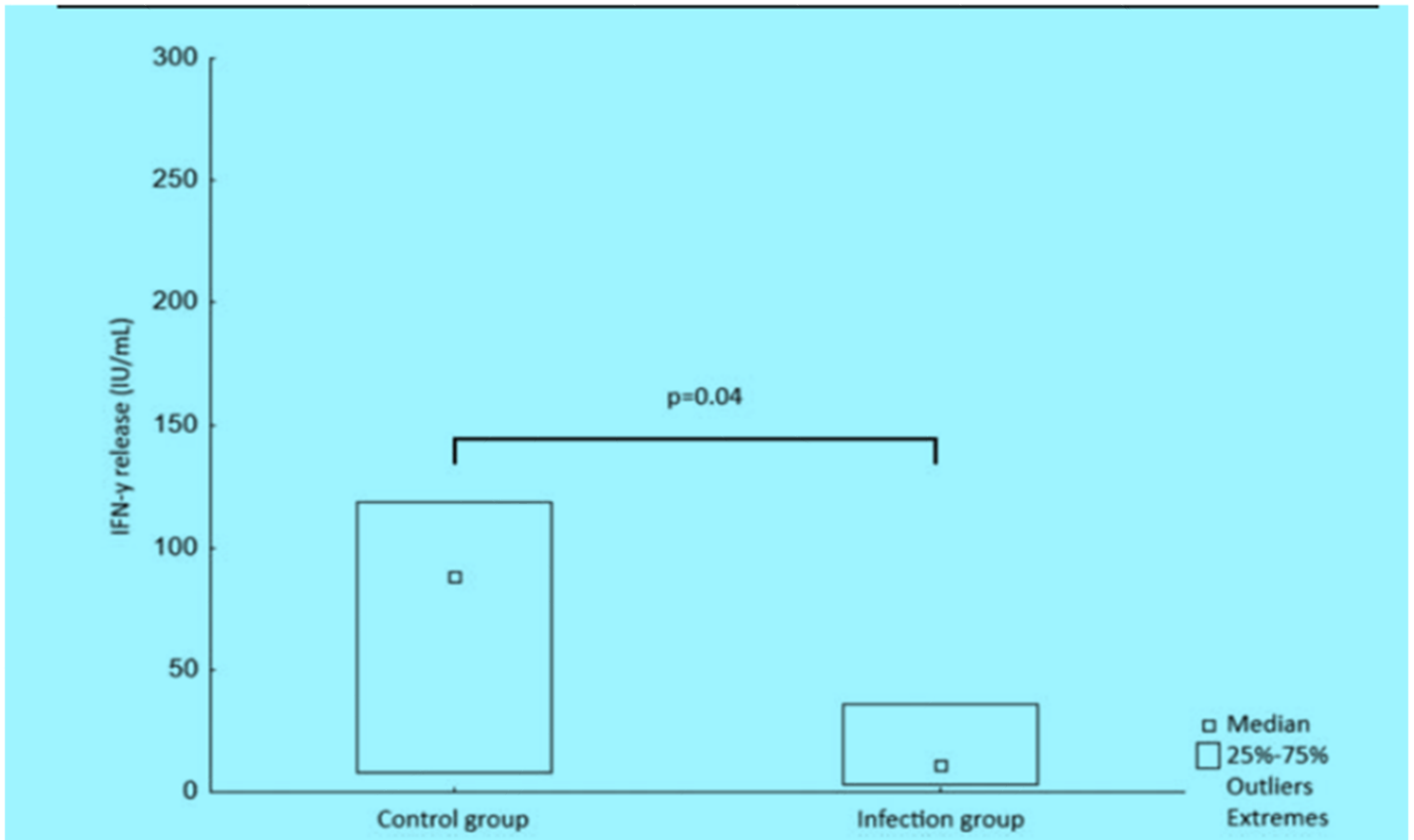


Figure 1. IFN-γ release difference between control and infection group exluding viral infections.

Référence: Medicine 2020; 97 (2)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (1-3)

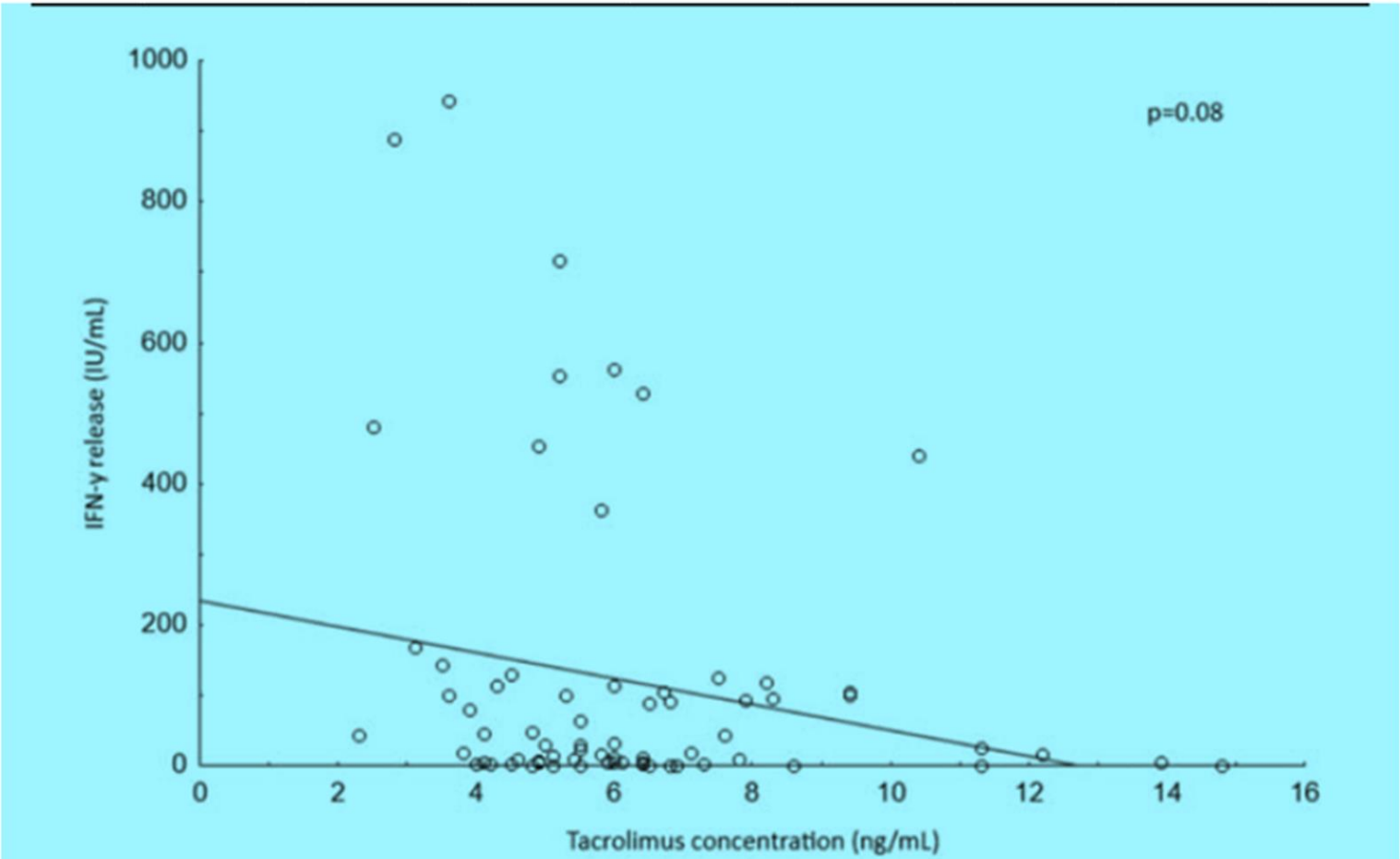


Figure 2. Correlation of Tacrolimus concentration and IFN-γ release.

Référence: Medicine 2020; 97 (2)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (1-4)

Table 3

Multivariate logistic regression analysis with bacterial infection as a dependent variable.

	Odds ratio	−95% CI	+95% CI	*P* value
IFN-γ release	0.98	0.97	1.00	.07
Tac concentration	1.11	0.85	1.44	.44
Steroid dose	1.24	0.98	1.56	.07

IFN-γ = interferon gamma, MPA = mycophenolic acid, Tac = tacrolimus.

Référence: Medicine 2020; 97 (2)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (2)

P-2.33

THE UTILITY OF QUANTIFERON MONITORING BASED ASSAY IN ASSESSING CLINICAL EVENTS AMONG KIDNEY TRANSPLANT RECIPIENTS

Maisarah Jalalonmuhali[1], Soo Jin Lim[2], Chee Sian Kuan[3], Xue Zheng Wong[1], Soo Kun Lim[1], Kok Peng Ng[1]
[1]Division of Nephrology, Department of Medicine, University Malaya Medical Centre, Kuala Lumpur, Malaysia; [2]Sunway Medical Centre Velocity, Kuala Lumpur, Malaysia; [3]Neogenix Laboratoire Sdn Bhd, Selangor, Malaysia.

Background: Immediate post transplantation care is crucial and requires close monitoring. Traditionally, transplant physicians relied on the crude markers such as therapeutic drug monitoring and clinical events to guide in the management of immunosuppression therapy. Quantiferon Monitor (QFM) is an immune based monitoring assay assessing IFN-γ which can be used as an objective marker of net immune function among kidney transplant recipients. Thus, the objective of this study is to look at the IFN-γ level post transplantation in relation to the incidence of Cytomegalovirus (CMV) viraemia, BK viraemia and hospitalisation.

Methodology: This is a prospective longitudinal study recruited all new kidney transplant recipients at University Malaya Medical Centre. The QFM were performed either at 1-month, 3-month, 6-month or 12-month post kidney transplantation. Based on the manufactured guidelines, IFN-γ (IU/mL) level < 15 IU/mL is low IFN-γ response, 15 – 1000 IU/mL is moderate IFN-γ response and > 1000 IU/mL is high IFN-γ response to innate and adaptive immune stimulants. CMV polymerase chain reaction (PCR), BKV PCR and protocol biopsy were performed according to standard protocol. Hospital admissions for any source of infection were recorded from the electronic medical report.

Results: A total of 85 patients with 206 samples for QFM were collected at designated interval. The mean IFN-γ level were 44.49 ± 74.07 IU/mL at 1-month, 94.21 ± 141.57 IU/mL at 3-month, 132.47 ± 168.33 IU/mL at 6-month and 221.52 ± 219.31 IU/mL at 12-month post transplantation. The levels were in increasing manner. This was correlated with the reduction of immunosuppression post transplantation. The incidence of CMV viraemia, BK viraemia and hospitalisation for any source of infection were significantly associated with low IFN-γ.

Conclusion: IFN-γ is a potential marker of net immune function among renal transplant recipients immediate post transplantation. The initial level would be able to serve as guiding tools for further reduction in immunosuppression and ultimately reduce the risk of infection. **Référence: Transplantation 2020; 103 (S4)**

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (3-1)

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Evaluation of a Novel Global Immunity Assay to Predict Infection in Organ Transplant Recipients

Muhtashim Mian, Yoichiro Natori, Victor Ferreira, Nazia Selzner, Shahid Husain, Lianne Singer, S. Joseph Kim, Atul Humar[a], and Deepali Kumar[a]

Multi-Organ Transplant Program, University Health Network, Toronto, Ontario, Canada

Conclusions. We show that a novel global immunity assay is able to quantify the level of immunosuppression and predict the risk of subsequent infection episodes in organ transplant recipients.

Référence: Clin Infect Dis 2018; 66 (9)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (3-2)

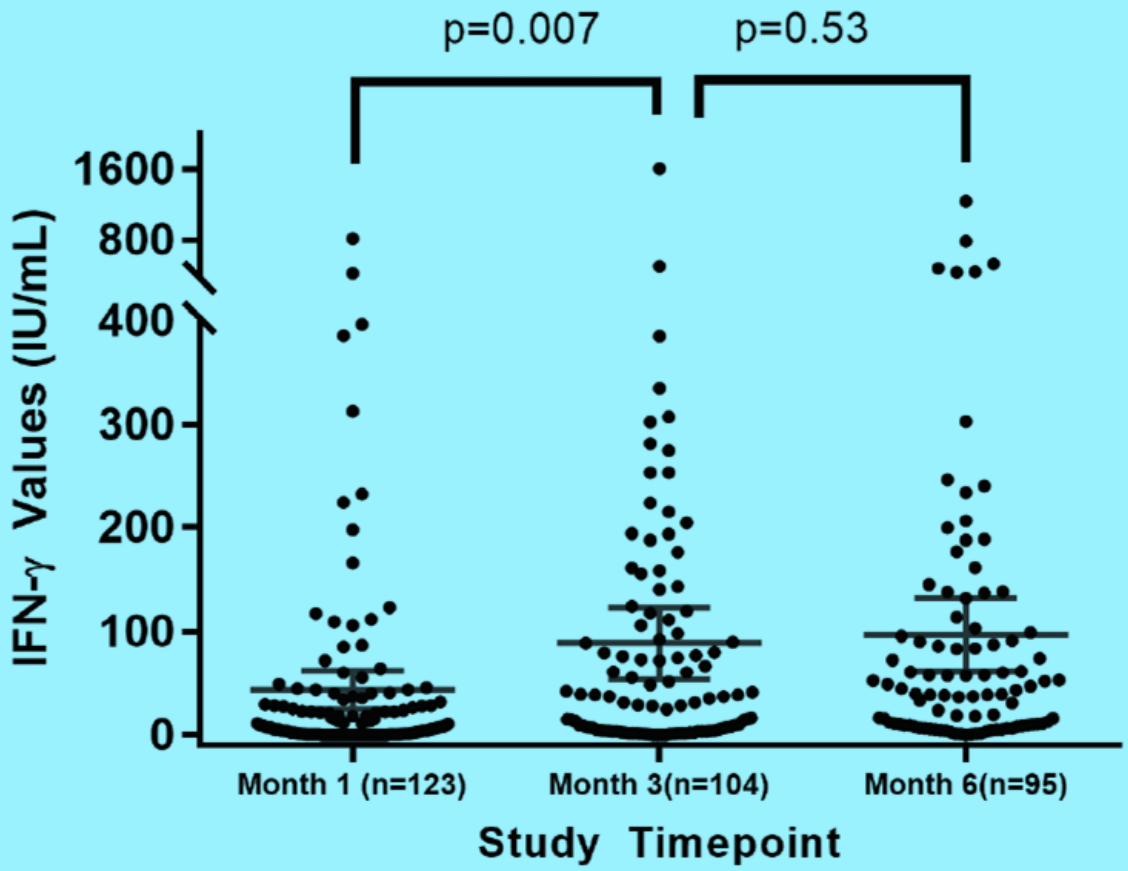


Figure 1. Global cell-mediated immunity (measured by QuantiFERON Monitor assay) at months 1, 3, and 6 posttransplant. Horizontal line represents mean and 95% confidence interval. Abbreviation: IFN-γ, interferon gamma.

Référence: Clin Infect Dis 2018; 66 (9)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (3-3)

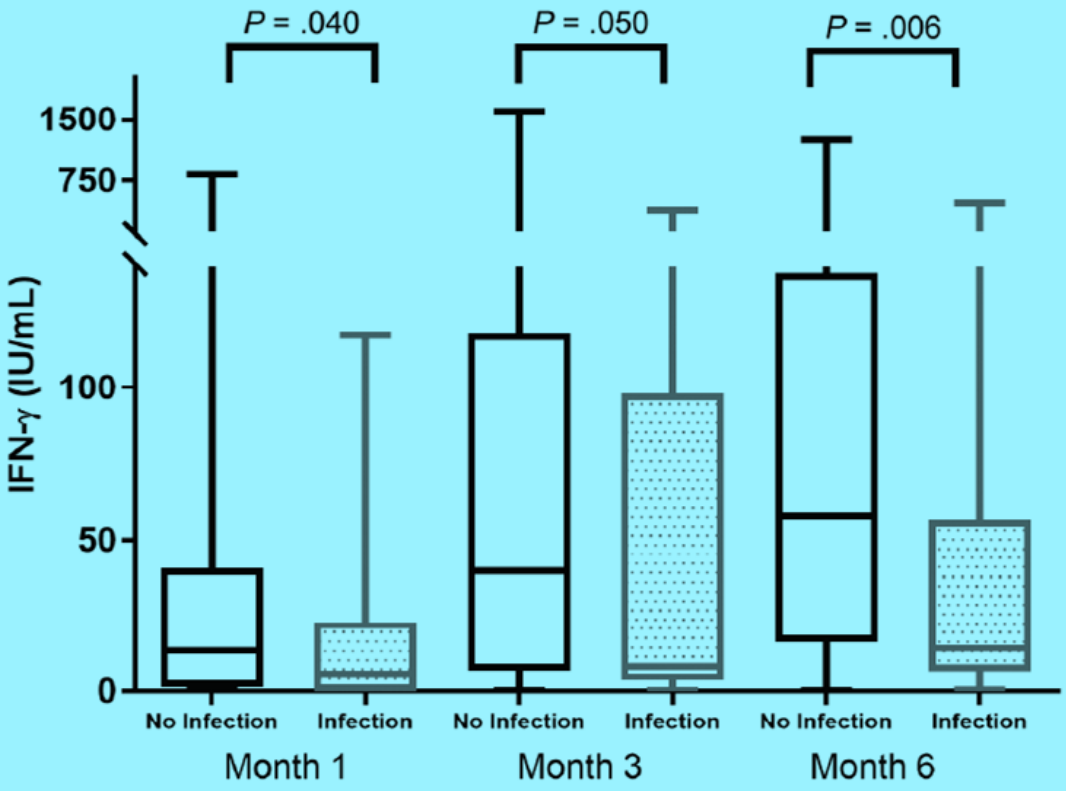


Figure 2. Global cell-mediated immunity at months 1, 3, and 6 in patients with at least 1 episode of infection vs patients with no infectious episodes. Error bars represent median with range of values. Abbreviation: IFN-γ, interferon gamma.

Référence: Clin Infect Dis 2018; 66 (9)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (3-4)

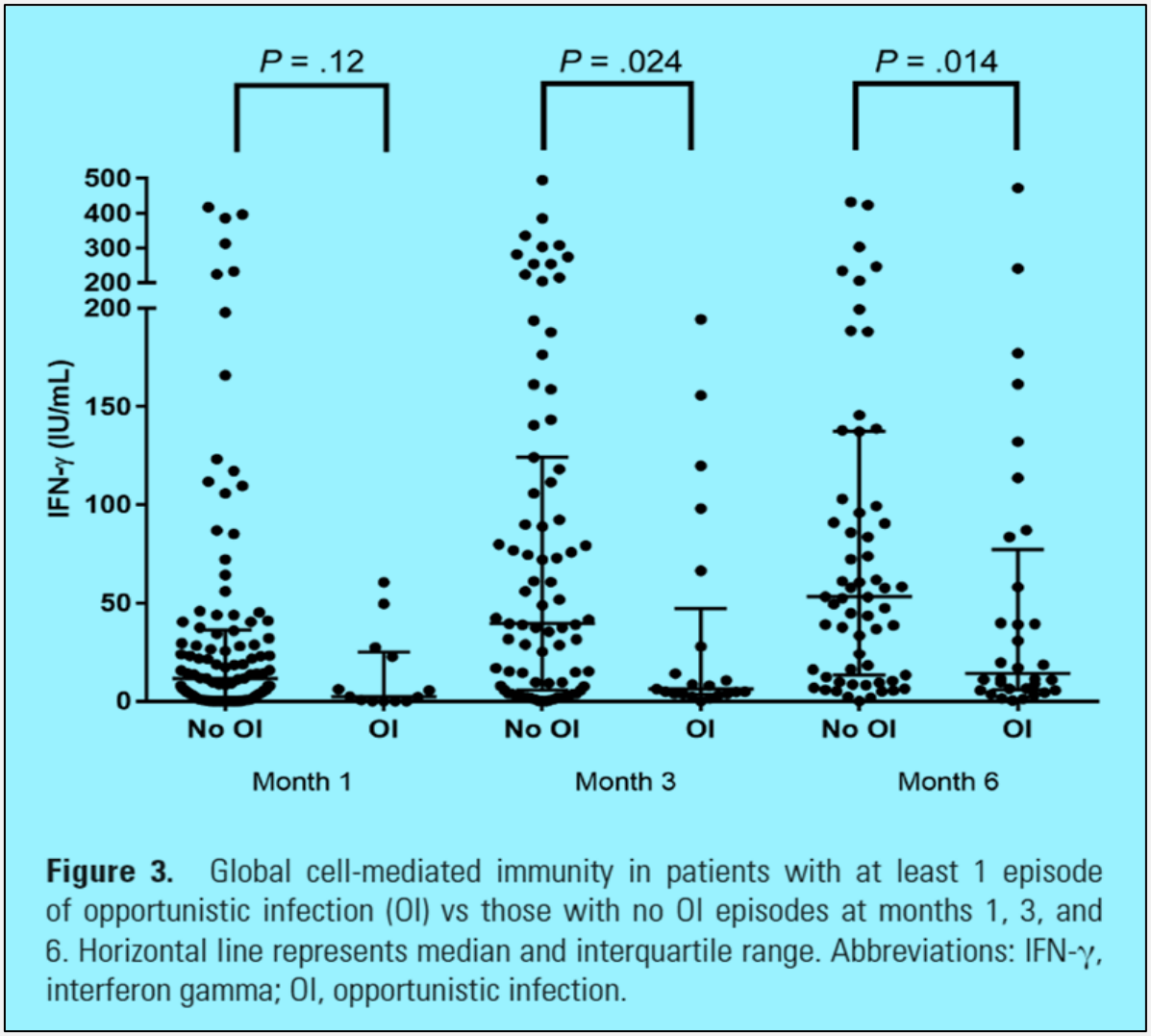


Figure 3. Global cell-mediated immunity in patients with at least 1 episode of opportunistic infection (OI) vs those with no OI episodes at months 1, 3, and 6. Horizontal line represents median and interquartile range. Abbreviations: IFN-γ, interferon gamma; OI, opportunistic infection.

Référence: Clin Infect Dis 2018; 66 (9)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (4-1)

Received: 20 June 2019 | Revised: 24 November 2019 | Accepted: 2 February 2020

DOI: 10.1111/tid.13260

Check for updates

ORIGINAL ARTICLE

WILEY

The QuantiFERON Monitor® assay is predictive of infection post allogeneic hematopoietic cell transplantation

Abby P. Douglas[1,2,3] | Lijia Yu[2,4] | Vijaya Sundararajan[2,5] | Jeff Szer[2,3,6] | David Ritchie[2,3,6] | Monica A Slavin[1,2,3] | Joe Sasadeusz[1,2] | Kumar Visvanathan[2,4]

Conclusion: This is a promising assay to demonstrate immune recovery and predict risk of infection after alloHCT and may allow tailoring of immunosuppression, antimicrobial treatment, and prophylaxis.

Référence: Transplant Infect Dis 2020; 22 (3)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (4-2)

Abstract

Introduction: Following allogeneic hematopoietic stem cell transplantation (alloHCT), excessive immunosuppression can be complicated by infection, while inadequate immunosuppression can result in graft-vs-host disease (GVHD). An accurate method to assess overall immune status post HCT is lacking. The QuantiFERON Monitor® (QFM) assay measures interferon gamma (IFN-γ) release from whole blood following incubation with both innate (Toll-like receptor 7, TLR7) and adaptive (CD3 antibody) stimulants and may result in a more complete assessment of the immune system.

Methods: Whole blood samples were prospectively collected from alloHCT recipients at conditioning followed by days 10, 30, 60, 90, 120, and 180 post-transplant and assayed by the QFM test. IFN-γ levels were correlated to time post HCT and episodes of infection and GVHD.

Results: Forty patients were enrolled in the study (68% male; median age 47 years; 58% matched related donors, 42% unrelated; 33% myeloablative). Post-stimulation IFN-γ levels rose steadily over the first 180 days post transplantation. IFN-γ levels were significantly lower in those with active infection compared to those without during the neutropenic period ($P < .001$). The assay was predictive of CMV reactivation (VL > 1000 copies/mL) post alloHCT ($P = .001$).

Référence: Transplant Infect Dis 2020; 22 (3)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (4-3)

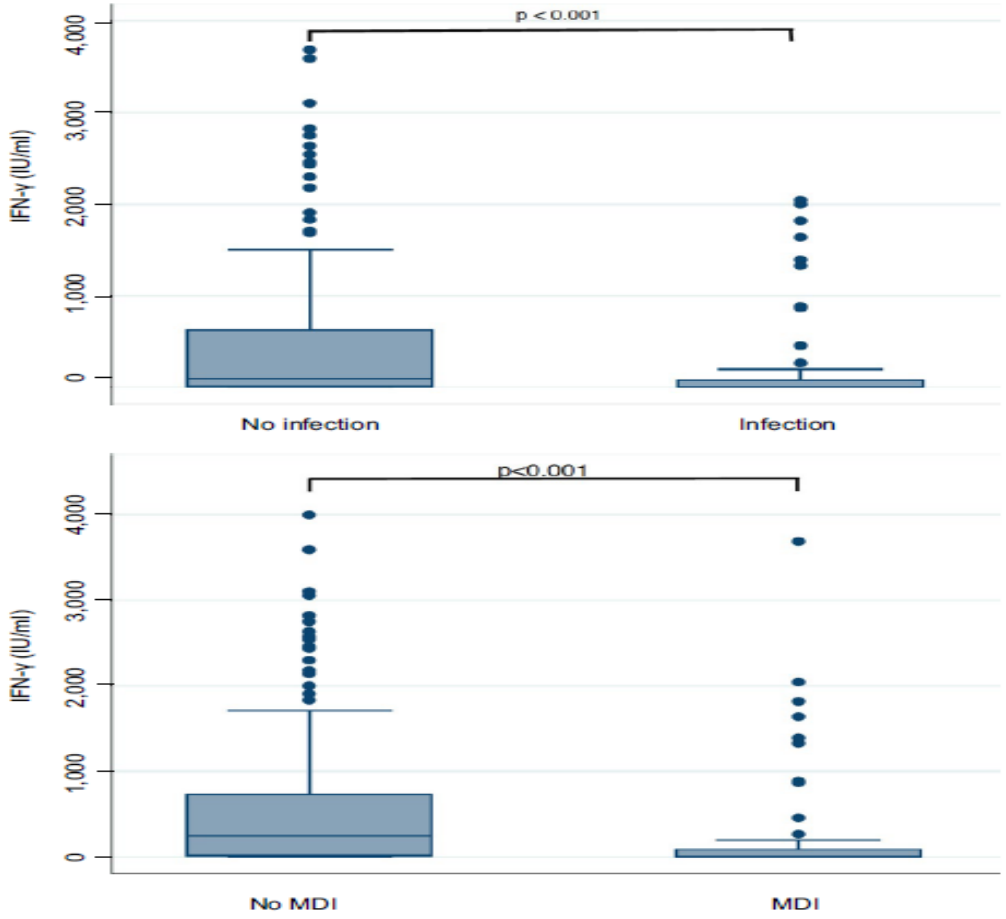


FIGURE 3 A, IFN-γ levels stratified for patients who did and did not develop infection at a particular time point post-transplant (n = 200 time points). B, IFN-γ levels stratified for patients who did and did not develop a microbiologically defined infection (MDI) at a particular time point post-transplant

Référence: Transplant Infect Dis 2020; 22 (3)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (5-1)

> Transpl Infect Dis. 2021 Jun;23(3):e13550. doi: 10.1111/tid.13550. Epub 2021 Jan 5.

Evaluation of Quantiferon®-Monitor as a biomarker of immunosuppression and predictor of infection in lung transplant recipients

Bradley J Gardiner [1], Sue J Lee [1], Yvonne Cristiano [2], Bronwyn J Levvey [2], Lucy C Sullivan [2 3], Gregory I Snell [2], Anton Y Peleg [1 4], Glen P Westall [2]

Conclusions: QFM values declined significantly post-transplant, with patients recovering at different rates. Prednisolone dose significantly impacted QFM results. Low levels were associated with infection beyond 3 months post-transplant, suggesting that QFM may be able to identify overly immunosuppressed patients who could be targeted for dose reduction. Larger prospective studies are needed to further evaluate this promising assay.

Référence: Transplant Infect Dis 2021; 223(3)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (5-2)

Abstract

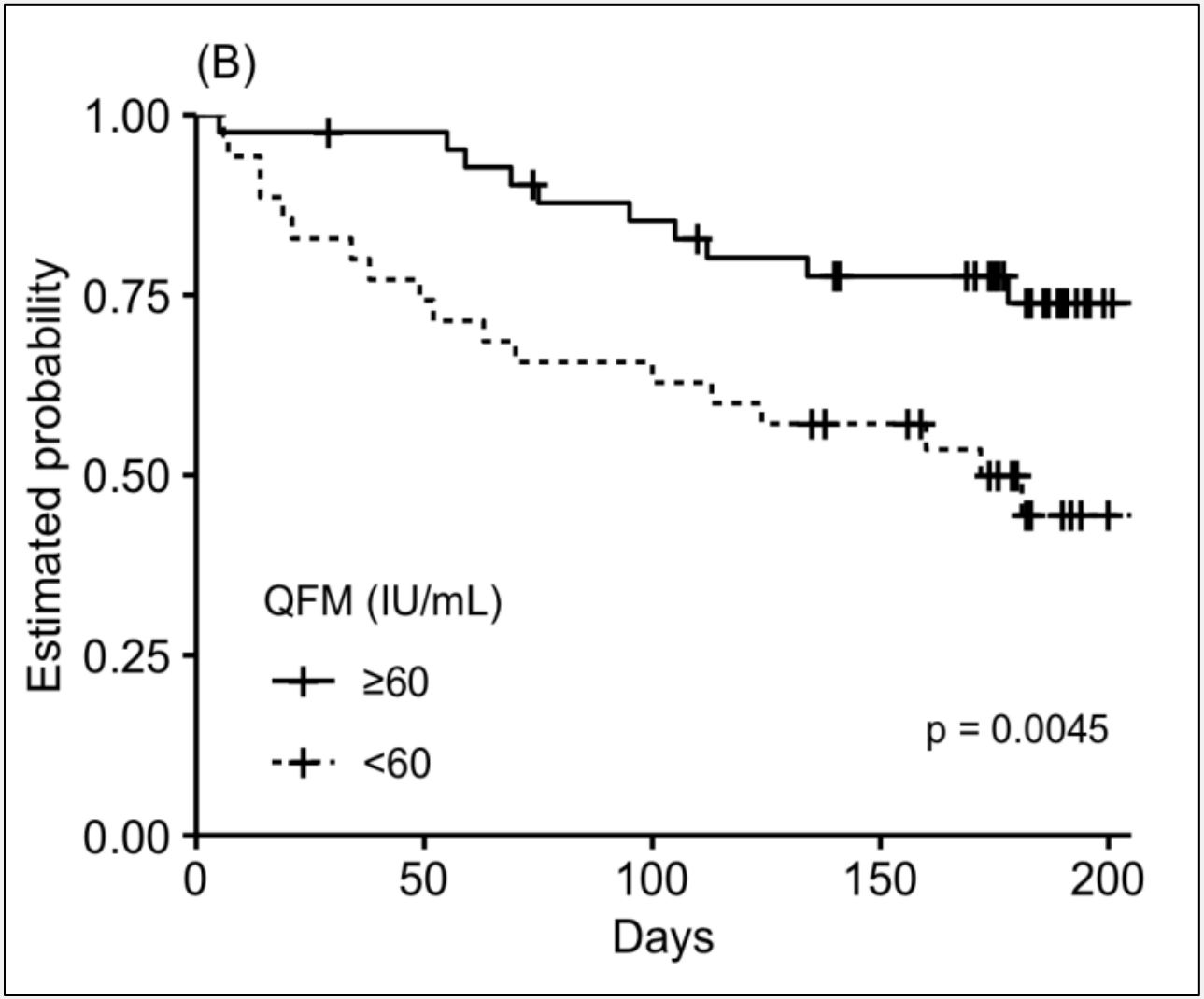
Background: Optimizing immunosuppression in lung transplant recipients (LTR) is crucially important in minimizing the risk of infection and rejection. Quantiferon®-Monitor (QFM) is a candidate immune function biomarker which has not yet been rigorously evaluated in the lung transplant setting. The aim of this prospective cohort study was to explore relationships between QFM results, immunosuppression, and infection/rejection in LTR.

Methods: QFM, which measures interferon-γ after stimulation with innate and adaptive immune antigens, was tested before and at 2, 6, 12, 24 and 52 weeks post-transplant. Immunosuppression relationships were assessed with linear mixed effects models. Clinical outcomes were analyzed based on the preceding QFM result.

Results: Eighty LTR were included. Median pre-transplant QFM levels were 171 IU/mL (IQR 45-461), decreasing to 3 IU/mL (IQR 1-8) at 2 weeks post-transplant then progressively recovering toward baseline with time from transplant. Prednisolone was strongly inversely associated with QFM level (0.1 mg/kg dose increase correlating with 88 IU/mL QFM decrease, 95% CI 61-114, P < .001). Patients with QFM values <10 and <60 IU/mL were more likely to develop a serious opportunistic infection between 3 and 6 months (HR 6.38, 95% CI 1.37-29.66, P = .02) and 6-12 months (HR 3.25, 95% CI 1.11-9.49, P = .03) post-transplant, respectively.

Référence: Transplant Infect Dis 2021; 223(3)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (5-3)



Référence: Transplant Infect Dis 2021; 223(3)

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (6-1)

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

ABSTRACT | VOLUME 37, ISSUE 4, SUPPLEMENT , S19-S20, APRIL 2018

Quantiferon Monitor Assay Identifies Over-Immunosuppressed Patients with Adverse Outcomes After Heart Transplantation: Towards the Definition of a Phenotype of Immune Frailty

L. Potena • A. Gaudenzi • A. Chiereghin • ... S. Boschi • T. Lazzarotto • F. Grigioni • Show all authors

Conclusion: QFM assay provide accurate risk stratification for infections and poor prognosis after HT. QFM appears an accurate assay to identify patients excessively immunosuppressed, and may represent a marker of immune frailty. Further studies are needed to assess how modulation in immunosuppression may influence QFM assay results.

Référence: J Lung and Heart Transplant 2018; 37 (4)- Suppl.

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (6-4)

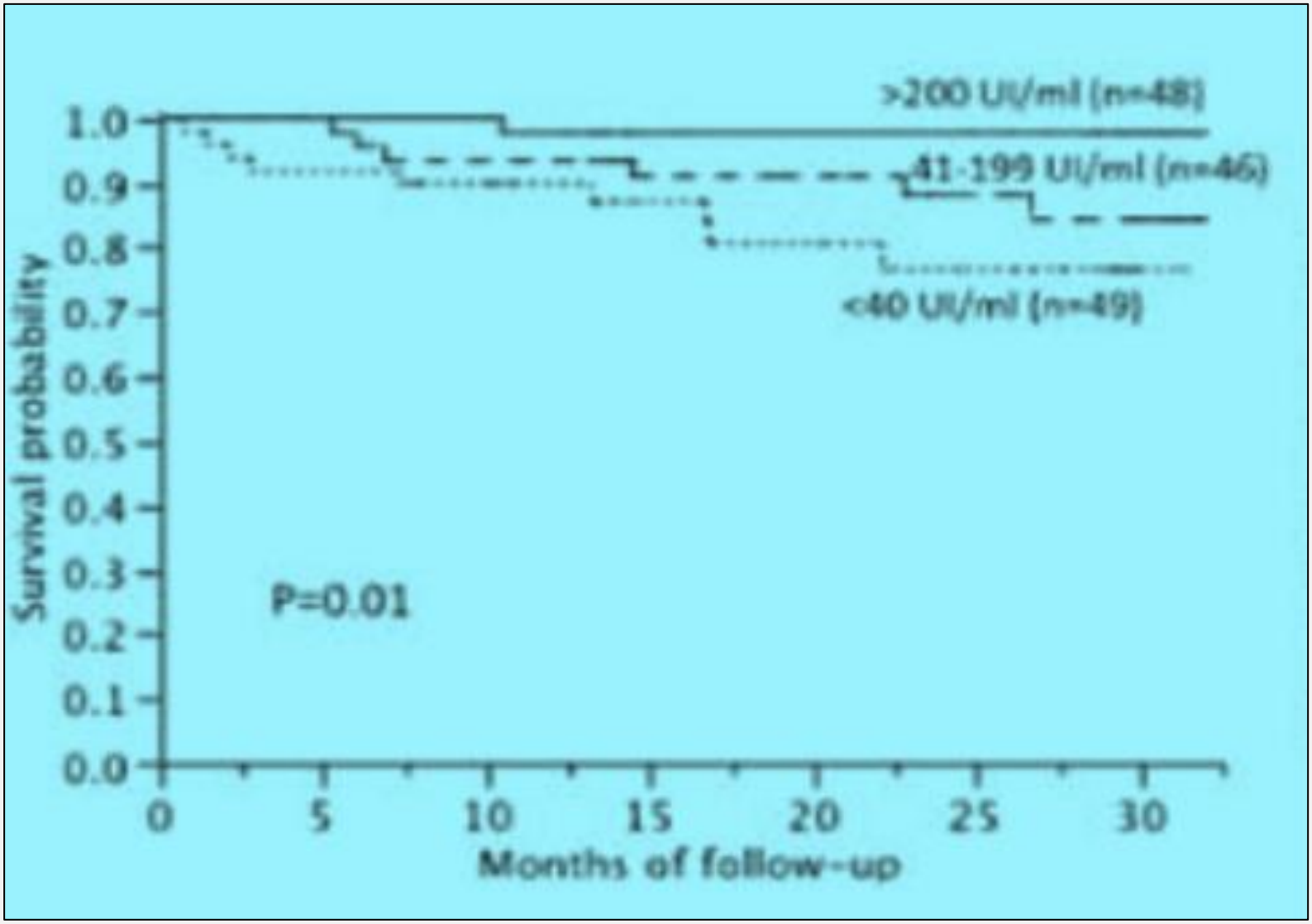
Purpose: Optimal balance between protection from rejection and the adverse consequences of over-immunosuppression is an important unmet need in clinical practice after heart transplant (HT). We tested the clinical utility of Quantiferon monitor (QFM), a novel immune monitoring test, to detect conditions of under-immunosuppression after organ transplantation and identify patients at risk of adverse outcomes.

Methods: QFM was performed at study entry. After overnight incubation of 1ml of whole blood with lyophilized antigens that stimulate NK-cells, with a TLR-7 agonist, and CD3 T lymphocytes with a TCR agonist, interferon-gamma (IFN-g) was assayed by the Quantiferon ELISA platform. Study enpoints were: 1) overall mortality, and combined incidence of death and hospitalization; 2) Occurrence of infection during the 3-6 months after assay.

Results: 143 patients were enrolled (58+13 y; 69% males; 5[1-16]y from HT). During a median follow-up of 26[14-31] months, 16 (11%) patients died, and 45(31%) presented the combined endpoint; 42(30%) develop at least one infection in the 3-6 months post-assay. By dividing study population in tertiles of IFN-g levels, endpoints incidence was 50% of patients in the lowest IFN-g tertile (<40UI/ml), vs. 26% of those with concentrations 41-199 UI/ml, and 12.5% in those with levels >200/ml. Figure shows Kaplan-meier survival estimate for overall survival and survival free death/hospitalization. After adjusting for potential confounders, QFM persisted independently associated with infection occurrence and death/hospitalization risk.

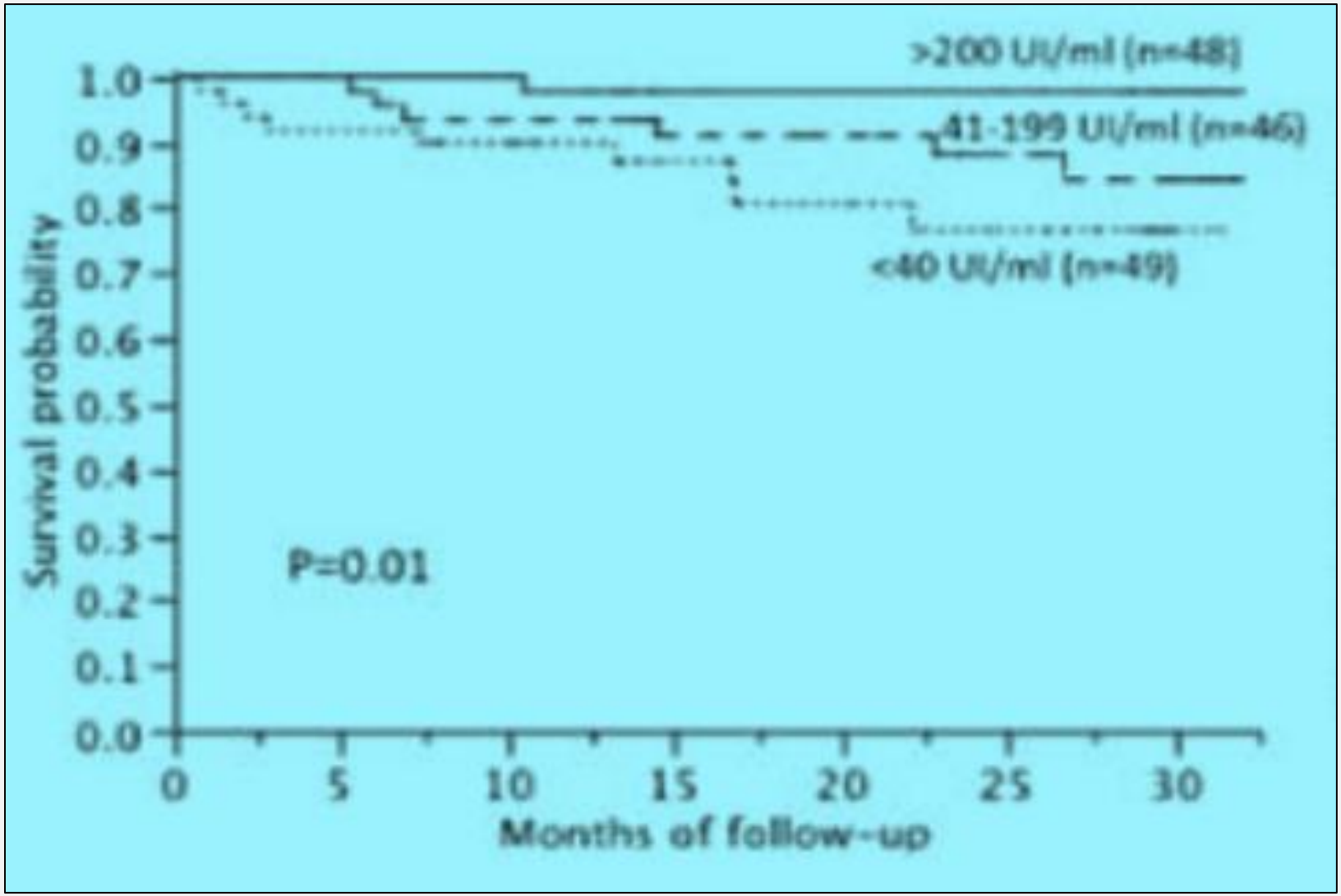
Référence: J Lung and Heart Transplant 2018; 37 (4)- Suppl.

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (6-2)



Référence: J Lung and Heart Transplant 2018; 37 (4)- Suppl.

Quantiféron Monitor en Néphrologie, Transplantation d'Organes (6-3)



Référence: J Lung and Heart Transplant 2018; 37 (4)- Suppl.

Quantiféron Monitor en Néphrologie, MRC Stade 5 – Dialyse & Traitement conservateur

ELSEVIER

Clinica Chimica Acta

Volume 502, March 2020, Pages 287-292

Functional immune assay using interferon-gamma could predict infectious events in end-stage kidney disease

S. Boyer-Suavet [a c 1], M. Cremoni [a 1], T. Dupeyrat [a], K. Zorzi [c], V. Brglez [c], S. Benzaken [b], V. Esnault [a], B. Seitz-Polski [a b c]

- **Etude prospective**
- **54 patients : HD : 30 ,DP: 13, CM :11**
- **Une faible production d'INFG : risque 10 fois plus de développer une infection.**
- **QFM permet de sélectionner les patients qui pourraient bénéficier une intervention pour restaurer l'immunité cellulaire et minimiser le risque d'infection et de rejet après transplantation rénale .**

Quantiféron Monitor en Néphrologie, Apport

- Réduit la morbi-mortalité liées aux infections
- La néphrotoxicité des anticalcineurines
- Réduit le cout de la greffe:

  *Réduit le nombre et la durée d'hospitalisation.

  *Réduit le recours aux ATB et antiviraux.

  *rationnalise l'utilisation de la chimio-prophylaxie anti CMV et *pneumocystis carinii*

Quantiféron Monitor en Néphrologie, Limites

- QFM : mesure qualitative et quantitative de la fonction immunitaire.
- Il se peut que les résultats de QFM ne quantifient pas directement le niveau d'immunodépression.
- Les résultats des tests QFM doivent être utilisés conjointement avec la présentation clinique, les antécédents médicaux et d'autres paramètres cliniques, lors de l'établissement du statut immunitaire d'un patient.
- Le seuil du test QFM peut varier selon le niveau d'immunodépression du sujet et les paramètres de transplantation individuels.

Quantiféron Monitor en Néphrologie, Conclusions

- La prise en charge des transplantés rénaux est confronté au défit de l'optimisatiion du traitement immunosuppresseur et de trouver l'équilibre entre le duel efficacité et tolérance.
- Elle s'appuie actuellement sur des marqueurs bruts tels que le suivi thérapeutique des médicaments et les événements cliniques pour guider la gestion du traitement immunosuppresseur.
- Le QFM est un test in vitro utilisé pour apprécier la fonction immunitaire à médiation cellulaire.
- Certaines travaux ont étudié sa place dans l'évaluation du risque d'infection ou de rejet de greffe après transplantation d'organes solides.
- Un faible résultat QFM peut être associé à un risque accru d'infection, tandis qu'un résultat élevé peut être associé à un risque de rejet de greffe.
- La littérature suggère que QFM peut fournir une stratification et une prédiction précise du risque de rejet et d'infection après la transplantation.

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