WOM
AGAINST HIV

# Toxicité tubulaire du ténofovir

**Dr Vincent Bourquin** - service de néphrologie - http://nephrohug.com

# Rein et infection par le VIH

# Rein et infection par le VIH

2

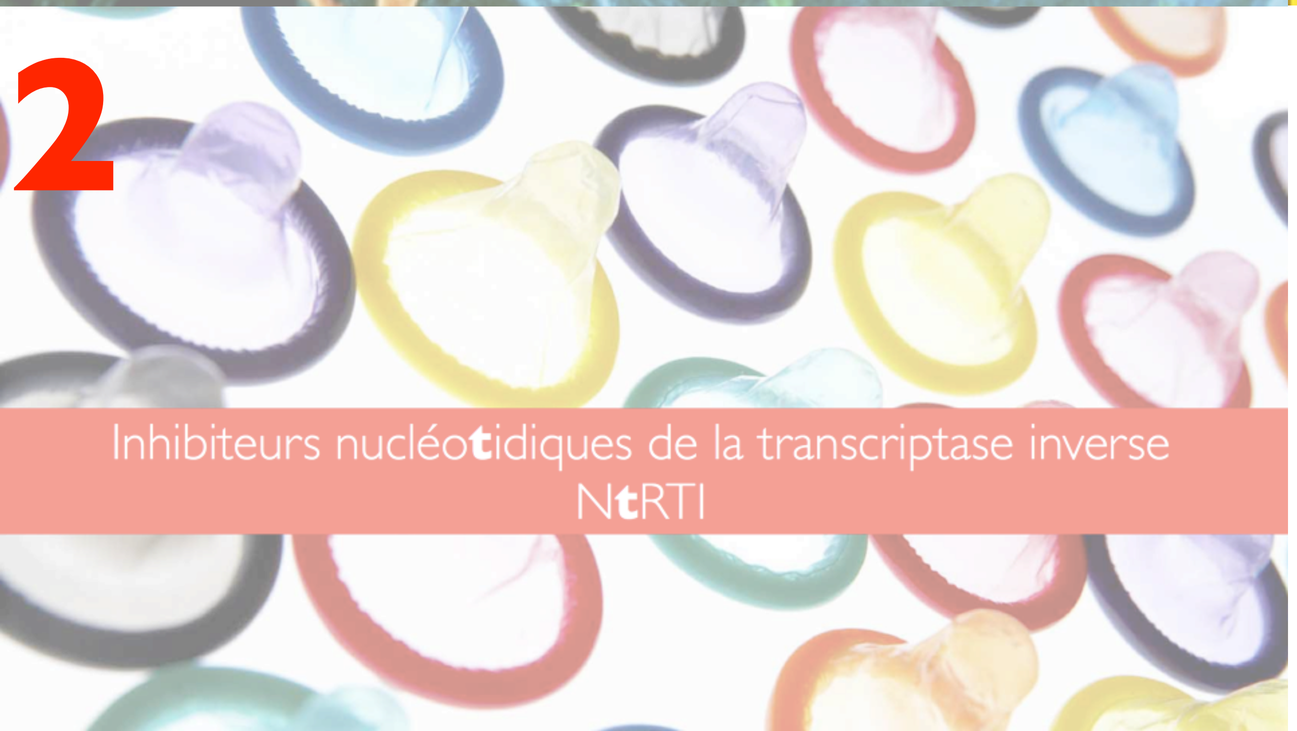
# Inhibiteurs nucléotidiques de la transcriptase inverse NtRTI

1

Rein et infection par le VIH

3

Quel suivi et quel bilan ?



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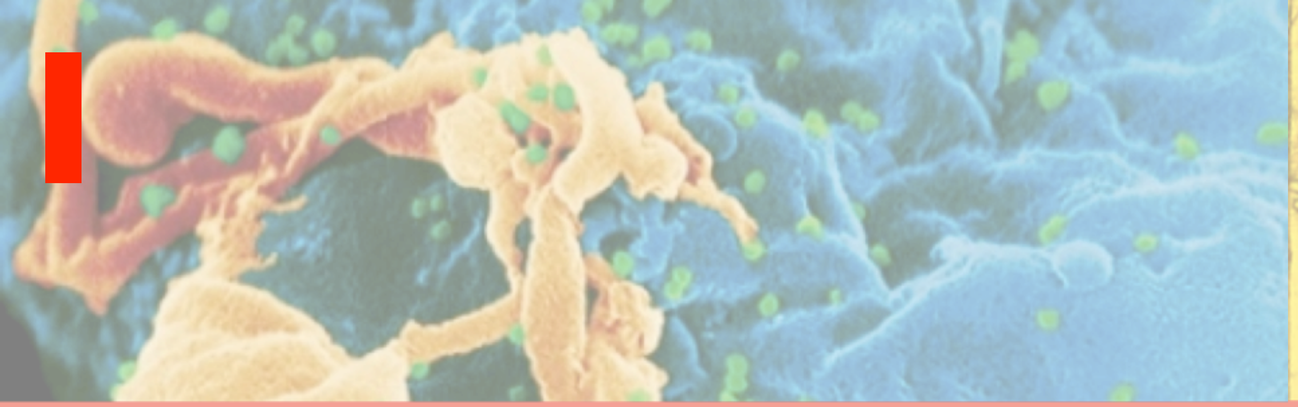
Inhibiteurs nucléo**t**idiques de la transcriptase inverse
N**t**RTI



1

Rein et infection par le VIH

3

Quel suivi et quel bilan ?

2

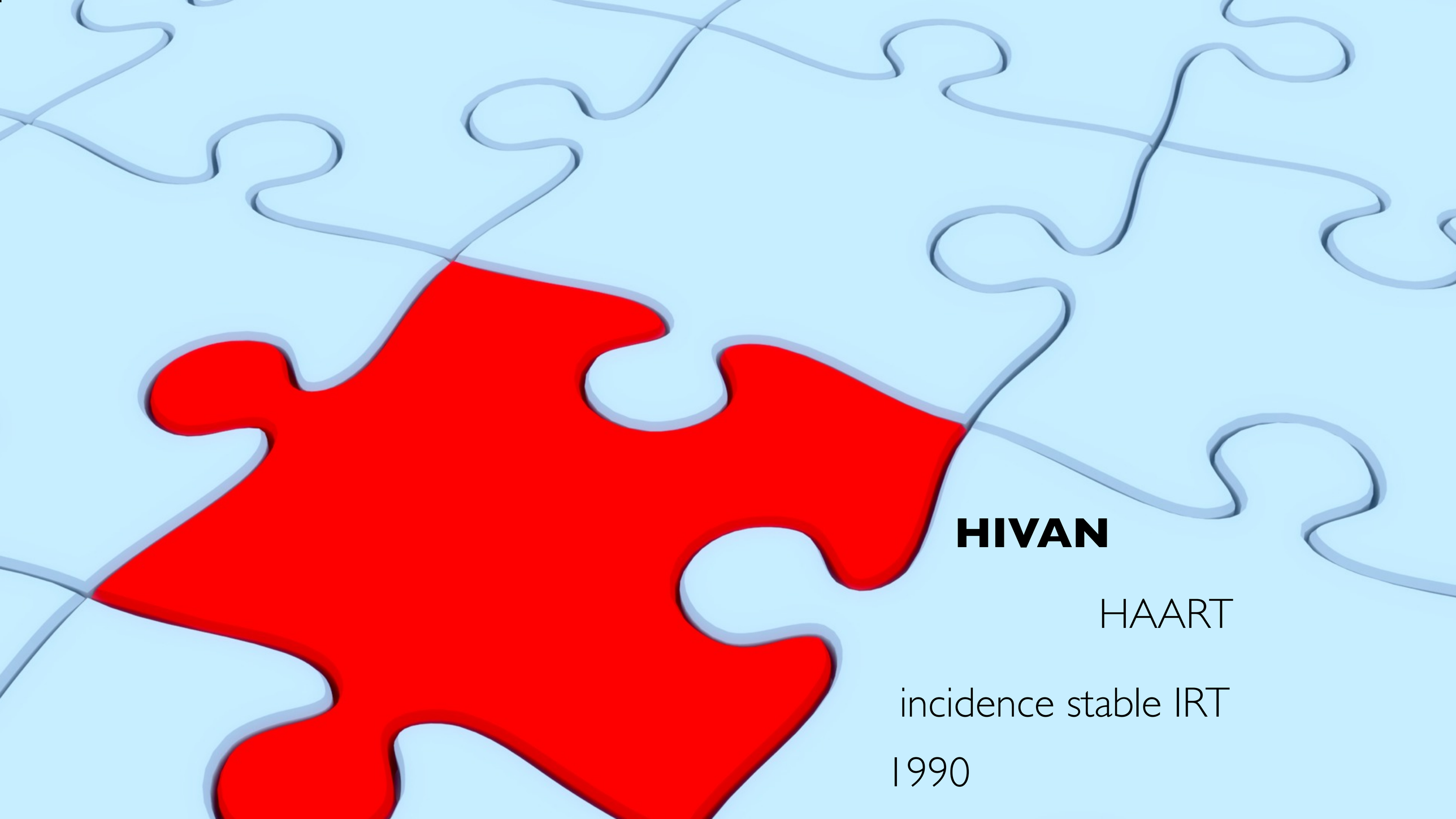
Inhibiteurs nucléo**t**idiques de la transcriptase inverse
N**t**RTI

Cas cliniques et discussion

# Rein et infection par le VIH

L'épidémiologie des néphropathies chez les patients infectés par le VIH s'est considérablement modifiée...

**Source**: Plaisier et coll. Presse Med 2012

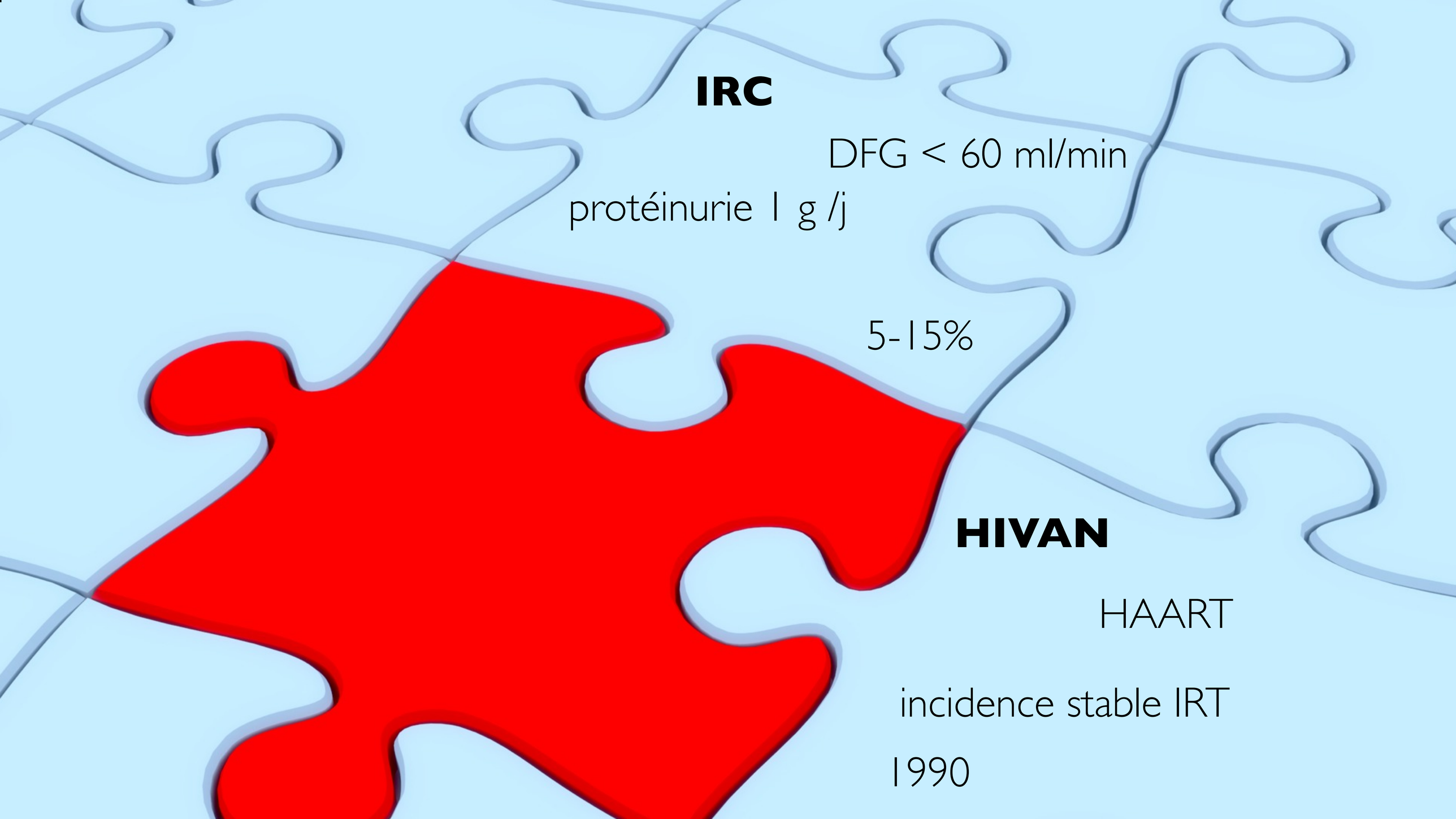


**HIVAN**

HAART

incidence stable IRT

1990


IRC
DFG < 60 ml/min
protéinurie 1 g /j
5-15%
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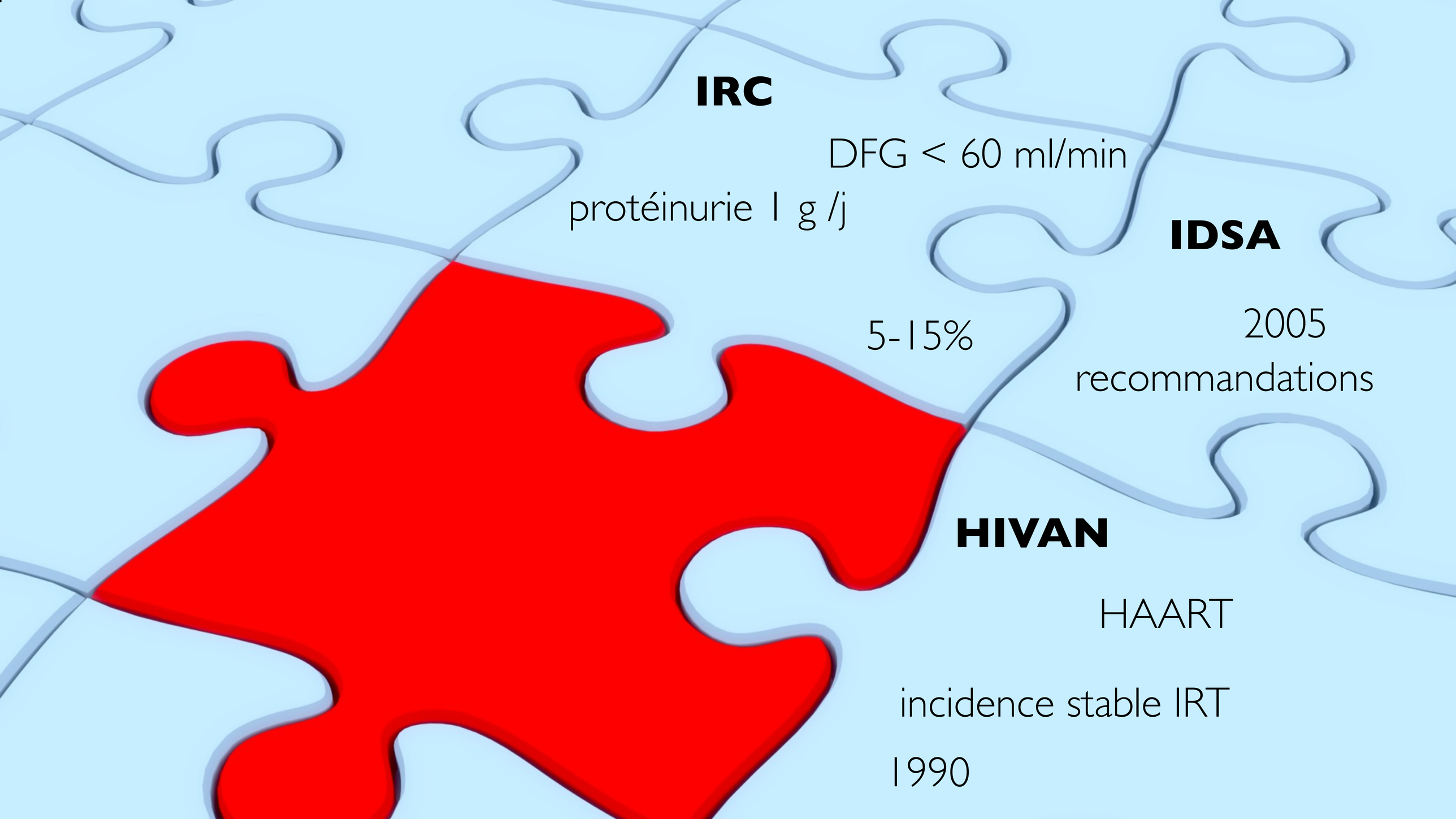
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**Glomérulopathies**

**complexes**

**immuns**

**IRC**

DFG < 60 ml/min

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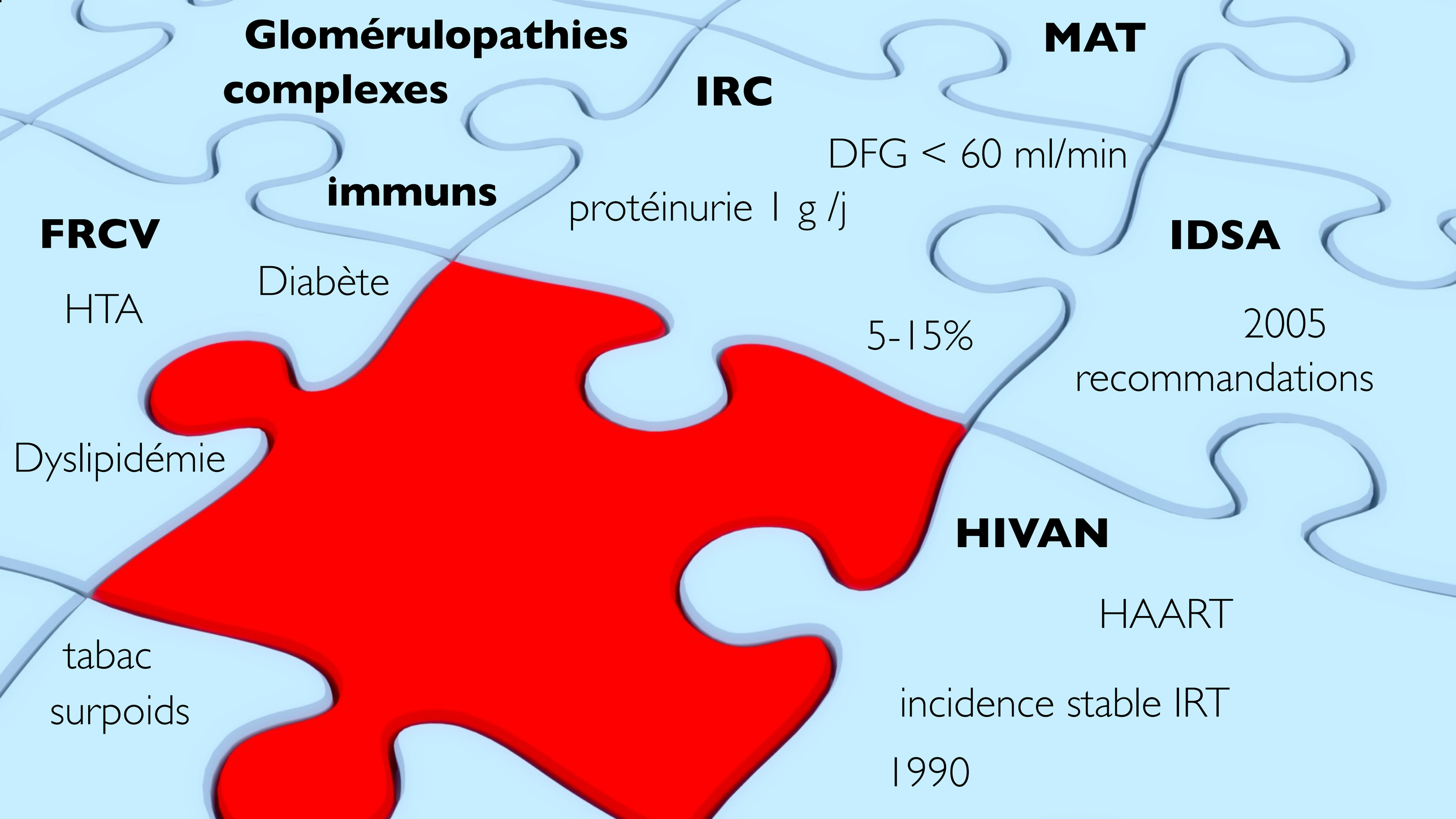
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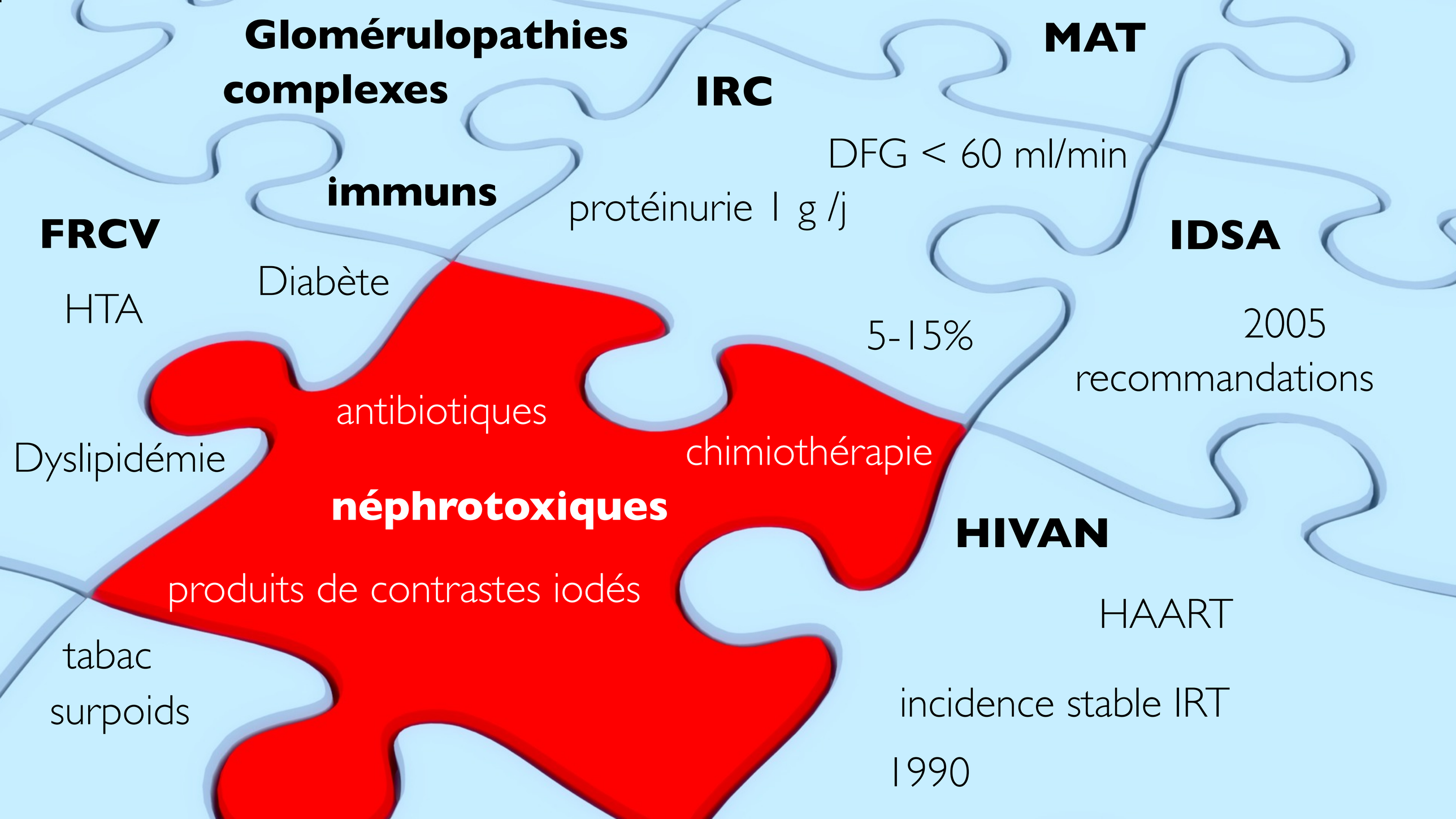
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antibiotiques
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chimiothérapie
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produits de contrastes iodés
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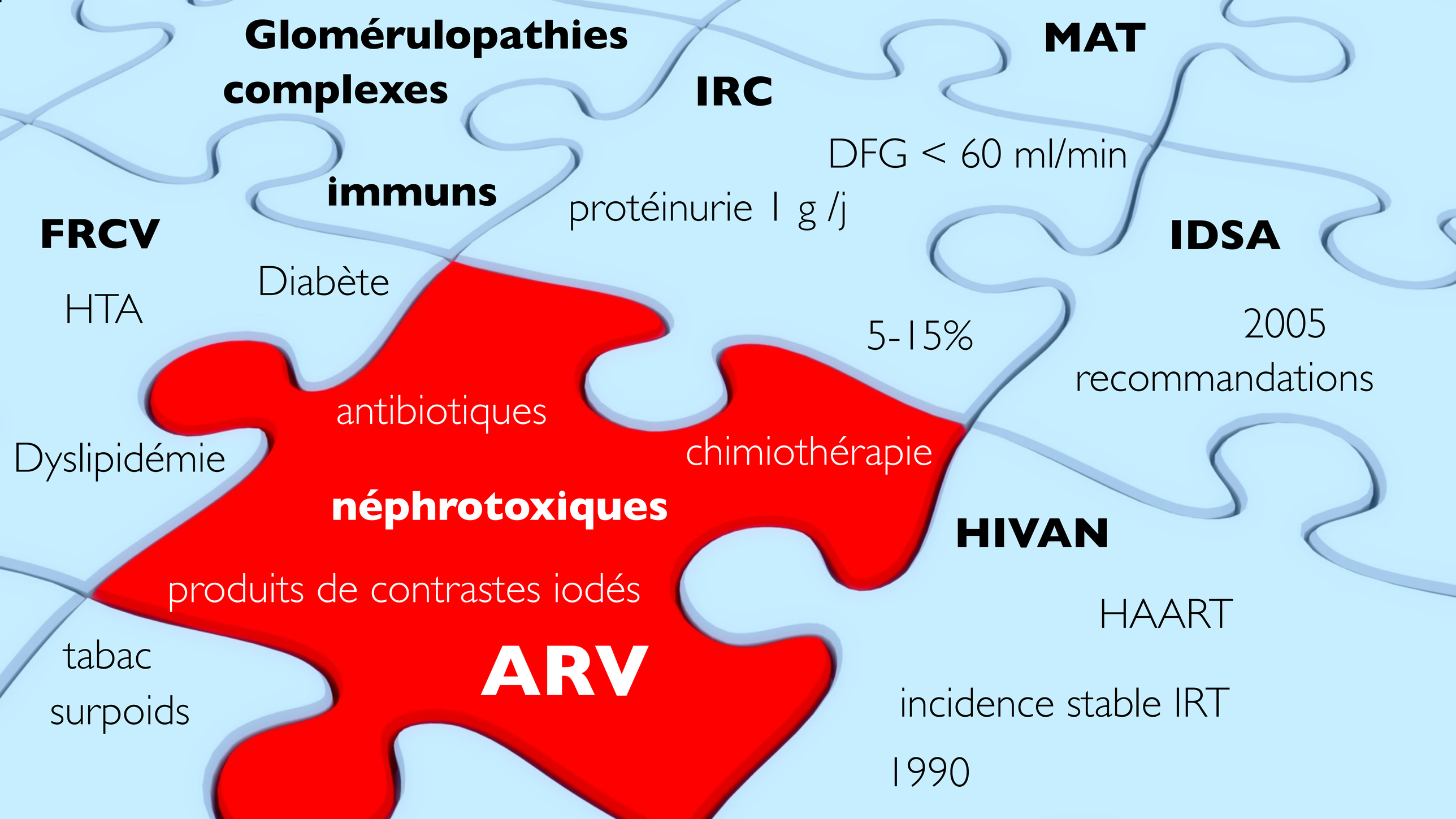
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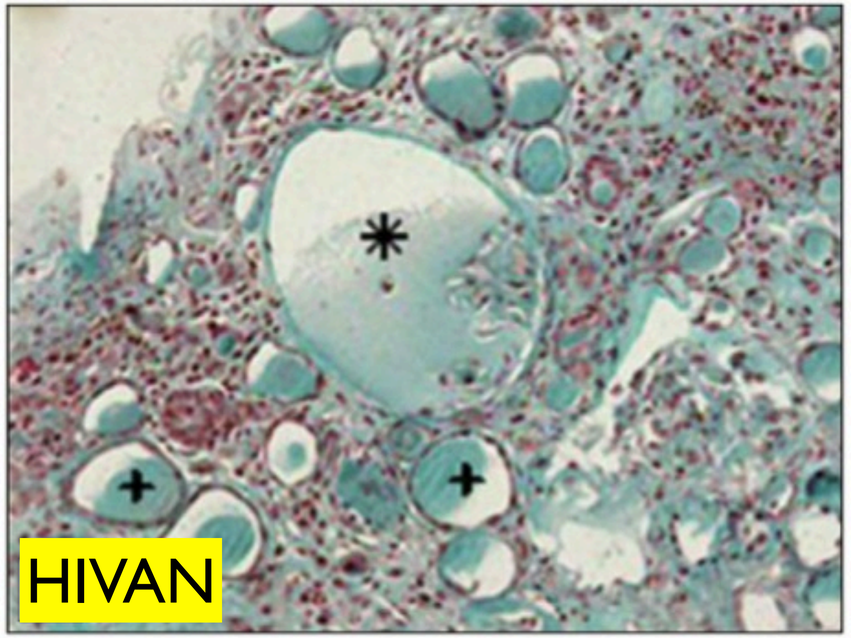
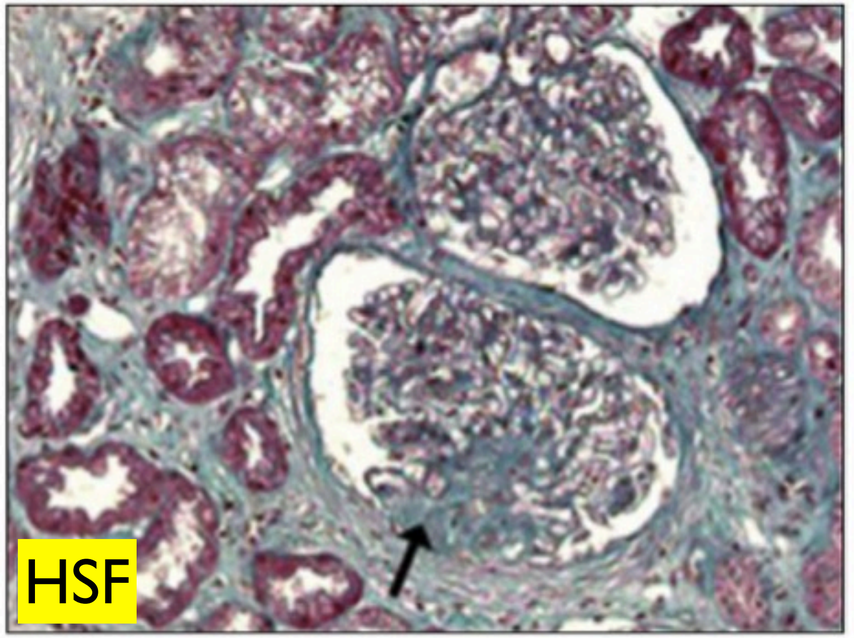
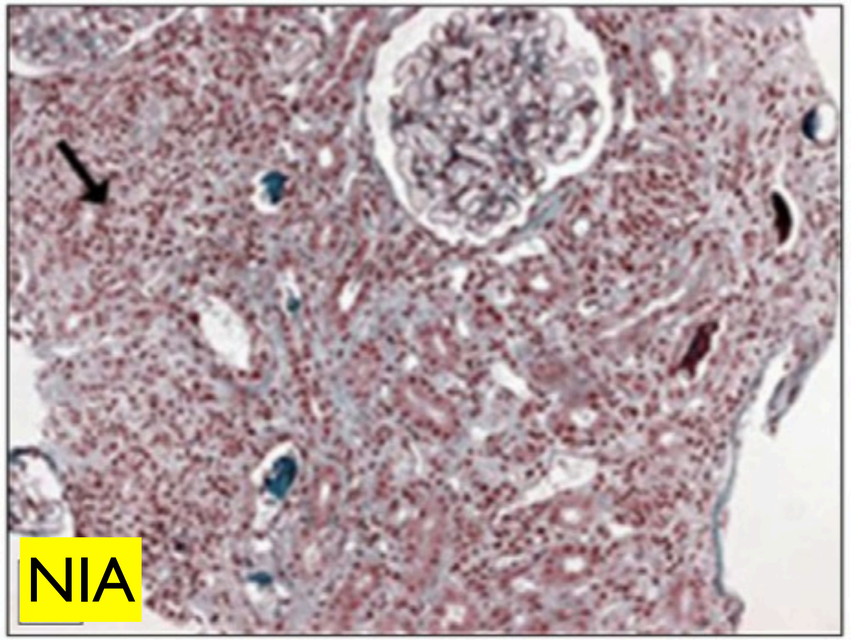
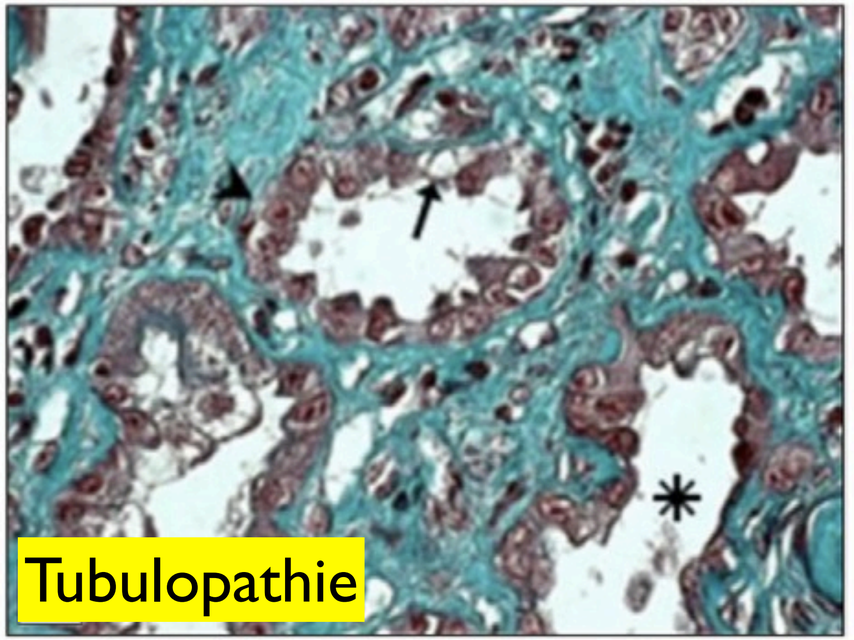


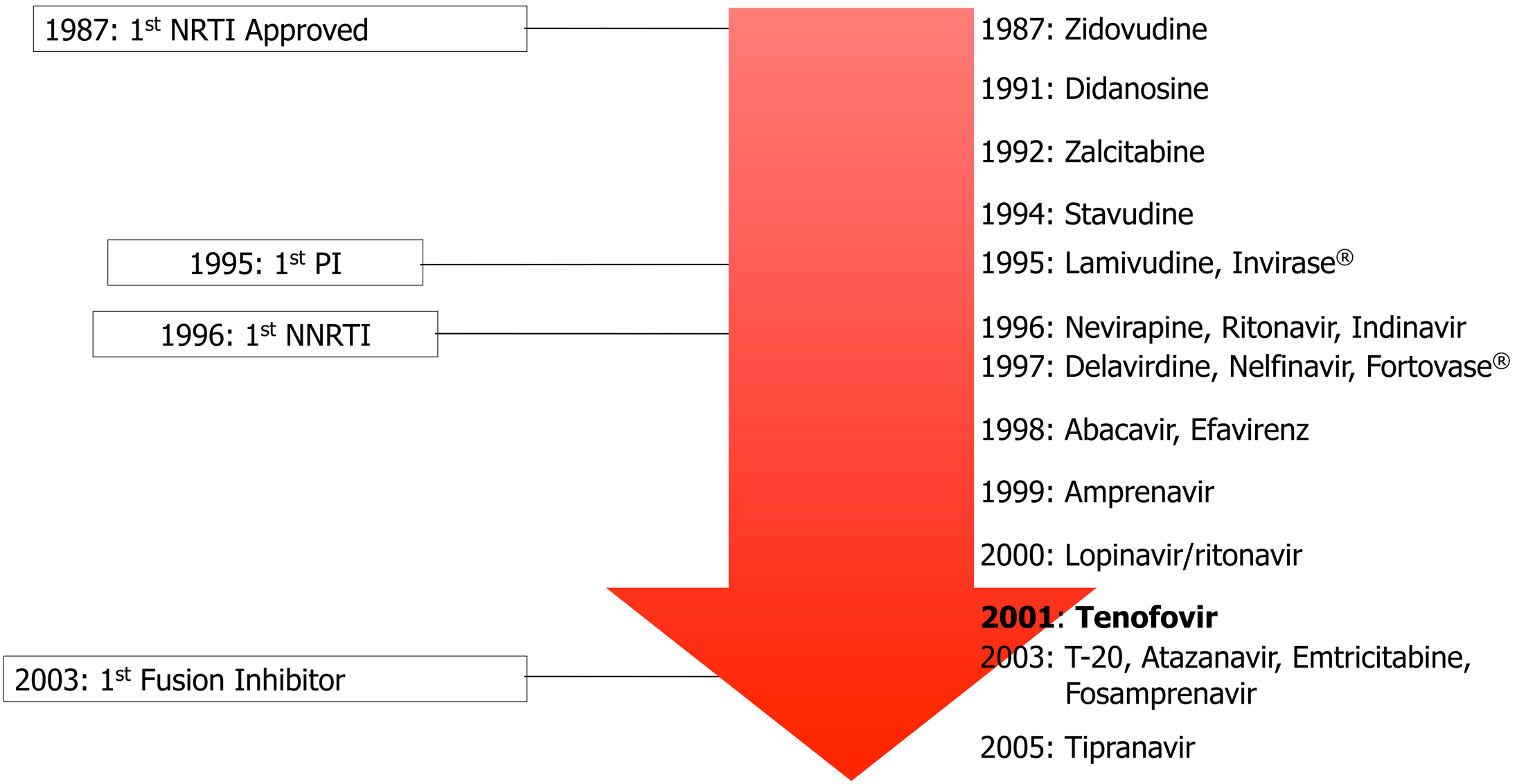




**Source**: Plaisier et coll. Presse Med 2012

# Timeline of ARV approval



| Stades | Description | DFG (ml/min/1.73 $m^2$) |
|---|---|---|
| **1** | Maladie rénale avec DFG normal | **≥ 90** |
| **2** | Maladie rénale avec faible baisse du DFG | **60-89** |
| **3** | Baisse modérée du DFG | **30-59** |
| **4** | Baisse sévère du DFG | **15-29** |
| **5** | Insuffisance rénale terminale | **< 15 ou dialyse** |

Classification K/DOQI selon le DFG de l'insuffisance rénale chronique

| Evaluation du risque par DFGe et protéinurie (KDIGO 2009) | | | | Stade de protéinurie, description et valeurs (mg/mg) | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | A1 | | A2 | A3 | |
| | | | | Optimal et normal-haut | | haut | Très haut et néphrotique | |
| | | | | <0.01 | 0.01-0.029 | 0.03-0.29 | 0.3-1.99 | ≥ 2 |
| DFGe, stades, description et valeurs | G1 | Haut et optimal | > 105 | | | | | |
| | | | 90-104 | | | | | |
| | G2 | Moyen | 75-89 | | | | | |
| | | | 60-74 | | | | | |
| | G3a | Moyen à modérée | 45-59 | | | | | |
| | G3b | Modéré à sévère | 30-44 | | | | | |
| | G4 | Sévère | 15-29 | | | | | |
| | G5 | IRT | <15 | | | | | |

Source: http://nephrohug.com/2011/11/07/proteinurie-aspects-pratiques/

| | **Formule Cockroft-Gault**<br>Nephron 1976 | **Equation MDRD**<br>Ann Int Med 1999 |
|---|---|---|
| **Prediction Model** | Best Fit | Stepwise LInear Regression Model |
| **Response variable** | 24h urine creatinine clearance | $^{125}$I Iothalamate clearance |
| **Validation** | > 200 hospitalized male patients with wide range of clearance values | Approx. 1600 patients with CKD and mean GFR 23 ml/min/1.73m$^2$ |
| **Caveats** | Not validated in special populations, including HIV | Not validated in special population, including HIV |
| **Clinical Uses** | In dose adjustment for drugs excreted by kidneys | More sensitive estimate of renal function |

**Source**: Gupta et coll. CID 2005

# Infectious Disease Society of America (IDSA)

**Dépistage systématique** de l'insuffisance rénale chronique au diagnostic de la maladie VIH par la recherche d'une protéinurie à la bandelette urinaire et l'estimation du DFG.

**Source**: Gupta et coll. CID 2005

# Infectious Disease Society of America (IDSA)

Ce bilan doit être répété **annuellement** chez les patients issus de population noire, diabétique, hypertendus, co-infectés par le virus de l'hépatite C dont les CD4 sont inférieurs à 200/ $mm^3$ ou la charge virale VIH est supérieure à 4'000 copies/mL

**Source**: Gupta et coll. CID 2005

# Infectious Disease Society of America (IDSA)

**Evaluation néphrologique** est recommandée en présence d'une protéinurie d'une croix ou plus et/ou si le DFG est inférieur à 60/ml/min/1.73 $m^2$

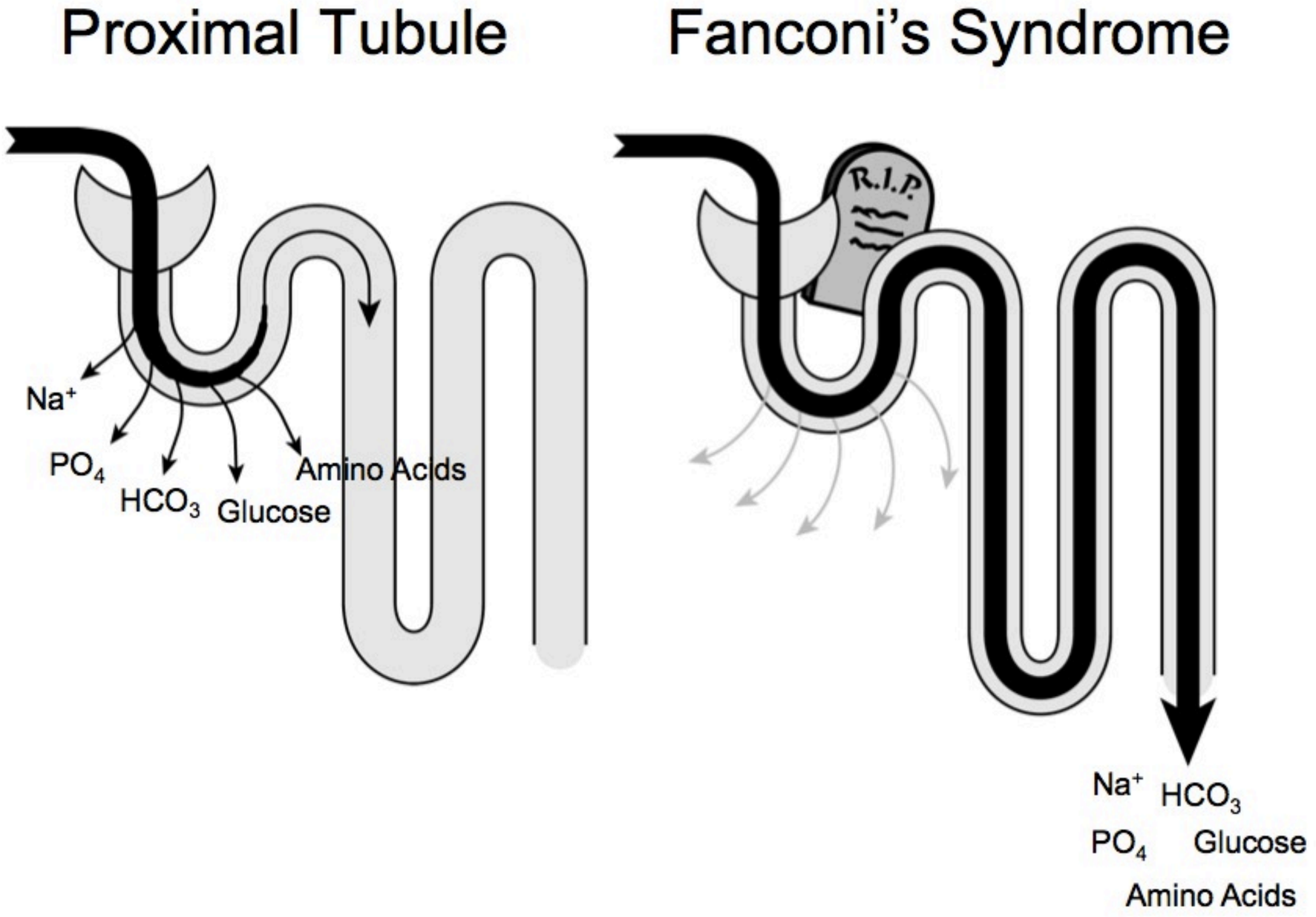
**Source**: Gupta et coll. CID 2005

| | Débit de filtration glomérulaire (mL/min/1,73 m²) | | | | Hémodialyse |
|---|---|---|---|---|---|
| | > 50 | 30–49 | 10–29 | < 10 | |
| Didanosine (Videx®) | 400 mg/24 h (≥ 60 kg) | 200 mg/24 h | 150 mg/24 h | 100 mg/24 h | 100 mg/24 h |
| | 250 mg/12 h (< 60 kg) | 150 mg/24 h | 100 mg/24 h | 75 mg/24 h | 75 mg/24 h |
| Emtricitabine (Emtriva®) | 200 mg/24 h | 200 mg/48 h | 200 mg/72 h | 200 mg/4 jours | 200 mg fin séance |
| Lamivudine (Epivir®) | 150 mg/12 h ou 300 mg/24 h | 150 mg/24 h | Dose de charge de 150 mg puis 25 à 100 mg/24 h | | |
| Stavudine (Zerit®) | 40 mg/12 h (≥ 60 kg) | 20 mg × 2/24 h | 20 mg/24 h | 20 mg/24 h | 20 mg/24 h |
| | 30 mg/12 h (< 60 kg) | 15 mg × 2/24 h | 15 mg/24 h | 15 mg/24 h | 15 mg/24 h |
| Zidovudine (Retrovir®) | 300 mg/12 h | 300 mg/12 h | 150 mg/12 h | 150 mg/12 h | 150 mg/12 h |
| Ténofovir (Viread®) | 300 mg/24 h | 300 mg/48 h | 300 mg/72 h | 300 mg 1 fois par semaine | |
| Maraviroc (Celsentri®) | | | | Non évalué | |
| + IP/ritonavir | 150 mg/24 h[1] | 150 mg/24 h | 150 mg/24 h | | |
| + Saquinavir/ritonavir | 150 mg/24 h[1] | 150 mg/48 h | 150 mg/72 h | | |
| Emtricitabine/Ténofovir (Truvada®) | 1 cp/24 h | 1 cp/48 h | Non recommandé<br>Utiliser Emtriva® et Viread® séparément en adaptant les posologies | | |
| Abacavir/Lamivudine (Kivexa®) | 1 cp/24 h | Non recommandé<br>Utiliser séparément abacavir (Ziagen®) et Epivir® en adaptant les posologies d'Epivir® | | | |
| Névirapine (Viramune®) | 400 mg/j | | | | 200 mg/j, fin séance |
| Nelfinavir (Viracept®) | 1250 mg/j | | | | 1250 mg/j, fin séance |

**Source**: Plaisier et coll. Presse Med 2012

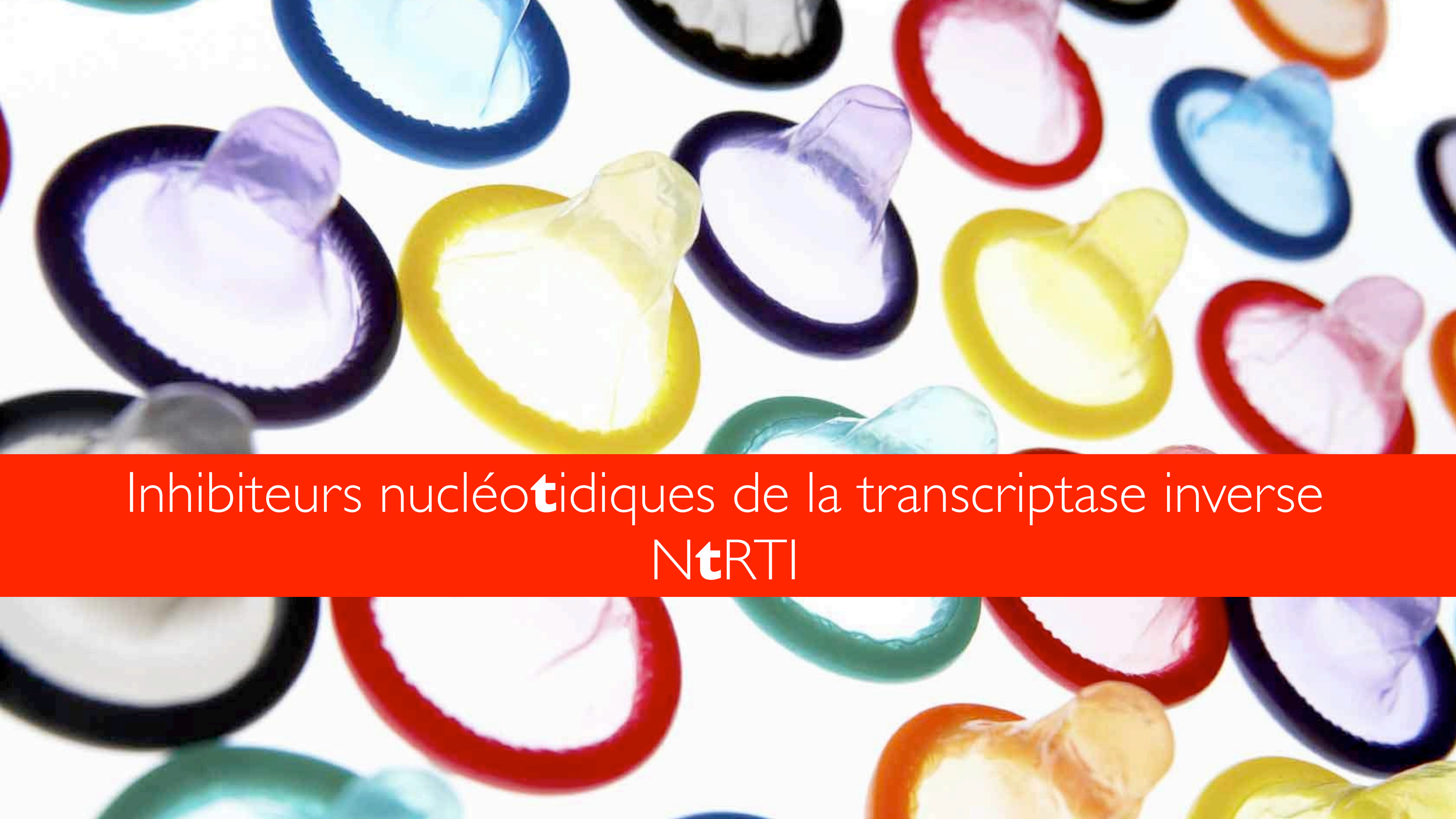
| | Précipitation intratubulaire/Lithiases | Tubulopathie proximale | Néphrite interstitielle aiguë | Inconnue (IRA) |
|---|---|---|---|---|
| *Inhibiteurs des protéases* | | | | |
| Indinavir | X | | X | |
| Nelfinavir/Saquinavir | X | | | |
| Lopinavir | X | | | |
| Atazanavir | X | | | |
| Ritonavir | | | | X |
| Amprenavir | X | | | |
| *Inhibiteurs nucléos(t)idiques de la transcriptase inverse* | | | | |
| Didanosine | | X | | |
| Abacavir | | | X | |
| Stavudine | | | | X |
| Ténofovir | | X | | |
| *Inhibiteurs non nucléosidiques de la transcriptase inverse* | | | | |
| Efavirenz | X | | X | |
| Nevirapine | | | X | |

**Source**: Plaisier et coll. Presse Med 2012

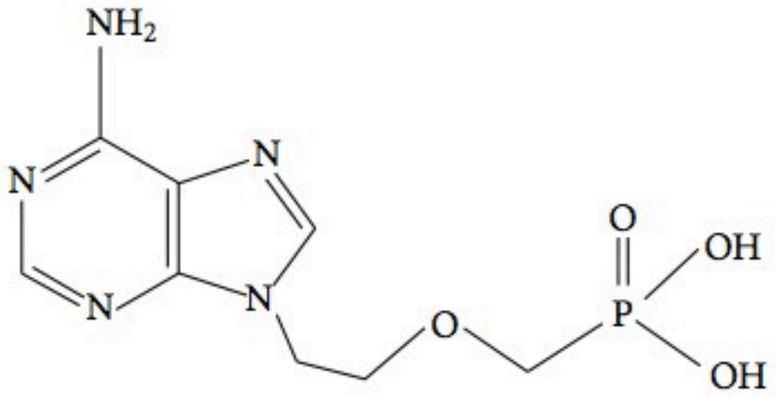



**Source**: http://nephrohug.com/2012/03/06/tout-savoir-du-syndrome-de-fanconi/

# Evaluation néphrologique

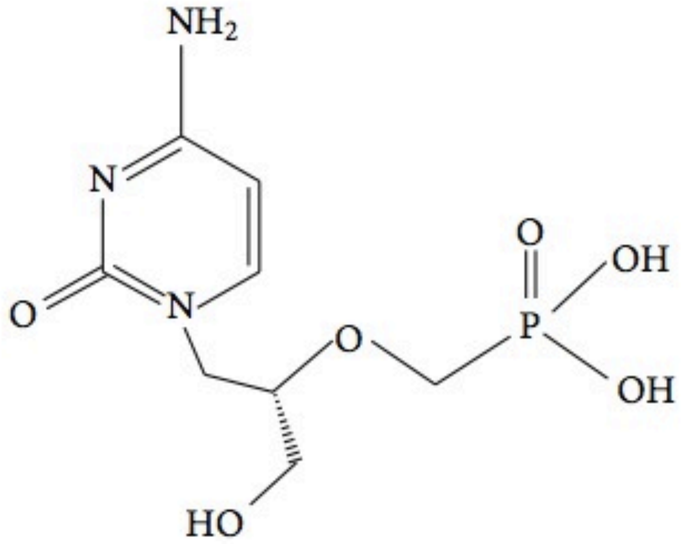


# Inhibiteurs nucléo**t**idiques de la transcriptase inverse
# N**t**RTI



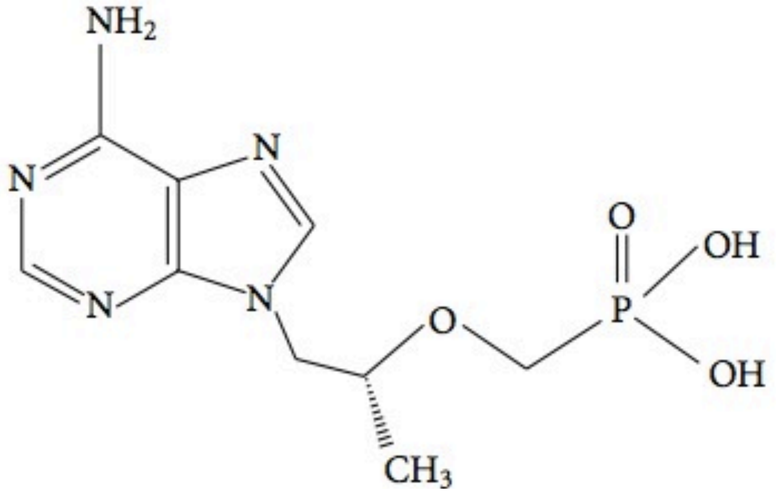

# Adéfovir

Hepsera®



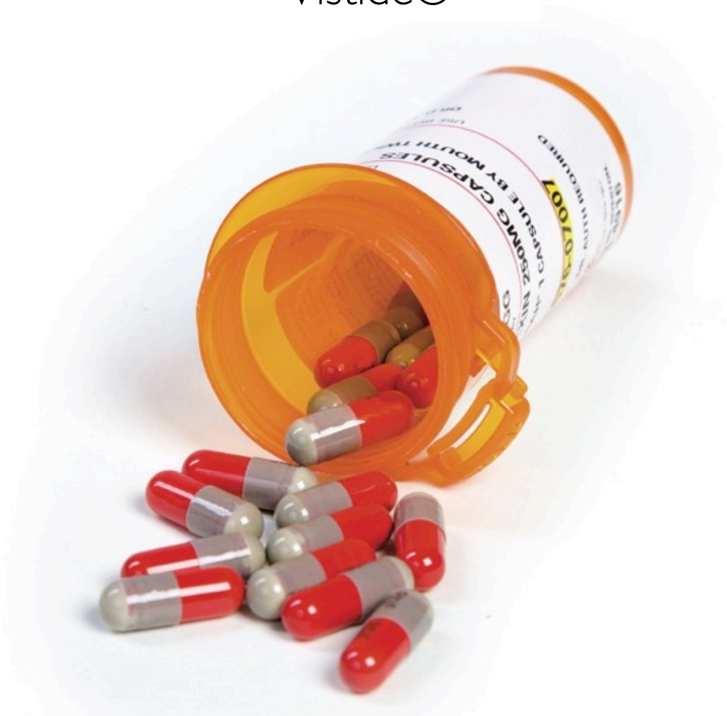

# Cidofovir

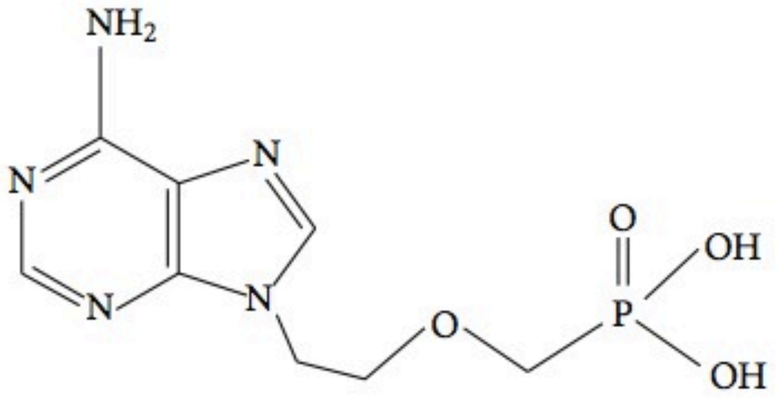
Vistide®




# Ténofovir

Viread®, Truvada®, Atripla®



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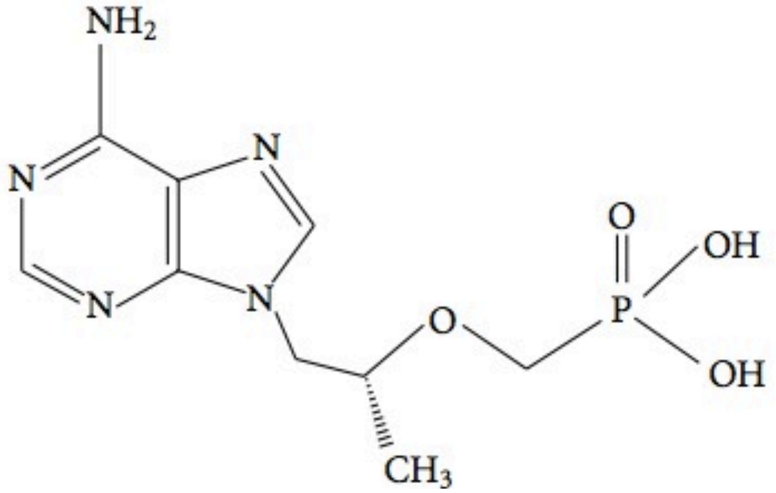


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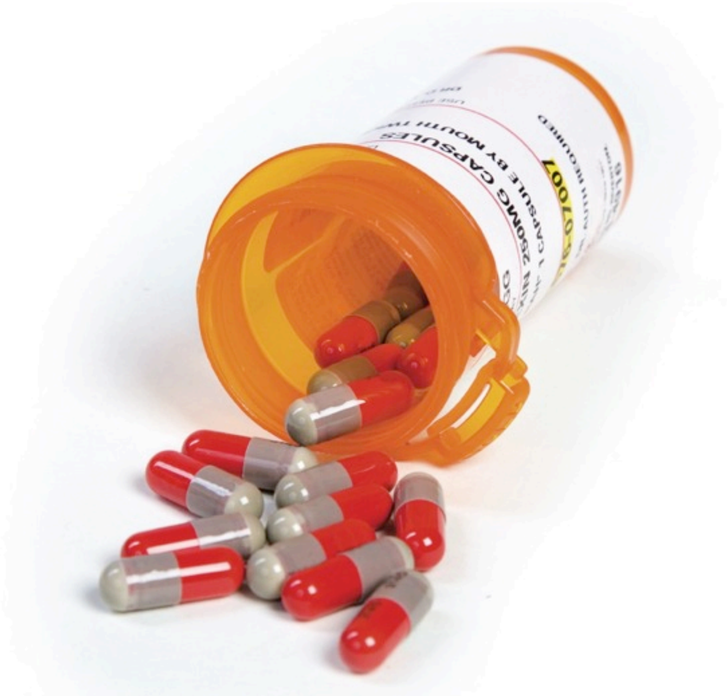


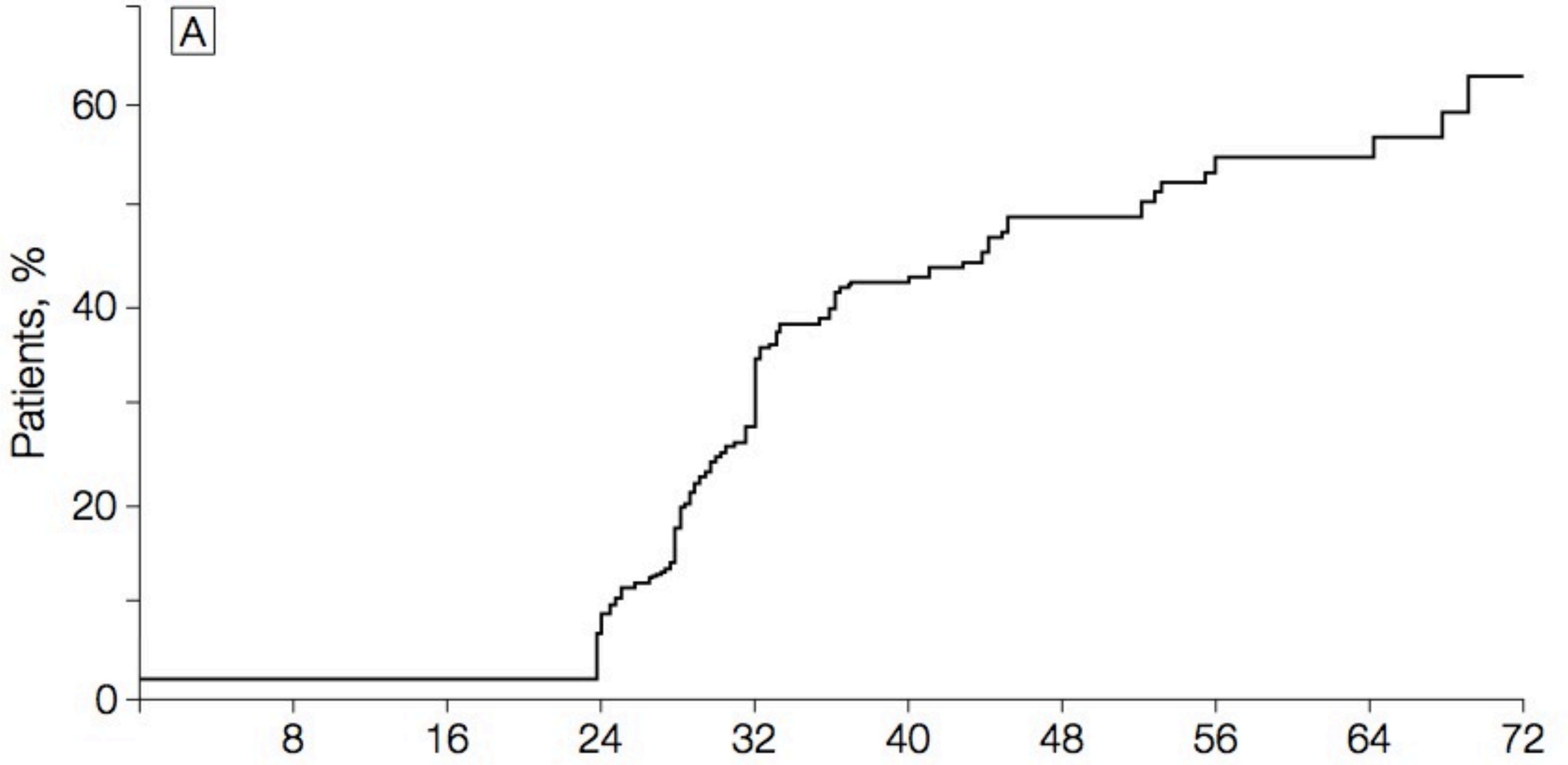
ORIGINAL CONTRIBUTION

# Efficacy and Safety of Adefovir Dipivoxil With Antiretroviral Therapy

## A Randomized Controlled Trial

**Source**: Kahn et coll. JAMA 1999

# Temps jusqu'à Pi < 0.65 mmol/l




**Source**: Kahn et coll. JAMA 1999

# Conclusion

This study suggests that once-daily adefovir [120 mg] therapy reduces HIV RNA and is active against isolates resistant to lamivudine or lamivudine and zidovudine. **Nephrotoxicity** occured when treatment extended beyond 24 weeks but was reversible.

**Source**: Kahn et coll. JAMA 1999

## Adéfovir

Hepsera®




## Cidofovir

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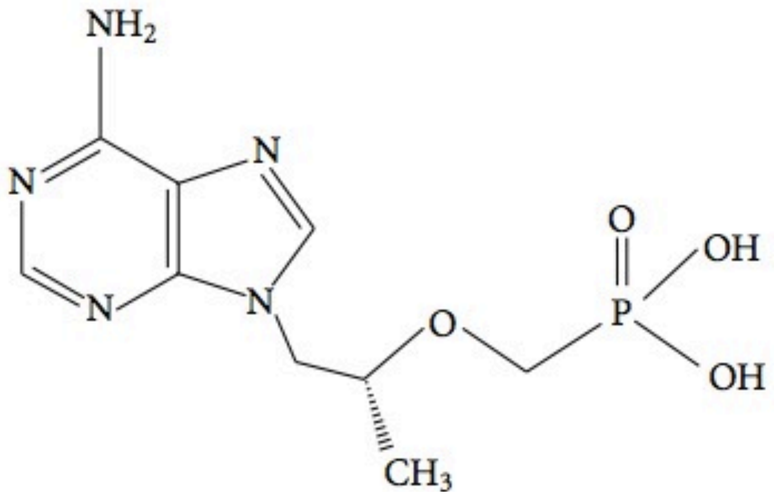


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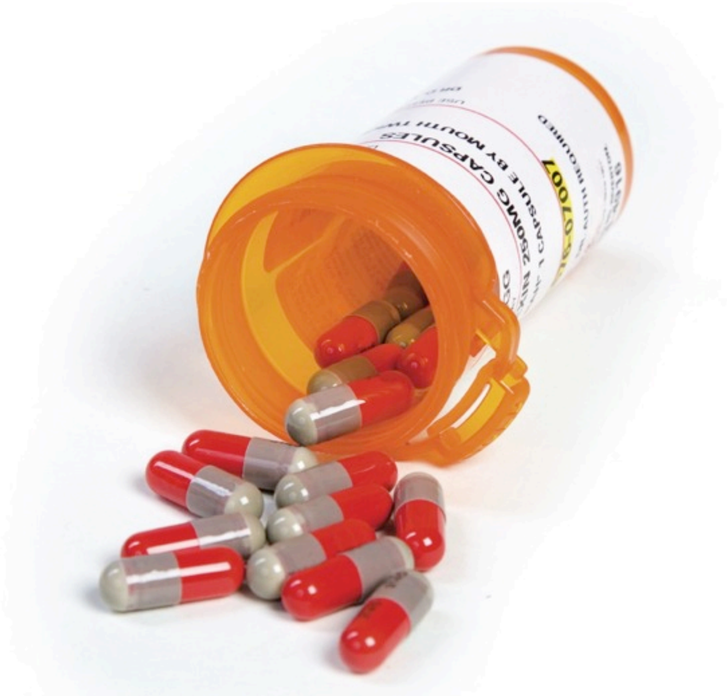


ORIGINAL CONTRIBUTION

# Efficacy and Safety of Tenofovir DF vs Stavudine in Combination Therapy in Antiretroviral-Naive Patients

## A 3-Year Randomized Trial

**Source**: Gallant et coll. JAMA 2004

# Comment

There have been **case reports of renal toxicity** in patients with antiretroviral regimens containing tenofovir DF. **However**, through 3 years in this study in patients with normal renal function at baseline, the **renal safety profile was similar** between the tenofovir DF and stavudine groups.

**Source**: Gallant et coll. JAMA 2004

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Tenofovir DF, Emtricitabine, and Efavirenz vs. Zidovudine, Lamivudine, and Efavirenz for HIV

Joel E. Gallant, M.D., M.P.H., Edwin DeJesus, M.D., José R. Arribas, M.D., Anton L. Pozniak, M.D., Brian Gazzard, M.D., Rafael E. Campo, M.D., Biao Lu, Ph.D., Damian McColl, Ph.D., Steven Chuck, M.D., Jeffrey Enejosa, M.D., John J. Toole, M.D., Ph.D., and Andrew K. Cheng, M.D., Ph.D., for the Study 934 Group*

**Source**: Gallant et coll N Engl J Med 2006

# Safety and tolerability

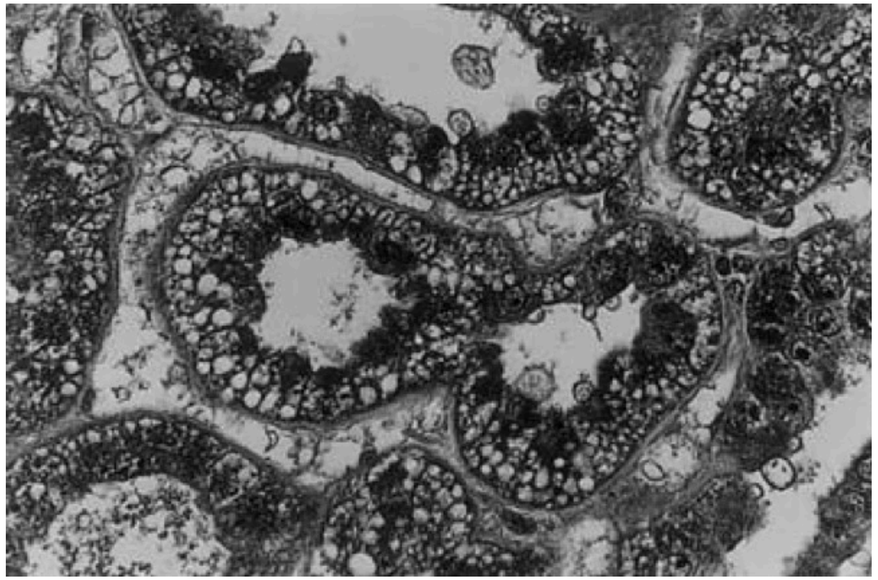
We closely followed markers of renal function. [...]
There were **no cases of Fanconi's syndrome**.

**Source**: Gallant et coll N Engl J Med 2006

**Pourtant dans la vraie vie...**

Fanconi syndrome and renal failure induced by tenofovir:

# A first case report



**Source**: Verhelst et coll. Am J Kidney Dis 2002

# Case report

Laboratory results showed elevated serum creatinine 194 mcmol/L, and urea levels 6 mmol/L], **decreased bicarbonate level** (14 mEq/L) with normal anion gap, hypokaliema (2.9 mEq/L), and **hypophosphatemia** 0.48 mmol/L. Serum protein concentration was unchanged 79 g/L. In a urine sample, sodium was 18 mEq/L, potassium 12 mEq/L, urea 50.6 mmol/L, and creatinine 1.6 mcmol/L. Urinalysis results showed a **proteinuria** (2 g/d) containing only 30% of albumin.

**Source**: Verhelst et coll. Am J Kidney Dis 2002

# Case report

Further investigations **confirmed the existence of a Fanconi syndrome**, characterized by the association of **decreased maximal transport of bicarbonate** (15 mEq/L of glomerular filtrate; normal >27 mEq/L), **decreased maximal transport of phosphate** (0.34 mg/dL of glomerular filtrate; normal >2.38 mg/dL), **normoglycemic glucosuria**, **generalized aminoaciduria**, and **high urinary excretion of β2-microglobulin** (23.10 mg/L; normal <0.30 mg/L).

**Source**: Verhelst et coll. Am J Kidney Dis 2002

**Série**

http://www.kidney-international.org

original article



see commentary on page 1060

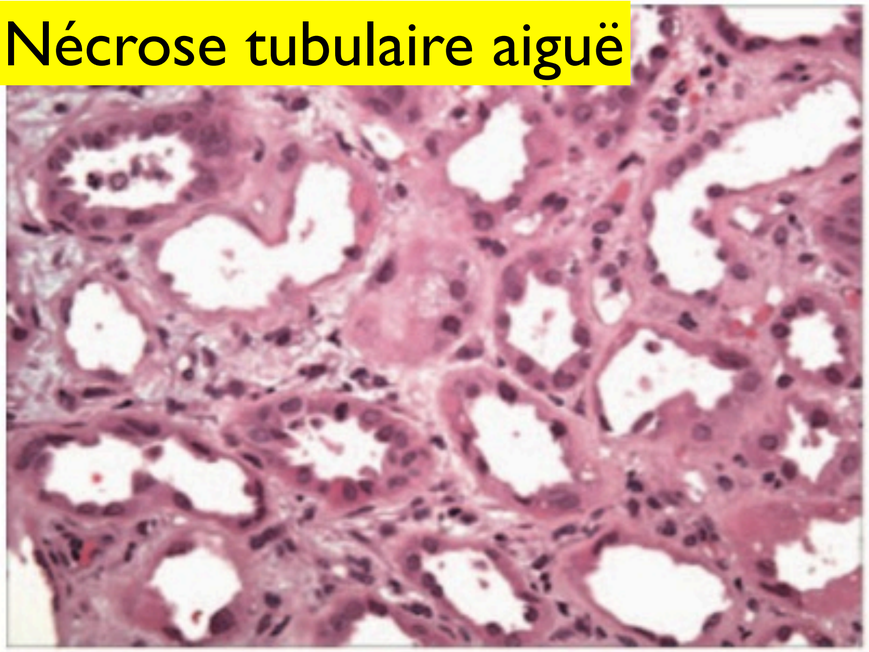
# Tenofovir nephrotoxicity: acute tubular necrosis with distinctive clinical, pathological, and mitochondrial abnormalities

Leal C. Herlitz[1], Sumit Mohan[3], Michael B. Stokes[1], Jai Radhakrishnan[2], Vivette D. D'Agati[1] and Glen S. Markowitz[1]

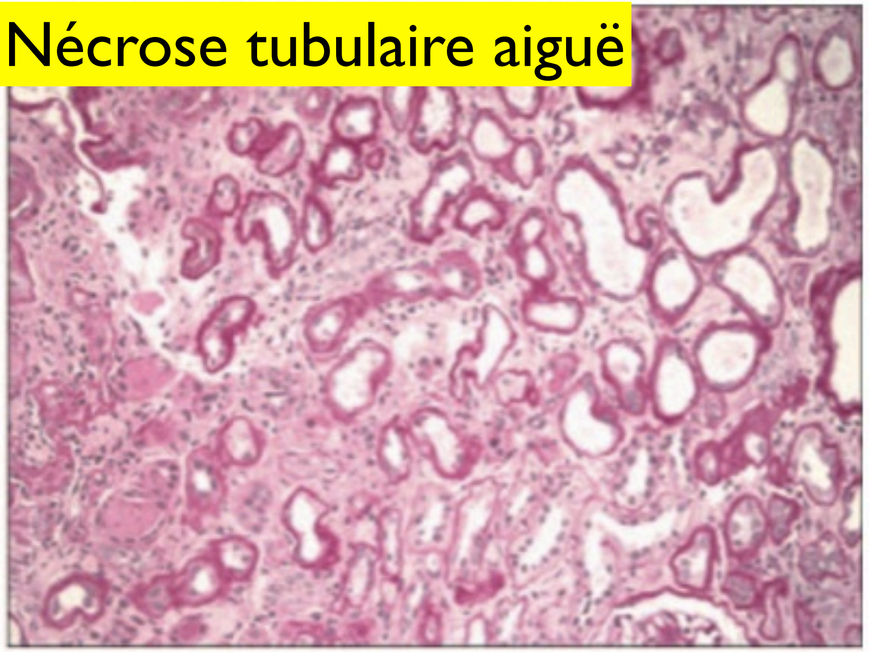
*[1]Department of Pathology, Columbia University College of Physicians and Surgeons, New York, New York, USA; [2]Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York, USA and [3]Department of Medicine, Harlem Hospital Center and Columbia University College of Physicians and Surgeons, New York, New York, USA*

**Source**: Herlitz et coll. Kidney International 2010

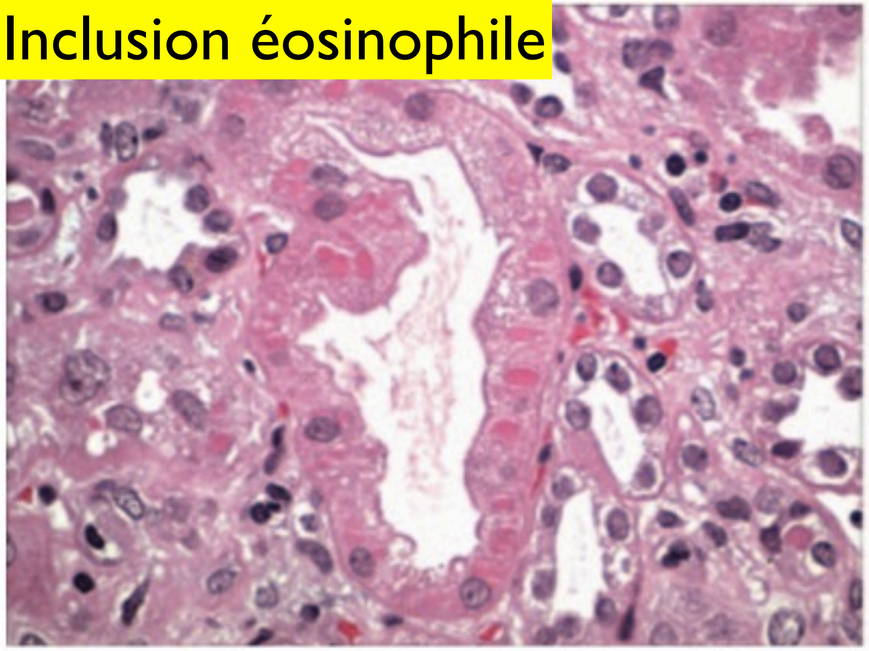
Nécrose tubulaire aiguë



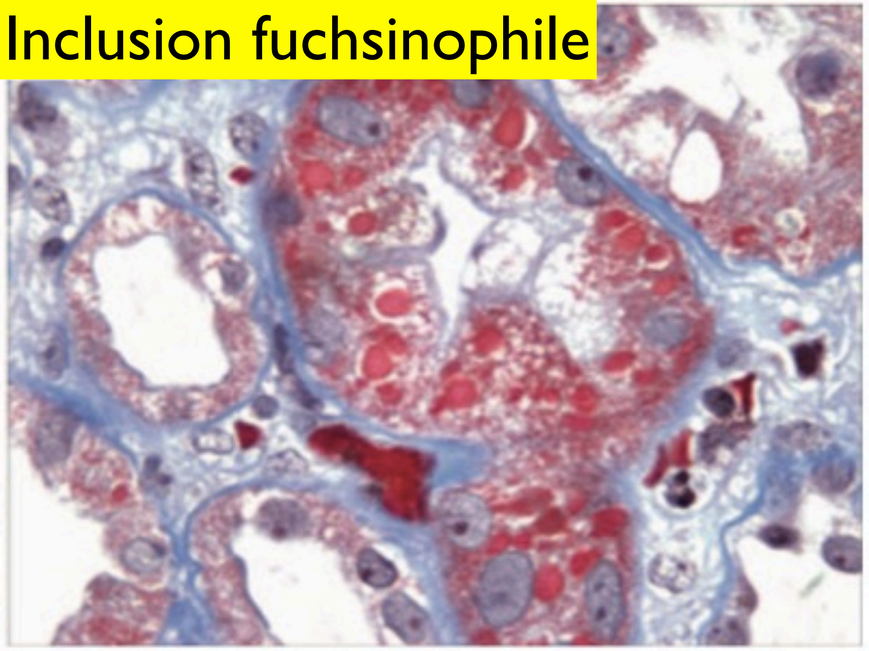
Nécrose tubulaire aiguë



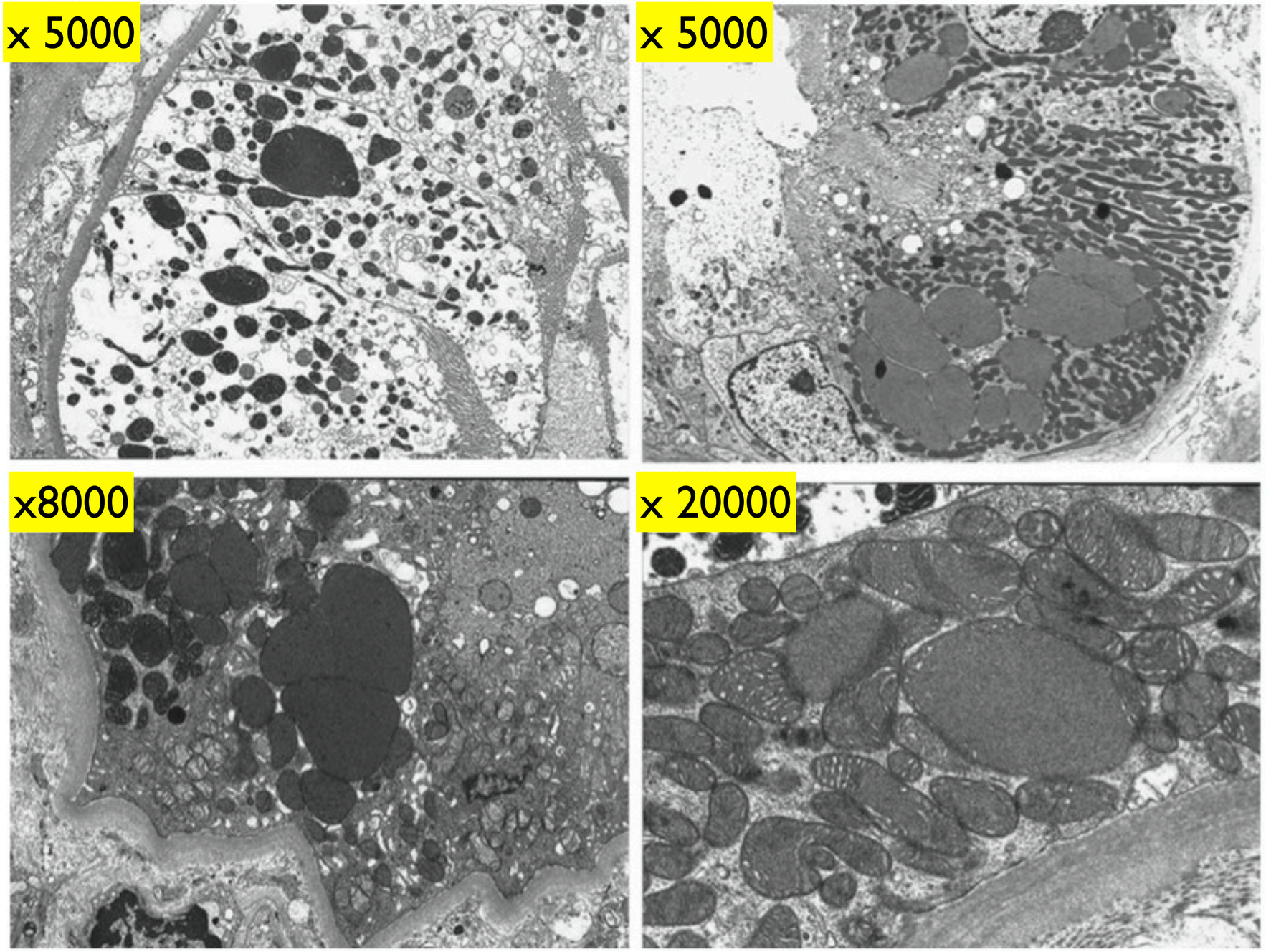
Inclusion éosinophile



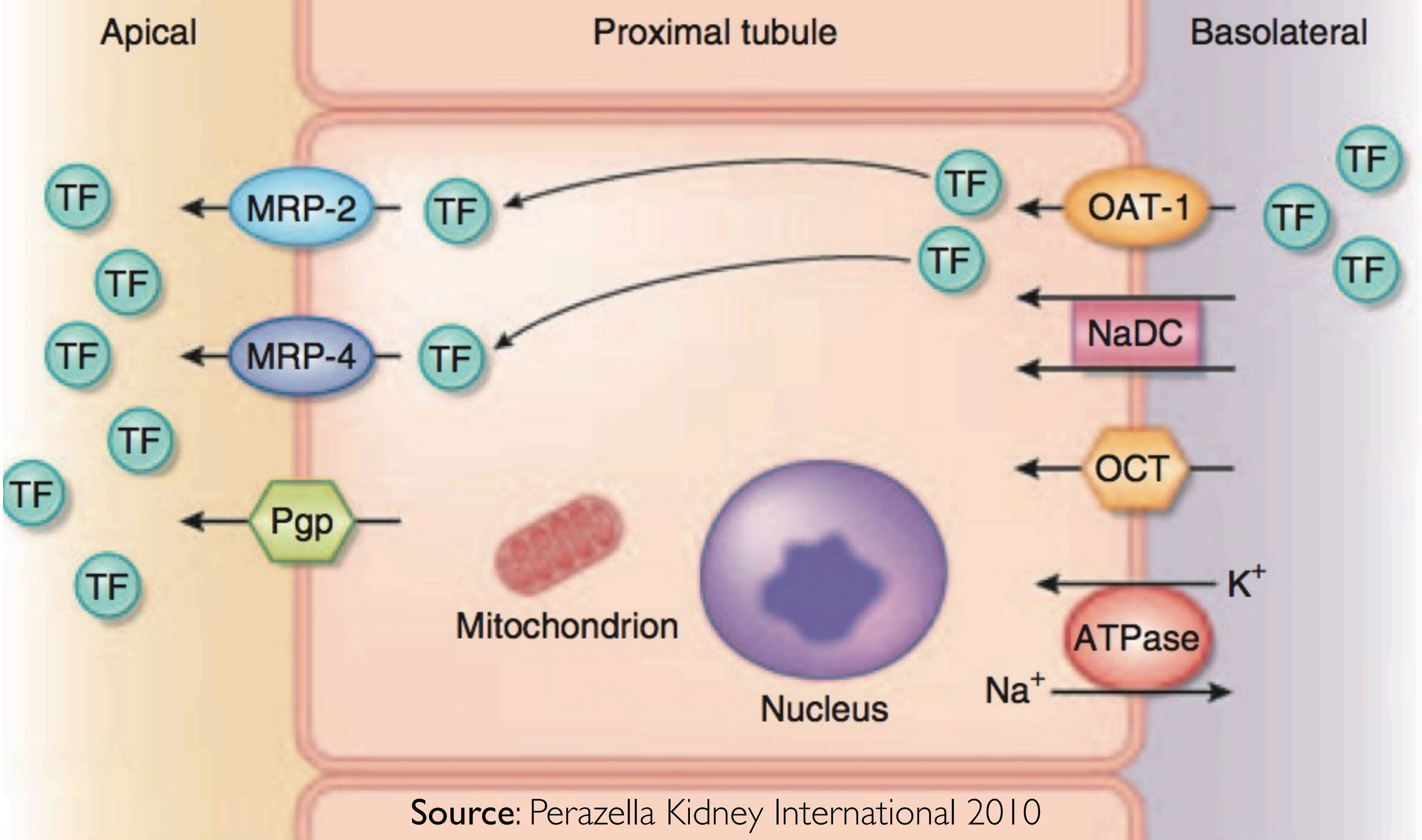
Inclusion fuchsinophile



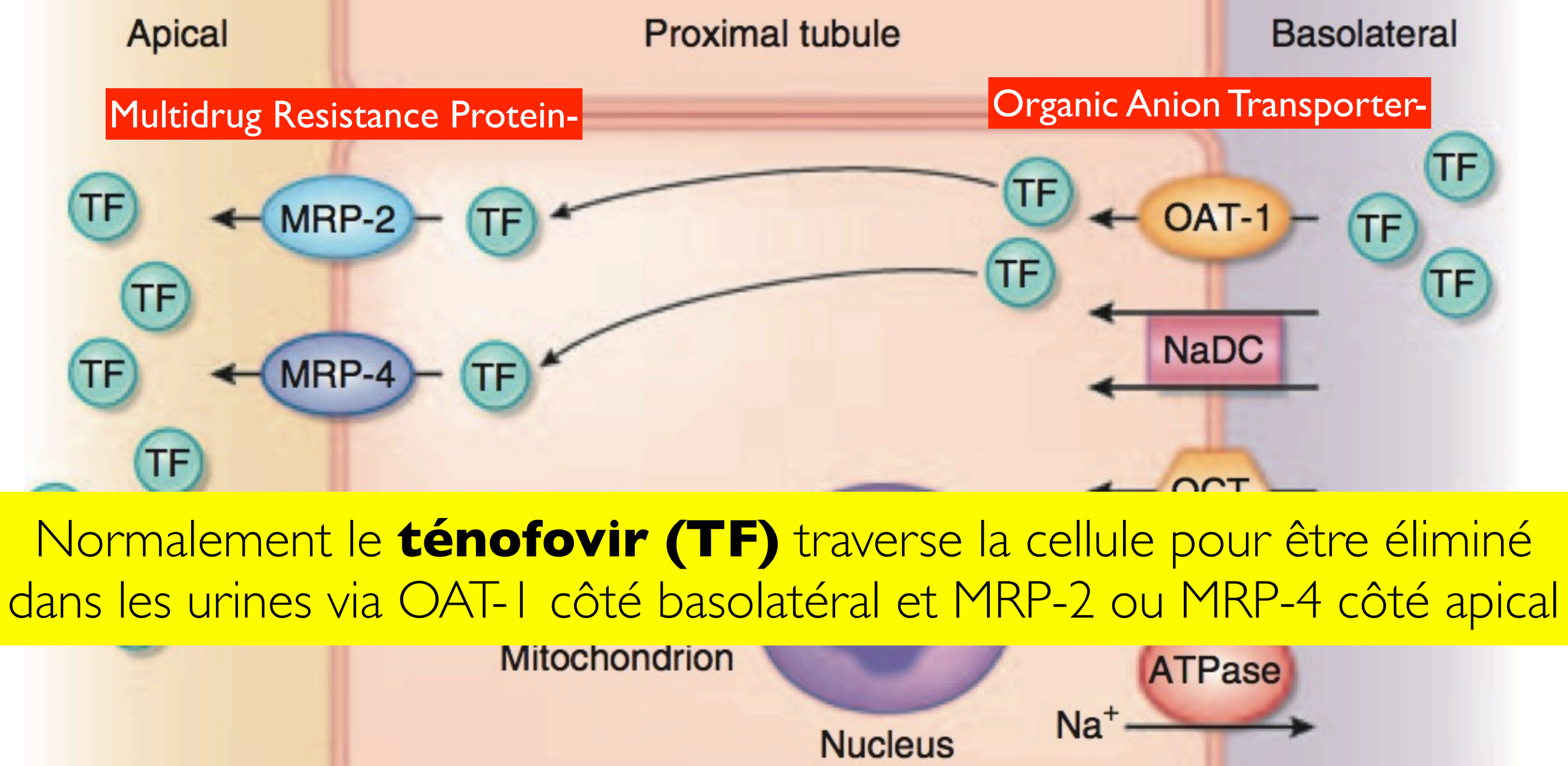
**Source**: Herlitz et coll. Kidney International 2010




**Source**: Herlitz et coll. Kidney International 2010

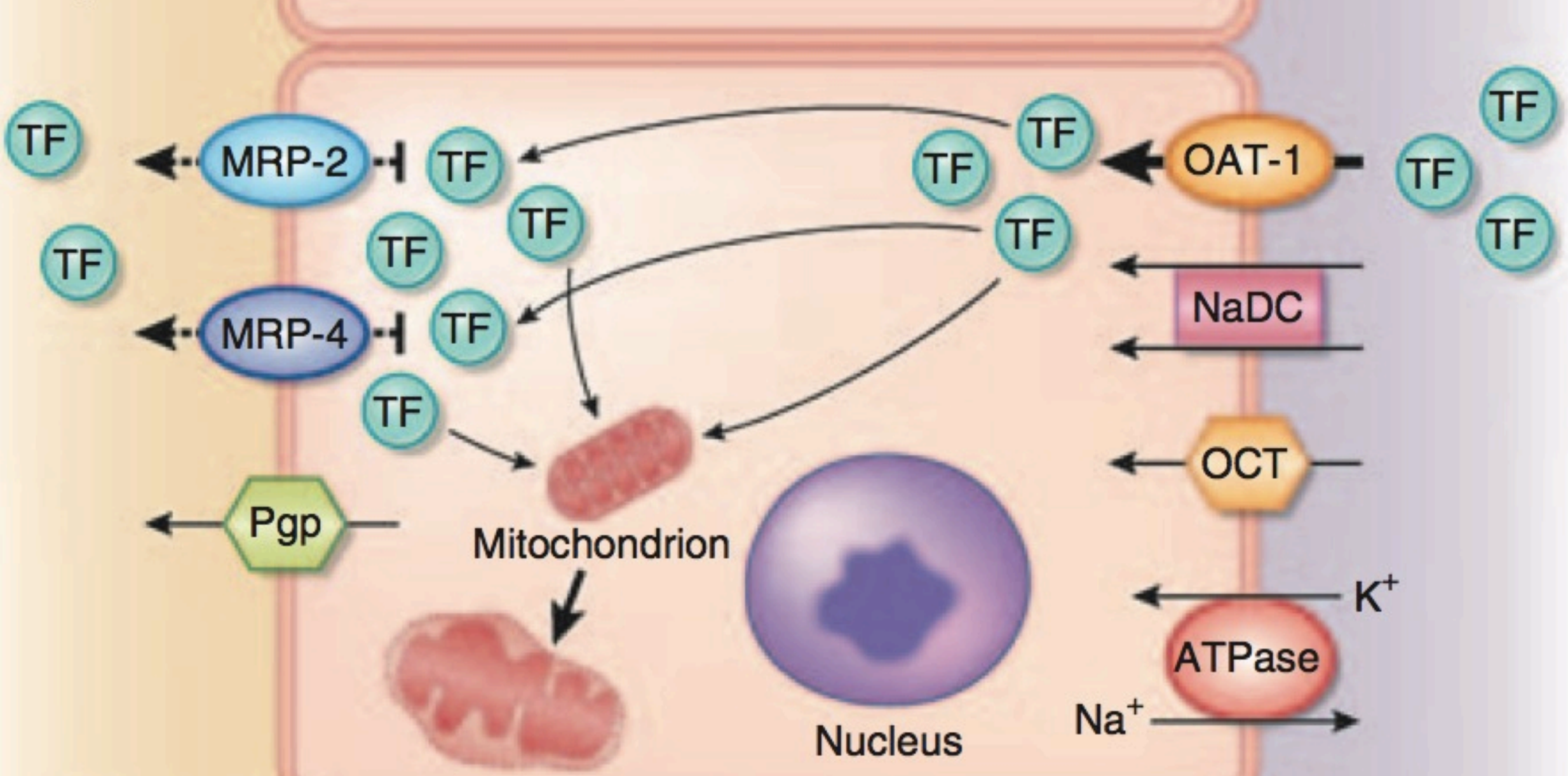



**Source**: Perazella Kidney International 2010

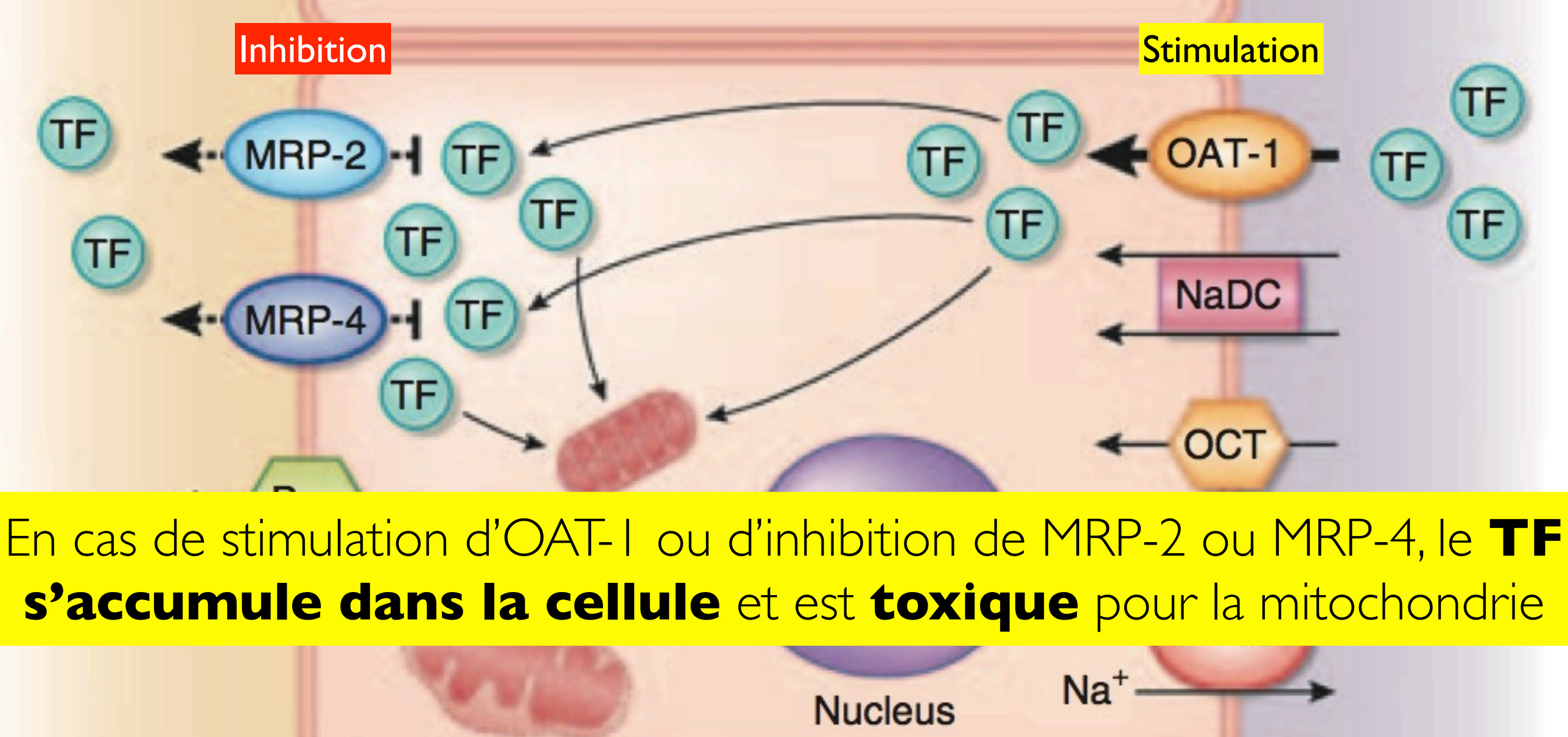



Normalement le **ténofovir (TF)** traverse la cellule pour être éliminé dans les urines via OAT-1 côté basolatéral et MRP-2 ou MRP-4 côté apical

**Source**: Perazella Kidney International 2010



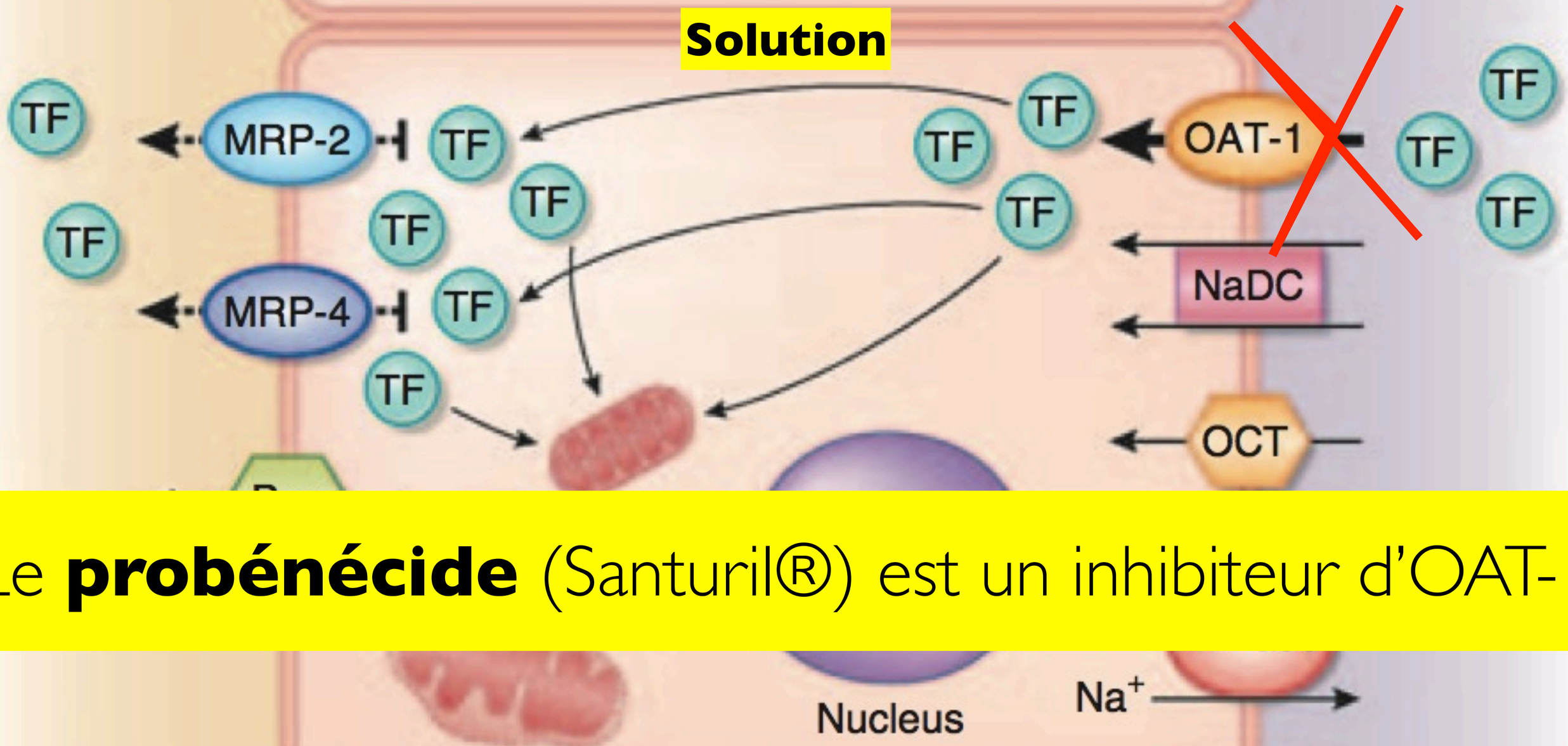

**Source**: Perazella Kidney International 2010




En cas de stimulation d'OAT-1 ou d'inhibition de MRP-2 ou MRP-4, le **TF s'accumule dans la cellule** et est **toxique** pour la mitochondrie

**Source**: Perazella Kidney International 2010

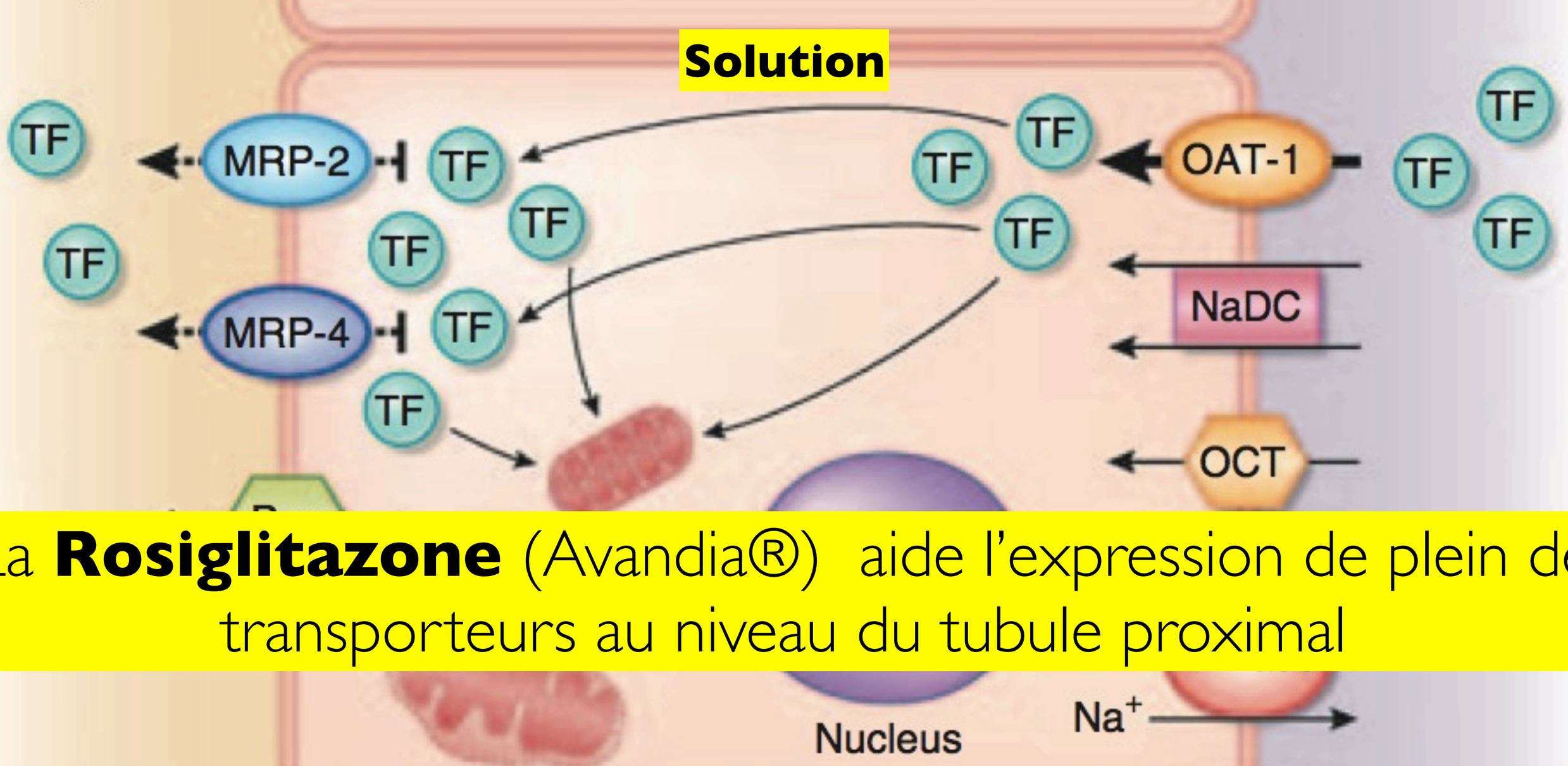
**Solution**




Le **probénécide** (Santuril®) est un inhibiteur d'OAT-1

**Source**: Perazella Kidney International 2010

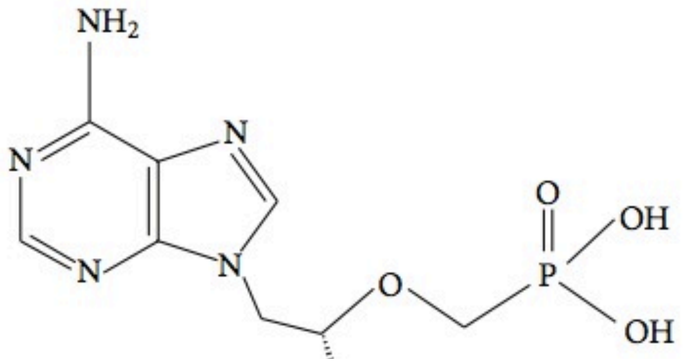
## Solution




La **Rosiglitazone** (Avandia®) aide l'expression de plein de transporteurs au niveau du tubule proximal

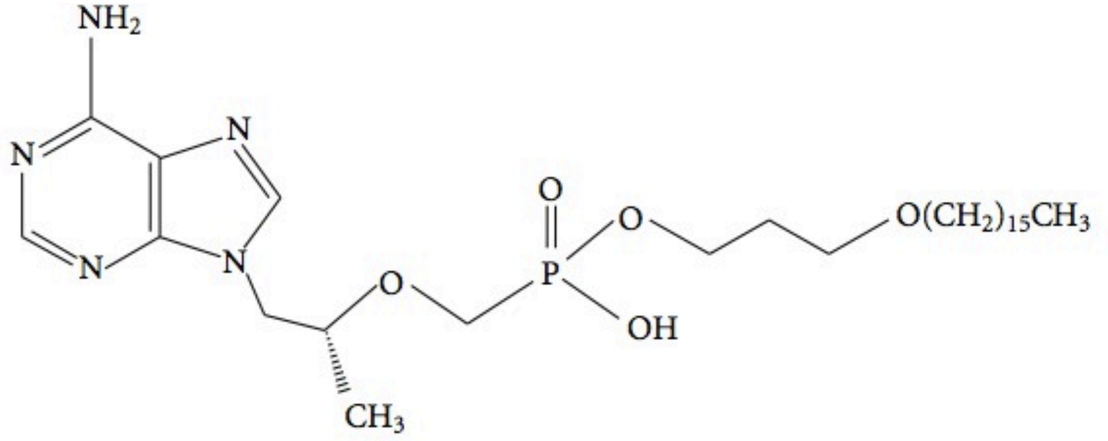
**Source**: Perazella Kidney International 2010

# Solution



## Ténofovir

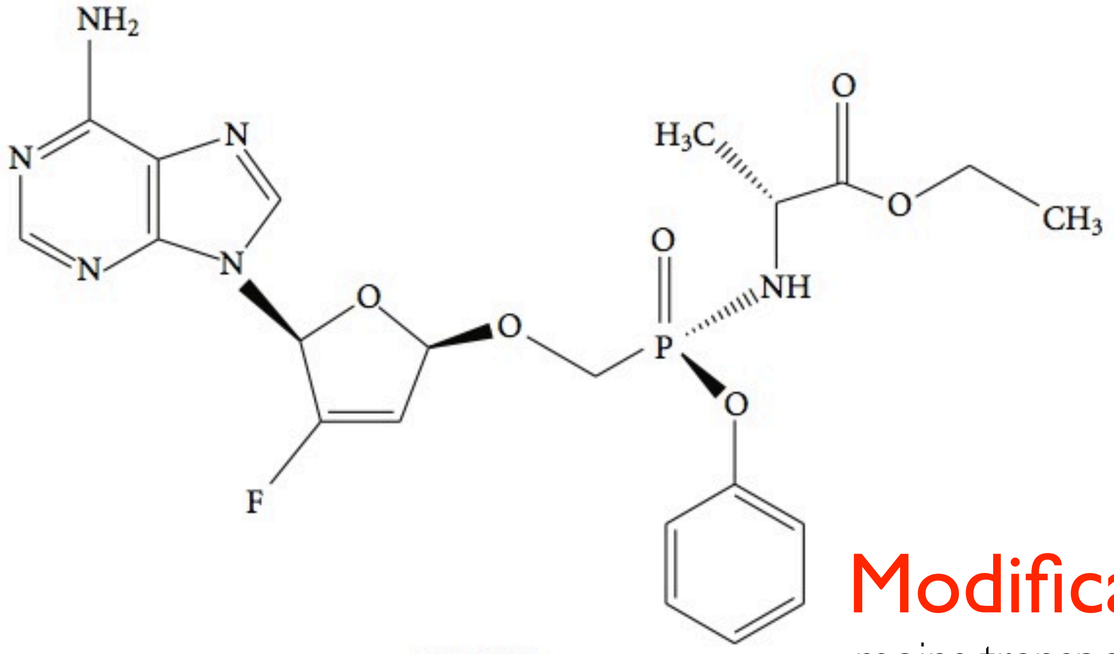
Viread®, Truvada®, Atripla®



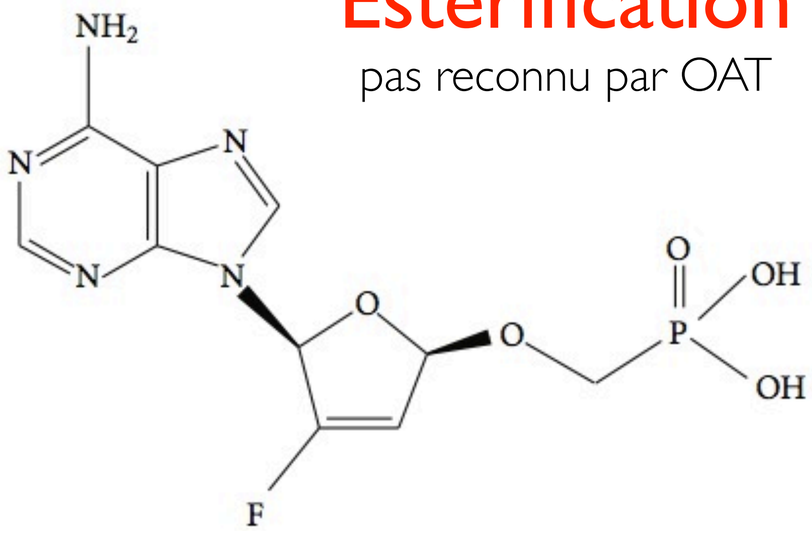
Hexadeciloxypropil-tenofovir (CMX157)

## Estérification

pas reconnu par OAT



GS-9131



GS-9148

## Modification ribose

moins transportée à travers cellule

**Il fallait le dire...**

The most effective treatment of tenofovir nephrotoxicity is stopping tenofovir.

**Source**: Fernandez-Fernandez et coll. AIDS Research and Treatment 2011

# Quel suivi et quel bilan ?

# Predictors of significant renal function decline

Preexisting renal impairment

Older age

Advanced HIV disease

Vasculometabolic disease

Concomitant use of nephrotoxic drugs or protease inhibitors

Low body weight

ABCC2 gene (encoding the outward tenofovir transporter MRP-2) polymorphisms

**Source**: Fernandez-Fernandez et coll. AIDS Research and Treatment 2011

MAJOR ARTICLE

# Systematic Review and Meta-analysis: Renal Safety of Tenofovir Disoproxil Fumarate in HIV-Infected Patients

**Ryan D. Cooper,[1] Natasha Wiebe,[1] Nathaniel Smith,[4] Philip Keiser,[5] Saraladevi Naicker,[6] and Marcello Tonelli[1,2,3]**

Departments of [1]Medicine and [2]Public Health Sciences and [3]Division of Critical Care Medicine, University of Alberta, Edmonton, Canada; [4]Center for Public Health Practice, Arkansas Department of Health, Little Rock, Arkansas; [5]University of Texas, Medical Branch, Galveston, Texas; and [6]Department of Internal Medicine, University of Witwatersrand, Johannesburg, South Africa

**Source**: Cooper et coll. CID 2010

| Study authors, year [reference] | Country (study) | Design | ART-naive participants | Treatment[a] | Comparator | Cotreatment | CG-GFR (in mL/min) or other exclusion | Sample size | Duration of follow-up, weeks |
|---|---|---|---|---|---|---|---|---|---|
| Campbell et al, 2009 [36] | UK | Registry | Both[b] | TDF-containing regimen | TDF-sparing regimen[c] | Any HAART | … | 3439 | 104–520 |
| De Jesus et al, 2009 [37] | US | RCT | No | TDF, EFV, FTC | Any HAART, no restrictions[d] | None | <60 | 306 | 48 |
| Guaraldi et al, 2009 [39] | Italy | PC | No | TDF-containing regimen | TDF-sparing regimen | Any HAART | MDRD ≤60 and >90 | 99 | 48 |
| Kinai et al, 2009 [40] | Japan | PC | No | TDF-containing regimen | TDF-sparing regimen | Any HAART | MDRD <80 | 63 | 96 |
| Martinez et al, 2009 [41] | Spain (BICOMBO) | RCT | No | TDF; FTC-containing regimen | ABC; 3TC-containing regimen | Any PI or NNRTI | SCr >2 mg/dL | 335 | 48 |
| Smith et al, 2009 [44] | US (HEAT) | RCT | Yes | TDF; FTC | ABC; 3TC | LPV/r[e]; no NNRTIs | <50 | 694 | 96 |
| Arribas et al, 2008 [34] | Spain, UK, and US | RCT | Yes | TDF; FTC | ZDV; 3TC | EFV; no PIs | ≤50 | 517 | 144 |
| Goicoechea et al, 2008 [18] | US | PC (nested in RCT) | No | TDF; PI/r-containing regimen; NNRTI-containing regimen | TDF-sparing regimen | Any HAART | … | 146 | 48 |
| Fux et al, 2007 [16] | Switzerland (HIV Cohort Study) | PC | Both[b] | TDF-containing regimen | TDF-sparing regimen | Any HAART | … | 1078 | 86[f] |
| Young et al, 2007 [20] | US (HOPS) | PC | No | TDF-containing regimen | TDF-sparing regimen | Any HAART | <50 | 1114 | 44[f] |
| Moyle et al, 2006 [42] | UK (RAVE) | RCT | No | TDF-containing regimen | ABC-containing regimen | Any HAART; no d4T; ZDV | SCr >1.25 ×ULN | 105 | 48 |
| Winston et al, 2006 [19] | Australia | PC | No | TDF-containing regimen | TDF-sparing regimen | Any HAART | … | 948 | 121 |
| Gallant et al, 2005 [17] | US (John Hopkin's HIV Clinical Cohort) | PC | Both[b] | TDF-containing regimen | TDF-sparing regimen | Any HAART | … | 658 | 46 |
| Gallant et al, 2004 [38] | US, South America, and Europe | RCT | Yes | TDF | d4T | 3TC (150 mg BID); EFV (600 mg QD) or NVP (200 mg BID); no PIs | <60 | 600 | 144 |
| Squires et al, 2003 [45] | US and UK | RCT | No | TDF | Placebo | Any HAART, no restrictions[d] | <60 | 552 | 24 |
| Schooley et al, 2002 [43] | US | RCT | No | TDF (75, 150, or 300 mg QD) | Placebo | Any HAART | … | 189 | 48 |
| Barditch-Crovo et al, 2001 [35] | US | RCT | No | TDF (75, 150, 300, or 600 mg QD) | Placebo | None | <60 | 49 | … |

# Meta-analysis

13 studies (> 5767 patients) reported a **significantly faster loss of kidney function** (-5.4 ml/min) in patients receiving tenofovir compared with control subjects (mean difference between group in GFR loss estimated by CG formula: 3.9 ml/min; 95% CI 2.1-5.7 ml/min)

**Source**: Cooper et coll. CID 2010

# Association of tenofovir exposure with kidney disease risk in HIV infection

Rebecca Scherzer[a], Michelle Estrella[b], Yongmei Li[a], Steven G. Deeks[c], Carl Grunfeld[a] and Michael G. Shlipak[a]


**Source**: Scherzer et coll. AIDS 2012

# 10'841 HIV-infected patients from VHA (1997-2007)

**Table 2. Association of tenofovir exposure with risk[a] of kidney disease outcomes.**

| | Demographic-Adjusted Model[b] | | Time-Dependent Cox Model[c] | | Marginal Structural Model[d] | |
|---|---|---|---|---|---|---|
| | Hazard Ratio (95% CI) | P Value | Hazard Ratio (95% CI) | P Value | Hazard Ratio (95% CI) | P Value |
| Cumulative Exposure to Tenofovir (per year) | | | | | | |
| Proteinuria *(n = 3400 events)* | 1.30 (1.22–1.37) | <0.0001 | 1.34 (1.25–1.45) | <0.0001 | 1.24 (1.17–1.32) | <0.0001 |
| Rapid decline[e] *(n = 3078 events)* | 1.17 (1.11–1.24) | <0.0001 | 1.11 (1.03–1.18) | 0.0033 | 1.16 (1.09–1.23) | <0.0001 |
| CKD *(n = 553 events)* | 1.44 (1.30–1.60) | <0.0001 | 1.33 (1.18–1.51) | <0.0001 | 1.36 (1.22–1.51) | <0.0001 |
| Ever Exposure to Tenofovir | | | | | | |
| Proteinuria *(n = 3400 events)* | 1.70 (1.57–1.85) | <0.0001 | 1.68 (1.52–1.85) | <0.0001 | 1.51 (1.36–1.66) | <0.0001 |
| Rapid decline *(n = 3078 events)* | 1.51 (1.39–1.64) | <0.0001 | 1.36 (1.23–1.50) | <0.0001 | 1.50 (1.36–1.67) | <0.0001 |
| CKD *(n = 553 events)* | 2.11 (1.76–2.54) | <0.0001 | 1.71 (1.38–2.12) | <0.0001 | 1.88 (1.50–2.36) | <0.0001 |

[a]Each analysis excludes patients who had the condition at baseline. *Abbreviations*: Confidence Interval (CI); Chronic kidney disease (CKD).
[b]Demographic adjusted Cox model includes drug exposure, age, sex, race, and time.
[c]Time-dependent multivariable adjusted model includes exposure to tenofovir and all other antiretroviral drugs, age, sex, race, baseline comorbid conditions (diabetes, hypertension, dyslipidemia, prevalent cardiovascular disease, smoking, drug abuse, hepatitis B and C virus infection), baseline measurements (CKD or proteinuria, BMI category), and current measurements (CD4 count, viral load, CKD or proteinuria, lipids, diabetes, and hypertension). Rapid decline model controls for both baseline CKD and proteinuria. Proteinuria model controls for baseline CKD, and CKD model controls for baseline proteinuria.
[d]Marginal structural model includes all baseline variables in multivariable model.
[e]Rapid decline in kidney function was defined as an annual decline of 3 ml/min/1.73m2 or more for two consecutive years.

**Source**: Scherzer et coll. AIDS 2012

# Conclusion

Tenofovir exposure was independently associated with increased risk for three types of kidney disease events, and **did not appear to be reversible**. Because subtle kidney function decline affects long-term morbidity and mortality, the balance between efficacy and probable adverse effects requires further study.

**Source**: Scherzer et coll. AIDS 2012

"What it does mean is you need to be **monitoring these patients closely.** You need to be checking kidney function, and if the signs are trending toward worsening function, consider alternatives."

**Source**: Michael Horberg, director of HIV/AIDS at Kaiser Permanente

# Regular Follow-up

| | | eGFR1 [i] | | |
|---|---|---|---|---|
| | | ≥ 60 mL/min | 30-59 mL/min | < 30 mL/min |
| Proteinuria [ii] | UP/C [iii] < 50 | Regular Follow-up | | • Check risk factors for CKD and nephrotoxic medication including ART [iv]<br>• Discontinue or adjust drug dosages where appropriate [v]<br>• Perform renal ultrasound<br>• Urgent referral to nephrologist |
| | UP/C [iii] 50-100 | • Check risk factors for CKD and nephrotoxic medication including ART [iv]<br>• Discontinue or adjust drug dosages where appropriate [v]<br>• Perform renal ultrasound<br>• If haematuria present with any level of proteinuria refer to nephrologist.<br>• Refer to nephrologist if new CKD or progressive decline in eGFR | | |
| | UP/C [iii] > 100 | | | |

**Source**: EACS Guidelines version 6.0 - October 2011

# Infectious Disease Society of America (IDSA)

Patients recevant du ténofovir et ayant un DFG < 90 ml/min, des comorbidités (diabète ou hypertension), ou qui reçoivent du ritonavir («boosted protease inhibitor») doivent être dépistés **au moins 2x par an** (fonction rénale, phosphore sérique, protéinurie et glycosurie)

**Source**: Gupta et coll. CID 2005

# Recommandations HUG

Patients recevant du ténofovir ~~et ayant un DFG < 90 ml/min, des comorbidités (diabète ou hypertension), ou qui reçoivent du ritonavir («boosted protease inhibitor»)~~ doivent être dépistés **au moins 2x par an** (fonction rénale, phosphore sérique, protéinurie et glycosurie)

# Questions en suspend

Patients avec DFG < 60 ml/min (?)
Patients avec facteurs de risque (?)
Quand arrêter le ténofovir (?)
Faut-il le commencer (?)
PEP (?)

**Il faut le dire…**

Mise en évidence d'une néphrotoxicité d'un médicament que l'on savait être néphrotoxique, mais moins que les autres NtRTI…

# Cas cliniques et discussion


# http://nephrohug.com

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