Prévention et traitement du diabète post-greffe

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Néphrologie - Transplantation

Conflits intérêts

- Honoraire consultance / advisory board:
  - Astra Zeneca (Evusheld)
  - Hansa (Inflimidase)

- Aucun en rapport avec thématique traitée dans cette présentation

Diabète post greffe

DEFINITION

Définition

POSTTRANSPLANTATION DIABETES MELLITUS

Recommendations

2.20 After organ transplantation, screening for hyperglycemia should be done. A formal diagnosis of posttransplantation diabetes mellitus is best made once the individual is stable on an immunosuppressive regimen and in the absence of an acute infection. **B**

2.21 The oral glucose tolerance test is the preferred test to make a diagnosis of posttransplantation diabetes mellitus. **B**

2.22 Immunosuppressive regimens shown to provide the best outcomes for patient and graft survival should be used, irrespective of posttransplantation diabetes mellitus risk. **E**

ADA, Diabetes Care, 2022

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*
OR
2-h PG ≥200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
OR
A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

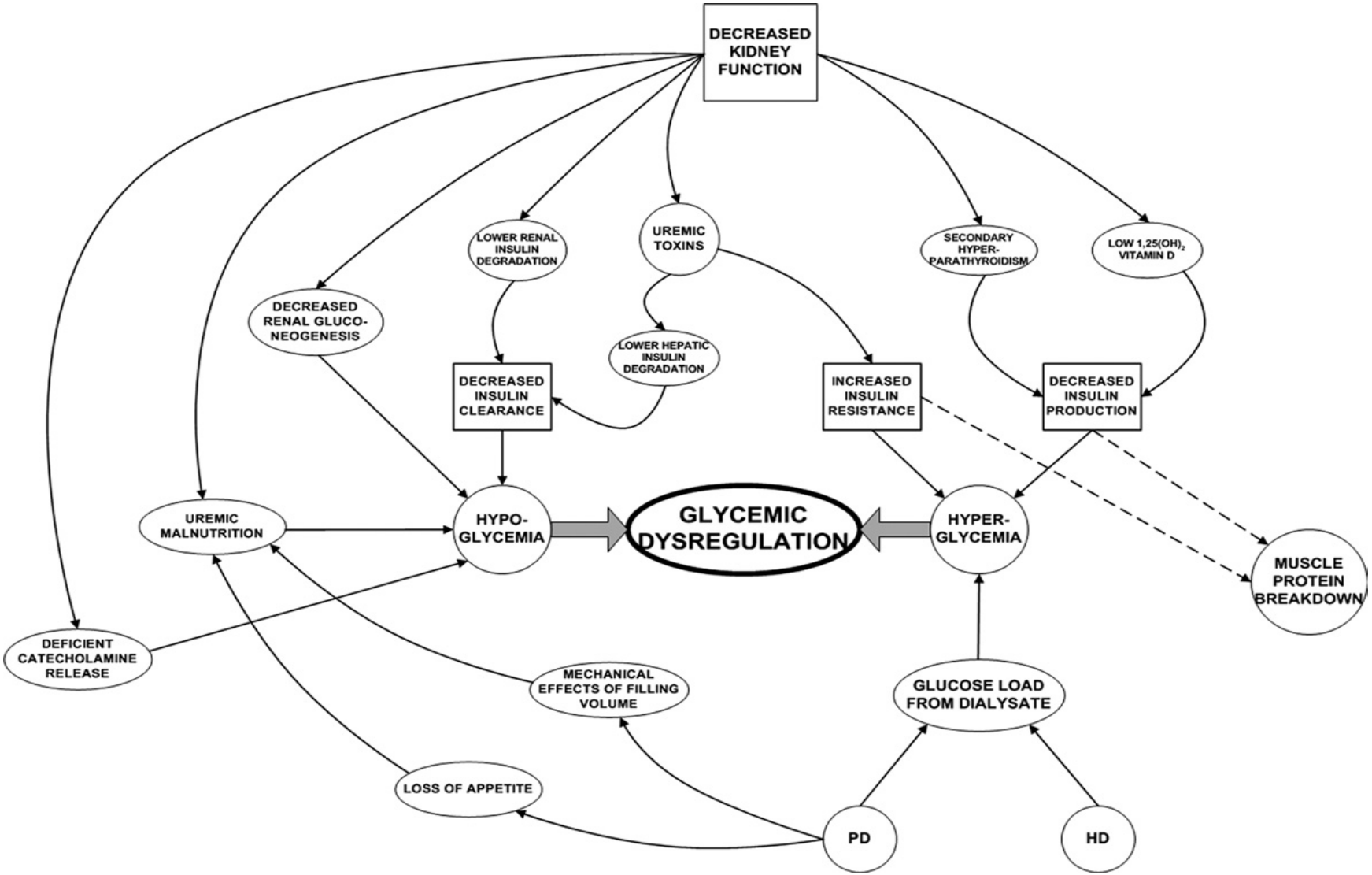
- **NODAT**: New Onset Diabetes After Transplantation
- **PTDM**: Post-Transplant Diabetes Mellitus
- 90% des transplantés rénaux ont une hyperglycémie transitoire les premières semaines post-greffe qui ne doit pas être étiquetée de Diabète post-greffe

« Proceedings From an International Consensus Meeting on Posttransplantation Diabetes Mellitus: Recommendations and Future Directions » ; American Journal of Transplantation , 2014

Diabète post greffe

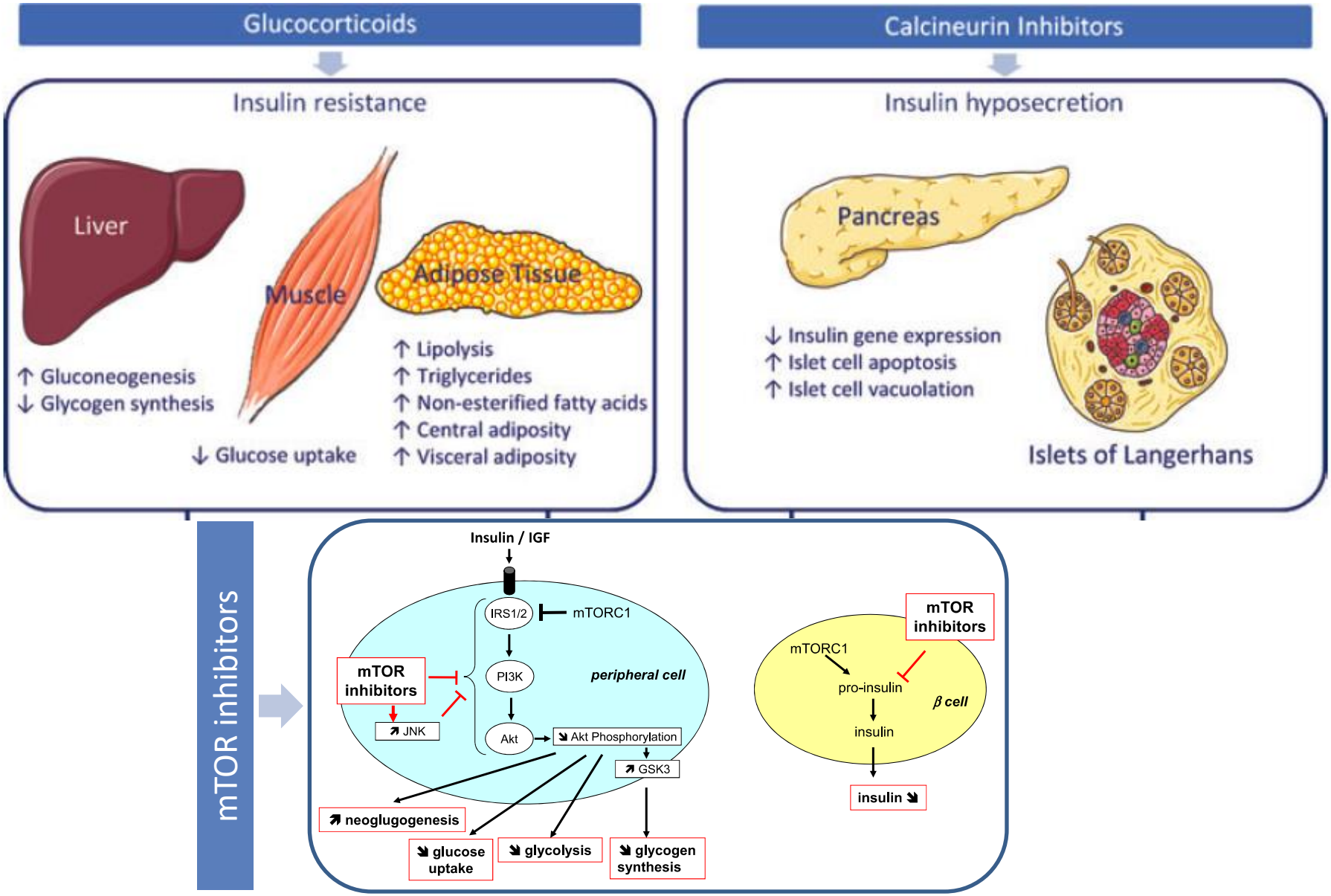
PHYSIOPATHOLOGIE

Mécanismes « dérégulation » glycémique IRC



C. Kovesdy, Am J Kidney Dis 52:766-777

Physiopathologie PTDM

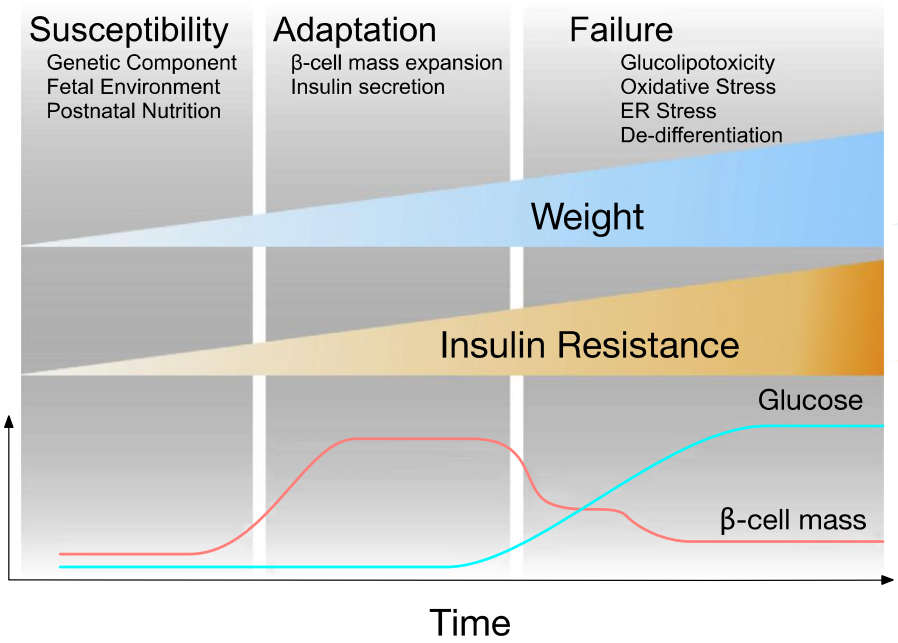


Yates et al ; American Journal of Transplantation ; 2012

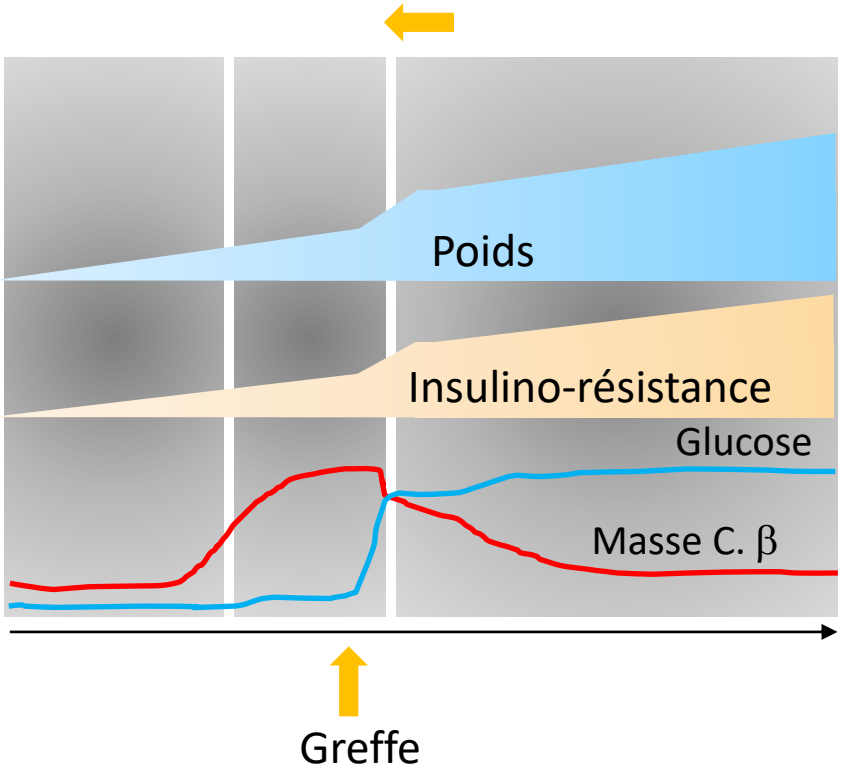
B. Vergès ; Diabetes research and clinical practice ; 2015

Histoire naturelle du diabète

Diabète de type 2

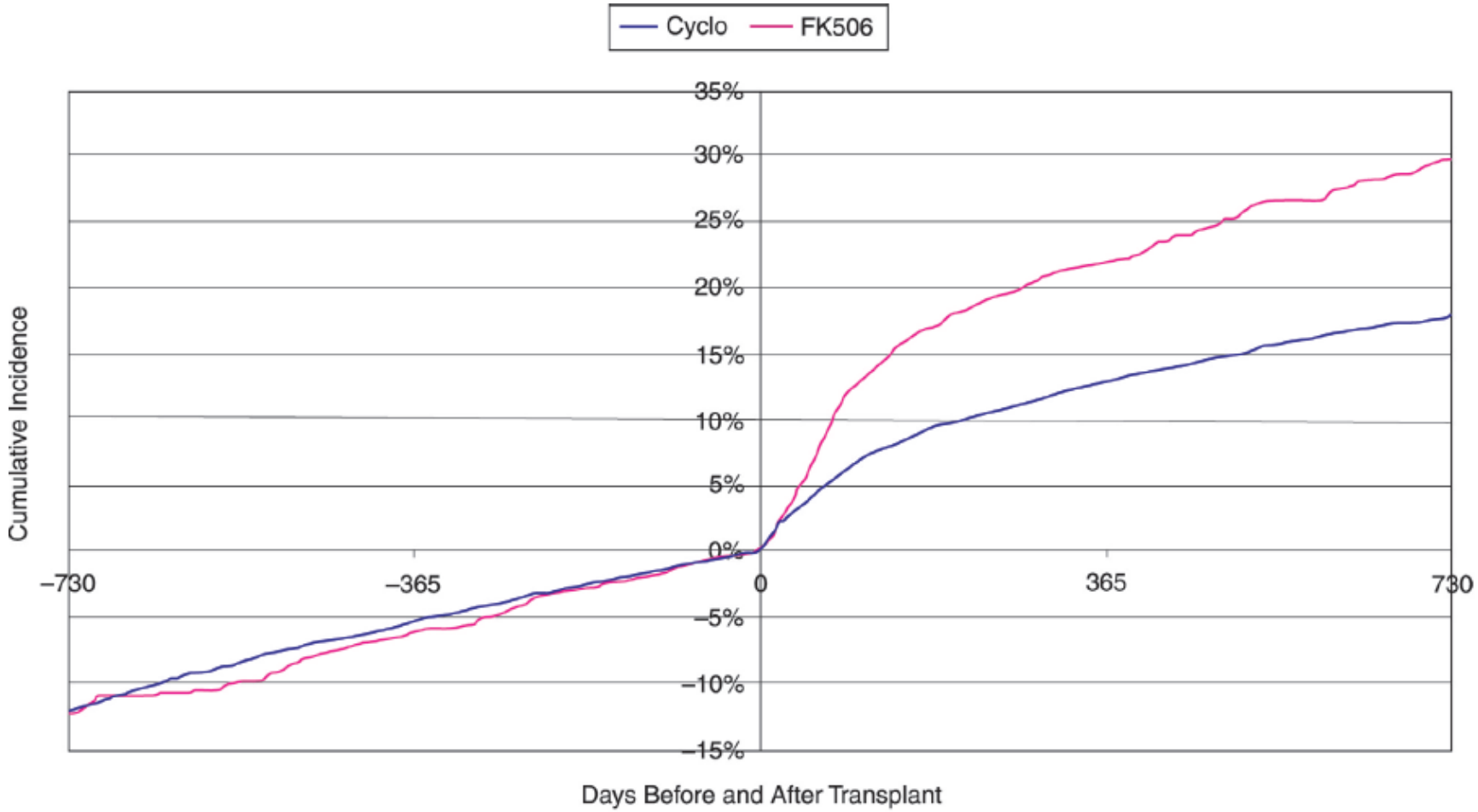


PTDM



Alejandro et al. ; Molecular Aspects of Medicine ; 2015

Incidence cumulée de diabète avant et après greffe rénale



Woodward et al. ; AJT ; 2003

Diabète post greffe

EPIDEMIOLOGIE

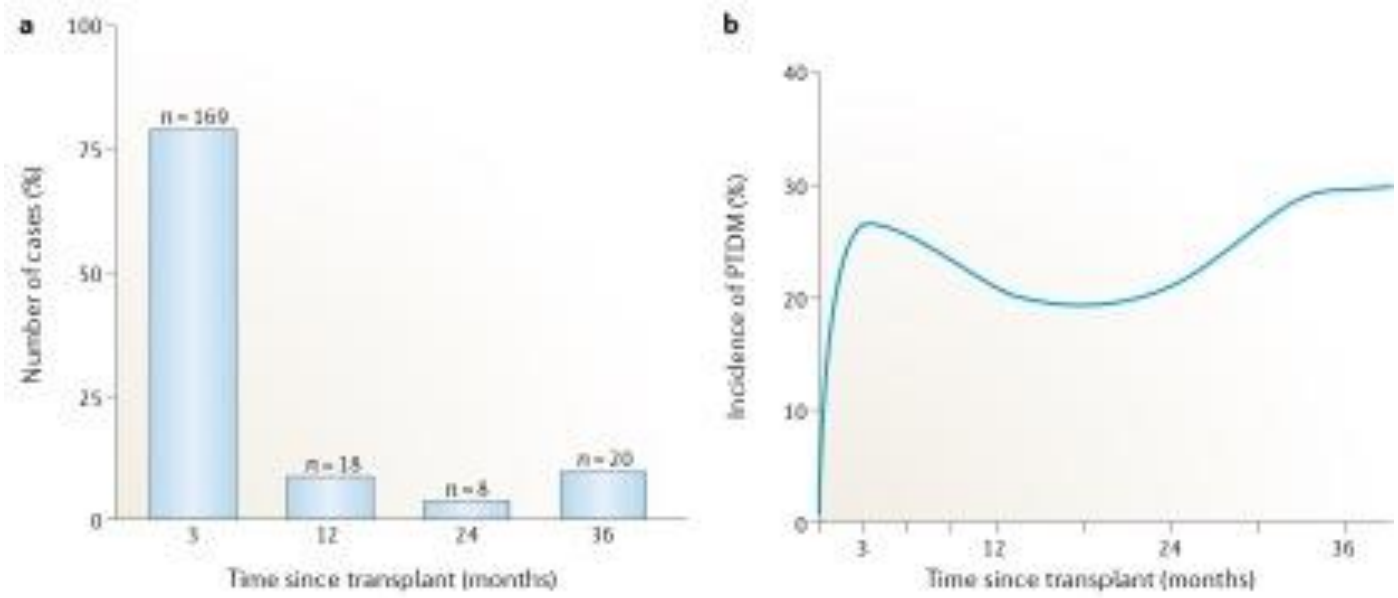
Incidence du NODAT

Study	N	Definition	NODAT incidence (%) Months post 1	2	3	6	Years post 1	4	6	7	Population	Primary maintenance immunosuppressive regimen
Hagen et al. (2003) (Ref. 9)	63	OGTT		19				22			White Norwegian	Pred, CsA, Aza
David-Neto et al. (2007) (Ref. 10)	84	OGTT	14	18		19	9				Nonobese Brazilian	Pred, Tac, MMF
Hur et al. (2007) (Ref. 11)	77	OGTT					39			35	Korean	Pred, CsA, MMF
Porrini et al. (2008) (Ref. 12)	154	OGTT			31		20				Spanish	Pred, Tac, MMF
Valderhaug et al. (2009) (Ref. 13)	1637	OGTT		17[2]							White Norwegian	Pred, CsA, Aza/MMF
Luan et al. (2010) (Ref. 14)	591	FBG						15[1]			White/African American	Pred, CsA, MMF/ Sirolimus

Pred = prednisone/prednisolone; CsA = cyclosporine A; Tac = tacrolimus; Aza = azathioprine; MMF = mycophenolate mofetil.

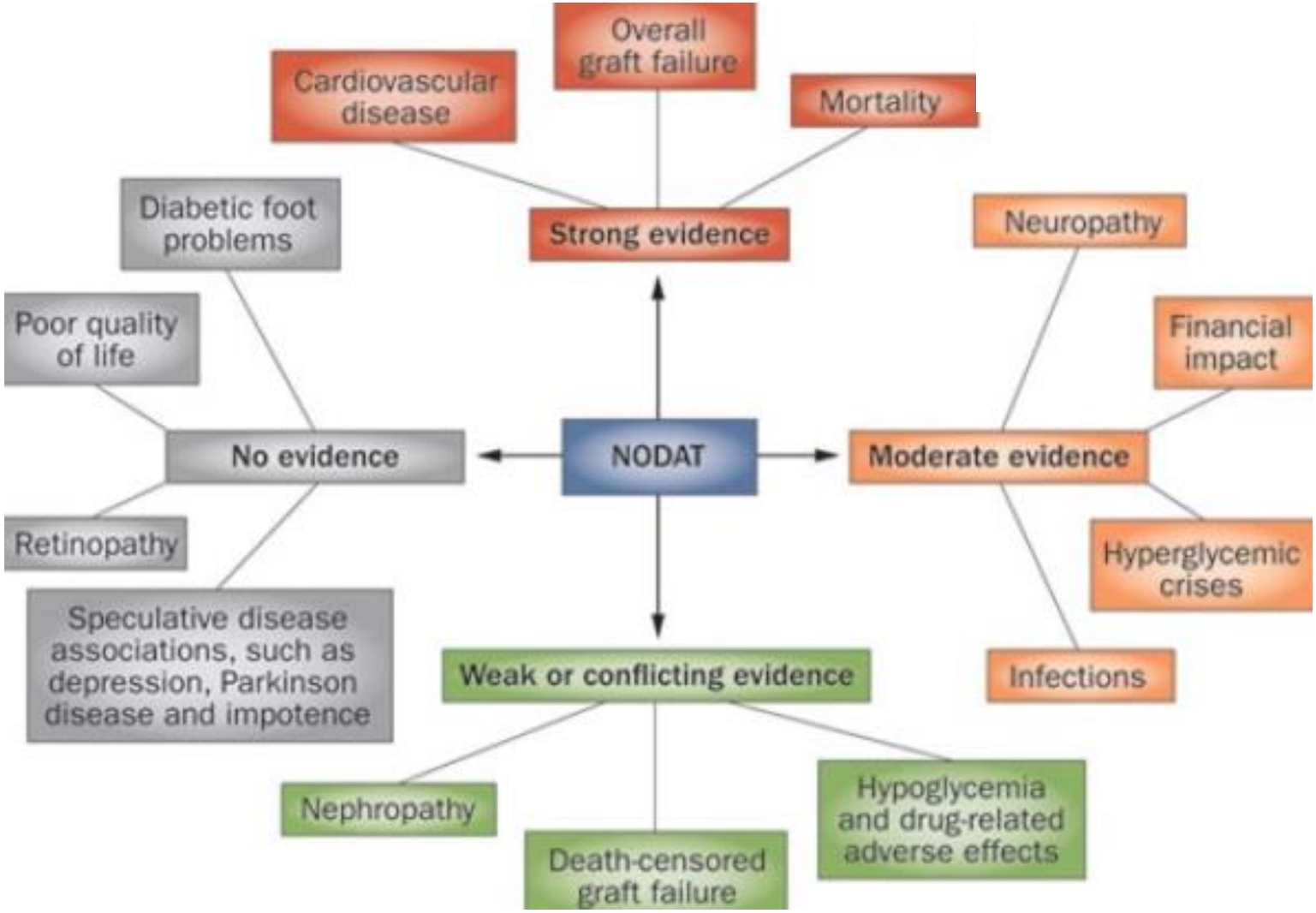
=> Incidence : **9** à **39%**

Yates et al ; American Journal of Transplantation ; 2012



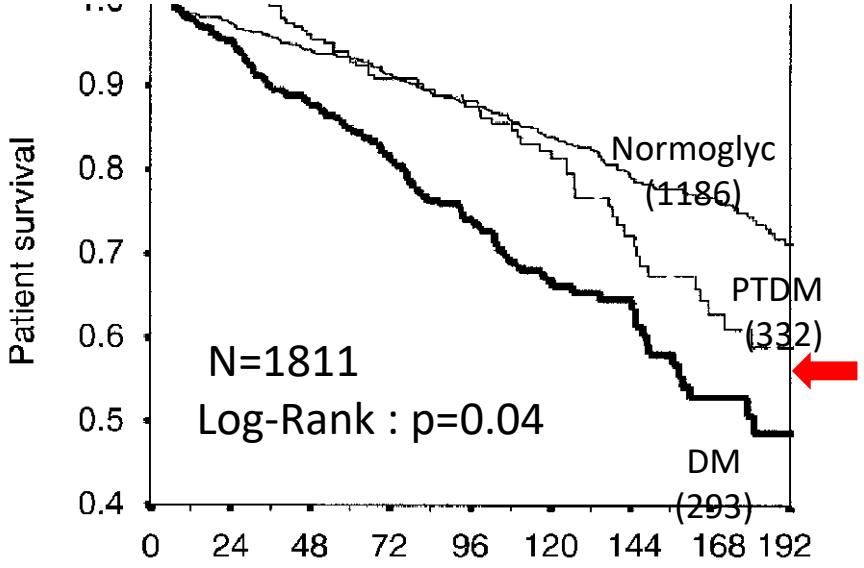
Jenssen et al; Nature Reviews Endocrinology ; 2019

Effets délétères <u>associés</u> avec le NODAT



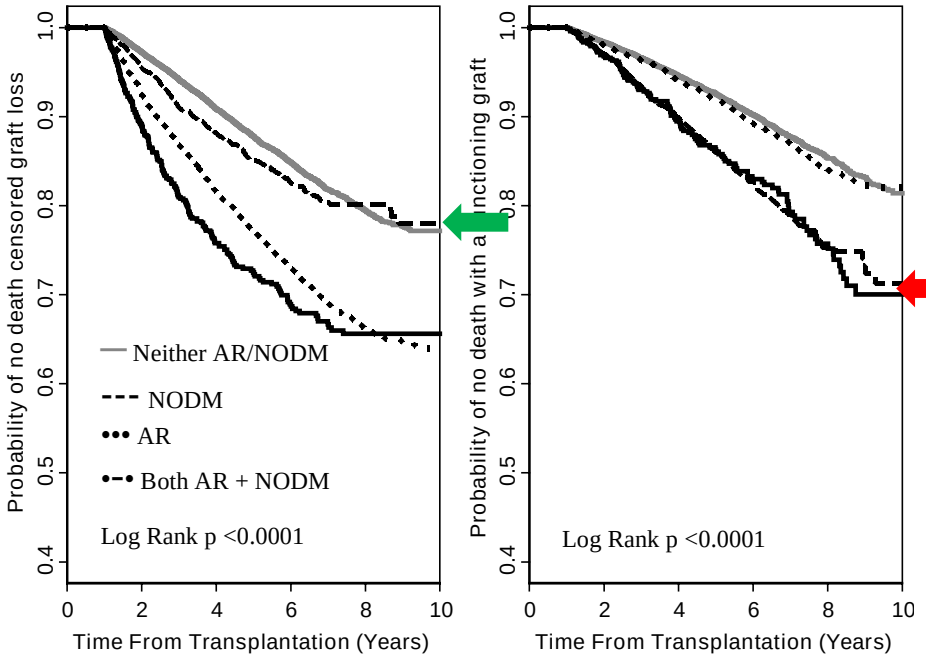
A. Sharif et al ; *Nat Rev Nephrol* **;** 2012

Mortalité post-greffe



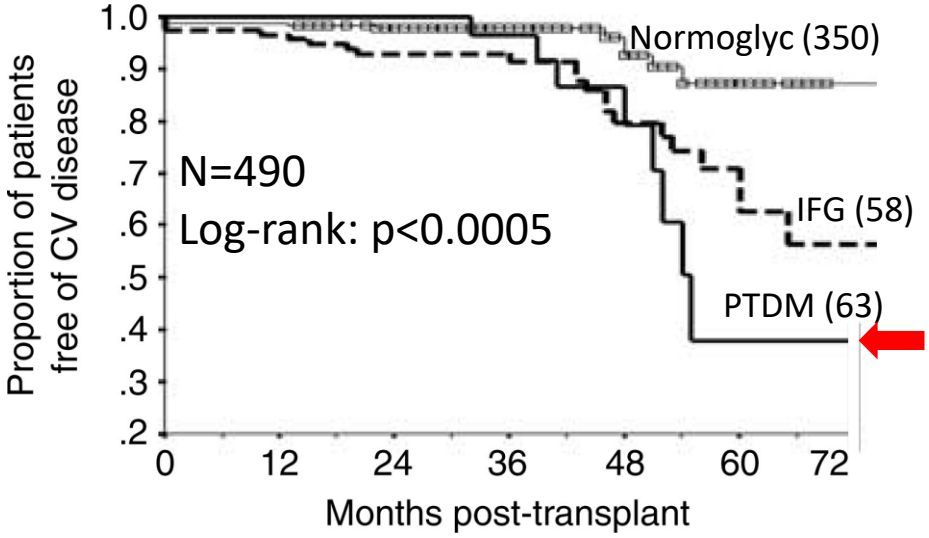
Cosio et al. ; Kidney International ; 2002

Survie greffon (censurée pour décès ou non)



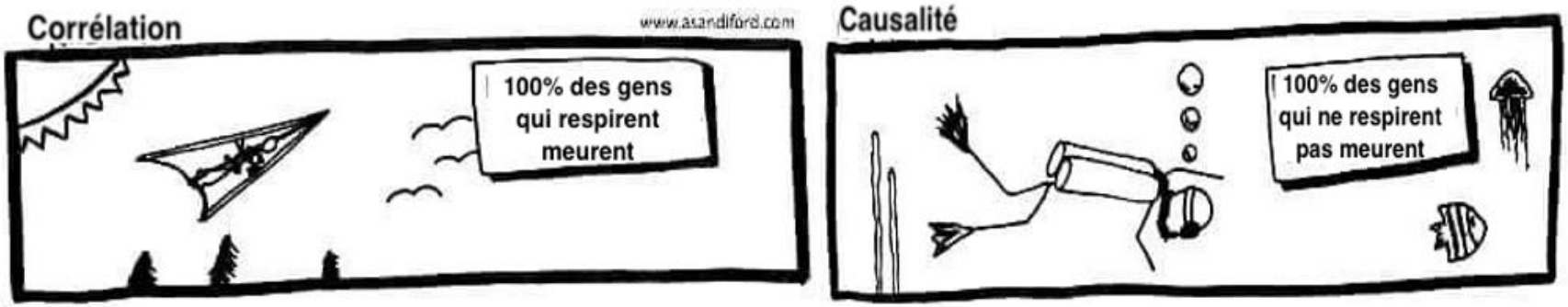
Cole et al. ; Clin J Am Soc Nephrol ; 2008

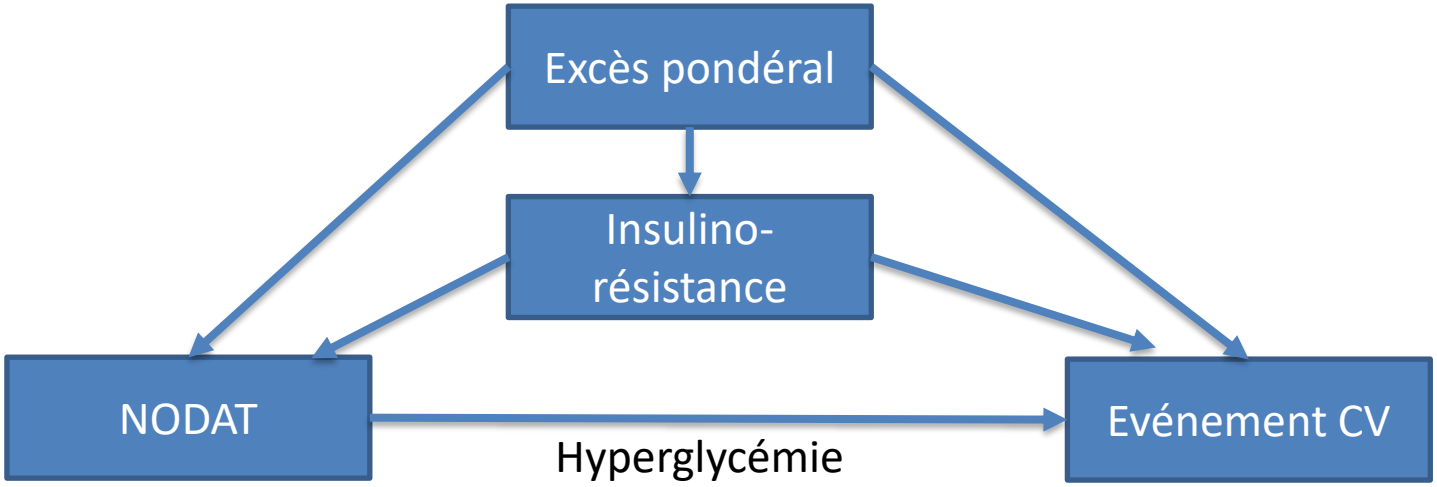
Evénements cardio-vasculaires



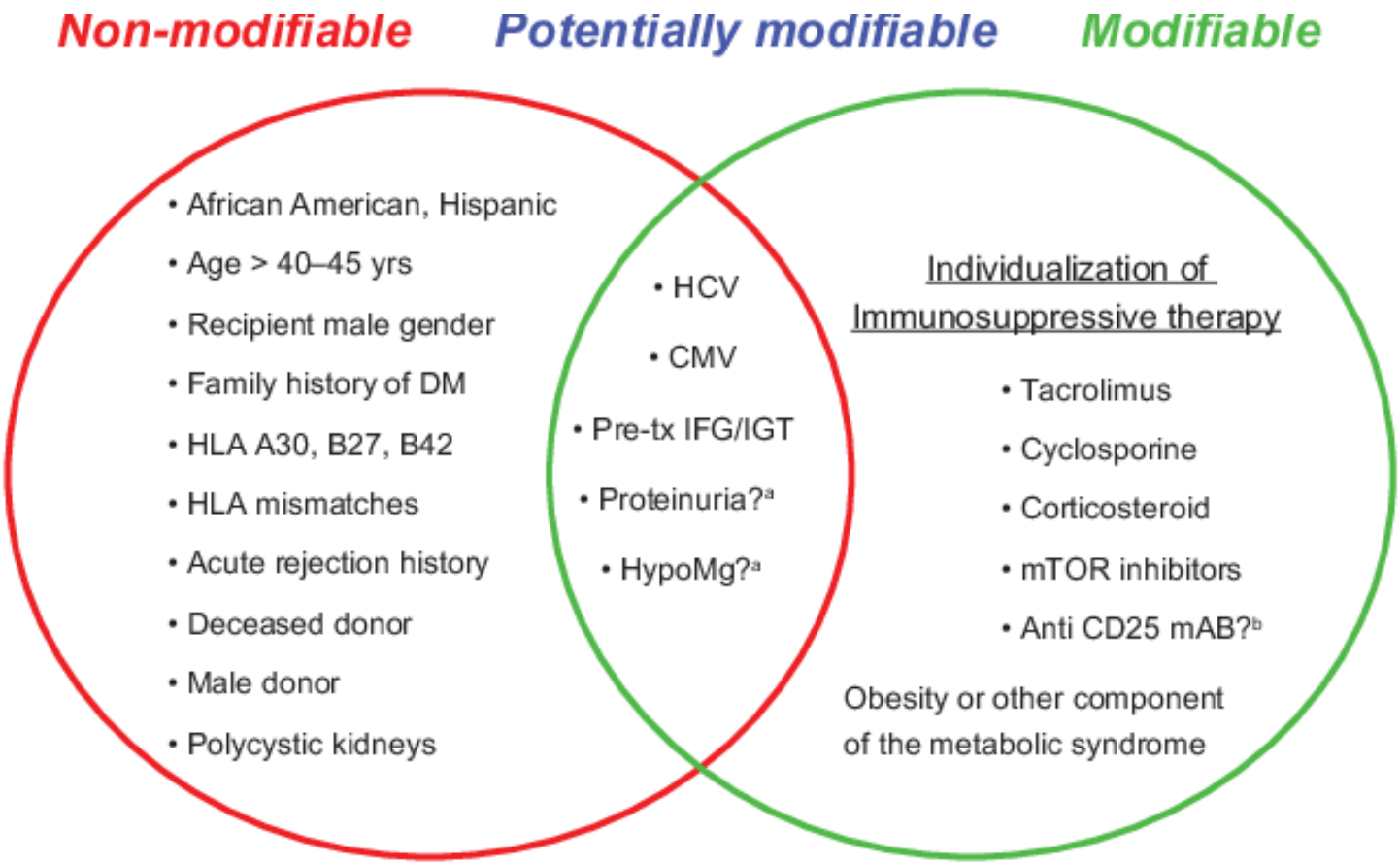
Cosio et al. ; Kidney International ; 2005

Effet causal ou facteur confondant?





Facteurs de risque

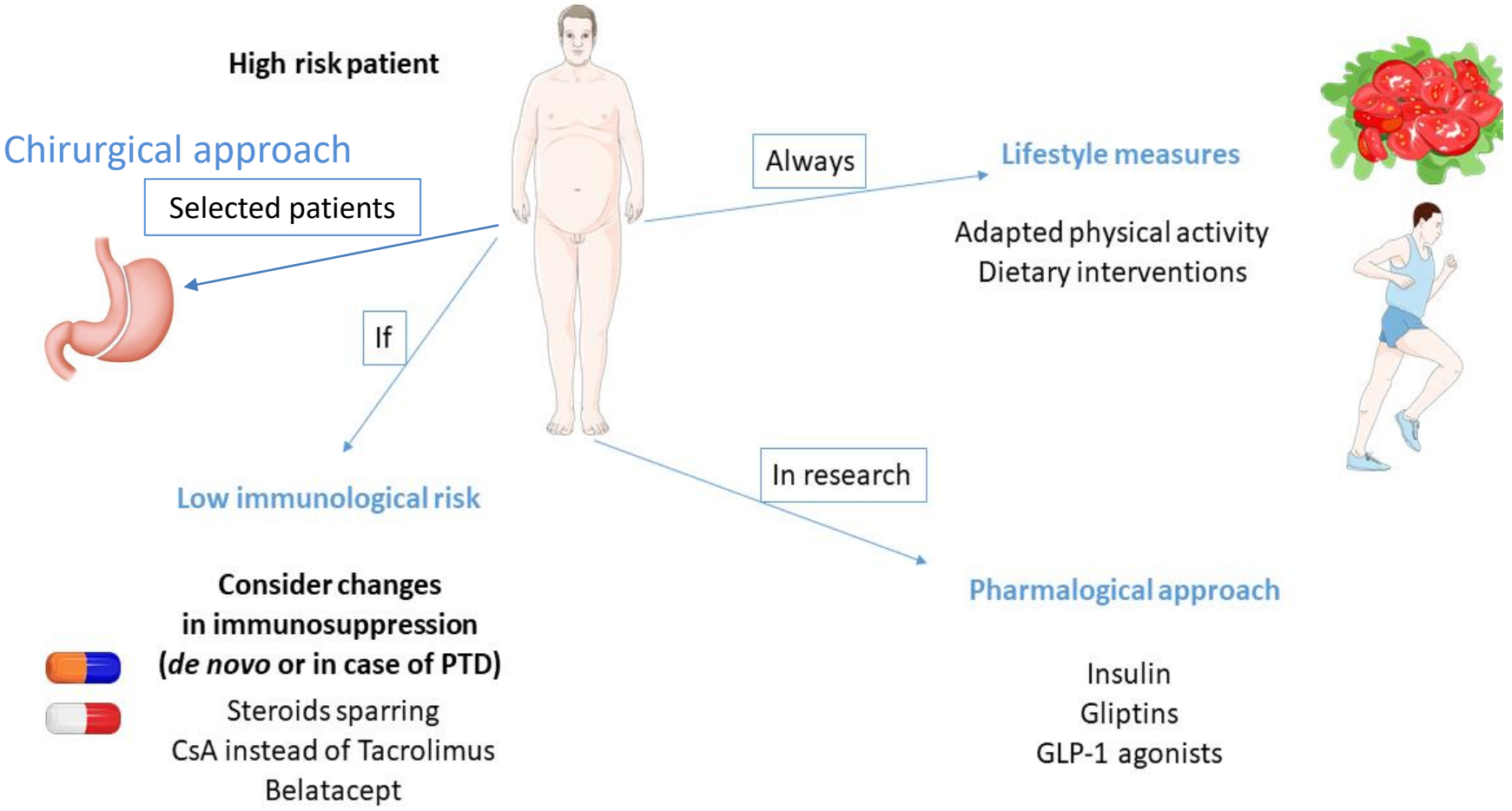


Pham et al ; Diabetes, metabolic syndrome and obesity : targets and therapy ; 2011

Diabète post greffe

MESURES PRÉVENTIVES

Prévention du PTDM



Ducloux D., Courivaud C. ; *J. Pers. Med. ;* 2022

Etude CAVIAR (Glycaemic Benefits of Active Versus Passive Lifestyle Intervention in Kidney Allograft Recipients

- Essai randomisé contrôlé 1:1
- N=130 (3 à 24 mois post-KTx)
- Intervention:
  - Visite chez diététiciens
  - Méthodologie visant à une modification du style de vie
- Suivi à 6 mois
- 20 % d'arrêts prématurés de l'étude
- Critères de jugements:
  - 1^{aire} : Mesure ssb à l'insuline (HOMA)
  - 2^{aire} : PTDM,…

Clinical outcomes at 6-mo

Parameter		Active	Passive	Mean difference	*P*
Weight (kg) ± SD	Baseline	79.03 ± 16.10	81.28 ± 14.73	–2.47 [–4.01 to –0.92]	0.002
	Follow-up	77.91 ± 16.50	82.66 ± 14.72		
	Δ Change	–1.20 ± 4.38	+1.26 ± 3.32		
Waist–hip ratio ± SD	Baseline	0.947 ± 0.102	0.950 ± 0.086	–0.007 [–0.032 to 0.017]	0.552
	Follow-up	0.940 ± 0.098	0.948 ± 0.095		
HbA1c (mmol/mol) ± SD	Baseline	38.7 ± 5.2	39.7 ± 5.9	–0.46 [–2.08 to 1.16]	0.572
	Follow-up	39.0 ± 6.0	40.6 ± 6.8		
	Δ Change	+0.32 ± 4.01	+0.78 ± 4.08		
Impaired fasting glucose		18 (32.1%)	15 (31.9%)	–	0.575
Impaired glucose tolerance		10 (22.7%)	9 (23.7%)	–	0.562
Posttransplantation diabetes		5 (7.6%)	10 (15.6%)	–	0.123
Any anti–glycemic medication		1 (1.5%)	3 (4.7%)	–	0.298

K. Kuningas et al ; Transplantation ; 2020

Intérêt de la chirurgie bariatrique

Population (pré-)greffe

Management of obesity in kidney transplant candidates and recipients: A clinical practice guideline by the DESCARTES Working Group of ERA

Gabriel C. Oniscu[1], Daniel Abramowicz[2], Davide Bolignano[3], Ilaria Gandolfini[4], Rachel Hellemans[5], Umberto Maggiore[6], Ionut Nistor[7], Stephen O'Neill[8], Mehmet Sukru Sever[9], Muguet Koobasi[10] and Evi V. Nagler[11]

We suggest considering bariatric surgery in kidney transplant candidates with a BMI ≥40 kg/m^2 (2C).

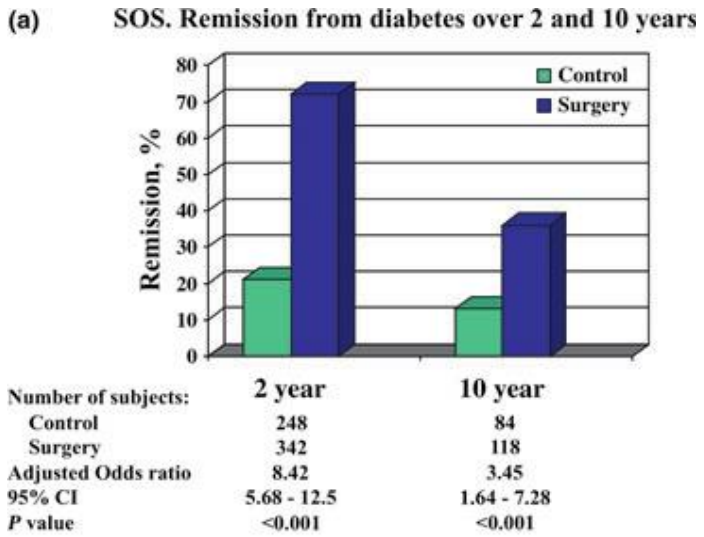
We suggest considering bariatric surgery in kidney transplant candidates with a BMI ≥35 kg/m^2 with at least one major obesity-related condition that can be improved by weight loss (2D).

We suggest laparoscopic sleeve gastrectomy over other forms of bariatric surgery in kidney transplant candidates (2D).

- 831 références répertoriées
- 32 études contrôlées retenues (aucune étude randomisées)
- 6 études portant sur chir bariatrique avant KTx
- 3 rapportent effet sur PTDM :
  - 133 chir vs. 192 contrôles
  - PTDM 0-9% vs. 11-43%

Nephrol Dial Transplant ; 2022

Population générale



L. Sjostrom ; Journal of Internal Medicine ; 2013

Early Postoperative Basal Insulin Therapy versus Standard of Care for the Prevention of Diabetes Mellitus after Kidney Transplantation: a Multicenter, Randomized Trial

JASN®
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

METHODS

263 Non-Diabetic
Kidney Transplant Recipients

& Triple Immunosuppression

Randomization (1:1)

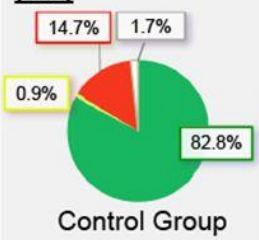
Blood Glucose Monitoring & **Basal Insulin Treatment**

Standard-of-Care **Control**

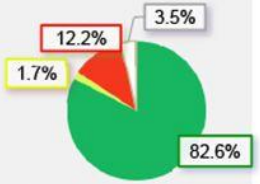
RESULTS

Month 12

Intention-To-Treat (ITT)



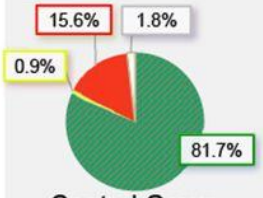
Control Group



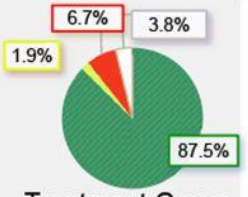
Treatment Group

Diabetic
Non-Diabetic
Missing Data
FPG ≥126 mg/dL
(FPG=fasting plasma glucose at OGTT)

Per-Protocol (PP)



Control Group



Treatment Group

OUTCOME

Post-Transplant Diabetes Mellitus (PTDM) at Month 12

Odds Ratio$_{unadjusted}$*	Number Needed to Treat
ITT: 0.82 (0.39-1.76)	**ITT:** 44
PP: 0.40 (0.16-1.01)	**PP:** 12

High-Risk Population

ITT: 0.53 (0.23-1.22)	**ITT:** 9
PP: 0.20 (0.07-0.59)	**PP: 5** *p<0.01*

Difference between ITT and PP

**After adjustment for polycystic kidney disease (PTDM risk factor) and glomerular nephritis (both being significantly different between groups at baseline), the Odds Ratio for the PP analysis became significant. *Four patients were mislabeled and 3 patients did not follow the protocol at all.*

CONCLUSIONS

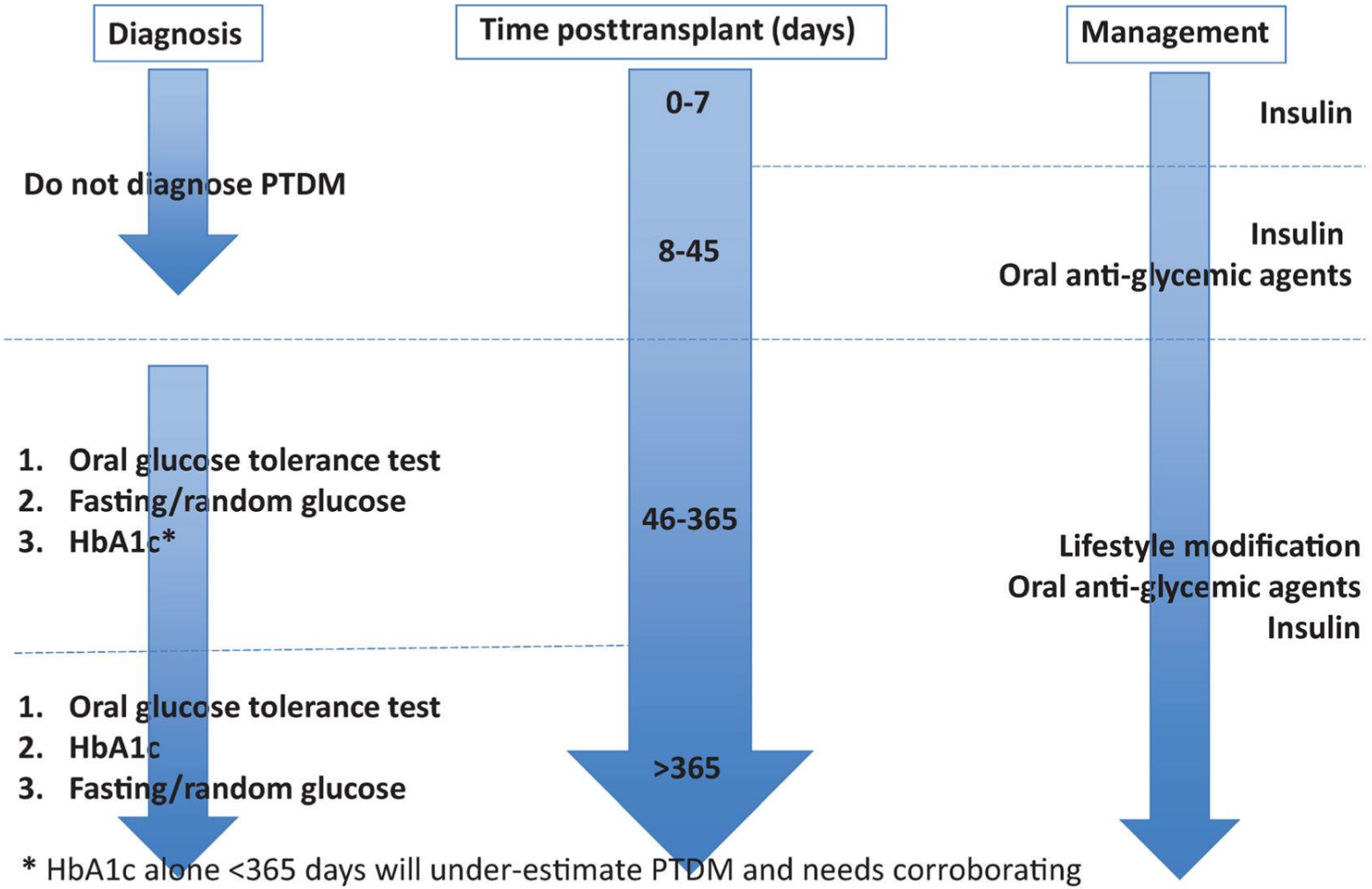
Early postoperative basal insulin administration has the potential to decrease sustained PTDM, but the therapeutic benefit depends on protocol adherence. This intervention may be particularly beneficial in patients who are at higher risk of developing hyperglycemia.

doi: 10.1681/ASN.2021010127

Diabète post greffe

TRAITEMENT DU DIABÈTE AVÉRÉ

Prise en charge séquentielle du PTDM

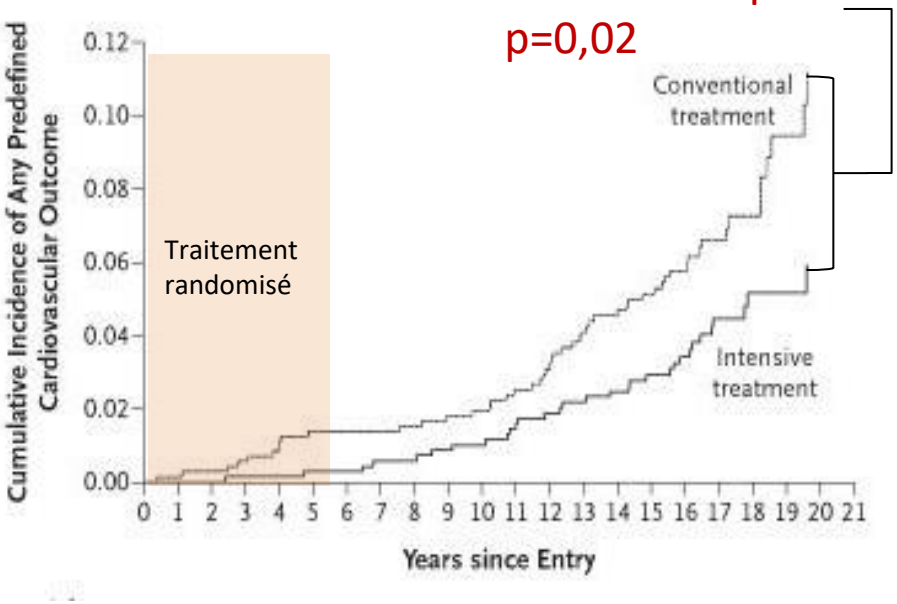


A. Sharif ; *Am J Transplant*. ; 2014

Contrôle stricte de la glycémie

DCCT/EDIC
D1, 5-6 ans (n=1441)

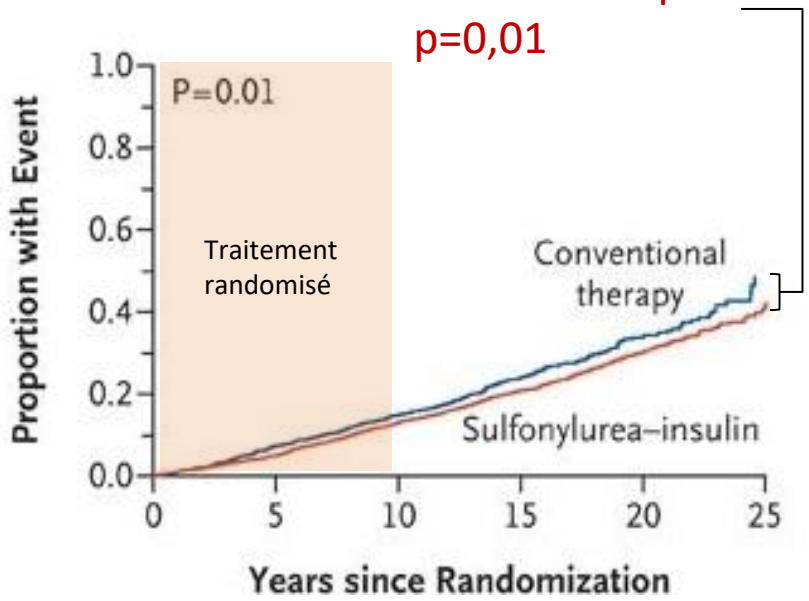
42% réduction du risque
p=0,02



Nathan et al ; NEJM ; 2005

UKPDS
D2, 9,5 ans (n=4209)

15% réduction du risque
p=0,01



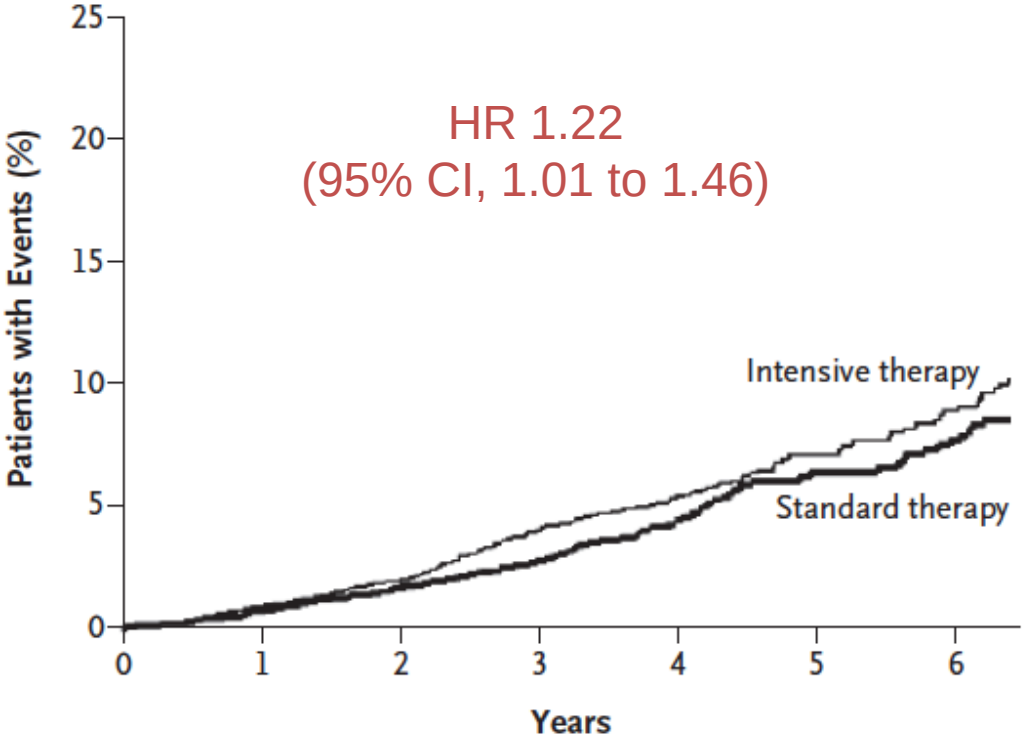
Hollman et al ; NEJM ; 2008

HbA1c: « the lower , the better » ?

ACCORD

D2; n= 10.251 ; HbA1c 8,1% => <6% vs 7-7,9%

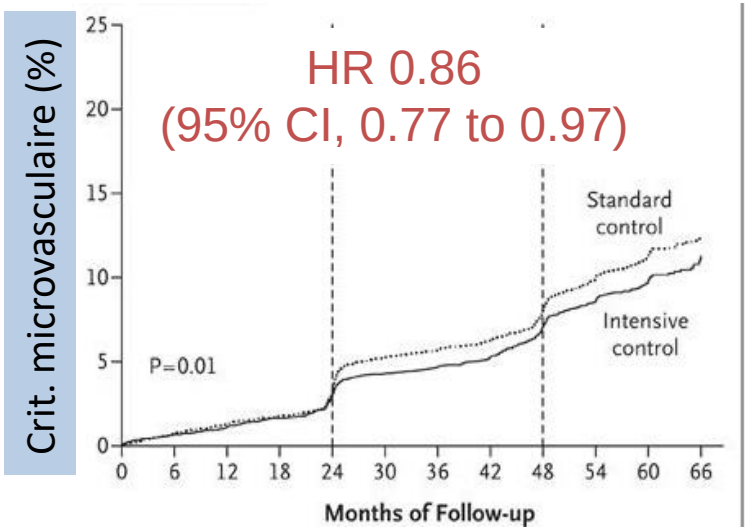
Mortalité toute cause (%)

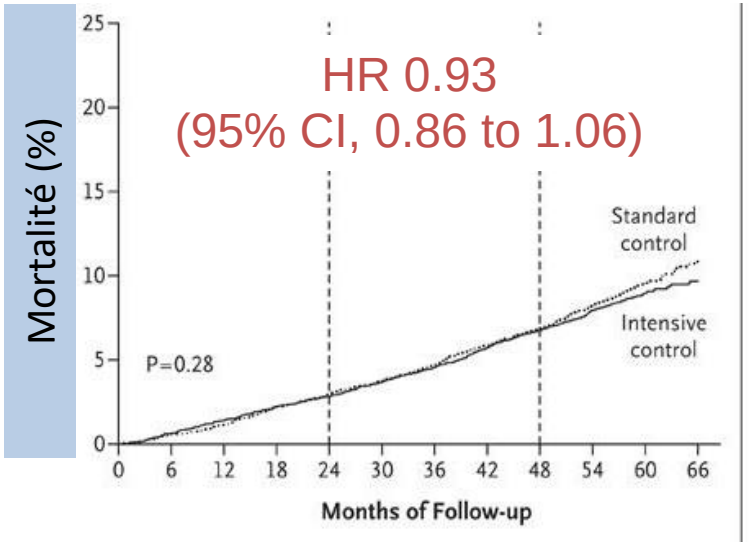


ACCORD Study Group; NEJM; 2008

ADVANCE

D2 ; n=11.140 ; objectif HbA1c < = 6,5%

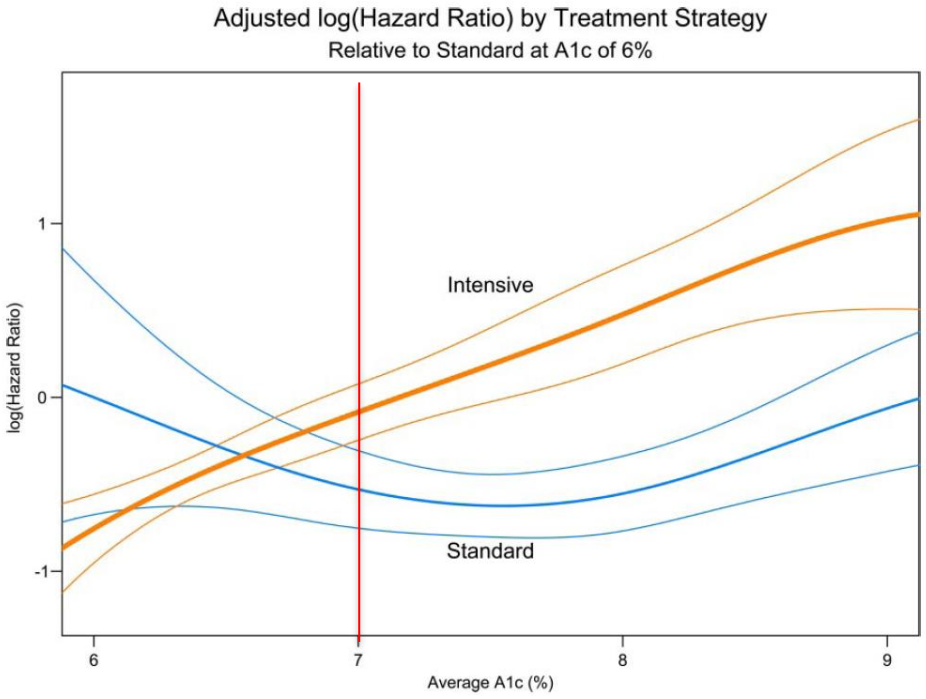




ADVANCE Collaborative Group ; NEJM ; 2008

HbA1c: « the lower, the better » ?

ACCORD
relation complexe HbA1c -

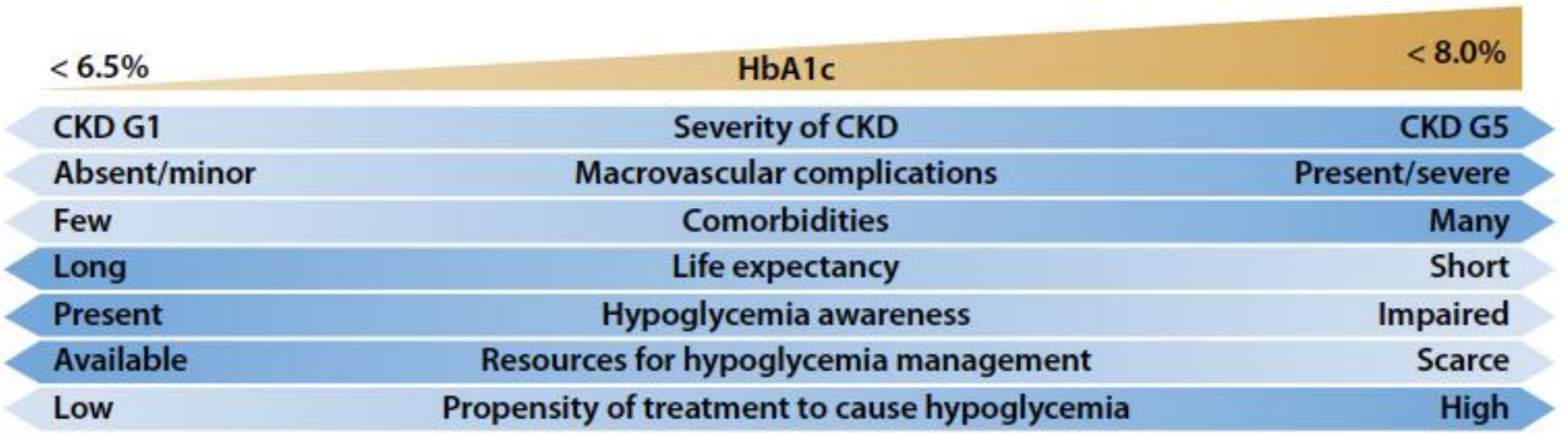


ADVANCE
Rôles des hypoglycémies sévères

Clinical Outcome and Interval after Hypoglycemia	No. of Events	Hazard Ratio Adjusted for Treatment Assignment (95% CI)	P Value
Macrovascular events	1147	4.05 (2.86–5.74)	<0.001
3 mo		3.27 (1.22–8.73)	0.02
6 mo		2.61 (1.17–5.83)	0.02
Microvascular events	1131	2.39 (1.60–3.59)	<0.001
3 mo		2.90 (1.09–7.74)	0.03
6 mo		3.24 (1.62–6.50)	<0.001
Death from any cause	1031	4.86 (3.60–6.57)	<0.001
3 mo		10.4 (6.02–18.00)	<0.001
6 mo		7.28 (4.50–11.80)	<0.001
Death from cardiovascular cause	542	4.87 (3.17–7.49)	<0.001
3 mo		6.25 (2.34–6.70)	<0.001
6 mo		4.20 (1.74–10.10)	<0.01
Death from noncardiovascular cause	489	4.82 (3.16–7.35)	<0.001
3 mo		14.20 (7.35–27.60)	<0.001
6 mo		10.30 (5.78–18.20)	<0.001

Zoungas; NEJM ; 2010

Objectifs glycémiques



Traitements actifs

Cochrane Library

Cochrane Database of Systematic Reviews

Glucose-lowering agents for treating pre-existing and new-onset diabetes in kidney transplant recipients (Review)

Lo C, Toyama T, Oshima M, Jun M, Chin KL, Hawley CM, Zoungas S

Cochrane Database of Systematic Reviews 2020

Types d’interventions

- Insulinothérapie intensive
- Inhibiteurs du DDP-4
- (Glitazone)
- Gliptine – Agonistes du GLP-1 => pas d’étude
- Gliflozine

Insulinothérapie intensive vs moins intensive

Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with less intensive insulin therapy	Risk difference with more intensive insulin therapy
Transplant or graft survival assessed with: graft loss/rejection TIme frame: 13 months to 5 years	301 (4)	⊕⊝⊝⊝ VERY LOW [1, 2, 3, 4]	RR 1.12 (0.32 to 3.94)	63 per 1,000	8 more per 1,000 (43 fewer to 186 more)
Delayed graft function Time frame: 1 to 3 years	153 (2)	⊕⊝⊝⊝ VERY LOW [3, 5, 6, 7]	RR 0.63 (0.42 to 0.93)	430 per 1,000	159 fewer per 1,000 (250 fewer to 30 fewer)
HbA1c Time frame: 13 months	16 (1)	⊕⊝⊝⊝ VERY LOW [3, 8, 9]	--	Barbosa 1983 reported HbA1c changed from 15 ± 2.3% (mean ± SEM: 140 ± 25 mmol/mol, month 7) to 13 ± 0.9% (119 ± 10 mmol/mol, month 13) in the less intensive group, and changed from 11 ± 0.4% (97 ± 4 mmol/mol, month 7) to 10 ± 0.8% (86 ± 9 mmol/mol, month 13) in the more intensive group	
FBG (mmol/L) Time frame: 13 months	24 (1)	⊕⊝⊝⊝ VERY LOW [3, 8, 9]	--	Barbosa 1983 reported that intensive insulin therapy achieved a lower FBG (mean ± SEM: 7.22 ± 0.50 mmol/L) compared with less intensive insulin therapy (13.44 ± 1.22 mmol/L) at 13 months (the study lasted for 2 years)	
Kidney function markers: creatinine, eGFR Time frame: 1 year	36 (1)	⊕⊝⊝⊝ VERY LOW [3, 4, 9, 10]	--	HiRT 2016 reported eGFR increased by 4.6 (95% CI -9.75, 18.95) mL/min/1.73 m^2, and serum creatinine changed by -10.6 (95% CI -37.0, 15.7) µmol/L after 1 year follow-up of 36 participants	
Death (any cause) Time frame: 1 to 5 years	208 (3)	⊕⊝⊝⊝ VERY LOW [3, 4, 11]	RR 0.68 (0.29 to 1.58)	118 per 1,000	38 fewer per 1,000 (84 fewer to 69 more)
Hypoglycaemia Time frame: 13 months to 5 years	301 (4)	⊕⊝⊝⊝ VERY LOW [1, 3, 5]	--	Barbosa 1983 reported in the narrative that intensive insulin therapy resulted in more frequent and severe episodes of hypoglycaemia compared with standard insulin therapy. Barbosa 1994 reported only severe hypoglycaemic episodes, that is, those requiring third party assistance. More intensive insulin therapy resulted in a higher rate of severe hypoglycaemia compared with less intensive insulin therapy (1.7 episodes/patient/year versus < 0.1episodes/patient/year, P < 0.001). Of the 29 episodes of severe hypoglycaemia resulting in hospital admission, 26 occurred in the intensive insulin group. A patient in the intensive insulin group remained comatose for 6 days and required a 2-week hospital admission. In Hermayer 2012, intensive insulin therapy may have increased the risk of severe hypoglycaemia (< 2.2 mmol/L), however the 95% CI indicated there may be no difference (RR 3.90, 95% CI 0.85 to 17.78) compared to less intensive insulin therapy. HiRT 2016 reported no episodes of hypoglycaemia in either arm	
Discontinuation of medication due to adverse events Time frame: 1 year	60 (1)	⊕⊝⊝⊝ VERY LOW [3, 10]	No events	HiRT 2016 reported the outcome, but no events were observed (n = 60)	

Inhibiteur du DDP-4 vs placebo

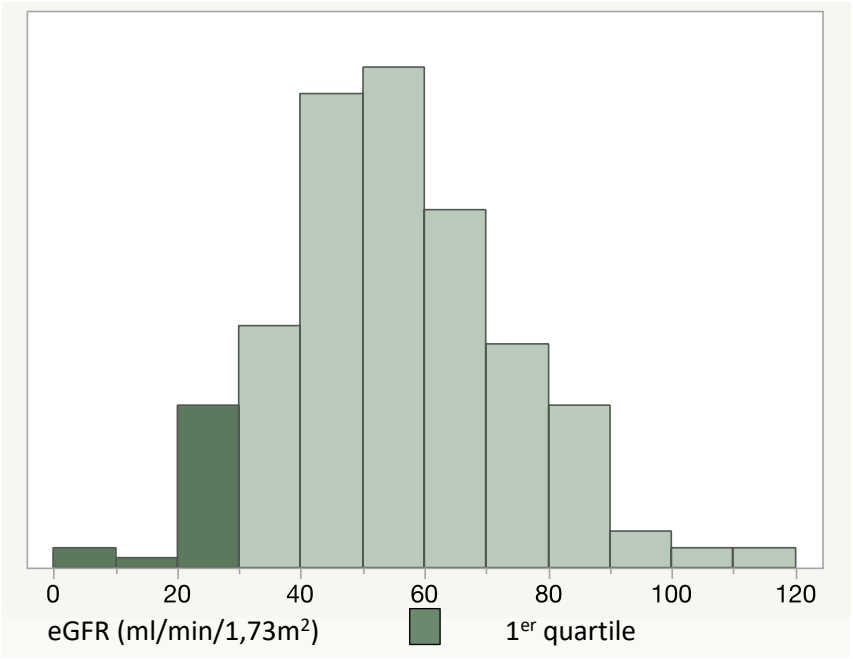
Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with placebo	Risk difference with DPP-4 inhibitors
Transplant or graft survival	Not reported	--	--	--	--
Delayed graft function	Not reported	--	--	--	--
HbA1c Time frame: 3 months	32 (1)	⊕⊕⊖⊖ LOW [1, 2]	-	The mean HbA1c in the placebo group was -0.1% (-1 mmol/mol)	The mean HbA1c was 0.5% lower in the DPP-4 inhibitors group (0.85% lower to 0.15% lower); 5 mmol/mol lower (9 lower to 2 lower)
FBG Time frame: 3 months	32 (1)	⊕⊕⊖⊖ LOW [1, 2]	--	The mean FBG in the placebo group was -0.18 mmol/L	The mean FBG was 0.75 mmol/L lower in the DPP-4 inhibitors group (1.48 lower to 0.02 lower)
Kidney function markers assessed with: eGFR Time frame: 3 months	32 (1)	⊕⊕⊖⊖ LOW [1, 2]	--	The mean eGFR in the placebo group was 2.1 mL/min/1.73 m^2	The mean eGFR in the DPP-4 inhibitor group was 0.2 mL/min/1.73 m^2 lower (6.07 lower to 5.67 higher)
Death (any cause)	Not reported	-	--	-	-
Hypoglycaemia Time frame: 8 to 16 weeks	51 (2)	⊕⊖⊖⊖ VERY LOW [1, 3]	--	Haidinger 2010 did not report any hypoglycaemia in the vildagliptin group (n = 16) Strom Halden 2014 reported 2 patients had asymptomatic moderate hypoglycaemia in the sitagliptin group (n = 19) although these patients were also receiving glipizide	
Discontinuation of medication due to adverse events Time frame: 8 to 16 weeks	51 (2)	⊕⊖⊖⊖ VERY LOW [1, 3]	--	Haidinger 2010 reported no discontinuation of medication due to adverse events (n = 32) Strom Halden 2014 reported one event in the sitagliptin group (n 19)	

Gliflozine vs. Placebo

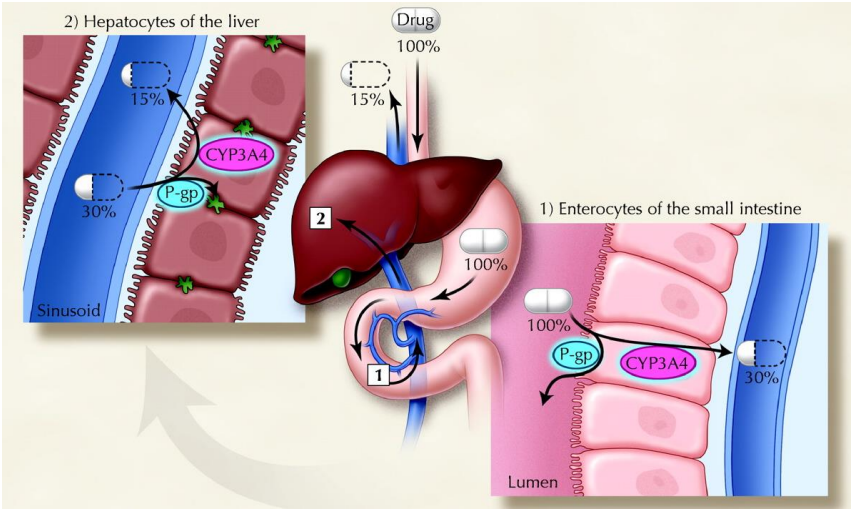
Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Impact
Transplant or graft survival assessed with: graft loss/rejection Time frame: 24 weeks	44 (1)	⊕⊕⊕⊖ MODERATE [1]	EMPA-Renal Tx 2019 reported that no patients in either the group receiving empagliflozin or placebo were suspected of having a kidney graft rejection. Follow-up, however was only over 24 weeks
Delayed graft function	Not reported	--	--
HbA1c Time frame: 24 weeks	44 (1)	⊕⊕⊖⊖ LOW [1, 2]	EMPA-Renal Tx 2019 reported that in patients with pre-existing or new onset diabetes receiving a kidney graft, empagliflozin significantly reduced the median HbA1c compared to placebo (-0.2%, (-0.6, -0.1) vs 0.1%, (-0.1, 0.4), P = 0.025 (-2.0 mmol/mol (-6.5, -1.0) vs 1.0 mmol/mol (-0.75, 3.8), P = 0.018))
FBG (mmol/L) Time frame: 24 weeks	44 (1)	⊕⊕⊖⊖ LOW [1, 2]	EMPA-Renal Tx 2019 reported that in patients with pre-existing or new onset diabetes receiving a kidney graft, empagliflozin did not reduce the median FBG compared to placebo (-0.65 mmol/L, (-1.2, -0.13) vs 0.30 mmol/L (-0.45, 0.55) P = 0.272)
Kidney function markers assessed with: creatinine, eGFR Time frame: 24 weeks	44 (1)	⊕⊕⊖⊖ LOW [1, 2]	EMPA-Renal Tx 2019 reported that in patients with pre-existing or new onset diabetes receiving a kidney graft, empagliflozin had a similar effect on change in eGFR compared to placebo at 24 weeks. (-3.0 mL/min/1.73 m^2, (-7.0, 0) vs -1.0 mL/min/1.73 m^2 (-2.8, 0.75) P = 1). However, at 8 weeks, there was a temporary decline in eGFR compared to placebo (−4.0 mL/min/1.73 m^2 (−7.0, −1.0) vs −1 mL/min/1.73 m^2 (−2.0, 2.0), P < 0.05)
Death (any cause)	Not reported	--	--
Hypoglycaemia Time frame: 24 weeks	44 (1)	⊕⊕⊕⊖ MODERATE [1]	EMPA-Renal Tx 2019 reported no episodes of hypoglycaemia in either the treatment or placebo group
Discontinuation of medication due to adverse events Time frame: 24 weeks	49 (1)	⊕⊕⊕⊖ MODERATE [1]	EMPA-Renal Tx 2019 reported that two patients receiving empagliflozin (2/24) withdrew from the study, one patient due to urosepsis, and one patient due to repeated urinary tract infections. One patient was withdrawn from the placebo arm due to colon cancer (1/25)

Spécificités pharmacologiques chez le transplanté

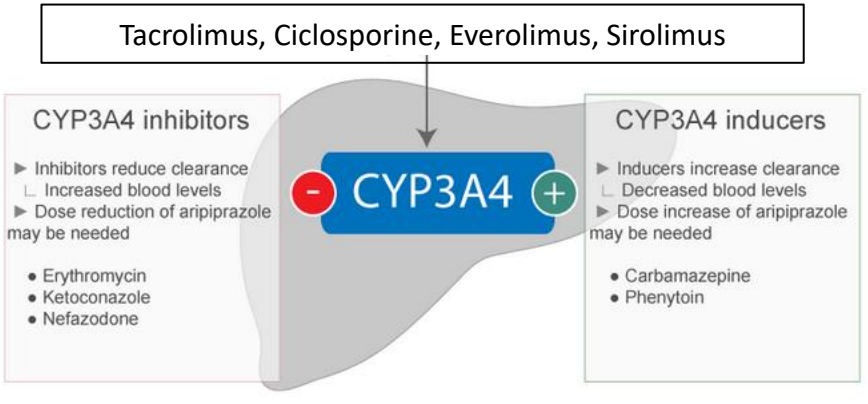
Fonction rénale



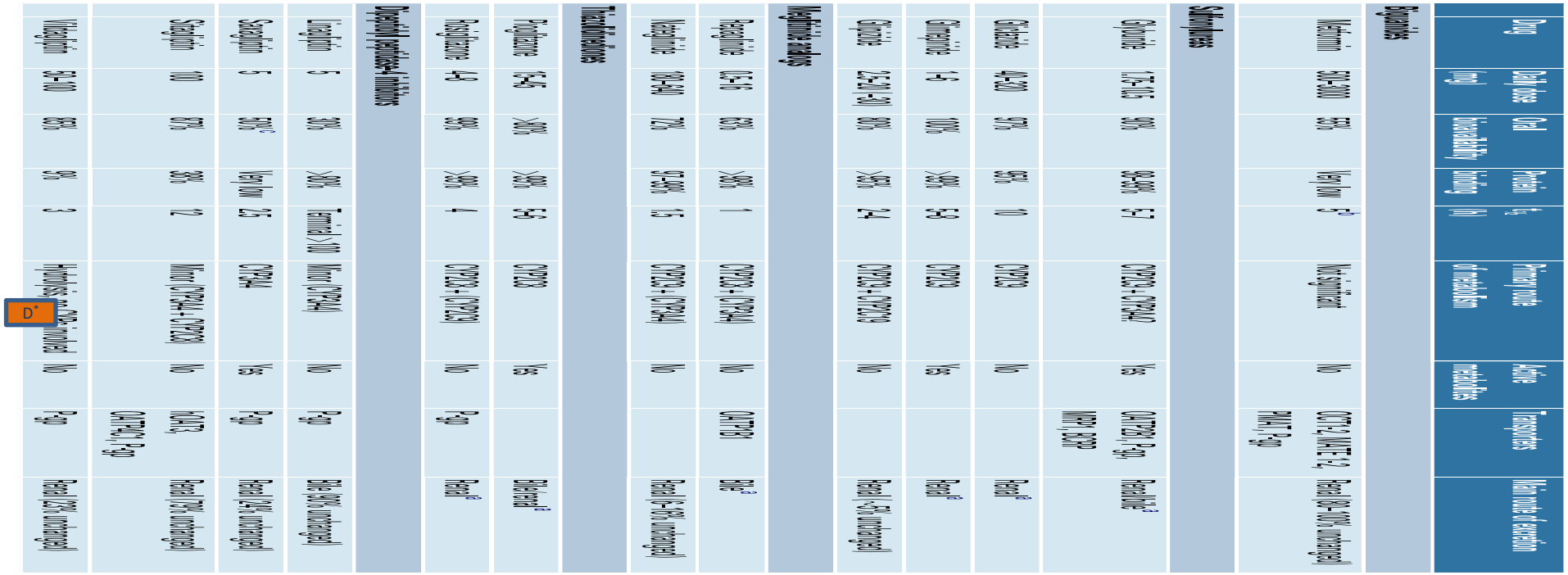
Interactions médicamenteuses



Bailey CMAJ, 2004



Interactions médicamenteuses cliniquement significatives



D* Lexicomp® : Ciclosporine + Repaglinide (Novonorm®), AUC +144% C_{max} +75% => risque hypo

A. Tornio, Trends in Pharmacological Sciences, 2012.

Inhibiteurs SGLT-2 (Glifozines)									
	Dapaglifozine	5-10	78%	91%	12.9	UGT1A9	No	?	Renal (glucoronoconjugate)
	Empaglifozine	10-25	?	86%	12.4	UGT2B7, UGT1A3, UGT1A8, UGT1A9	No	?	Renal (glucoronoconjugate) Feces (unchanged)

Pas d'interaction attendue avec les immunosuppresseurs

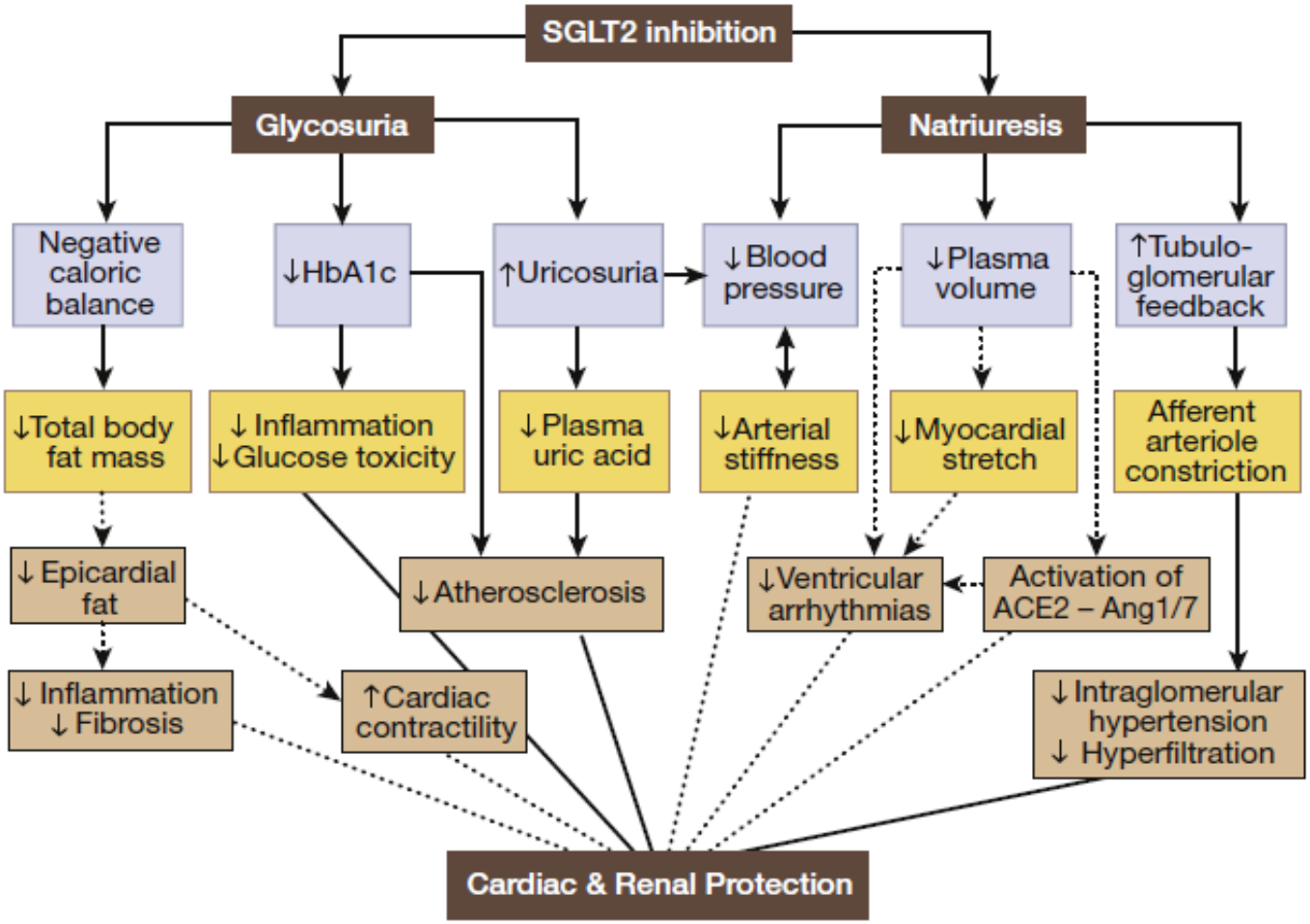
Agents hypoglycémiants et stade d'IRC

		CKD-1	CKD-2	CKD-3	CKD-4	CKD-5ND	CKD-5D
	Metformin	No adjustments		1,5g-850 mg/day*	500 mg/day**	Consider carefully/Awaiting further data	
Sulfonylureas	Chlorpropamide	No adjustments		100-125 mg/day	To be avoided		
	Acetohexamide	To be avoided					
	Tolazamide	To be avoided					
	Tolbutamide	250mg, 1-3 times/day				To be avoided	
	Glipizide	No adjustments					
	Glicazide	Start at low doses and dose titration every 1-4 weeks					
	Glyburide	To be avoided					
	Glimepiride	Recude dosage to 1 mg/day				To be avoided	
	Gliquidone	No adjustments					
	Repaglinide	No adjustments				Limited experience available	
	Nateglinide	No adjustments				Start at 60 mg/day	To be avoided
α-gluc inhibitors	Acarbose	No adjustments			use lowest dose and <50mg		
	Miglitol	Limited experience available					
	Pioglitazone	No adjustments					
DPP-IV inhibitors	Sitagliptin	No adjustments		Reduce to 50 mg/day	Reduce to 25 mg/day		
	Vildagliptin	No adjustments		Reduce to 50 mg/once daily			
	Saxagliptin	No adjustments		Reduce to 2,5 mg/once daily			
	Linagliptin	No adjustments					
	Alogliptin	No adjustments		Reduce to 12,5 mg/daily			
Incretin Mimetics	Exenatide	No adjustments	Reduce dose to 5 mcg/once to twice daily		To be avoided		
	Liraglutide	Limited experience available					
	Lixisenatide	No adjustments	Careful use if GFR 80-50 mL/min				No experience available
	Pramlintide	Limited experience available					
SGLT-2 inhibitors	Dapagliflozin	Limited experience available					
	Canagliflozin	Reduced efficacy		Careful monitoring		To be avoided	
	Empagliflozin	Limited experience available					

Diabète post greffe

GLIFLOZINES - INHIBITEURS DU SGLT-2 & TRANSPLANTATION RENALE

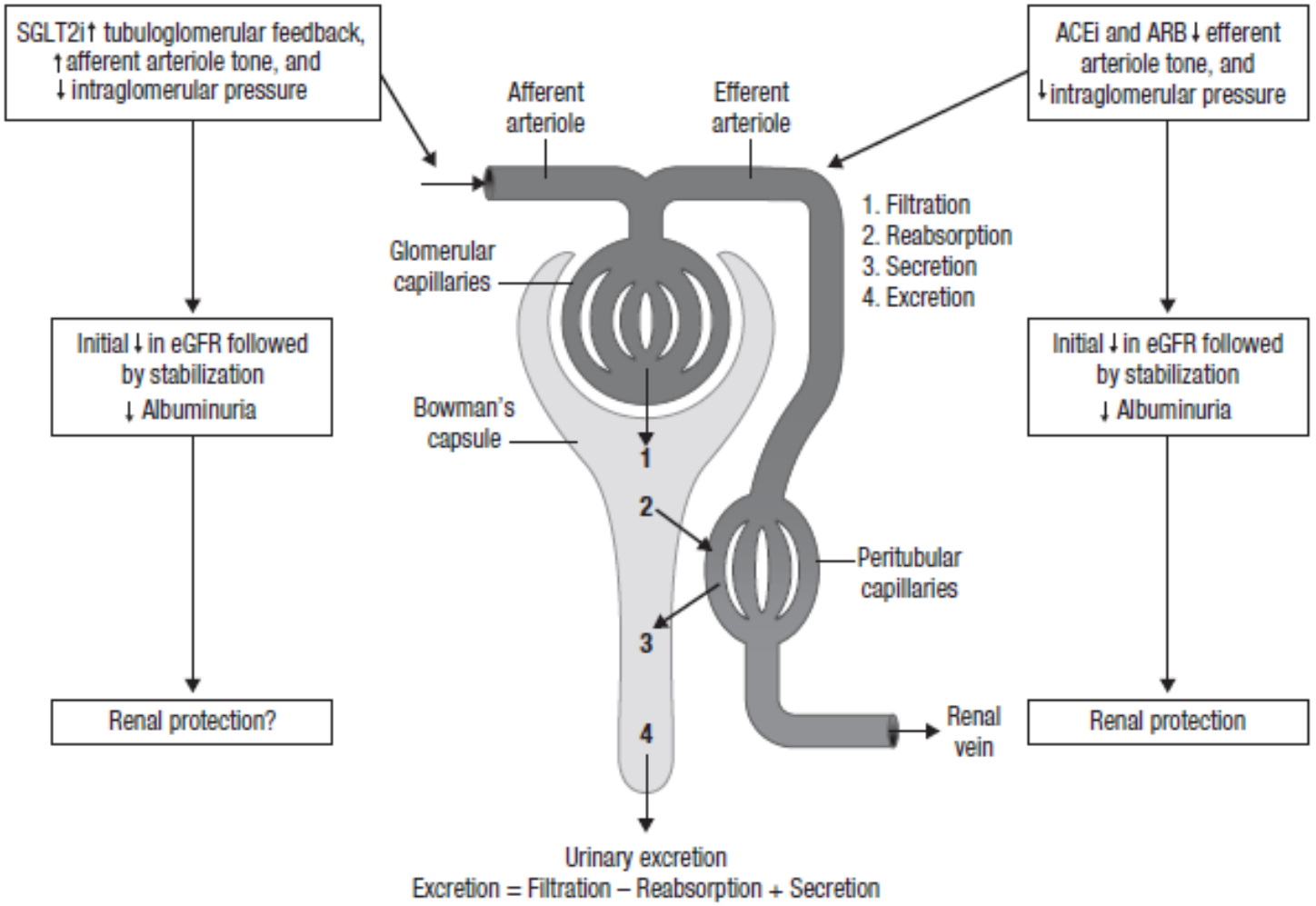
Sodium–glucose cotransporter 2 inhibition and cardiovascular risk reduction in patients with type 2 diabetes: the emerging role of natriuresis



Rajasekeran et al. KI; 2016

Effets rénaux des inhibiteurs SGLT-2 et du SRA

Current Medical Research & Opinion Volume 31, Number 12 December 2015



Etudes gliflozines en protection CV et rénale

	CREDENCE	DAPA-CKD	EMPA-REG	CANVAS	DECLARE-TIMI 58
Drug	Canagliflozin 100 mg once daily	Dapagliflozin 10 mg once daily	Empagliflozin 10 mg, 25 mg once daily	Canagliflozin 100 mg, 300 mg once daily	Dapagliflozin 10 mg once daily
Total of participants	4401	4304	7020	10,142	17,160
% with CVD	50	37.4	100	66	41
eGFR criteria for enrollment (ml/min per 1.73 m²)	30–90	25–75	≥30	≥30	CrCl ≥60 ml/min, 45% had eGFR 60–90
Mean eGFR at enrollment (ml/min per 1.73 m²)	56	43	74	76	85
% with eGFR <60	59	88	26	20	7.4
ACR	Criteria: ACR >300–5000 mg/g [30–500 mg/mmol] Median ACR 927 mg/g [92.7 mg/mmol]	ACR 200–5000 mg/g [20–500 mg/mmol] ACR Median DAPA: 965 mg/g [96.5 mg/mmol]; Placebo: 934 mg/g [93.4 mg/mmol]	No criteria ACR <30 mg/g [3 mg/mmol] in 60%; 30–300 mg/g [3–30 mg/mmol] in 30%; >300 mg/g [30 mg/mmol] in 10%	No criteria Median ACR 12.3 mg/g [1.23 mg/mmol]	No criteria
Follow-up (yr)	2.6	2.4	3.1	2.4	4.2
Primary outcome(s)	Composite kidney	First occurrence of a ≥50% decline in eGFR, the onset of kidney failure, or death from renal or CV causes	MACE	MACE	1) MACE; 2) Composite CV death or hospitalization for HF
CV outcome results	CV death, MI, stroke: HR: 0.80; 95% CI: 0.67–0.95; hospitalization for HF: HR: 0.61; 95% CI: 0.47–0.80	CV death: HR: 0.81; 95% CI: 0.59–1.21	MACE: HR: 0.86; 95% CI: 0.74–0.99; hospitalization for HF: HR 0.65; 95% CI 0.50–0.85	MACE: HR: 0.86; 95% CI: 0.75–0.97; hospitalization for HF: HR 0.67; 95% CI: 0.52–0.87	MACE: HF: 0.93; 95% CI: 0.84–1.03; CV death or hospitalization for HF: HR 0.83; 95% CI: 0.73–0.95
Kidney outcome	Composite of kidney failure outcomes, doubling SCr, or death from renal or CV causes	First occurrence of a ≥50% decline in eGFR, the onset of kidney failure, or death from renal or CV causes	Incident or worsening nephropathy (progression to severely increased albuminuria, doubling of SCr, initiation of KRT, or renal death) and incident albuminuria	Composite doubling in SCr, kidney failure, or death from renal causes	Composite of ≥40% decrease in eGFR to <60 ml/min per 1.73 m², kidney failure, CV or renal death
Kidney outcome results	Primary kidney: HR: 0.70; 95% CI: 0.59–0.82	Primary outcome: HR: 0.61; 95% CI: 0.45–0.73	Incident/worsening nephropathy: 12.7% vs. 18.8% in empagliflozin vs. placebo. [HR: 0.61; 95% CI: 0.53–0.70] Incident albuminuria: NS	Composite kidney: 1.5 vs. 2.8 1000 patient-years in the canagliflozin vs. placebo [HR: 0.53; 95% CI: 0.33–0.84]	Composite kidney: HR: 0.76; 95% CI: 0.67–0.87

PUBLIC REVIEW DRAFT KDIGO 2022 CLINICAL PRACTICE GUIDELINE FOR DIABETES MANGEMENT IN CHRONIC KIDNEY DISEASE

Empagliflozin Scores Topline Win in EMPA-KIDNEY Trial

Mitchel L. Zoler, PhD
March 17, 2022

Researchers running the EMPA-KIDNEY trial that's been testing the safety and efficacy of the SGLT2 inhibitor empagliflozin (Jardiance) in about 6600 patients with chronic kidney disease (CKD) announced on March 16 that they had stopped the trial early because of positive efficacy that met the study's prespecified threshold for early termination.

Empagliflozin Scores Topline Win in EMPA-KIDNEY Trial

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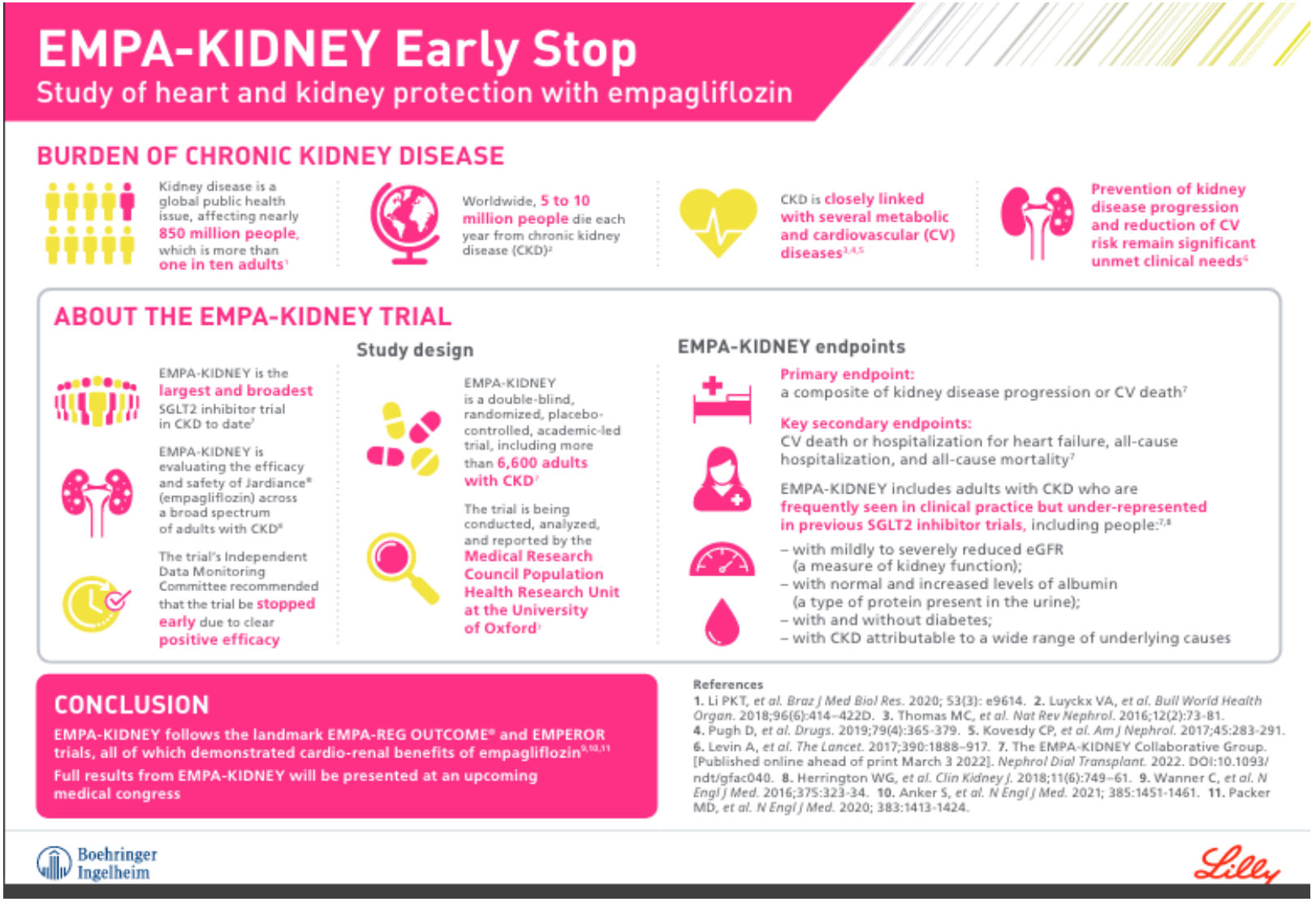
March 17, 2022



Particularité du diabète post-greffe

- Fréquence élevée d'infection urinaire (reflux sur le greffon, contexte immunosuppression, manœuvres urologiques)

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Drug Safety Communications

FDA warns about rare occurrences of a serious infection of the genital area with SGLT2 inhibitors for diabetes

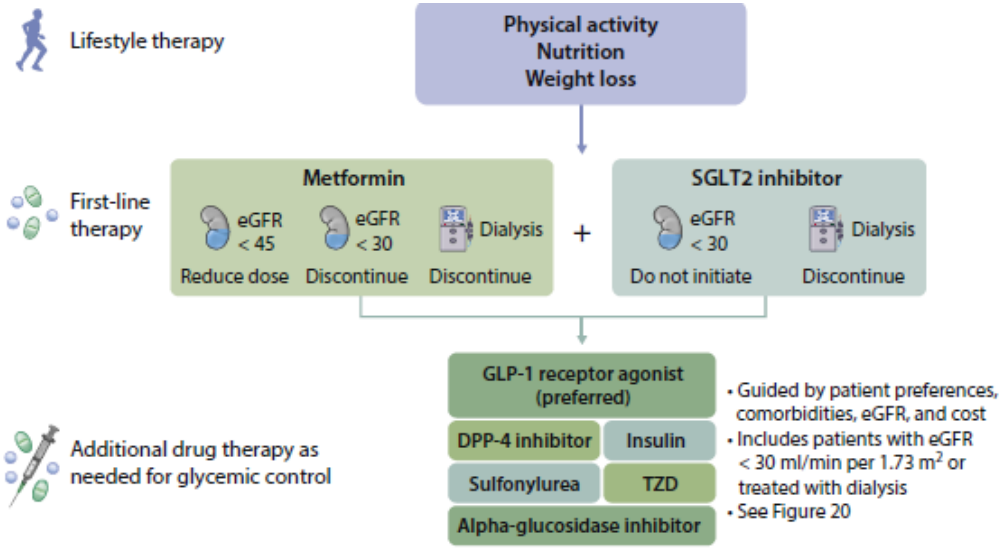
Safety Announcement

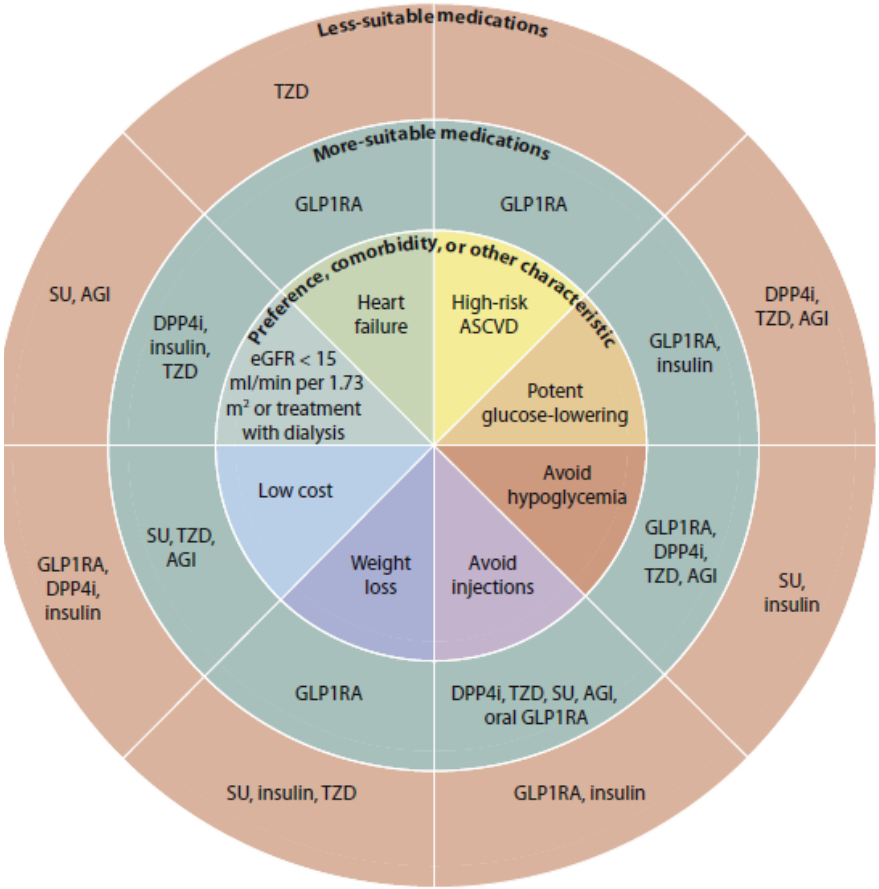
- Variabilité de la créatinine et absence de données solides sur la néphro-protection des inhibiteurs du RAS

Diabète post greffe

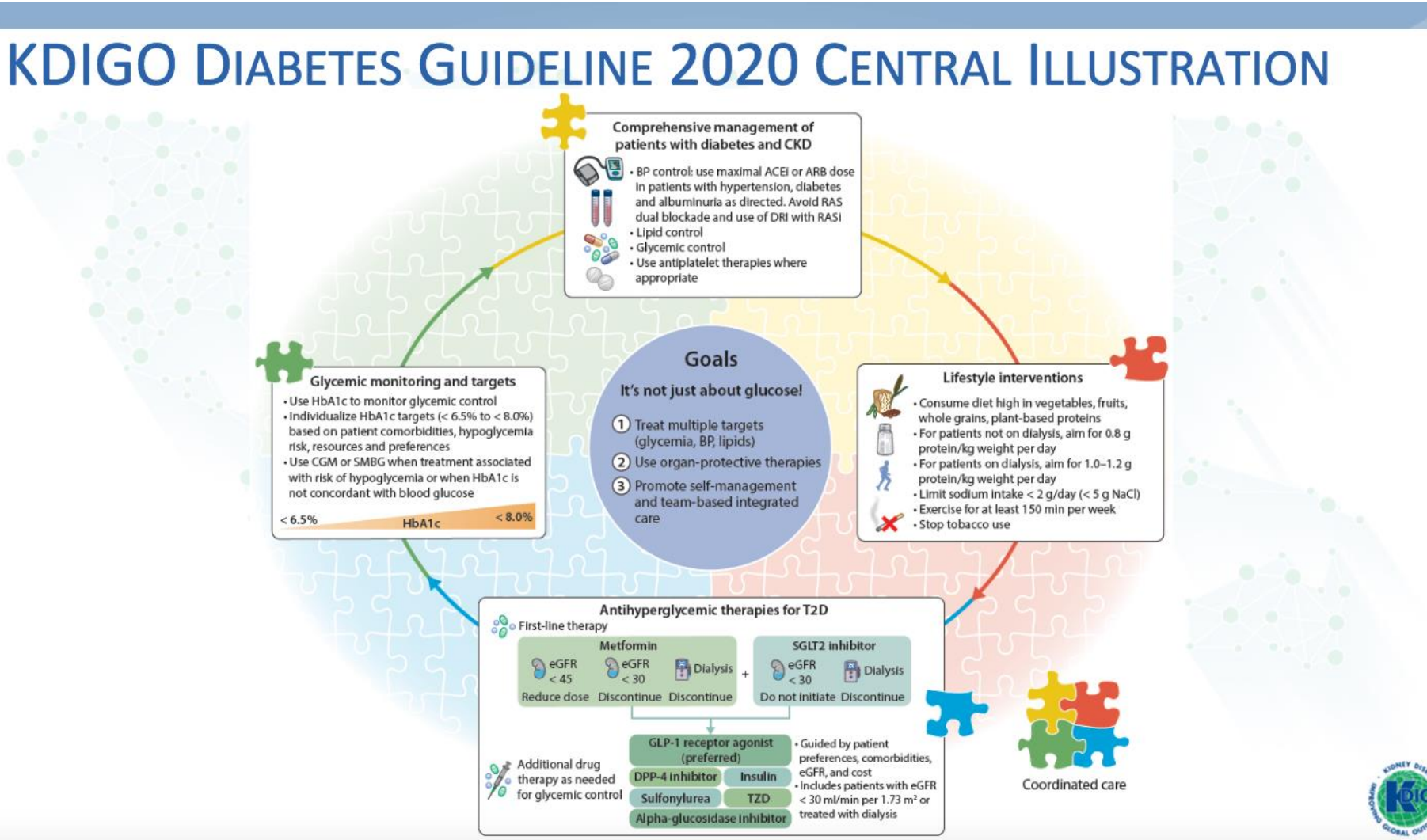
CONCLUSION

Choix de la stratégie thérapeutique: Post-greffe = MRC ?





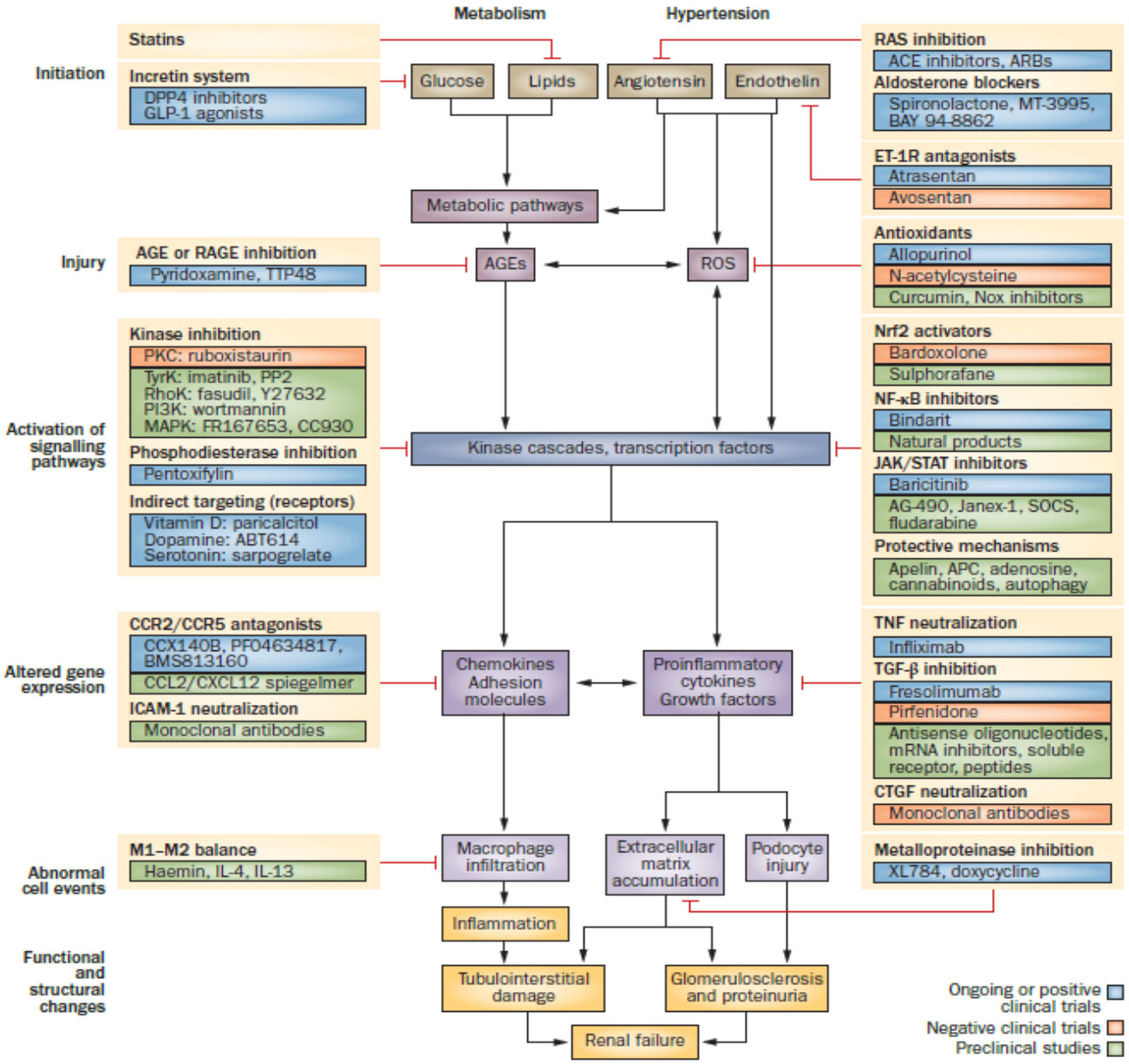
Approche intégrée



Merci de votre attention!

RDV à Liège en Octobre 2023.

Protection rénale et cardio-vasculaire



Nat. Rev. Nephrol. **10**, 325–346 (2014); published online 6 May 2014;