



Cas clinique

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Nice, février 2014

**Centre d'excellence européen en HTA
CHU Avicenne, Bobigny, France**

L'histoire

- Mr B., 40 ans adressé en avril 2012 en Cs
- Célibataire, Tabac 15PA, Poids 72kg
- Antécédents
- 3 coliques néphrétiques (2000,2005,2011)

L'histoire 2

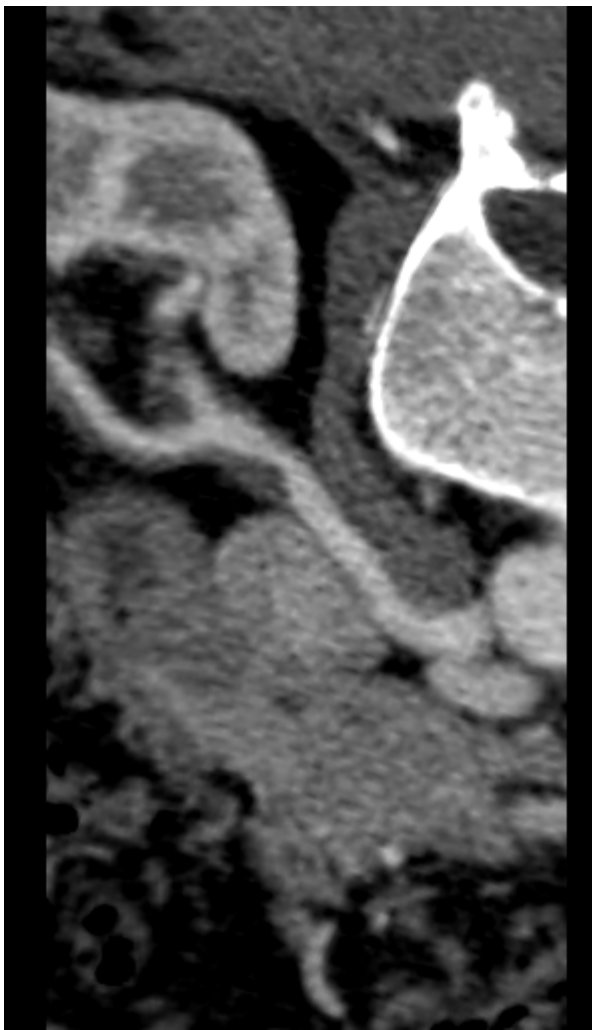
- HTA découverte systématique en Juin 2011 : 200/140 mmHg
 - Bilan hospitalier négatif.
 - Rupture thérapeutique en sept 2011
- Consultation Janvier 2012 Avicenne
 - Examen clinique normal . 240/160 mmHg
 - Refus d'hospitalisation; Mise sous trithérapie
- Consultation J15 : >180 mmHg en automesure, Kaliémie normale, Rénine stimuable, créat : 12 mg/l
 - Mise sous quadrithérapie et hospitalisation pour bilan

L'histoire 3

- En hospitalisation : PA 124/84 mmHg sous quadrithérapie
 - BU négative
 - Créatininémie : 103 $\mu\text{mol/l}$.
 - K⁺ : 3.9 mmol/l
 - Rénine 30 $\mu\text{UI/ml}$ (nl 5.4-50.8)
- Angioscanner des artères rénales et des surrénales







L'histoire 4

- Diagnostic

- Dissection d'une branche distale de l'artère rénale droite sans infarctus d'aval

Attitude thérapeutique ?

Attitude thérapeutique ?

- 1- Angioplastie et stent
- 2- Pontage chirurgical
- 3- AVK
- 4- ASA

Evolution

- Mise au traitement AAP (Kardegic 160 mg/j)
- Poursuite de la quadrithérapie anti-hypertensive.
- Scanner prévu à 6 Mois

3D
Ex: 33062

111

Set:3
No cut
Volume Rendering

DFOV 21.4cm

40
M

DoB: Jun 21 1972
Ex: Aug 29 2012

R
1
1
7

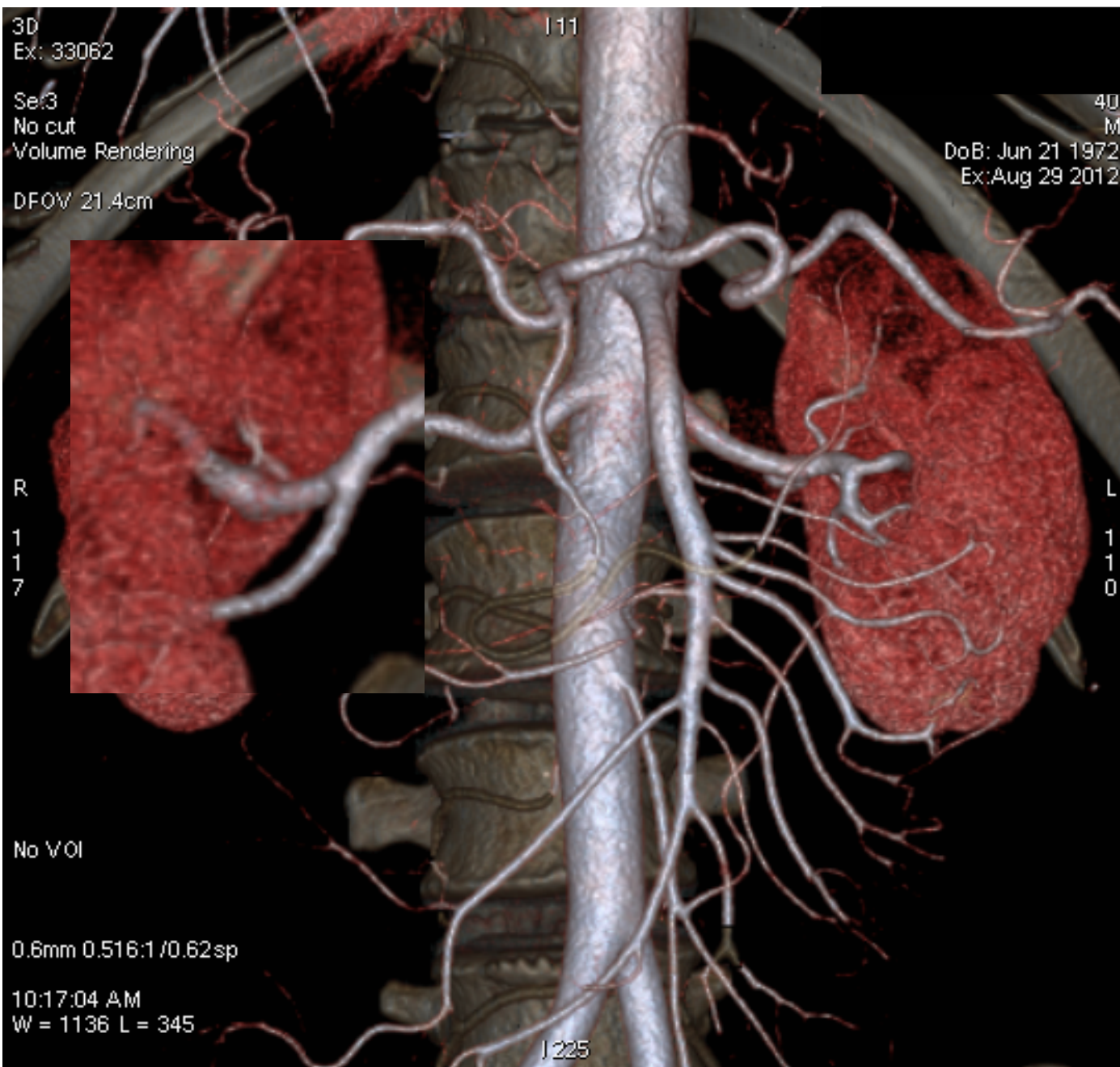
L
1
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No VOI

0.6mm 0.516:1 /0.62sp

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W = 1136 L = 345

1225



Curved
Ex: 33062

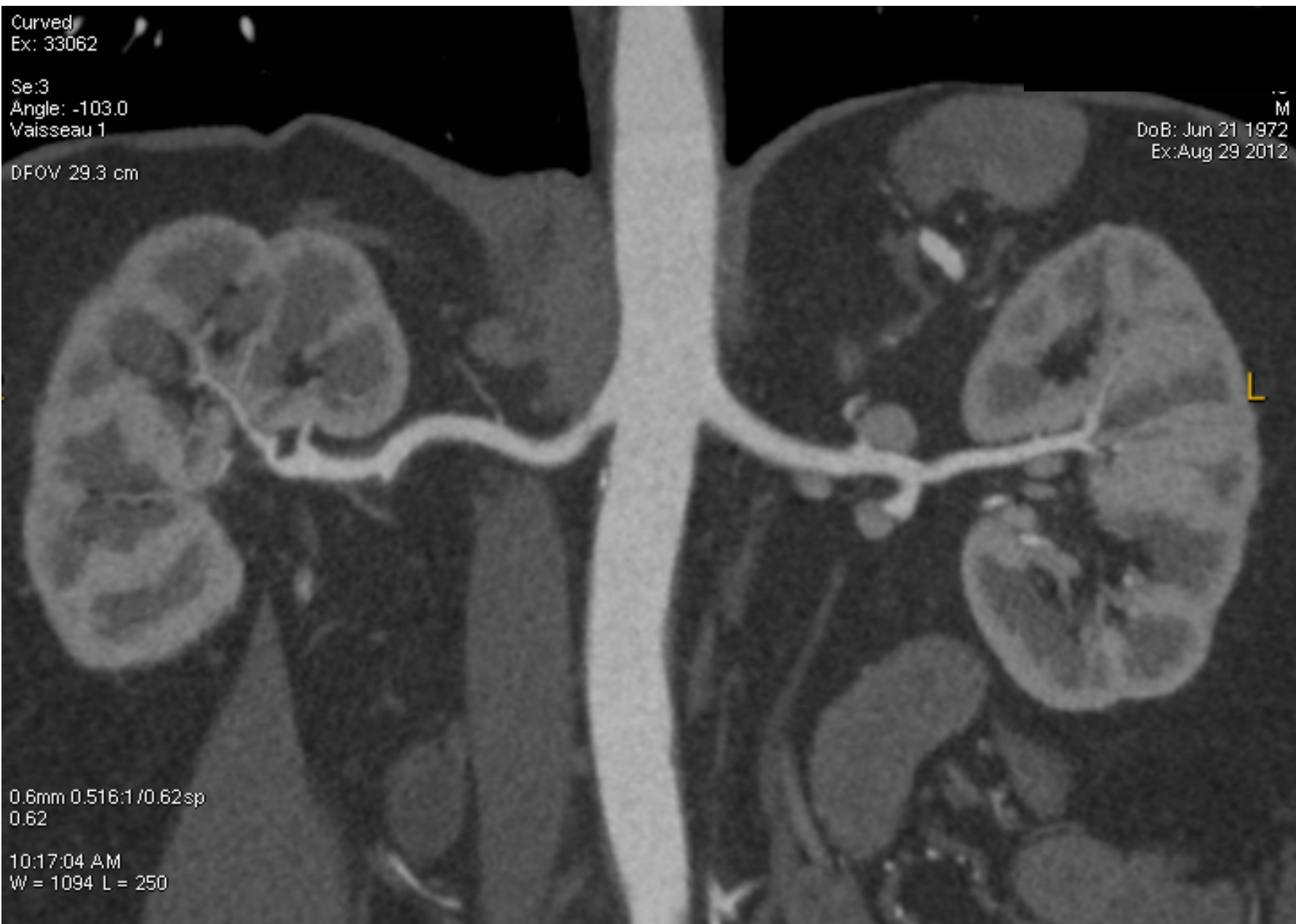
Se:3
Angle: -103.0
Vaisseau 1

DFOV 29.3 cm

DoB: Jun 21 1972
Ex: Aug 29 2012

0.6mm 0.516:1 / 0.62sp
0.62

10:17:04 AM
W = 1094 L = 250



Axial
Ex: 33062

A 49

+C
Se:3
I: 101.50
Im: 169
DFOV 15.6cm
STND/SS40

40
M
DoB: Jun 21 1972
Ex: Aug 29 2012

R
1
1
9

L
1
0
1

MIP
41.9
kV 100
mA 414
Rot 0.50s/HE+ 20.6mm/rot
0.6mm 0.516:1/0.62sp
Tilt: 0.0
10:17:04 AM

P 107



A: 4.96 (coi)

DoB: Jun 21 1972

Ex: Aug 29 2012

DFOV 11.2cm
STND/SS40

R
P

L
A

MIP
41.9
kV 100
mA Mod.
Rot 0.50s/HE+ 20.6mm/rot
0.6mm 0.516:1/0.62sp
Tilt: 0.0
10:17:04 AM

I 176



Curved
Ex: 33062

Se:3
Angle: -9.0
Vaisseau 1
DFOV 29.8 cm

40
M
DoB: Jun 21 1972
Ex: Aug 29 2012

0.6mm 0.516:1 / 0.62sp
0.62

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W = 1094 L = 250



Evolution

- Va bien
- PA 110/70 en automesure.
- Début de la décroissance antihypertensive

Spontaneous Dissection of Branch Renal Artery— Is Conservative Management Safe and Effective?

Vincent Misrai, Michaël Peyromaure,* Sylvain Poiree, Véronique Marteau and Claude Laurian

From the Departments of Vascular Surgery (VM, CL) and Radiology (VM), Hôpital Saint Joseph, Department of Urology, Hôpital Cochin (MP) and Department of Radiology, Hôpital Necker (SP), Paris, France

TABLE 1. Patient characteristics at diagnosis

Pt—Age No.	History	Clinical Presentation	Interval Before Diagnosis
1—50	Smoking, hyperuricemia	Isolated acute lumbar pain	14 Days
2—59	Smoking, family history of hypertension	Acute lumbar pain, hypertension	15 Days
3—49	Labile hypertension family history of hypertension	Acute lumbar pain, fever, hypertension	5 Days
4—47	None	Acute iliac pain, hypertension, hematuria	15 Days
5—52	Smoking, hyperuricemia, overwt	Isolated acute iliac pain	10 Days
6—51*	Hyperuricemia, smoking	Acute lumbar pain, hematuria, hypertension	6 Days
6—58†	Hypertension	Acute lumbar pain, high blood pressure	2 Days
7—54	Smoking, family history of hypertension	Acute lumbar pain, fever, hypertension	4 Days
8—48	Smoking	Acute lumbar pain, hematuria	6 Mos

TABLE 3. Anatomical results after medical treatment

Pt No.	Intermediate Arteriography (mos)	Followup CT Angiography	Followup (mos)
1	Permeable prepyelic artery, false lumen occlusion (12)	No evolution	87
2	—	Permeable narrow prepyelic artery, false lumen occlusion + nonsignificant stenosis	41
3	—	Permeable narrow prepyelic artery, false lumen occlusion + nonsignificant stenosis	85
4	—	Permeable narrow median branch	86
5	—	Complete recovery of initial retropyelic branch anatomy, false lumen occlusion	74
6	Dissection extension on retropyelic branch, permeable narrow superior branch, false lumen occlusion (72)	No evolution	100
6*	—	Residual nonsignificant stenosis, permeable narrow superior branch, retropyelic artery occlusion	48
7	Irregular trunk, retropyelic branch ectasia, superior branch occlusion	No evolution	82
8	—	Superior branch occlusion	48

* Second dissection.

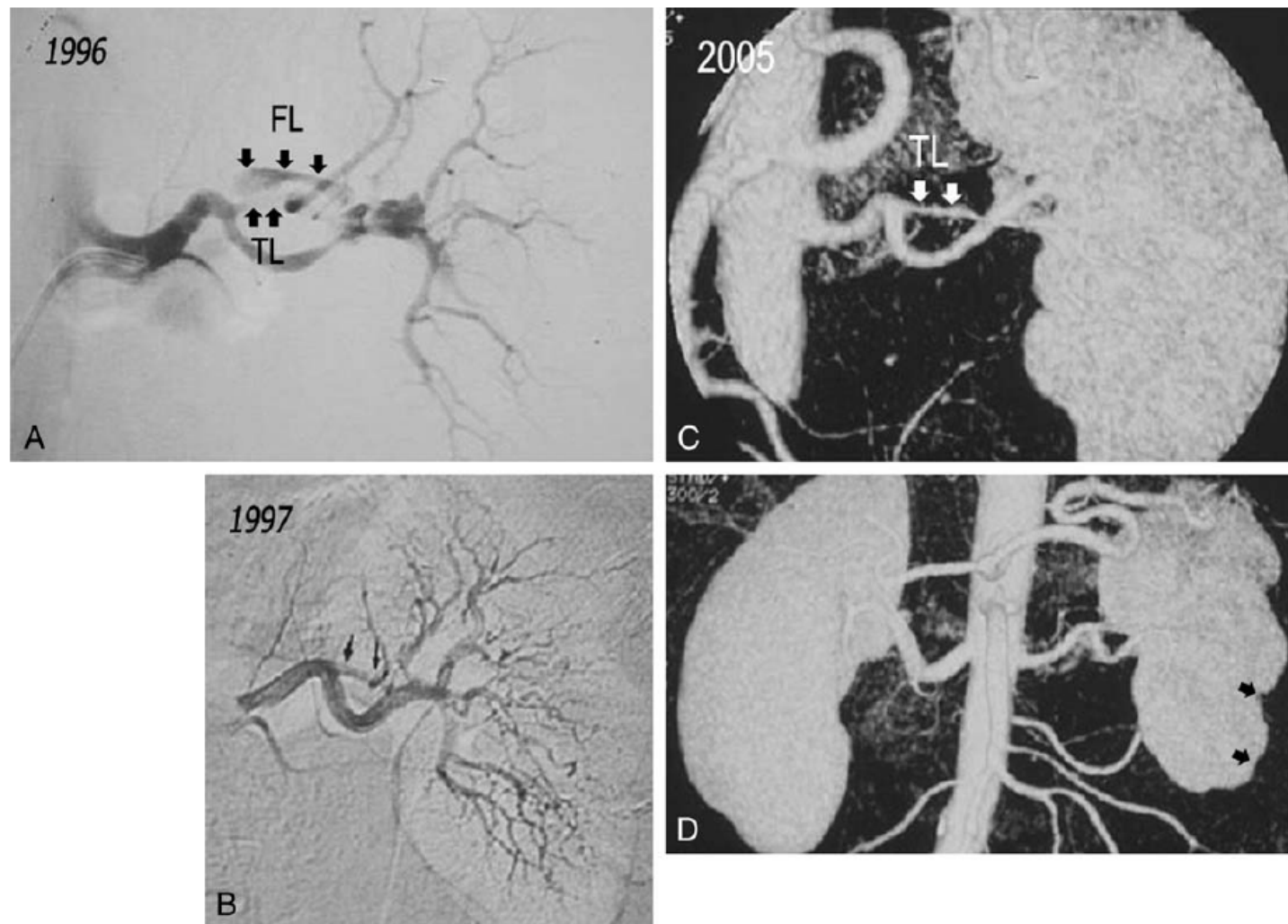


FIG. 1. A, angiography at diagnosis shows dissection of retroperitoneal branch with typical aspect of double lumen artery (arrows). *FL*, false lumen. *TL*, true lumen. B, angiography at intermediate followup reveals permeability of true lumen (arrows). C and D, angiography CT with 3D reconstruction demonstrates permeability of true lumen with inferior polar infarction (arrows).

Résumé

Dissections spontanées : Rare

Traitement antihypertenseur associé à ASA peut apparaître comme un traitement conservateur suffisant et efficace chez la plupart des patients

Le remodelage artériel survient à moyen terme et évolue peu vers l'occlusion ou la dilatation anévrysmale.

La revascularisation ne doit être proposée qu'en cas d'occlusion complète de l'artère principale, d'HTA maligne, d'altération de la fonction rénale ou d'HTA réfractaire au traitement.

Mr Jean-Jacques M. 48 ans, chiffres élevés
dépistés en médecine du travail.

PA : 150/95 mmHg (90)

créat : 80 μ mol/l

glycémie 0.96 g/l

HDL : 0.46g/l LDL:1.40 g/l CT : 2.26 g/l

Tabac=0

Automesure : 144/90 mmHg

Chez ce patient, recherchez vous une microalbuminurie?

1. OUI
2. NON
3. Ca dépend

Box 2. Subclinical organ damage in total cardiovascular risk stratification

- (1) In hypertension, assessment of total cardiovascular risk is important to optimize the decision about treatment initiation, intensity and goals.
- (2) Quantification of total cardiovascular risk must include a search for subclinical organ damage, which is common in hypertension and has independent prognostic significance.
- (3) In patients with hypertension, the presence of subclinical organ damage usually brings cardiovascular risk into the high range. Subclinical organ damage alone may not be sufficient to bring normotensive individuals into the high-risk category, although this may occur with multiple organ damage and the metabolic syndrome.
- (4) As detailed in the 2007 ESH/ESC guidelines, several measures of renal, cardiac and vascular damage can be considered for total cardiovascular risk quantification. Because of their simplicity, wide availability and limited cost measures based on urinary protein excretion (including microalbuminuria), eGFR (MDRD formula), and ECG are suitable for routine use. Cardiac and vascular ultrasounds are more and more easily available in Europe, and their use in the evaluation of the hypertensive patient can be encouraged.
- (5) Subclinical organ damage should be assessed both at screening and during treatment because a number of treatment-induced changes in organ damage relate to cardiovascular and renal outcomes, thereby offering information on whether the selected treatment is protecting patients from progressing organ damage and potentially from cardiovascular events.
- (6) Several other measures of subclinical organ damage have been shown to have prognostic significance, but their complexity, low availability, and high cost prevent their routine clinical use. It is likely that technological progress will make use of some of these measurements more common in the future. Any measure, however, should be considered only if it adds to the overall precision of cardiovascular risk quantification.

PRISE EN CHARGE DE L'HYPERTENSION ARTÉRIELLE DE L'ADULTE

*Jacques Blacher, Jean-Michel Halimi, Olivier Hanon, Jean-Jacques Mourad,
Atul Pathak, Bruno Schnebert, Xavier Girerd*
au nom de la Société Française d'Hypertension Artérielle.

3 - Réaliser un bilan initial comportant systématiquement :

- un examen clinique, avec recherche de facteurs provoquant ou aggravant une HTA,
- un bilan biologique comportant ionogramme sanguin, créatininémie avec débit de filtration glomérulaire estimé, glycémie à jeun, bilan lipidique et protéinurie, la recherche de la microalbuminurie n'est recommandée que chez le diabétique,
- un électrocardiogramme de repos.

Une hypokaliémie, une insuffisance rénale, une protéinurie doivent faire suspecter une HTA secondaire.

De l'(in)utilité du dosage de la microalbuminurie en pratique quotidienne chez l'hypertendu

*About the usefulness/uselessness of microalbuminuria
detection in hypertensive patients in daily practice*

J.J. Mourad*



Le dosage de la microalbuminurie est entré dans les (bonnes) pratiques courantes depuis 15 ans environ, largement favorisé par la conjonction

urinaire, faisant questionner la pertinence de proposer cet examen chez les patients hospitalisés ! Cet examen est coté B15, soit un peu moins de

Quelle est l'affirmation fausse concernant la microalbuminurie ?

- 1- Une recherche positive suffit pour affirmer le diagnostic.
- 2- Le dosage peut être faussement positif en cas de diabète déséquilibré
- 3- Le dosage peut être faussement positif en cas d'infection
- 4- Le dosage peut être faussement positif en cas d'activité physique importante
- 5- Le dosage peut être faussement positif en cas d'HTA déséquilibrée

Quelle est l'affirmation fausse concernant la microalbuminurie ?

- 1- C' est un marqueur du risque cardiovasculaire.
- 2- C' est un facteur du risque cardiovasculaire.
- 3- Son dosage coûte environ 5 euros
- 4- Sa présence signe l' existence d' une atteinte rénale qui peut être réversible

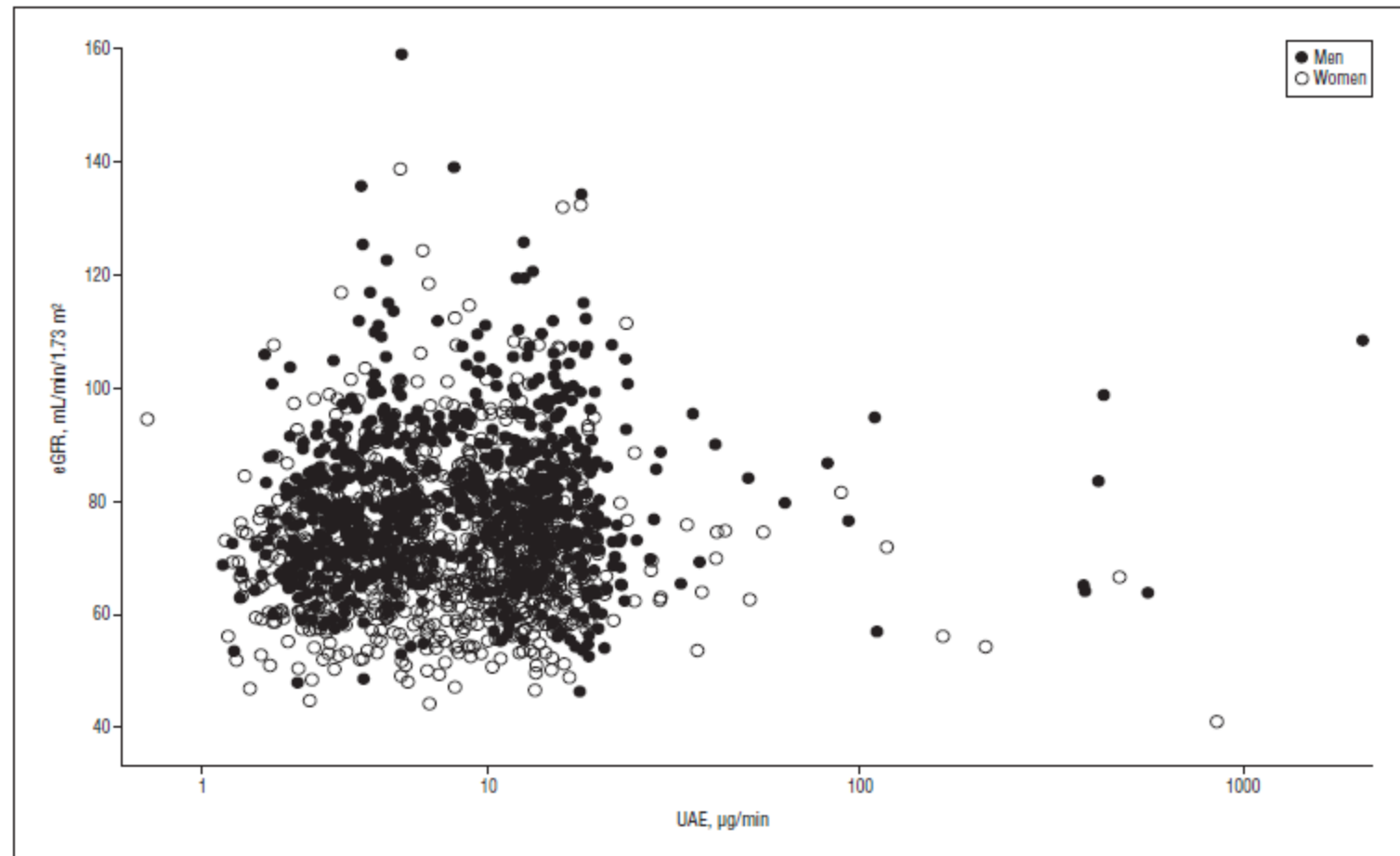
Focus sur la microalbuminurie

Application des recommandations:
Dépistage de la microalbuminurie à
l'ensemble des hypertendus

Definition of Kidney Dysfunction as a Cardiovascular Risk Factor

Use of Urinary Albumin Excretion and Estimated Glomerular Filtration Rate

Massimo Cirillo, MD; Maria Paola Lanti, MD; Alessandro Menotti, MD; Martino Laurenzi, MD;
Mario Mancini, MD; Alberto Zanchetti, MD; Natale G. De Santo, MD



Definition of Kidney Dysfunction as a Cardiovascular Risk Factor

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Table 2. Incidence of Cardiovascular Disease and Other Disease Events by Presence and Type of Baseline Kidney Dysfunction in Individuals Aged 45 to 64 Years

Cardiovascular and Other Disease Events, % of Patients	No Kidney Dysfunction	Composite Kidney Dysfunction ^a		
		Isolated High UAE ^b	High UAE and Low eGFR	Isolated Low eGFR ^c
Cerebrovascular disease	1.3	1.4	4.3	2.8
Ischemic heart disease	4.3	7.6	21.7	6.9
Peripheral artery disease	0.1	0.7	0.0	0.0
Any of the above	5.6	9.7	26.1	9.7
Nonfatal	4.5	6.9	17.4	7.6
Fatal	1.3	5.6	8.7	3.5
Other diseases	5.0	6.9	8.7	4.2

Abbreviations: eGFR, estimated glomerular filtration rate; UAE, urinary albumin excretion.

^a Indicates with high UAE (highest sex-specific decile) or with low eGFR (lowest sex-specific decile).

^b Indicates with high UAE and without low eGFR.

^c Indicates with low eGFR and without high UAE.

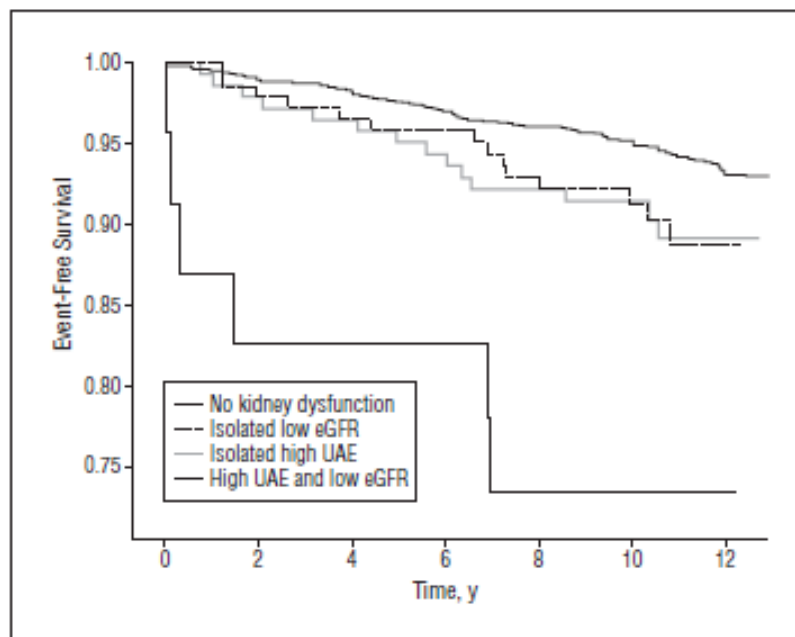


Figure 2. Kaplan-Meier plot of incident cardiovascular events in individuals aged 45 to 64 years. No kidney dysfunction (n=1354 without high urinary albumin excretion [UAE] and without low estimated glomerular filtration rate [eGFR]) compared with kidney dysfunction divided subjects into the following 3 subgroups: isolated high UAE (n=144 with high UAE and without low eGFR), isolated low eGFR (n=144 with low eGFR and without high UAE), and high UAE and low eGFR (n=23). High UAE was defined as a UAE in the highest sex-specific decile, and low eGFR was defined as an eGFR in the lowest sex-specific decile.

Definition of Kidney Dysfunction as a Cardiovascular Risk Factor

Use of Urinary Albumin Excretion and Estimated Glomerular Filtration Rate

Massimo Cirillo, MD; Maria Paola Lanti, MD; Alessandro Menotti, MD; Martino Laurenzi, MD;
Mario Mancini, MD; Alberto Zanchetti, MD; Natale G. De Santo, MD

Variable	No Kidney Dysfunction (n=1354)	Composite Kidney Dysfunction ^a		
		Isolated High UAE ^b (n=144)	High UAE and Low eGFR (n=23)	Isolated Low eGFR ^c (n=144)
UAE, mean (SD), µg/min	7.8 (4.4)	50.5 (179.2)	114.3 (210.4)	7.7 (4.6)
Serum creatinine level, mean (SD), mg/dL	0.93 (0.14)	0.93 (0.15)	1.26 (0.13)	1.21 (0.13)
eGFR, mean (SD), mL/min/1.73 m ²	77.8 (12.7)	77.7 (14.5)	57.2 (5.6)	56.0 (4.5)
Women, %	55.6	59.0	34.8	59.0
Age, mean (SD), y	54.5 (5.6)	55.5 (5.1)	57.7 (5.0)	56.9 (5.5)
Prevalent cardiovascular risk factors				
Systolic pressure, mean (SD), mm Hg	128.3 (17.0)	144.7 (21.6)	144.3 (17.5)	130.4 (17.9)
Diastolic pressure, mean (SD), mm Hg	77.7 (9.3)	85.5 (11.0)	84.4 (6.7)	78.8 (8.8)
Antihypertensive drug use, %	17.3	35.4	34.8	30.6
Hypertension, %	35.4	75.7	78.3	44.4
Serum total cholesterol level, mean (SD), mg/dL	225.2 (37.6)	262.4 (43.0)	266.7 (32.7)	233.9 (37.0)
Serum HDL cholesterol level, mean (SD), mg/dL	50.7 (12.8)	50.0 (13.1)	51.1 (15.1)	48.1 (11.1)
Hypercholesterolemia, %	34.9	75.7	78.3	41.0
Current smokers, %	30.1	36.1	43.5	32.6
Serum glucose level, mean (SD), mg/dL	94.3 (20.2)	99.1 (27.9)	96.9 (20.0)	92.1 (14.4)
Diabetes mellitus, %	5.7	6.3	4.4	3.5
Left ventricular hypertrophy, %	3.3	6.3	21.7	0.7
BMI, mean (SD)	27.8 (4.2)	30.1 (4.6)	31.2 (5.7)	28.0 (4.2)
Obesity, %	26.2	48.6	52.2	27.1
Prior cardiovascular disease, %				
Cerebrovascular disease	0.5	2.1	4.4	2.8
Ischemic heart disease	2.1	3.5	13.0	3.5
Peripheral artery disease	0.0	0.0	0.0	0.0
Any of the above	2.5	5.6	17.4	5.6

La microalbuminurie est définie comme l'élimination dans les urines d'une quantité d'albumine comprise entre 30 et 300 mg/24 h ou entre 30 et 300 µg par mg de créatinine sur un échantillon d'urine isolé. Une augmentation de la microalbuminurie témoigne d'une atteinte glomérulaire. La microalbuminurie constitue à la fois un indicateur diagnostique, de suivi thérapeutique et de pronostic, aussi bien dans le diabète de type 1 que de type 2. C'est également un facteur de risque indépendant dans l'hypertension artérielle et la maladie coronarienne. La microalbuminurie doit être mesurée dans des conditions strictes de prélèvement, au moins à deux reprises à visée diagnostique, et une fois par an au cours du suivi des patients. Son dosage actuel ne pose aucun problème, il est bien standardisé. Il fait appel à l'immunoturbidimétrie ou l'immunonéphélémétrie. Il est très rapide et fiable. Son interprétation est donc sûre.

Deux résultats positifs sur une période de 3 à 6 mois sont prédictifs d'une néphropathie débutante (HAS)

Guieu R; EMC 2008

Microalbuminurie et excrétion urinaire d'albumine : recommandations pour la pratique clinique

Microalbuminuria and urinary albumin excretion: clinical practice guidelines

Jean-Michel Halimi^{l,*}, Samy Hadjadj^{j,k}, Victor Aboyans^a,
François-André Allaert^{b,c}, Jean-Yves Artigou^d, Michel Beaufils^e,
Gilles Berrut^f, Jean-Pierre Fauvel^h, Henri Ginⁱ, Alain Nitenberg^m,
Jean-Charles Renversezⁿ, Emmanuel Rusch^o, Paul Valensi^p,
Daniel Cordonnier^g

Dans le cadre du soin

Pour des raisons pratiques, l' utilisation d' un échantillon sur les premières urines du matin suffit. Il est nécessaire de

répéter dans les semaines suivantes la recherche de microalbuminurie chez un patient chez qui une première recherche s' est révélée positive. **En cas de discordance, une troisième recherche de microalbuminurie est nécessaire.**

Il n' est pas nécessaire de répéter le dosage de l' excrétion urinaire d' albumine si une première recherche de microalbuminurie est négative. Dans le cadre du suivi, il est recommandé d' effectuer la recherche de microalbuminurie dans les mêmes conditions (conditions de prélèvement, méthode de dosage, laboratoire).

Définition de la microalbuminurie et valeurs de référence

	24 heures (mg/24h)	Echantillon d'urine (spot) (mg/g de créatinine)
Albuminurie normale	< 30	< 30
Microalbuminurie	30 – 300	30 – 300
Protéinurie	> 300	> 3000

Il a été observé que le dosage de la microalbuminurie pouvant varier d'un jour à l'autre chez le même individu.

Cette variabilité chez le même individu est assez importante estimée de 25 à 50% selon les études.

D'autres facteurs peuvent faire varier la microalbuminurie : élévation de la glycémie, élévation des chiffres tensionnels, infection urinaires, hyperthermie et infection générale, orthostatisme, activité physique...

Cette variabilité impose la nécessité d'obtenir au moins **deux dosages espacés de quelques semaines** avant de porter le diagnostic de microalbuminurie pathologique.

En dépit de cette variabilité, la valeur prédictive négative d'un dosage unique apparaît très bonne (supérieur à 90%) alors que la valeur prédictive positive n'est que de 75%.

Les éléments les plus importants qui vont influencer sur l'évolution de la microalbuminurie sont :

- Adopter une hygiène de vie protectrice pour la santé,
- Arrêt du tabac indispensable : fumer pour un sujet diabétique ou à risque cardiovasculaire augmente de façon importante le risque d'accident cardiovasculaire : infarctus mais aussi artériopathie des membres inférieurs,
- Bouger plus :
 - . Marche (au moins 30 mn) 3 ou 4 fois par semaine,
 - . Gérer le stress de la vie quotidienne,
 - . L'activité physique peut être une aide.
- Manger mieux :
 - . Limiter la consommation de graisses visibles ou cachées, manger au moins 5 légumes ou fruits par jour,
 - . Limiter la viande et le fromage,
 - . Privilégier le poisson au moins deux fois par semaine,
 - . Consommer du pain et des féculents,
 - . Ne pas resaler les aliments,
 - . Eviter l'excès de boissons alcoolisées (2 verres de vin par jour pour les femmes, 3 verres pour les hommes).
- Maîtriser la maladie diabétique :
 - . Maintenir l'HbA1c inférieure à 6 – 6.5 ou 7% selon le diabète : à définir pour chaque personne avec son médecin traitant (l'HbA1c est à demander tous les 3 mois, le dosage pouvant être réalisé non à jeun),
 - . Contrôler le bilan lipidique : le bilan doit être réalisé idéalement après 8 heures de jeun. Il faut s'intéresser au cholestérol total, au cholestérol LDL (« mauvais cholestérol »), au bon cholestérol (HDL), aux triglycérides. L'alimentation est une aide.

B EUROS

glucose	10	2,70
HbA1c	50	13,50
protéines glyquées		
cholestérol total	5	1,35
triglycérides	10	2,70
exploration d'une anomalie lipidique : comprenant dosage des triglycérides, du cholestérol total, l'aspect du sérum, et de l'Apo A1 ou de l'HDL-cholestérol par précipitation	45	12,15
Apo A 1	10	2,70
Apo B	20	5,40
lipoprotéinogramme	40	10,80
acide urique	10	2,70
calcium	15	4,05
créatinine	10	2,70
magnésium plasmatique ou globulaire	15	4,05
micro-albuminurie	40	10,80
phosphore	10	2,70
urée	10	2,70
urée et créatinine	10	2,70
albumine	30	8,10
fer sérique	15	4,05

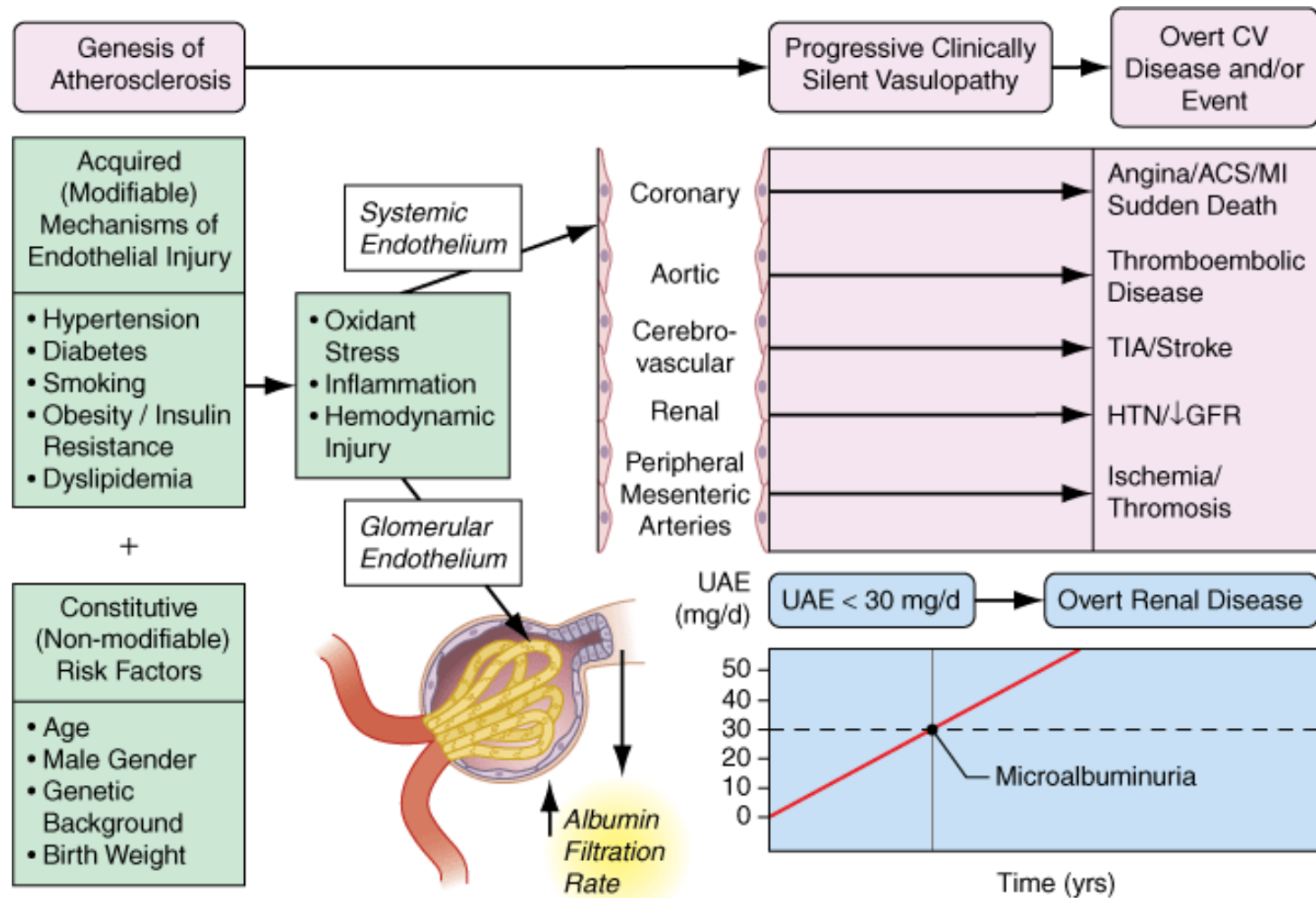
There is ample epidemiological evidence to suggest that **albuminuria is a powerful and independent predictor of progressive kidney and cardiovascular disease** in both the general population and in patients at high cardiovascular risk.

Table 2. Clinical studies reporting the risks associated with a positive microalbuminuria result*

Study	Population	Microalbuminuria Definition	Risk Associated with a Positive Microalbuminuria Result (95% CI)
Prospective studies			
HOPE (7)	Subjects at high cardiovascular risk (≥ 55 yr with CVD or with diabetes + ≥ 1 CVD risk factor; $n = 9040$)	ACR ≥ 2 mg/mmol in a first-morning spot urine sample	All-cause mortality: RR 2.09 (1.84 to 2.38)
PREVEND (8)	Residents of Groningen, the Netherlands, 28 to 75 yr ($n = 40,548$)	UAE 20 to 300 mg/L in an early-morning spot urine sample	Cardiovascular death: RR 1.29 (1.18 to 1.40) Noncardiovascular death: RR 1.12 (1.04 to 1.21)
PREVEND (21)	Residents of Groningen, the Netherlands, 28 to 75 yr ($n = 7530$)	UAE 30 to 300 mg in a 24-h urine sample	All-cause mortality: HR 3.3 (1.5 to 7.1) for patients with ST-T segment changes + microalbuminuria versus 0.9 (0.4 to 1.9) for ST-T segment changes alone Cardiovascular death: HR 10.4 (2.5 to 43.6) for patients with ST-T segment changes + microalbuminuria versus 2.7 (0.6 to 12.3) for ST-T segment changes alone
Heim Study (11)	Population-based: White individuals, 50 to 75 yr ($n = 631$)	ACR ≥ 2 mg/mmol in a first-morning spot urine sample	Cardiovascular death: RR 3.22 (1.28 to 8.00) All-cause mortality: RR 1.70 (0.86 to 3.34) All-cause mortality in patients with hypertension: RR 2.87 (1.22 to 6.33)
HUNT (12)	Non-diabetic, non-hypertensive residents of Nord-Trøndelag, Norway, ≥ 20 yr ($n = 2085$)	ACR ≥ 0.76 mg/mmol (> 60 th percentile) in a first-morning spot urine sample	All-cause mortality: RR 2.3 (1.0 to 5.4)
EPIC-Norfolk (13)	Residents of Norfolk, UK, 40 to 79 yr ($n = 20,911$)	ACR 2.5 to 25 mg/mmol in a random spot urine sample	All-cause mortality: HR 1.48 (1.20 to 1.79) Cardiovascular death: HR 2.03 (1.55 to 2.67) Fatal stroke: HR 1.58 (1.30 to 3.0) Coronary heart disease death: HR 2.01 (1.40 to 2.90)
EPIC-Norfolk (20)	Residents of Norfolk, UK, 40 to 79 yr ($n = 23,630$)	ACR 2.5 to 25 mg/mmol in a random spot urine sample	Stroke: HR 1.49 (1.13 to 2.14)
Third Copenhagen City Heart Study (14)	Residents of Copenhagen, Denmark, 30 to 70 yr, without coronary heart disease	UAE > 4.8 $\mu\text{g}/\text{min}$ (> 3 rd quantile) in a timed overnight urine sample	All-cause mortality: RR 1.9 (1.5 to 2.4) Coronary heart disease: RR 2.0 (1.4 to 3.0)
Danish MONICA (22)	Population-based: Individuals without ischemic heart disease, renal disease, urinary tract infection, or diabetes ($n = 2085$)	ACR > 0.65 mg/mmol (> 90 th percentile) in a first-morning spot urine sample	Ischemic heart disease: RR 2.3 (1.3 to 3.9)
Shibata Study (25)	Residents of Shibata, Japan, ≥ 40 yr ($n = 2651$)	Positive albumin dipstick test	Stroke: RR in men 2.5 (1.1 to 5.7)
Portland Study (26)	Older residents of Portland, Oregon, with previous stroke or transient ischemic attack ($n = 121$)	UAE 20 to 300 mg/L in a first-morning spot urine sample	Recurrent stroke: HR 4.9 (1.4 to 17.6)
Skewik <i>et al.</i> (27)	Patients admitted within 24 h of a first ischemic stroke ($n = 60$)	UAE 30 to 300 mg in a 24-h urine sample	Mortality: OR 6.0 (1.3 to 27.7)
Cross-sectional studies			
Zander <i>et al.</i> (28)	Patients with type 2 diabetes ($n = 1063$)	UAE 20 to 300 $\mu\text{g}/\text{min}$ in a timed overnight urine sample	PAD: OR 2.1 (1.4 to 3.2)
PREVEND (28)	Non-diabetic residents of Groningen, the Netherlands, 28 to 75 yr ($n = 7579$)	UAE 30 to 300 mg in a 24-h urine sample	Electrocardiography abnormalities: Ischemic pattern: OR 1.61 (1.12 to 2.32) Major ischemia: OR 1.43 (1.08 to 1.91) Minor ischemia: OR 1.32 (1.03 to 1.68)
PREVEND (28)	Non-diabetic residents of Groningen, the Netherlands, 28 to 75 yr ($n = 6660$)	UAE 30 to 300 mg in a 24-h urine sample	PAD: OR 0.98 (0.68 to 1.41) in multivariate analysis
Euris <i>et al.</i> (29)	Patients with type 1 diabetes and without CVD	UAE 20 to 300 $\mu\text{g}/\text{min}$ in a timed overnight urine sample	Stress myocardial ischemia: OR 6.3 (1.2 to 32.8)

*ACR, albumin-to-creatinine ratio; CI, confidence interval; CVD, cardiovascular disease; EPIC-Norfolk, European Prospective Investigation into Cancer in Norfolk; HOPE, Heart Outcomes Prevention Evaluation; HR, hazard ratio; HUNT, Nord-Trøndelag Health Study; OR, odds ratio; PAD, peripheral artery disease; PREVEND, Prevention of Renal and Vascular End Stage Disease; RR, relative risk.

The association between microalbuminuria and cardiovascular disease is probably explained by a **common pathophysiologic process**, such as **endothelial dysfunction or chronic, low-grade inflammation**.



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: <http://www.accessmedicine.com>

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Modifying Albuminuria

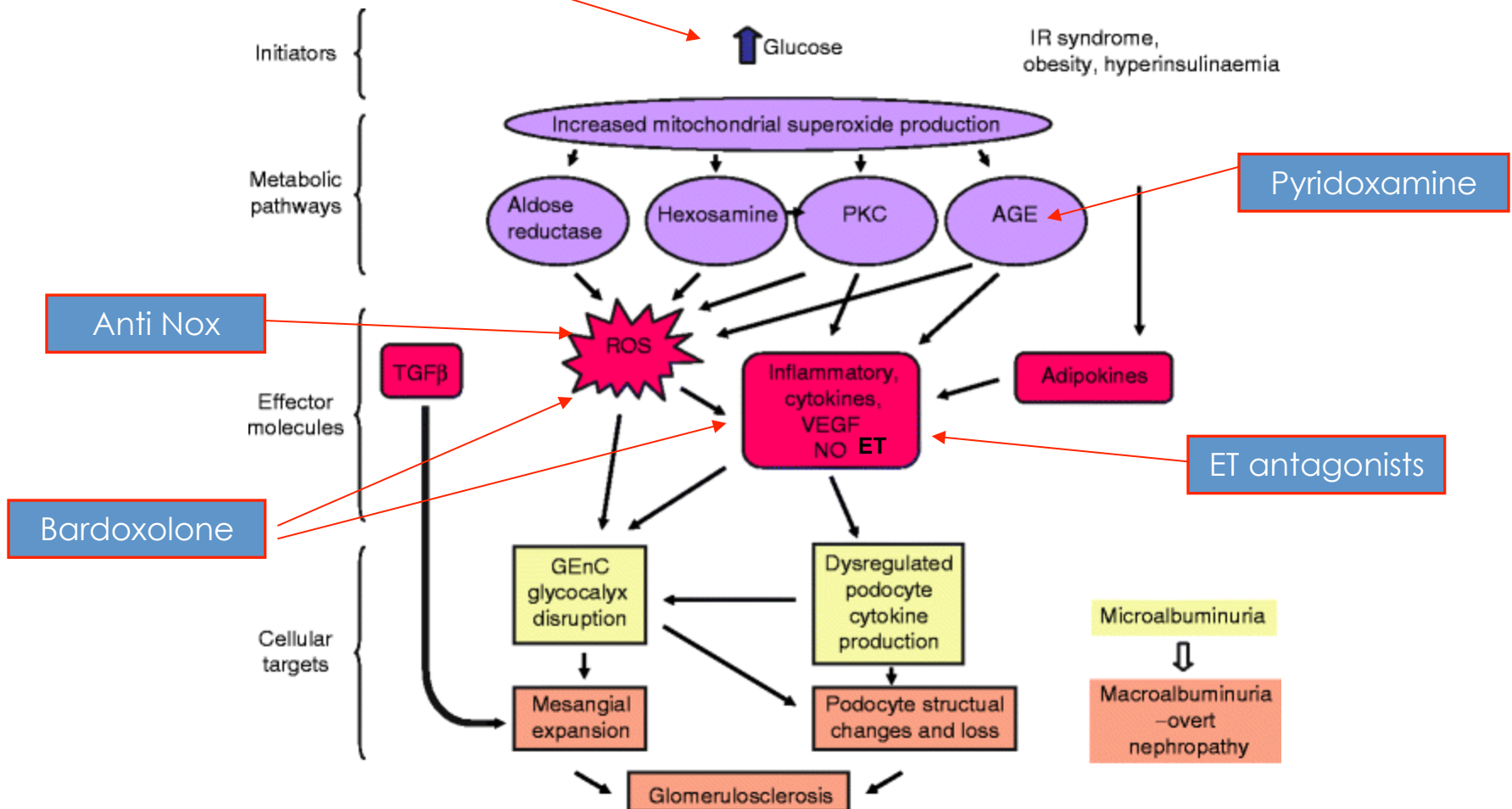
Regular exercise

Weight loss

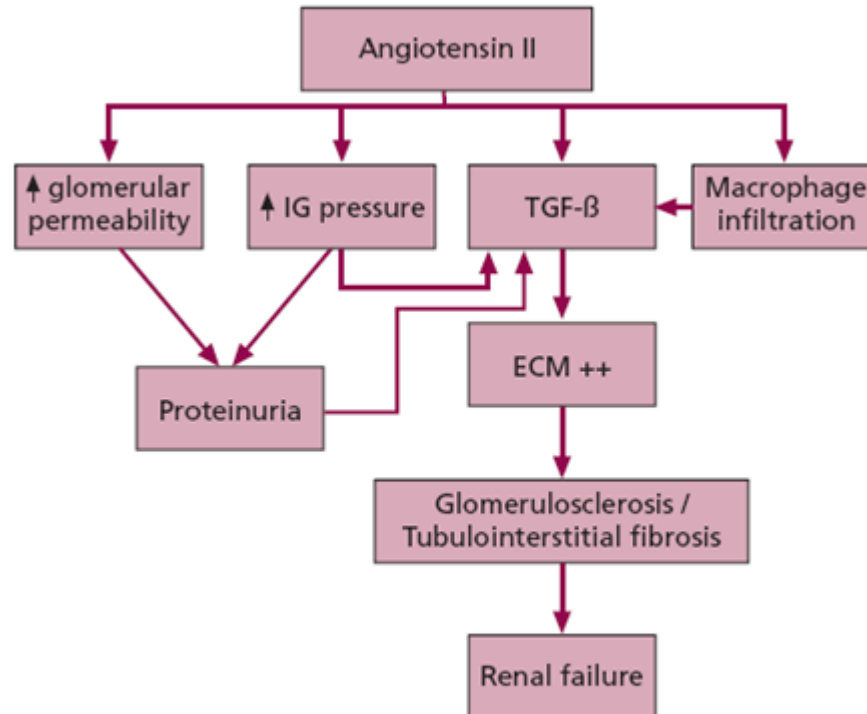
Blood sugar management

Pharmacological strategies

Glycemic control



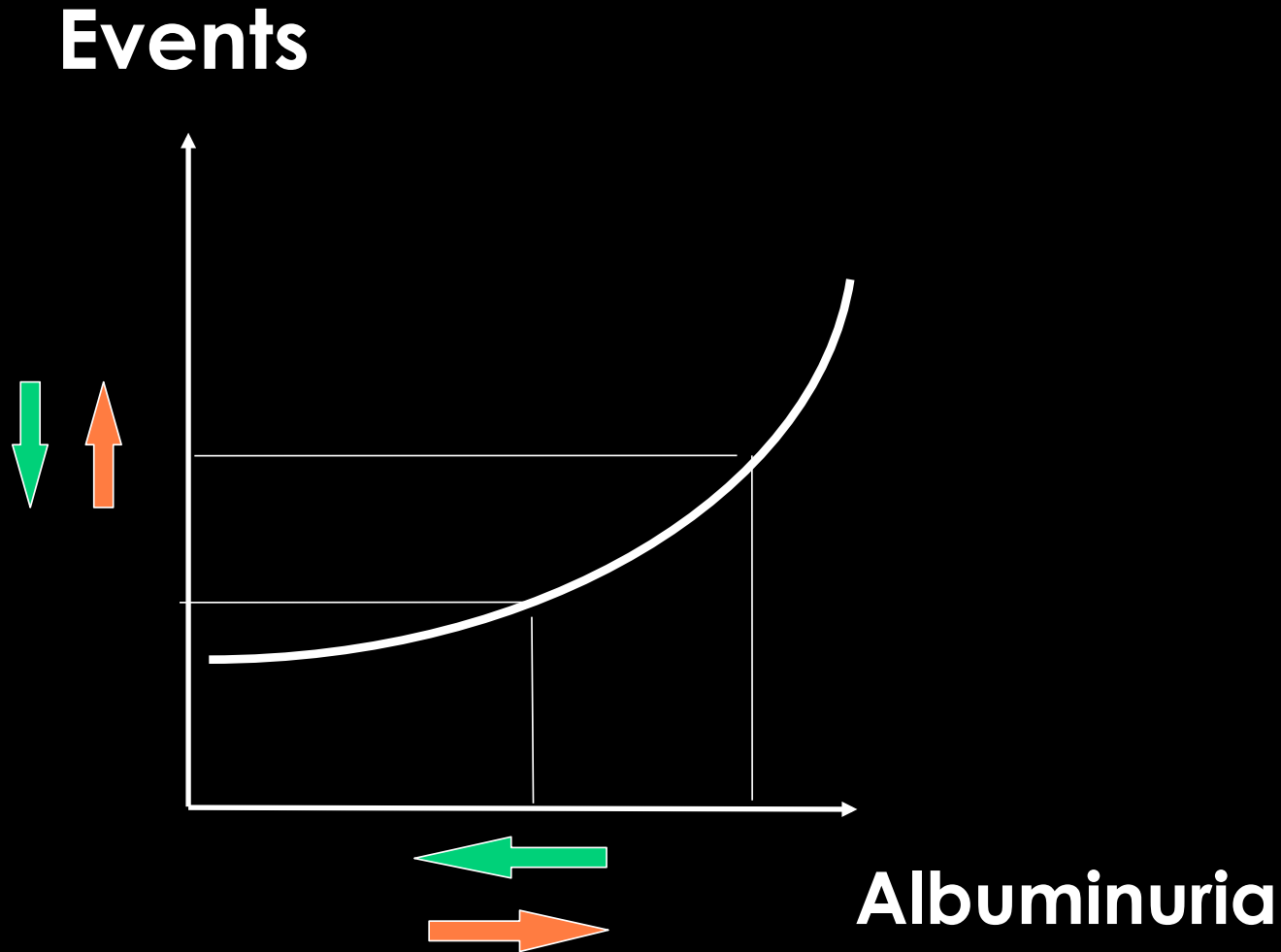
RAAS inhibitors

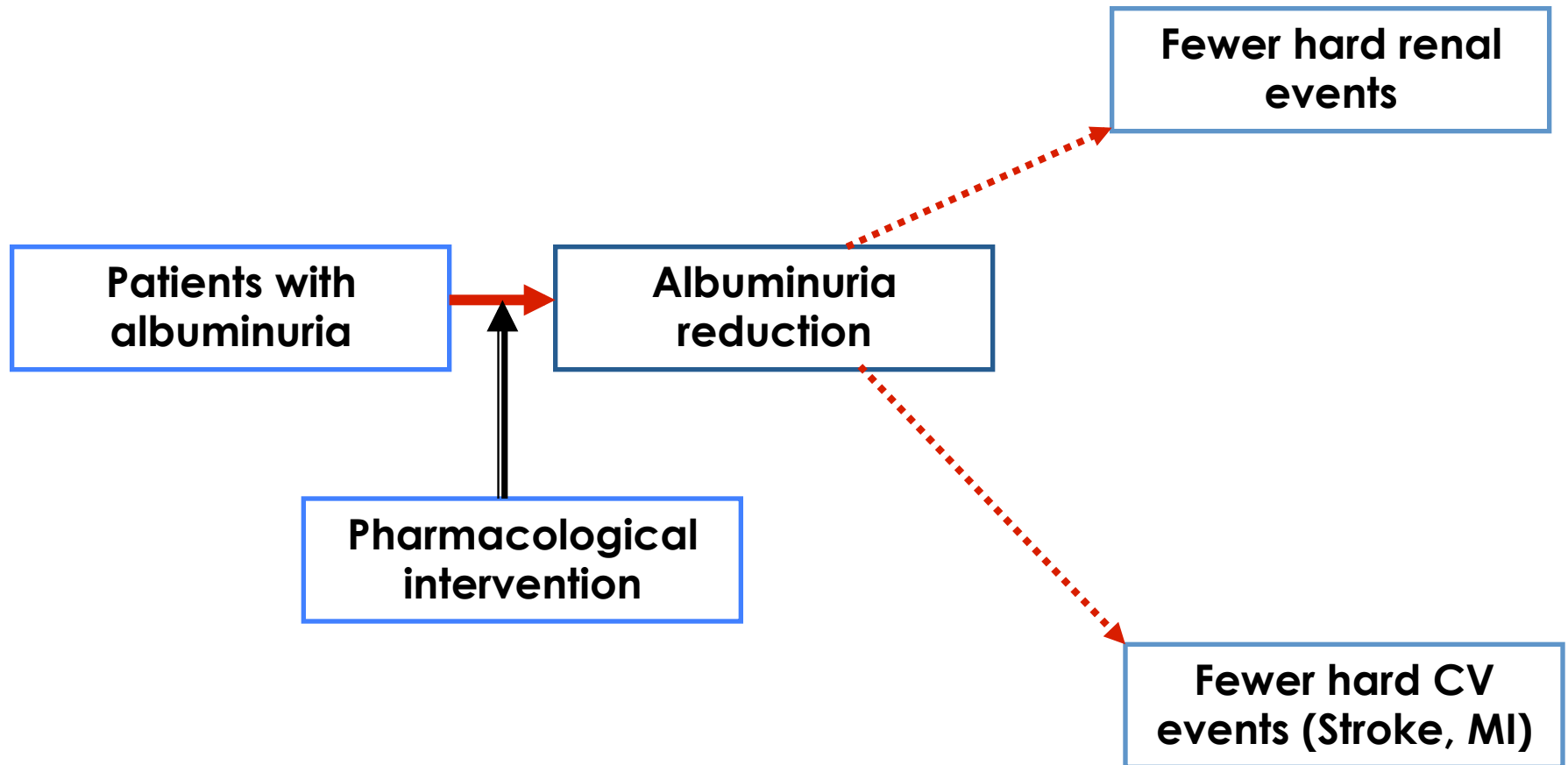


Key: ECM = extracellular matrix; IG = intra glomerular; TGF = transforming growth factor

Do treatment-induced **changes in albuminuria** predict cardiovascular and renal outcomes?

Numerous studies have been designed to confirm this hypothesis and would have been able to draw this figure





Subsidiary question : Is there any correlation between the achieved reduction in albuminuria and the risk reduction?

Intensive glucose control improves kidney outcomes in patients with type 2 diabetes

Vlado Perkovic¹, Hiddo Lambers Heerspink², John Chalmers¹, Mark Woodward^{1,3}, Min Jun¹, Qiang Li¹, Stephen MacMahon^{1,4}, Mark E. Cooper⁵, Pavel Hamet⁶, Michel Marre⁷, Carl Erik Mogensen⁸, Neil Poulter⁹, Giuseppe Mancina¹⁰, Alan Cass¹, Anushka Patel¹ and Sophia Zoungas^{1,11}, for the ADVANCE Collaborative Group

HbA1c : 7.3% vs 6.5%

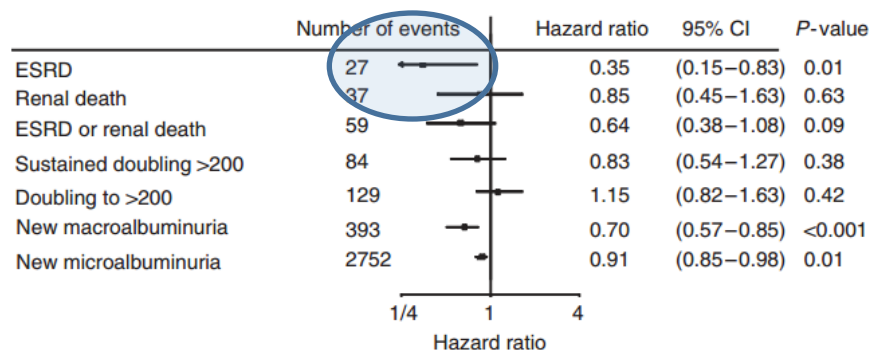


Figure 2 | Summary plot showing the effects of intensive glucose lowering compared with standard glucose lowering on renal outcomes. CI, confidence interval; doubling to >200, adjudicated doubling of serum creatinine to a value over 200 $\mu\text{mol/l}$; sustained doubling >200, doubling of creatinine as above that remained at least doubled at the final available follow-up reading; ESRD, end-stage renal disease.

Major Macrovascular Events

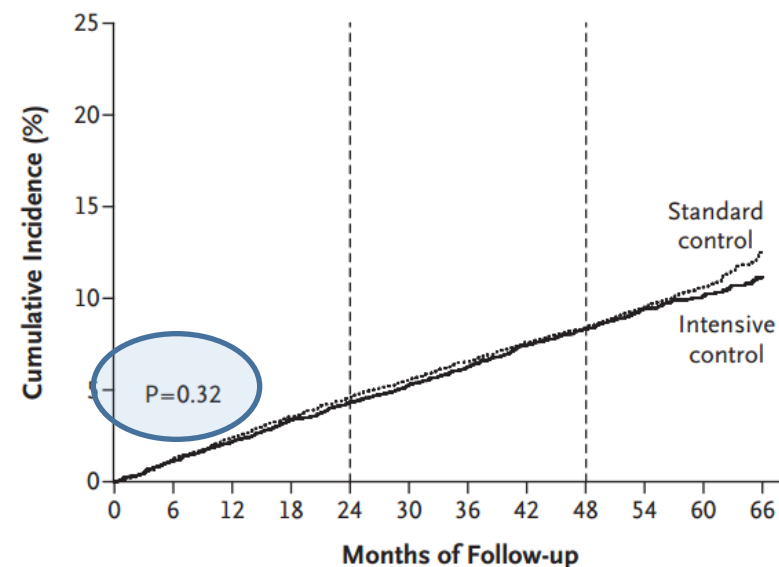
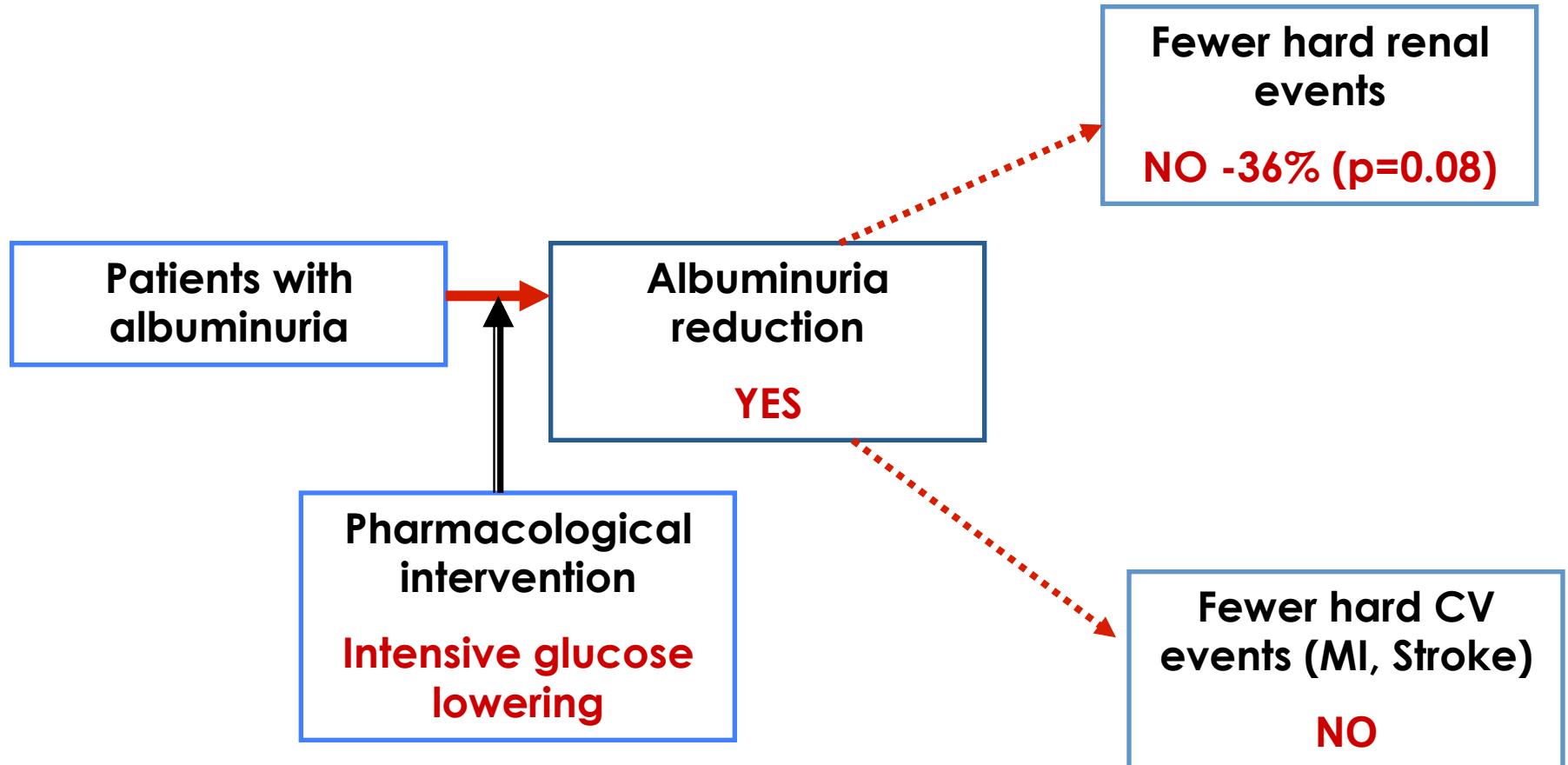


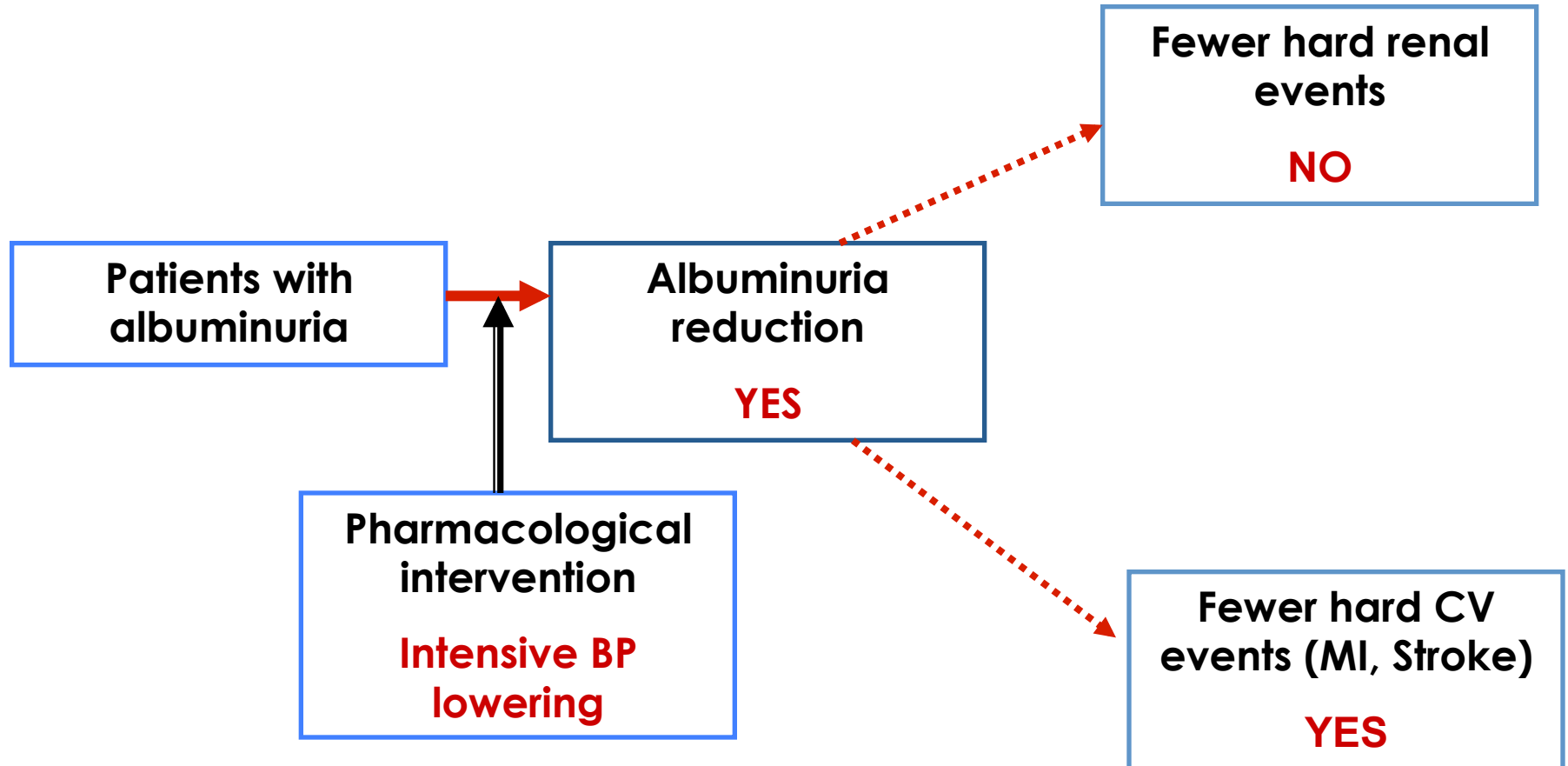
Table 2 | Effects of intensive compared with standard glucose control on albuminuria

Outcome	Intensive, n (%)	Standard, n (%)	Hazard ratio (95% confidence interval)	P-value
New-onset microalbuminuria	1318 (33.5)	1434 (36.3)	0.91 (0.85–0.98)	0.012
New-onset macroalbuminuria	162 (3.0)	231 (4.3)	0.70 (0.57–0.85)	0.0004
Progression of albuminuria by ≥ 1 stage ^a	1298 (23.3)	1410 (25.3)	0.90 (0.84–0.97)	0.0077
Regression of albuminuria by ≥ 1 stage ^b	1003 (61.2)	914 (56.3)	1.15 (1.05–1.26)	0.0020
Regression to normoalbuminuria	922 (56.3)	814 (50.2)	1.20 (1.09–1.31)	0.0002

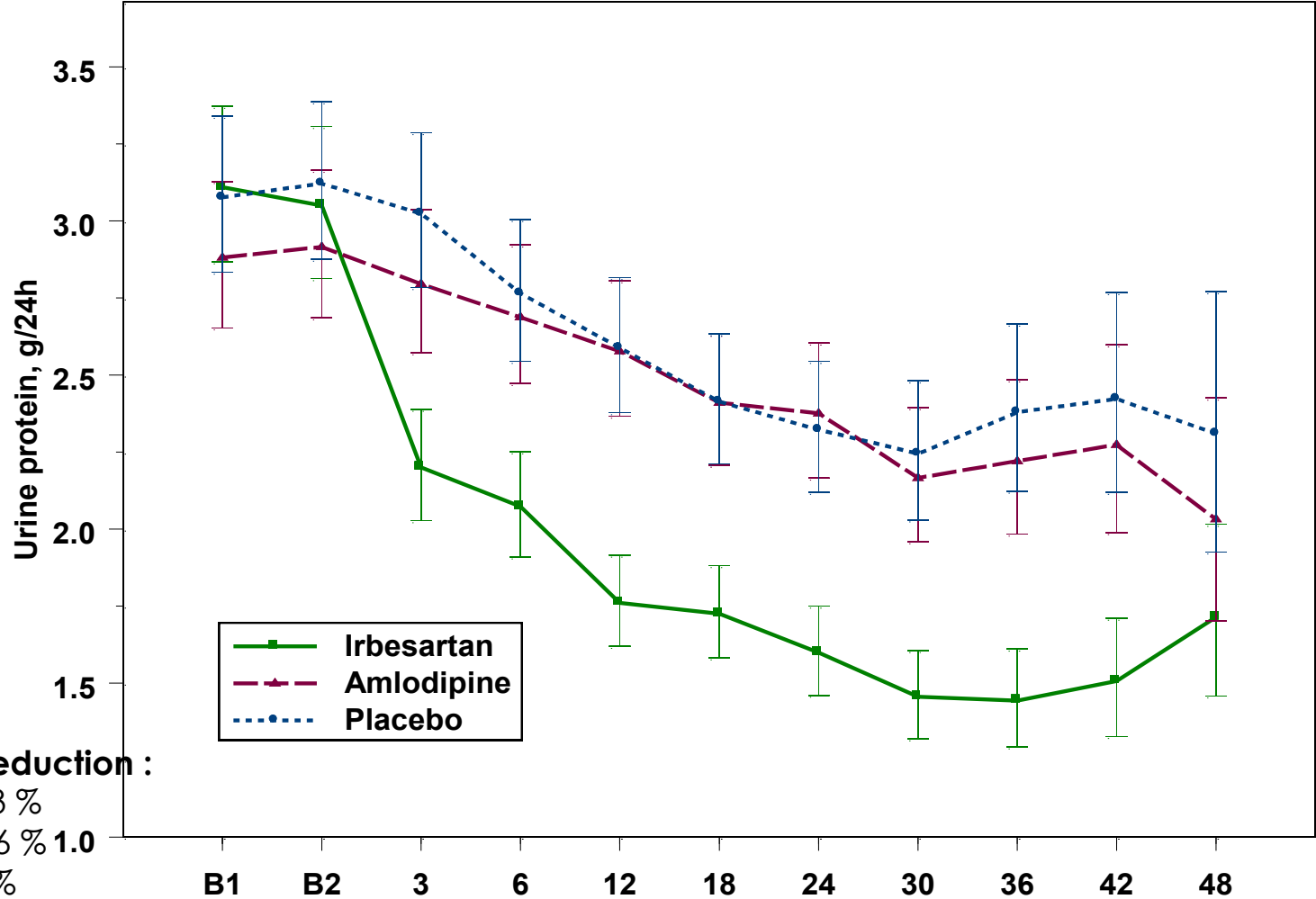
ADVANCE



ADVANCE



Geometric Mean 24 hour Urine Protein by Follow-up Visit
Corrected for Missing Data



Proteinuria reduction :
Irbesartan 33 %
Amlodipine 6 %
Placebo 10 %

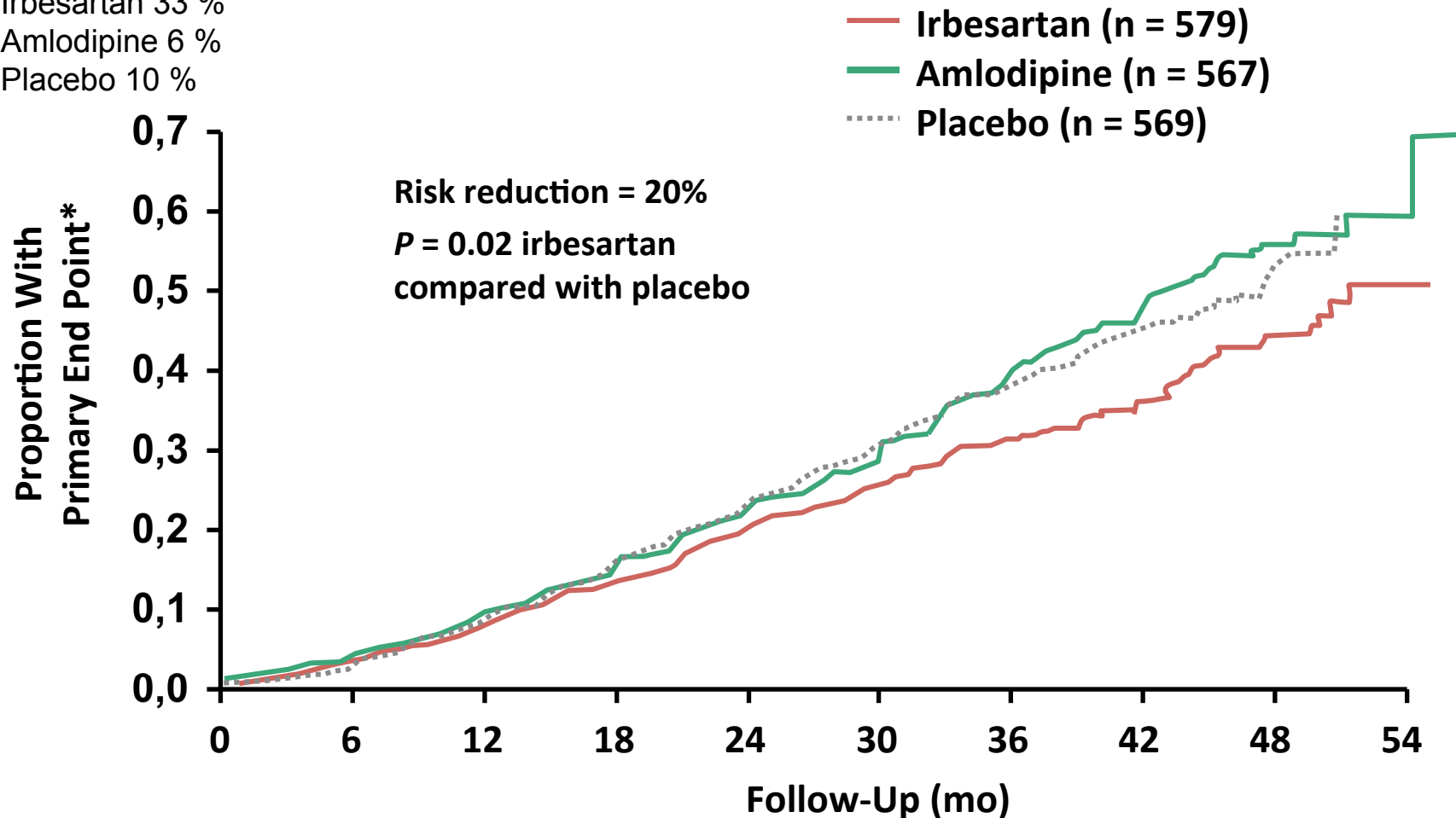
IDNT Study Demonstrates 20% Risk Reduction With Irbesartan Treatment

Proteinuria reduction :

Irbesartan 33 %

Amlodipine 6 %

Placebo 10 %



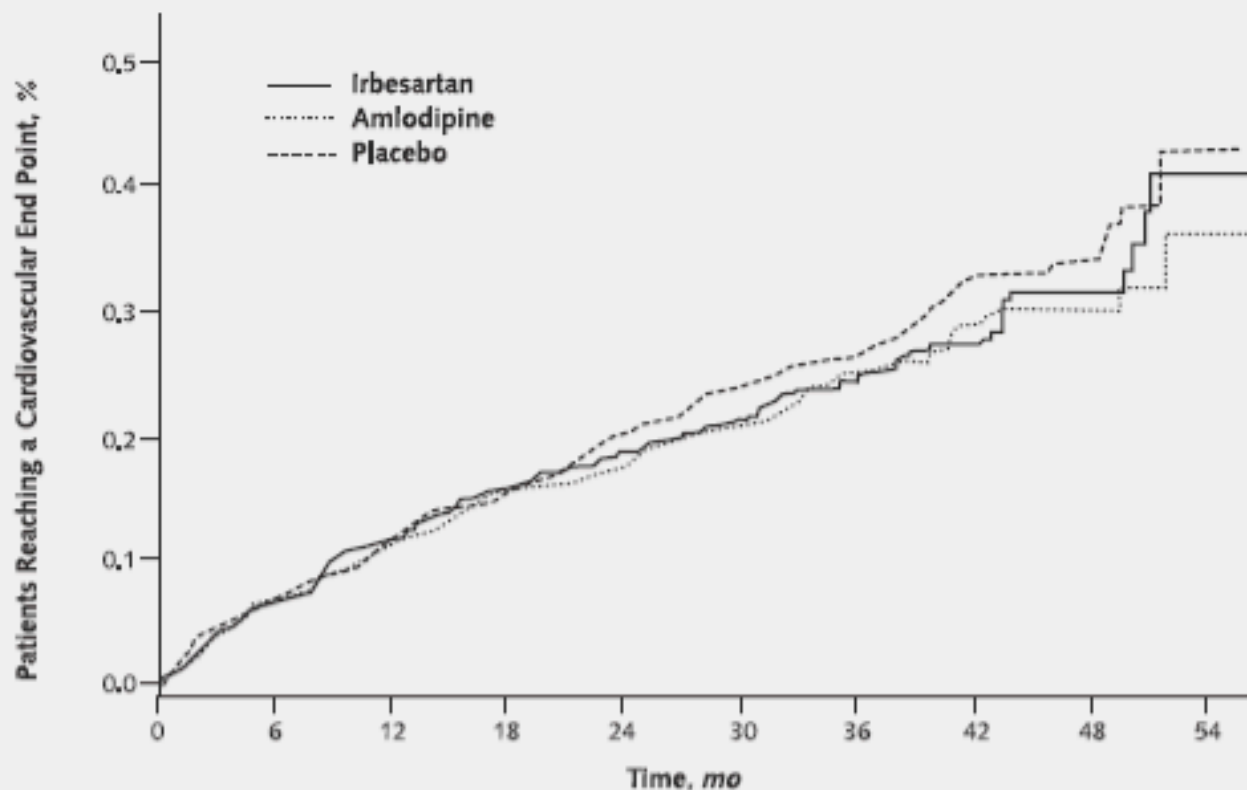
IDNT = Irbesartan in Diabetic Nephropathy Trial.

*Composite of a doubling of SCr, ESRD, or death.

Lewis et al for the Collaborative Study Group. *N Engl J Med.* 2001;345:851-860.

Cardiovascular Outcomes in the Irbesartan Diabetic Nephropathy Trial of Patients with Type 2 Diabetes and Overt Nephropathy

Tomas Berl, MD; Lawrence G. Hunsicker, MD; Julia B. Lewis, MD; Marc A. Pfeffer, MD, PhD; Jerome G. Porush, MD; Jean-Lucien Rouleau, MD; Paul L. Drury, MD, FRACP; Enric Esmatjes, MD; Donald Hricik, MD; Chirag R. Parikh, MD; Itamar Raz, MD; Philippe Vanhille, MD; Thomas B. Wiegmann, MD; Bernard M. Wolfe, MD, FRCPC; Francesco Locatelli, MD; Samuel Z. Goldhaber, MD; and Edmund J. Lewis, MD, for the Collaborative Study Group*



Patients at Risk, *n*

Irbesartan	579	528	486	449	368	282	194	133	59	4
Amlodipine	567	515	473	432	358	263	178	123	44	5
Placebo	569	519	475	432	359	258	172	111	43	2

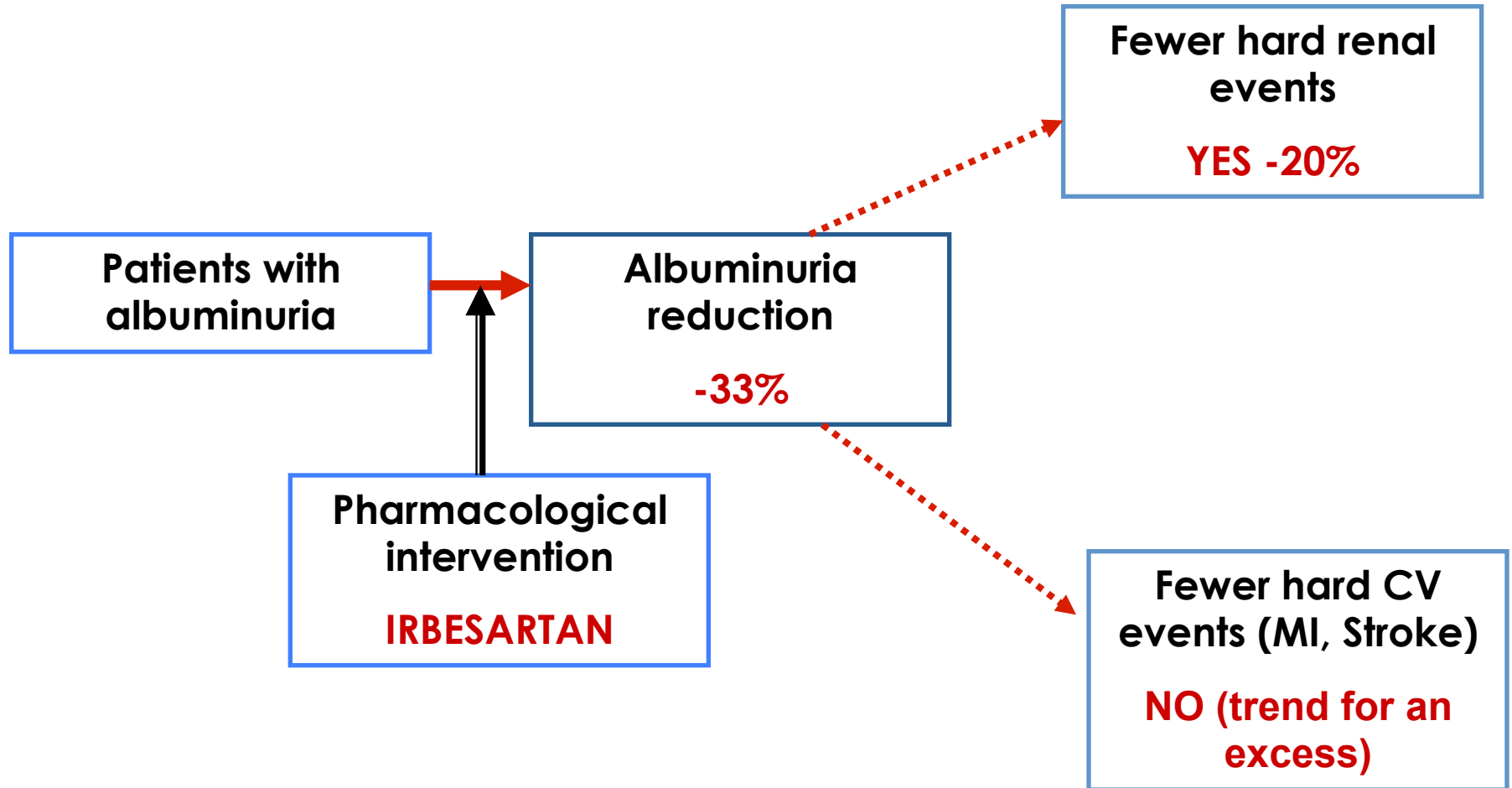
Table 3. Risk for Cardiovascular Outcomes by Treatment Group*

Cardiovascular Event	Events/Patients			Hazard Ratio (95% CI)†	P Value
	Irbesartan Group (n = 579)	Amlodipine Group (n = 567)	Placebo Group (n = 569)		
	$\longleftrightarrow n/n \longleftrightarrow$				
Cardiovascular composite	259/172	278/161	284/185		
Irbesartan vs. placebo				0.90 (0.74–1.10)	>0.2
Amlodipine vs. placebo				1.00 (0.83–1.21)	>0.2
Irbesartan vs. amlodipine				0.90 (0.74–1.10)	>0.2
Cardiovascular death	52/52	37/37	46/46		
Irbesartan vs. placebo				1.08 (0.72–1.60)	>0.2
Amlodipine vs. placebo				0.79 (0.51–1.22)	>0.2
Irbesartan vs. amlodipine				1.36 (0.89–2.07)	0.155
Congestive heart failure	80/60	143/93	113/72		
Irbesartan vs. placebo				0.72 (0.52–1.00)	0.048
Amlodipine vs. placebo				1.11 (0.83–1.50)	>0.2
Irbesartan vs. amlodipine				0.65 (0.48–0.87)	0.004
Myocardial infarction	48/44	29/27	51/46		
Irbesartan vs. placebo				0.90 (0.60–1.33)	>0.2
Amlodipine vs. placebo				0.58 (0.37–0.92)	0.021
Irbesartan vs. amlodipine				1.54 (0.97–2.45)	0.068
Cerebrovascular accident	30/28	18/15	28/26		
Irbesartan vs. placebo				1.01 (0.61–1.67)	>0.2
Amlodipine vs. placebo				0.65 (0.35–1.22)	0.18
Irbesartan vs. amlodipine				1.55 (0.84–2.87)	0.165
Cardiac revascularization	31/27	32/28	39/36		
Irbesartan vs. placebo				0.80 (0.49–1.30)	>0.2
Amlodipine vs. placebo				0.86 (0.54–1.38)	>0.2
Irbesartan vs. amlodipine				0.93 (0.55–1.55)	>0.2

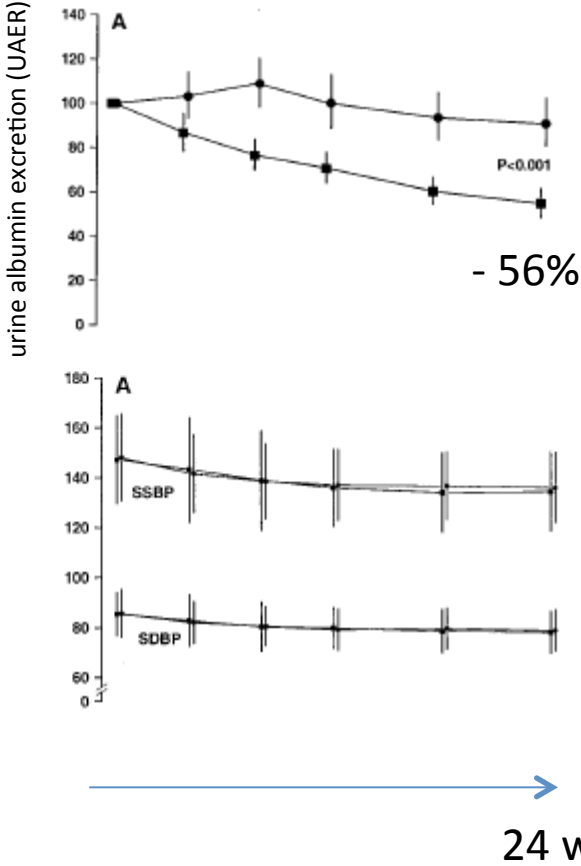
* All patients received conventional antihypertensive therapy that was initiated with irbesartan, amlodipine, or placebo.

† Hazard ratio for cardiovascular death (single end point) was estimated by using proportional hazards (Cox) regression modeling. Risk for subsequent events was estimated by using the counting process method of Anderson and Gill as modified by Lee et al. (18) to account for possible correlation of risk for events within patients.

IDNT



Microalbuminuria Reduction With Valsartan in Patients With Type 2 Diabetes Mellitus A Blood Pressure–Independent Effect

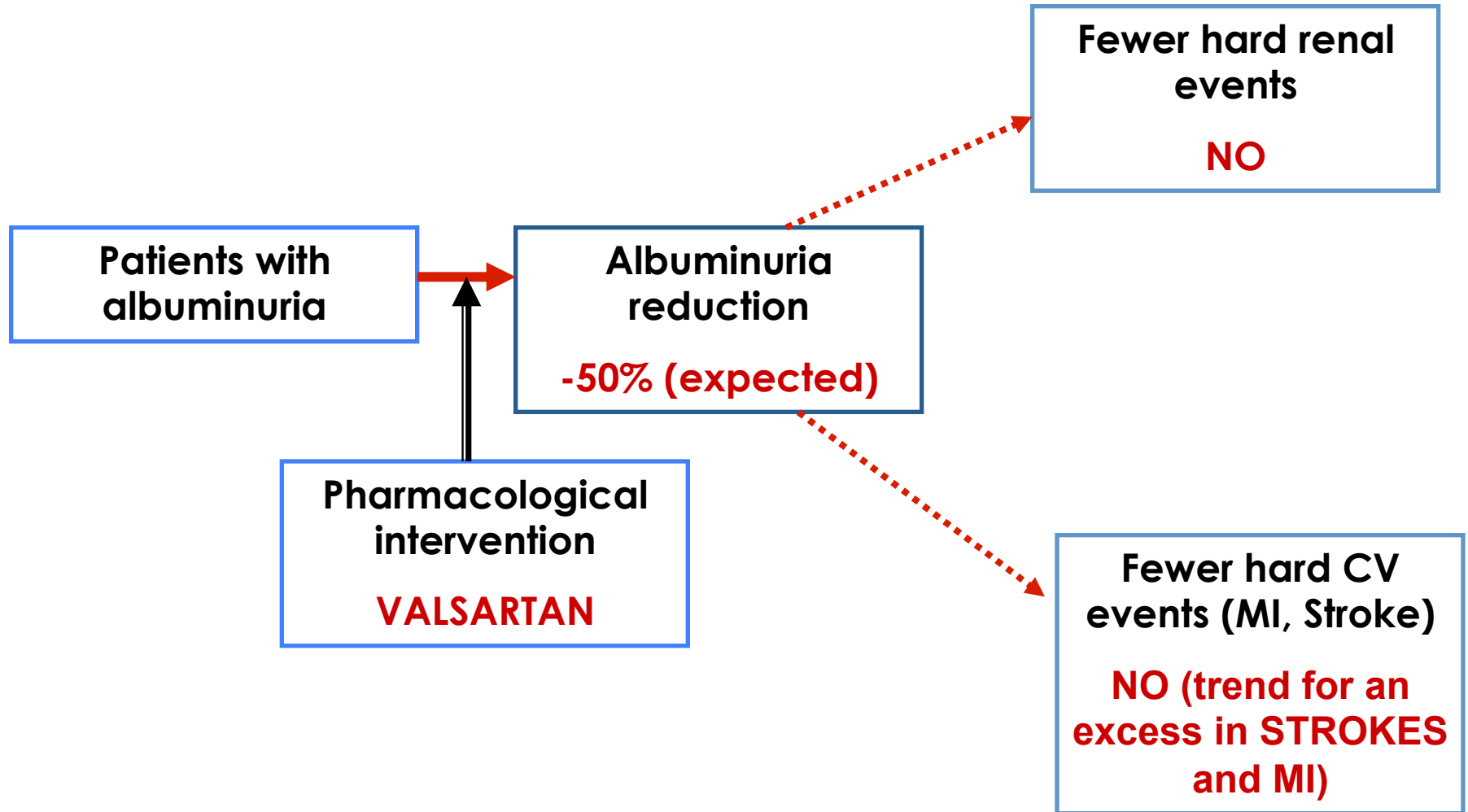


Outcomes in subgroups of hypertensive patients treated with regimens based on valsartan and amlodipine: an analysis of findings from the VALUE trial

Baseline variable		ΔSBP/DBP (V-A) mmHg	Valsartan %	Amlodipine %	HR (95% CI)	P
Smoking status	No (n = 11581)	2.32/1.58	10.9	10.9		0.879
	Yes (n = 3664)	1.46/1.51	9.6	8.7		0.207
Diabetes	No (n = 10422)	2.02/1.43	8.7	8.4		0.536
	Yes (n = 4823)	2.16/1.70	14.7	14.6		0.528
Cholesterol > 240 mg/dl	No (n = 10168)	2.17/1.54	11.1	10.7		0.366
	Yes (n = 5077)	2.13/1.52	9.6	9.8		0.936
LVH	No (n = 12473)	1.93/1.53	9.7	9.7		0.840
	Yes (n = 2772)	3.12/1.50	14.6	13.6		0.285
Proteinuria	No (n = 11810)	2.09/1.43	10.3	10.1		0.571
	Yes (n = 3435)	2.46/2.07	11.6	11.5		0.543
S. Creatinine > 1.7 mg/dl	No (n = 14695)	2.19/1.55	10.2	10.0		0.443
	Yes (n = 530)	0.70/0.70	19.7	21.9		0.670
CHD	No (n = 8264)	2.18/1.58	8.5	8.1		0.556
	Yes (n = 6981)	2.18/1.55	13.1	13.0		0.684
Stroke	No (n = 12231)	2.14/1.56	10.4	10.1		0.440
	Yes (n = 3014)	2.80/1.58	11.2	11.5		0.962
PAD	No (n = 13131)	2.23/1.59	10.1	9.9		0.528
	Yes (n = 2114)	1.69/1.09	13.4	13.6		0.633
ISH	No (n = 13217)	1.91/1.49	10.2	9.8		0.293
	Yes (n = 2025)	3.18/1.70	12.8	14.5		0.484

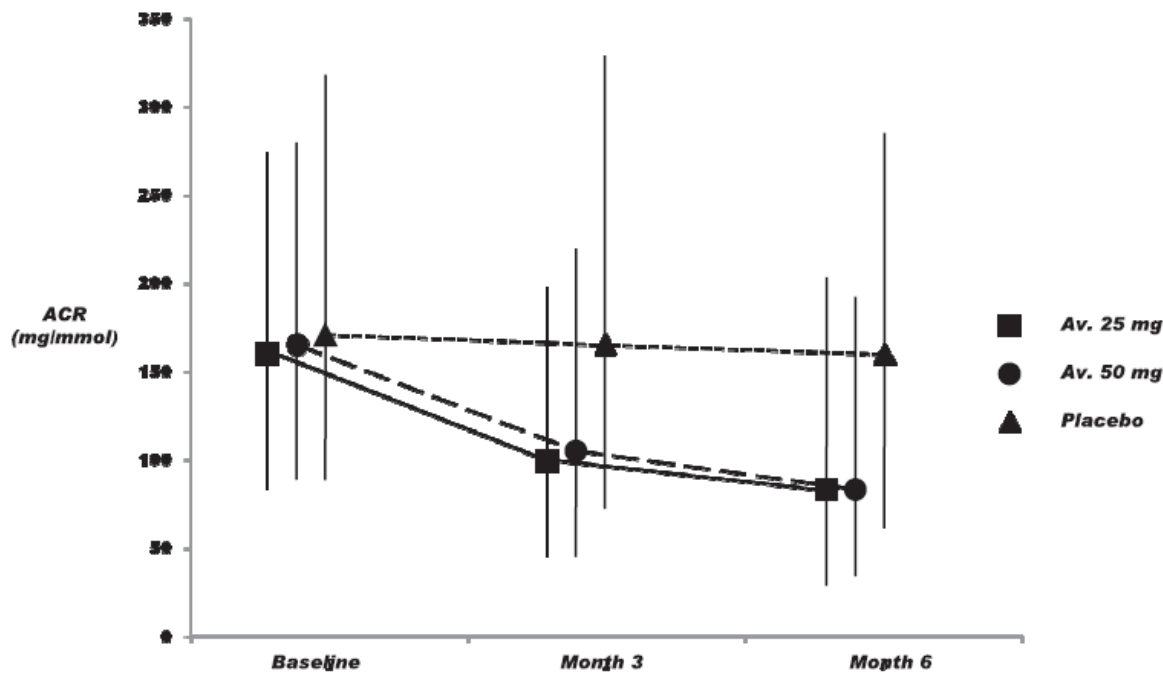
Primary endpoint (composite cardiac mortality and morbidity) in various subgroups of patients.

VALUE



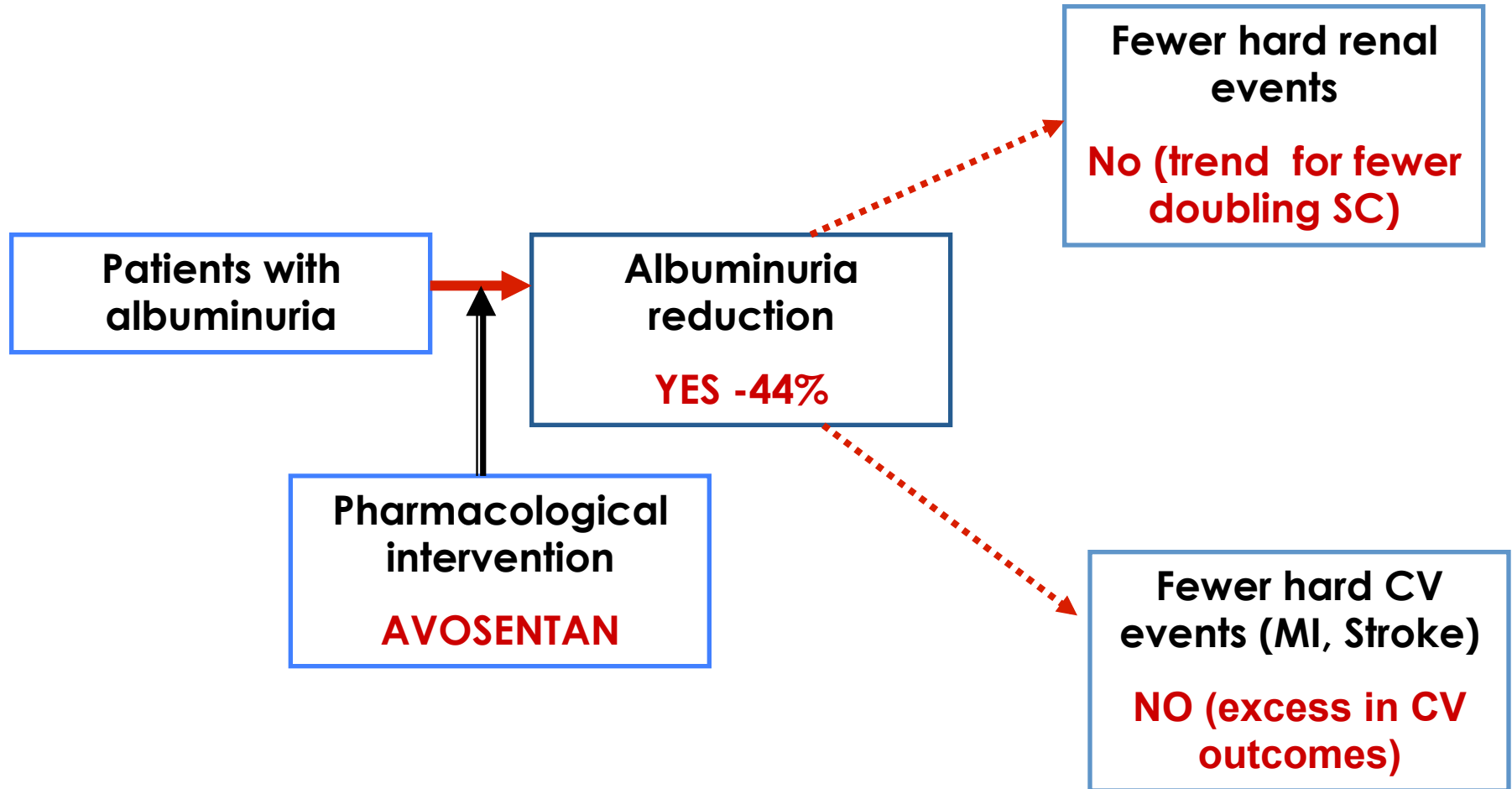
Avosentan for Overt Diabetic Nephropathy

Johannes F.E. Mann,^{*} Damian Green,[†] Kenneth Jamerson,[‡] Luis M. Ruilope,[§]
Susan J. Kuranoff,^{||} Thomas Littke,^{||} and Giancarlo Viberti,[¶] for the ASCEND Study Group



Parameter	Avosentan 25 mg (n = 455)	Avosentan 50 mg (n = 478)	Placebo (n = 459)	P	
				Avosentan 25 mg versus placebo	Avosentan 50 mg versus placebo
Primary composite outcome	37 (8.1)	41 (8.6)	44 (9.6)	0.557	0.791
death	21 (4.6) ^a	17 (3.6)	12 (2.6)	0.225	0.194
ESRD	20 (4.4)	24 (5.0)	30 (6.5)	0.136	0.405
doubling of serum creatinine	2 (0.4)	4 (0.8)	9 (2.0)	0.405	0.060
Cardiovascular outcome	68 (14.9)	71 (14.9)	47 (10.2)	0.049	0.089
CHF	27 (5.9)	29 (6.1)	10 (2.2)	0.008	0.050

ASCEND



Renal outcomes with different fixed-dose combination therapies in patients with hypertension at high risk for cardiovascular events (ACCOMPLISH): a prespecified secondary analysis of a randomised controlled trial

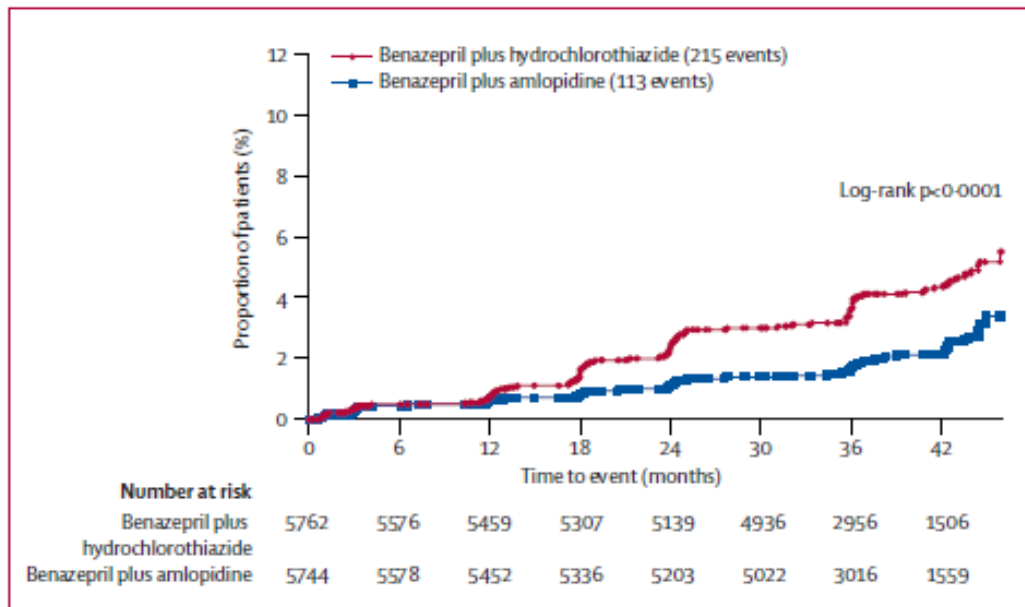
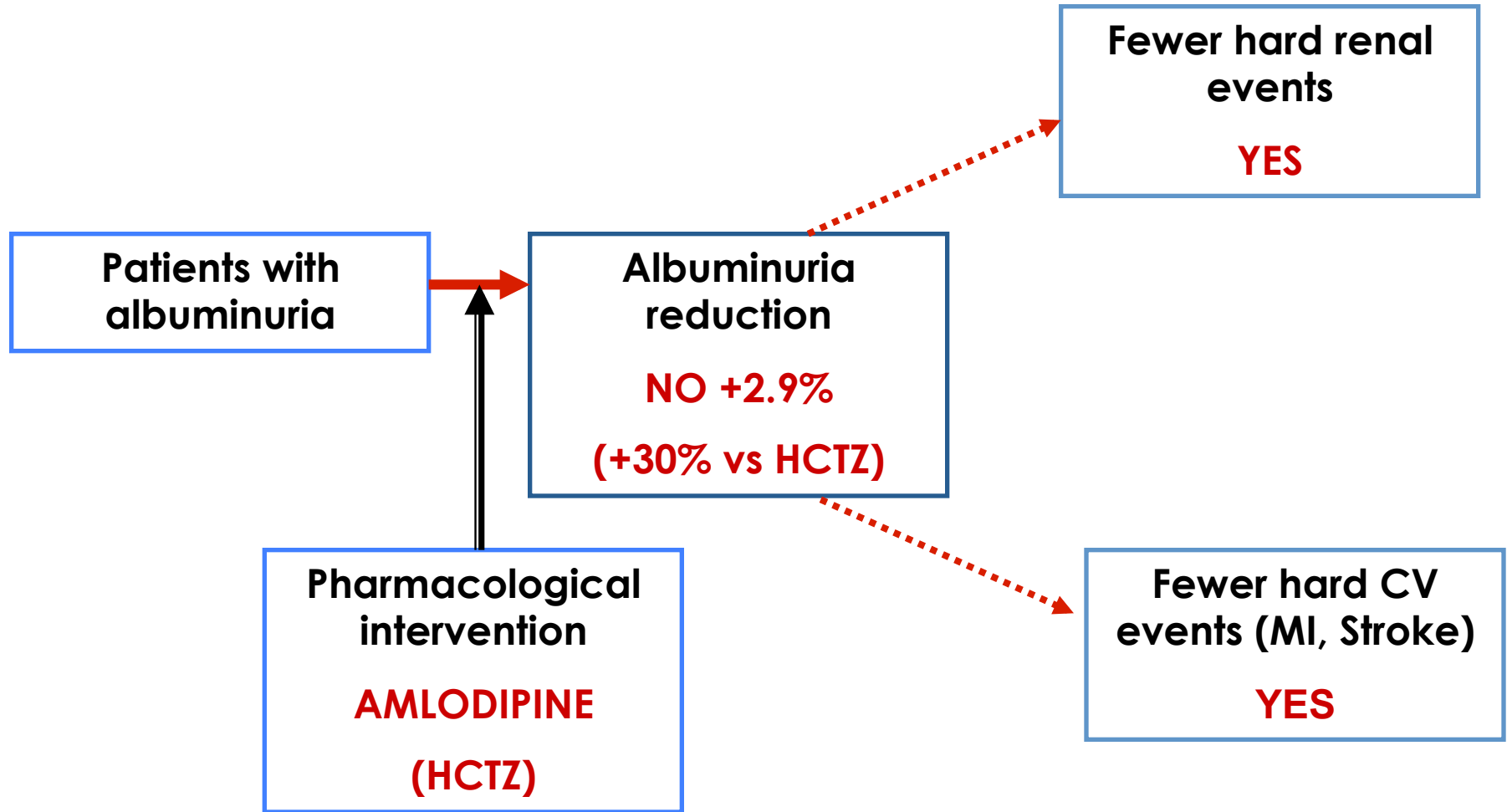


Figure 1: Kaplan-Meier curves for progression of chronic kidney disease for the intention-to-treat population
Progression of chronic kidney disease was defined as doubling of serum creatinine concentration, estimated glomerular filtration rate less than 15 mL/min/1.73 m², or need for dialysis.

At the final visit, a **reduction** in UACR from baseline was noted in the benazepril plus hydrochlorothiazide group (median change –26.8%) whereas **an increase** was seen in the benazepril plus amlodipine group (median change 2.9%);
 $p=0.0001$ for ratio of log mean change from baseline).

ACCOMPLISH



Effects of olmesartan on renal and cardiovascular outcomes in type 2 diabetes with overt nephropathy: a multicentre, randomised, placebo-controlled study

E. Imai • J. C. N. Chan • S. Ito • T. Yamasaki •
F. Kobayashi • M. Haneda • H. Makino •
for the ORIENT study investigators

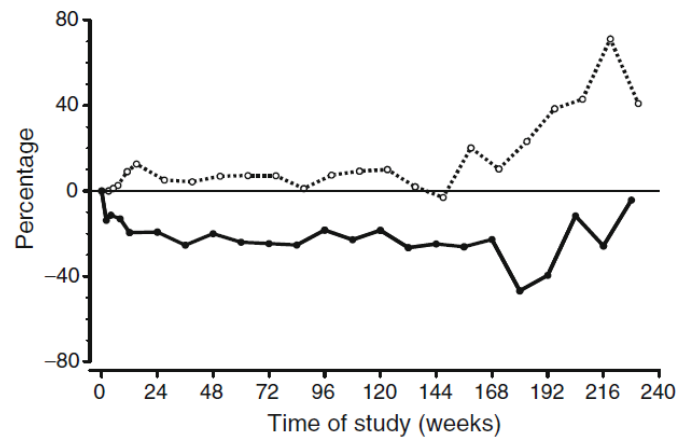


Fig. 3 Changes in proteinuria expressed as percentage change of urinary protein/creatinine ratio from baseline during treatment with olmesartan or placebo in type 2 diabetic patients with overt proteinuria and renal insufficiency. Solid line, black circles, olmesartan; dashed line, white circles, placebo. $p=0.005$

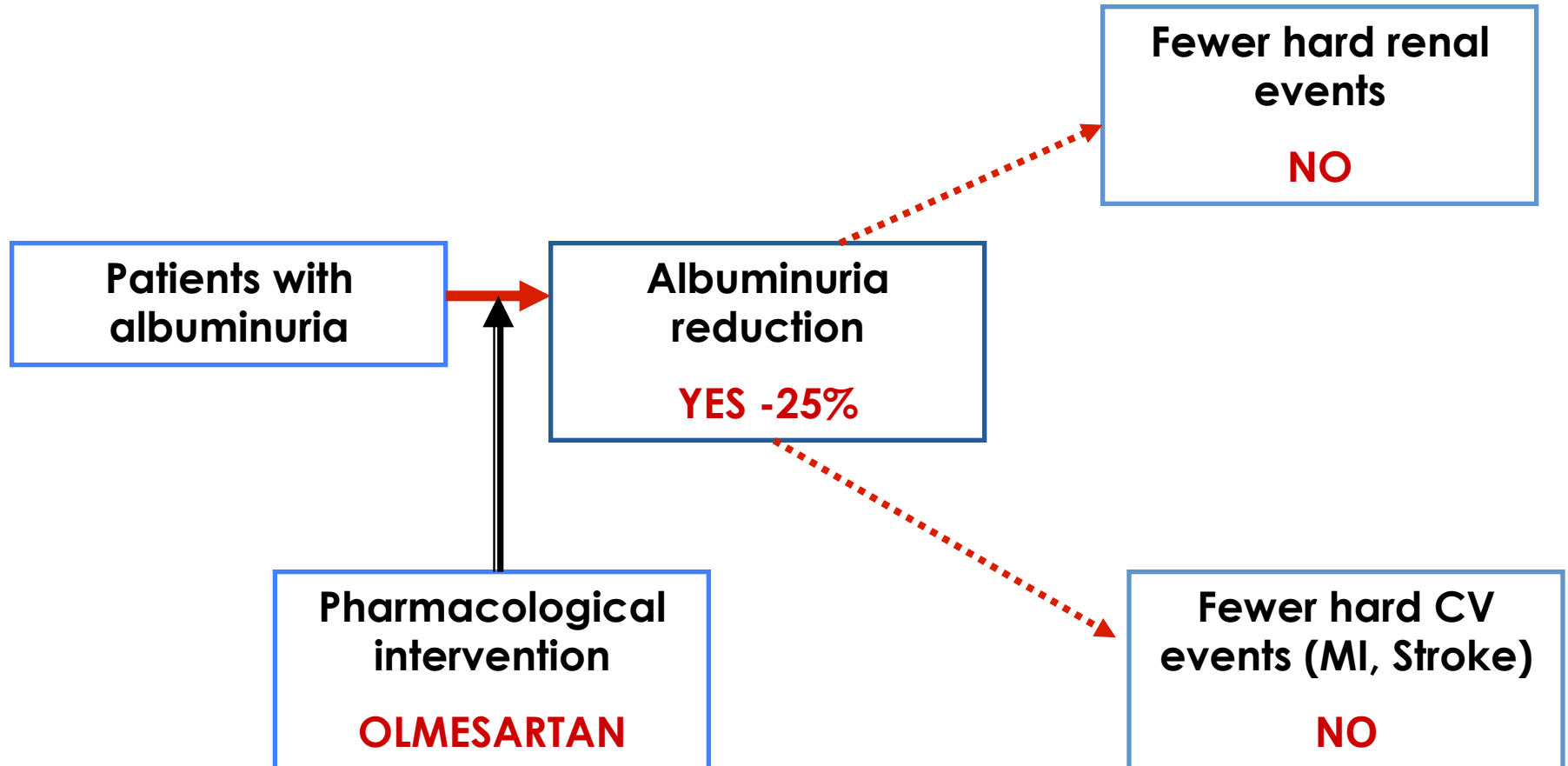
Outcome	<i>n</i> (%)		Olmesartan vs placebo
	Olmesartan	Placebo	HR (95% CI) (covariates: SCr, ACR and region)
All patients group (olmesartan <i>n</i> =282, placebo <i>n</i> =284)			
Renal composite outcome	116 (41.1)	129 (45.4)	0.97 (0.75, 1.24) [†]
Doubling of SCr	106 (37.6)	120 (42.3)	0.94 (0.73, 1.23)
ESRD	74 (26.2)	78 (27.5)	1.08 (0.78, 1.49)
Death from any cause	19 (6.7)	20 (7.0)	0.99 (0.53, 1.86)

Table 3 HR of secondary composite cardiovascular outcomes in type 2 diabetic patients with overt proteinuria and renal insufficiency treated with olmesartan or matching placebo during a 3.2 year study period

Outcome	n (%)		Olmesartan vs placebo	
	Olmesartan	Placebo	HR (95% CI) (covariates: ACR and age)	Adjusted HR (95% CI) (covariates: ACR, age and cardiovascular history)
All patients group (olmesartan $n=282$, placebo $n=284$)				
Cardiovascular composite outcome	40 (14.2)	53 (18.7)	0.73 (0.48, 1.09) [†]	0.64 (0.43, 0.98) [‡]
Cardiovascular death	10 (3.5)	3 (1.1)	3.38 (0.93, 12.29)	2.81 (0.76, 10.38)
Non-fatal stroke	8 (2.8)	11 (3.9)	0.73 (0.29, 1.82)	0.73 (0.29, 1.85)
Non-fatal myocardial infarction	3 (1.1)	7 (2.5)	0.43 (0.11, 1.66)	0.45 (0.11, 1.75)
Hospitalisation with unstable angina	5 (1.8)	3 (1.1)	1.67 (0.40, 6.98)	1.37 (0.31, 6.00)
Hospitalisation with heart failure	18 (6.4)	25 (8.8)	0.71 (0.39, 1.30)	0.59 (0.32, 1.10)
Coronary, carotid or peripheral revascularisation	8 (2.8)	21 (7.4)	0.37 (0.16, 0.84)	0.35 (0.15, 0.80)
Amputation	4 (1.4)	0 (0.0)	— (—)	— (—)

[†] $p=0.126$, [‡] $p=0.039$

ORIENT



Cardiovascular and Renal Outcomes With Telmisartan, Ramipril, or Both in People at High Renal Risk

Results From the ONTARGET and TRANSCEND Studies

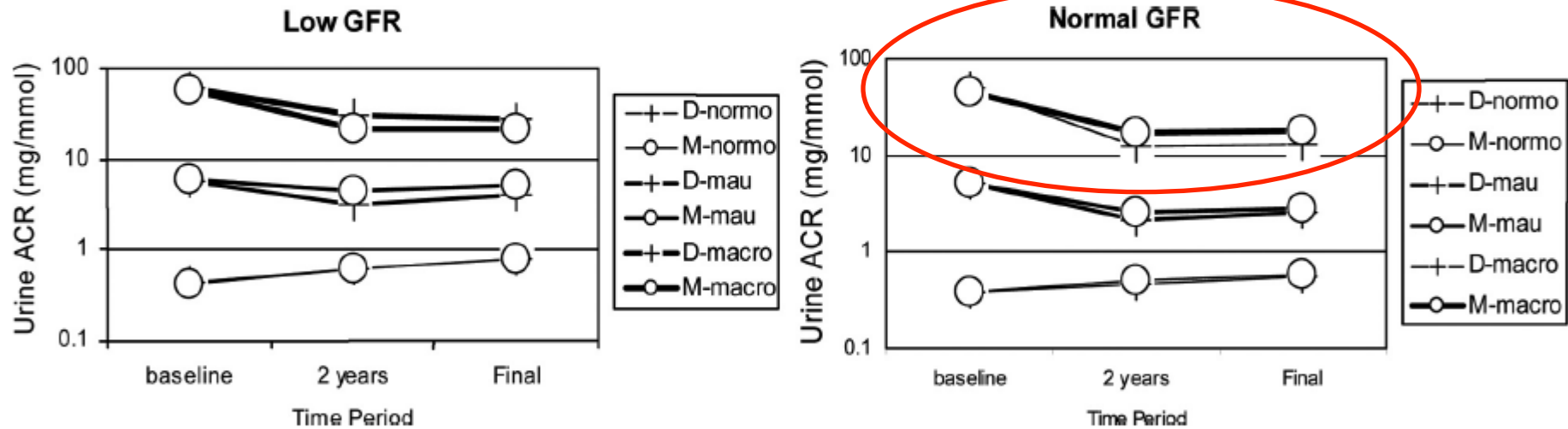


Figure 2. Change of albumin-to-creatinine ratio (ACR) at different time periods for estimated glomerular filtration rate (GFR) ≥ 60 mL/min per 1.73 m² (right) or < 60 mL/min per 1.73 m² (left). Normo indicates normoalbuminuria; mau, microalbuminuria; macro, macroalbuminuria; D, dual therapy; and M, monotherapy.

In patients with normal GFR, ACR fell more from baseline with dual therapy compared with monotherapy at 2 years.

(0.91 ratio of dual therapy/monotherapy; 95% CI, 0.86 to 0.96; $P < 0.001$)

Cardiovascular and Renal Outcomes With Telmisartan, Ramipril, or Both in People at High Renal Risk

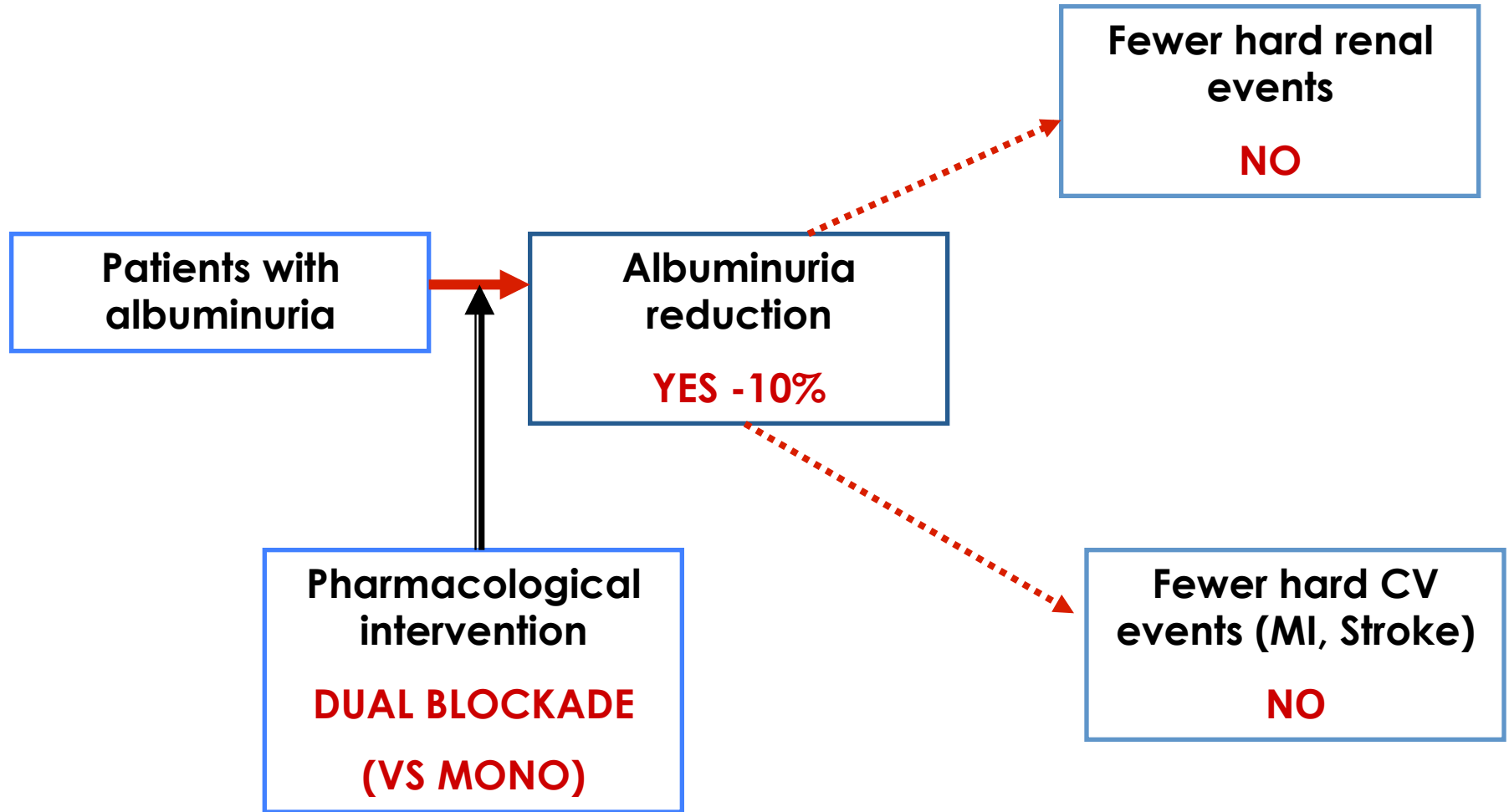
Results From the ONTARGET and TRANSCEND Studies

Table 2. ONTARGET: Major Outcomes Comparing Dual Therapy With Monotherapy

Outcome	Comparison Subgroup	Dual Therapy vs Monotherapy						
		Absolute Number (Rate/100 Person-Years)			Hazard Ratio (95% CI)			
		GFR ≥60 mL/min per 1.73 m ²	GFR <60 mL/min per 1.73 m ²	All	GFR ≥60 mL/min per 1.73 m ²	GFR <60 mL/min per 1.73 m ²	All	
Chronic dialysis or doubling of creatinine	Normoalbuminuria	71/4833 (0.32) vs 121/9656 (0.27)	13/1269 (0.23) vs 19/2568 (0.16)	84/6102 (0.30) vs 140/12224 (0.25)	1.18 (0.88–1.59)	1.40 (0.69–2.83)	1.21 (0.93–1.59)	P2=0.88
	Microalbuminuria	28/856 (0.74) vs 49/1775 (0.62)	15/411 (0.87) vs 27/767 (0.83)	43/1267 (0.78) vs 76/2542 (0.68)	1.20 (0.76–1.92)	1.84 (0.55–1.95)	1.15 (0.79,1.67)	
	Macroalbuminuria	12/216 (1.32) vs 32/463 (1.64)	36/191 (4.77) vs 46/417 (2.84)	48/407 (2.89) vs 78/880 (2.19)	0.81 (0.42–1.58)	1.63 (1.05–2.51)	1.31 (0.91,1.87)	
	All	111/5905 (0.41) vs 202/11894 (0.37)	64/1871 (0.79) vs 92/3752 (0.56)	175/7776 (0.50) vs 294/15646 (0.42)	1.12 (0.89–1.41)	1.46 (1.02–1.93)	1.21 (1.00–1.46)	
P1=0.27								P3=0.62
Chronic dialysis	Normoalbuminuria	2/4833 (0.01) vs 1/9656 (0.00)	3/1269 (0.05) vs 5/2568 (0.04)	5/6102 (0.02) vs 6/15646 (0.01)	4.02 (0.36–44.3)	1.23 (0.29–5.16)	1.68 (0.51–5.51)	P2=0.55
	Microalbuminuria	1/856 (0.03) vs 0/1775 (0.00)	4/411 (0.23) vs 13/767 (0.40)	5/1267 (0.09) vs 13/2542 (0.12)		0.58 (0.19–1.77)	0.78 (0.28–2.18)	
	Macroalbuminuria	2/216 (0.22) vs 9/463 (0.46)	21/191 (2.74) vs 26/417 (1.57)	23/407 (1.36) vs 35/880 (0.96)	0.48 (0.10–2.21)	1.69 (0.95–3.00)	1.39 (0.82–2.36)	
	All	5/5905 (0.02) vs 10/11894 (0.02)	28/1871 (0.34) vs 44/3752 (0.27)	33/7776 (0.09) vs 54/15646 (0.08)	1.01 (0.35–2.96)	1.28 (0.80–2.06)	1.24 (0.80–1.91)	
P1=0.69								P3=0.37
Doubling of creatinine	Normoalbuminuria	70/4833 (0.32) vs 121/9656 (0.27)	12/1269 (0.21) vs 14/2568 (0.12)	82/6102 (0.30) vs 135/12224 (0.24)	1.17 (0.87–1.57)	1.75 (0.81–3.78)	1.23 (0.93–1.62)	P2=0.98
	Microalbuminuria	27/856 (0.71) vs 49/1775 (0.62)	13/411 (0.75) vs 19/767 (0.58)	40/1267 (0.72) vs 68/2542 (0.61)	1.16 (0.73–1.86)	1.28 (0.63–2.59)	1.20 (0.81–1.77)	
	Macroalbuminuria	12/216 (1.32) vs 28/463 (1.43)	22/191 (2.84) vs 30/417 (1.82)	34/407 (2.02) vs 58/880 (1.61)	0.94 (0.48–1.84)	1.50 (0.87–2.61)	1.24 (0.81–1.90)	
	All	109/5905 (0.41) vs 198/11894 (0.36)	47/1871 (0.57) vs 63/3752 (0.38)	156/7776 (0.45) vs 261/15646 (0.37)	1.12 (0.89–1.42)	1.50 (1.03–2.19)	1.21 (1.00–1.48)	
P1=0.20								P3=0.83
Primary cardiovascular outcome	Normoalbuminuria	619/4833 (2.90) vs 1206/9656 (2.82)	230/1269 (4.27) vs 490/2568 (4.49)	849/6102 (3.18) vs 1696/12224 (3.16)	1.03 (0.94–1.14)	0.95 (0.81–1.11)	1.01 (0.93–1.09)	P2=0.60
	Microalbuminuria	175/856 (4.92) vs 379/1775 (5.10)	127/411 (8.11) vs 221/767 (7.43)	302/1267 (5.89) vs 600/2542 (5.76)	0.96 (0.81–1.15)	1.09 (0.88–1.36)	1.02 (0.89–1.17)	
	Macroalbuminuria	55/216 (6.39) vs 135/463 (7.58)	66/191 (9.25) vs 147/417 (9.61)	121/407 (7.69) vs 282/880 (8.52)	0.84 (0.62–1.16)	0.96 (0.72–1.28)	0.90 (0.73–1.12)	
	All	849/5905 (3.3) vs 1720/11894 (3.31)	423/1871 (5.52) vs 858/3752 (5.56)	1272/7776 (3.81) vs 2578/15646 (3.82)	1.00 (0.92–1.08)	0.99 (0.88–1.12)	1.00 (0.93–1.07)	
P1=0.95								P3=0.74
Cardiovascular death	Normoalbuminuria	242/4833 (1.09) vs 431/9656 (0.96)	120/1269 (2.11) vs 222/2568 (1.91)	362/6102 (1.30) vs 653/12224 (1.16)	1.13 (0.96–1.32)	1.11 (0.89–1.38)	1.12 (0.98–1.27)	P2=0.14
	Microalbuminuria	73/856 (1.90) vs 154/1775 (1.92)	60/411 (3.43) vs 110/767 (3.34)	133/1267 (2.38) vs 264/2542 (2.33)	0.99 (0.75–1.31)	1.03 (0.75–1.41)	1.02 (0.83–1.26)	
	Macroalbuminuria	28/216 (3.03) vs 69/463 (3.48)	36/191 (4.56) vs 99/417 (5.85)	64/407 (3.73) vs 168/880 (4.57)	0.87 (0.56–1.35)	0.77 (0.53–1.13)	0.81 (0.61–1.09)	
	All	343/5905 (1.27) vs 654/11894 (1.20)	216/1871 (2.63) vs 431/3752 (2.59)	559/7776 (1.59) vs 1085/15646 (1.52)	1.06 (0.93–1.21)	1.01 (0.86–1.19)	1.04 (0.94–1.16)	
P1=0.66								P3=0.50
All death	Normoalbuminuria	436/4833 (1.96) vs 784/9656 (1.75)	192/1269 (3.38) vs 342/2568 (2.94)	628/6102 (2.25) vs 1126/12224 (2.00)	1.12 (0.99–1.26)	1.15 (0.96–1.37)	1.13 (1.02–1.24)	P2=0.03
	Microalbuminuria	129/856 (3.36) vs 251/1775 (3.13)	97/411 (5.55) vs 168/767 (5.10)	226/1267 (4.04) vs 419/2542 (3.70)	1.07 (0.87–1.33)	1.09 (0.85–1.40)	1.09 (0.93–1.29)	
	Macroalbuminuria	46/216 (4.97) vs 120/463 (6.04)	56/191 (7.09) vs 152/417 (8.98)	102/407 (5.95) vs 272/880 (7.39)	0.82 (0.59–1.16)	0.78 (0.58–1.06)	0.80 (0.64–1.01)	
	All	611/5905 (2.26) vs 1155/11894 (2.11)	345/1871 (4.20) vs 662/3752 (3.98)	956/7776 (2.71) vs 1817/15646 (2.55)	1.07 (0.97–1.18)	1.05 (0.93–1.20)	1.07 (0.99–1.15)	
P1=0.84								P3=0.19

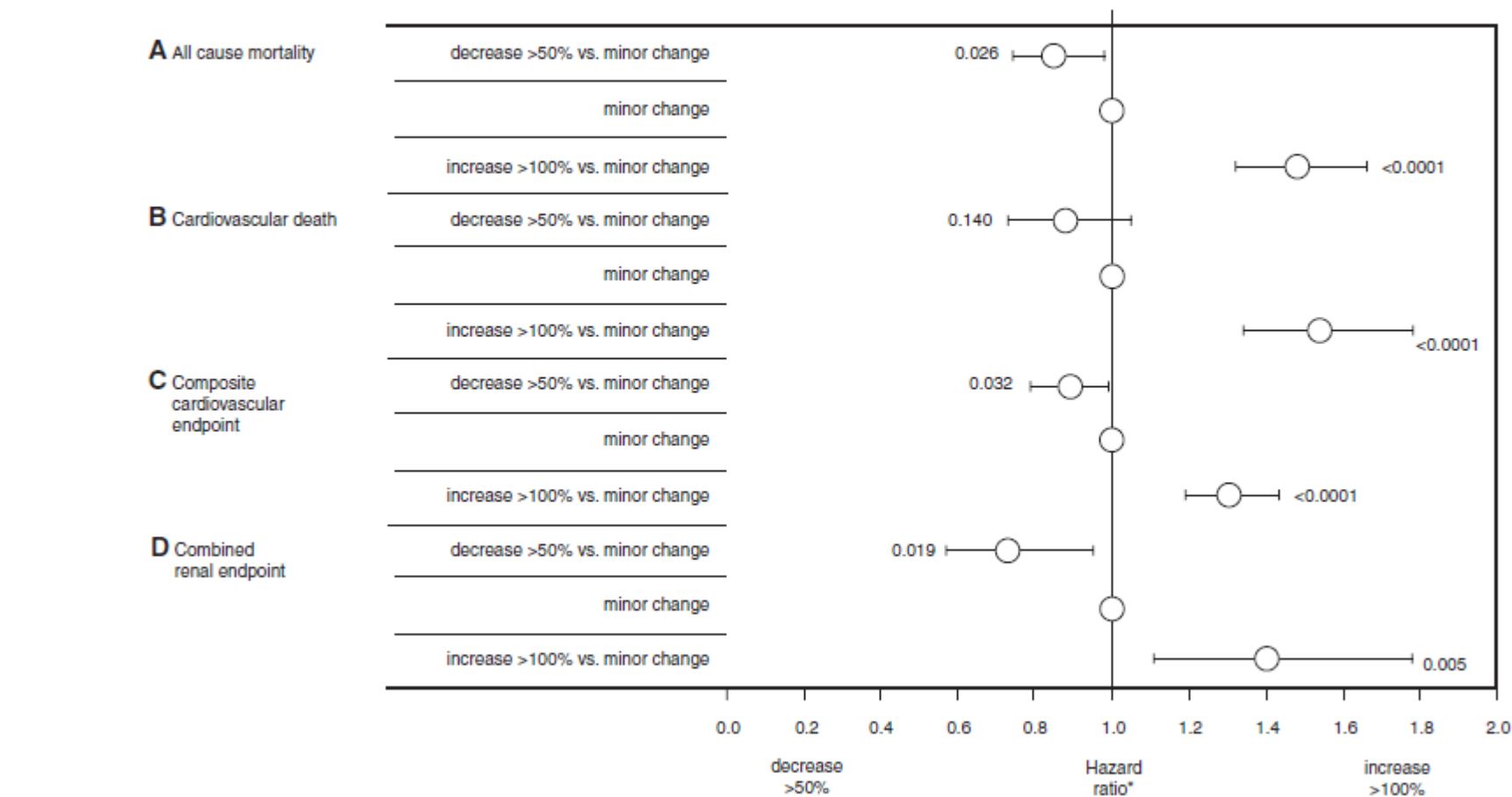
ONTARGET indicates Ongoing Telmisartan Alone and in Combination With Ramipril Global End Point Trial; GFR, glomerular filtration rate; CI, confidence interval; P1, effect of treatment difference according to estimated GFR; P2, effect of treatment difference according to albuminuria; and P3, effect of treatment difference according to both estimated GFR and albuminuria.

ONTARGET-TRANSCEND



Changes in Albuminuria Predict Mortality and Morbidity in Patients with Vascular Disease

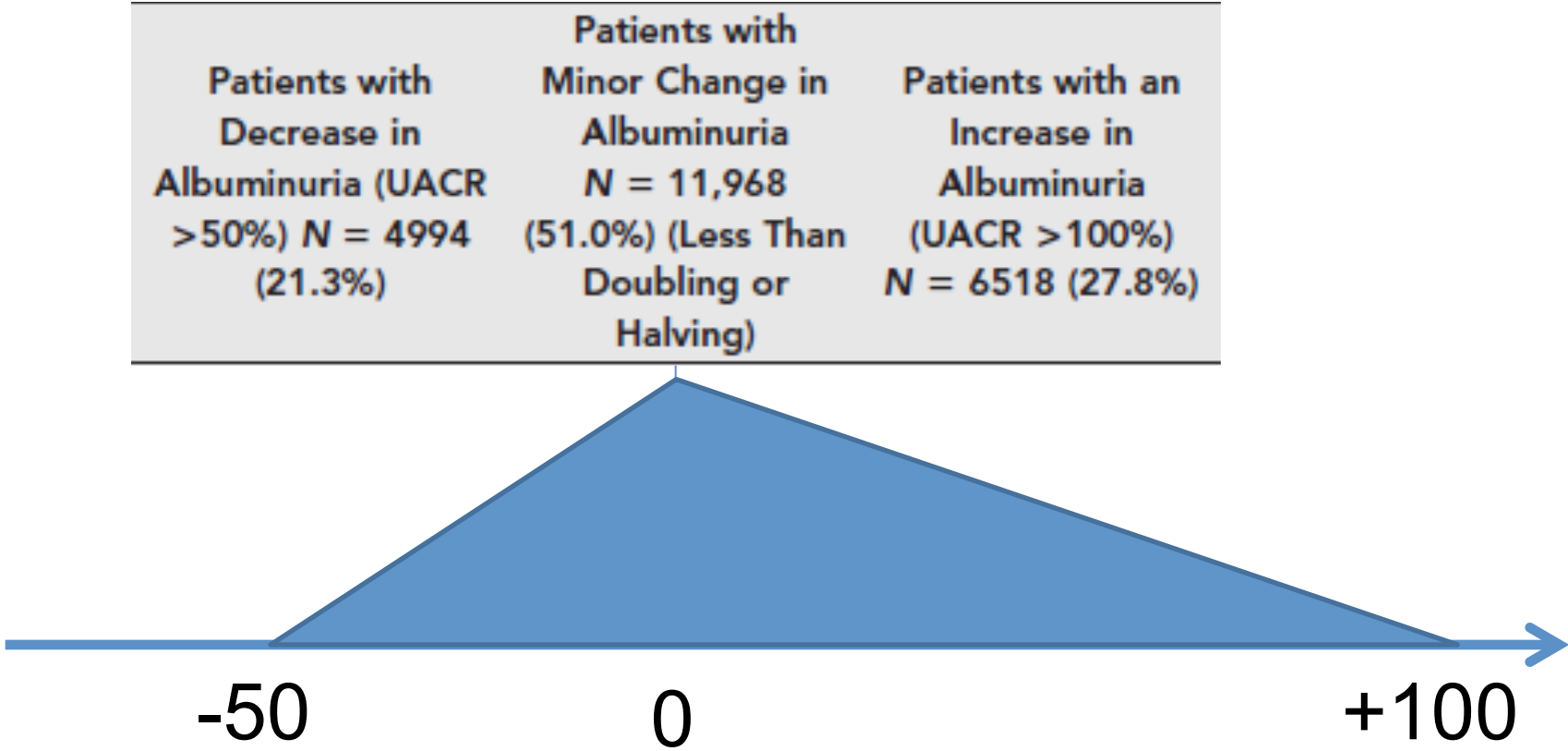
Roland E. Schmieder,* Johannes F. E. Mann,† Helmut Schumacher,‡ Peggy Gao,§
Giuseppe Mancina,|| Michael A. Weber,¶ Matthew McQueen,** Teo Koon,** and
Salim Yusuf,** on behalf of the ONTARGET Investigators



“In patients with vascular disease, changes in albuminuria predict mortality and cardiovascular and renal outcomes, independent of baseline albuminuria”

Changes in Albuminuria Predict Mortality and Morbidity in Patients with Vascular Disease

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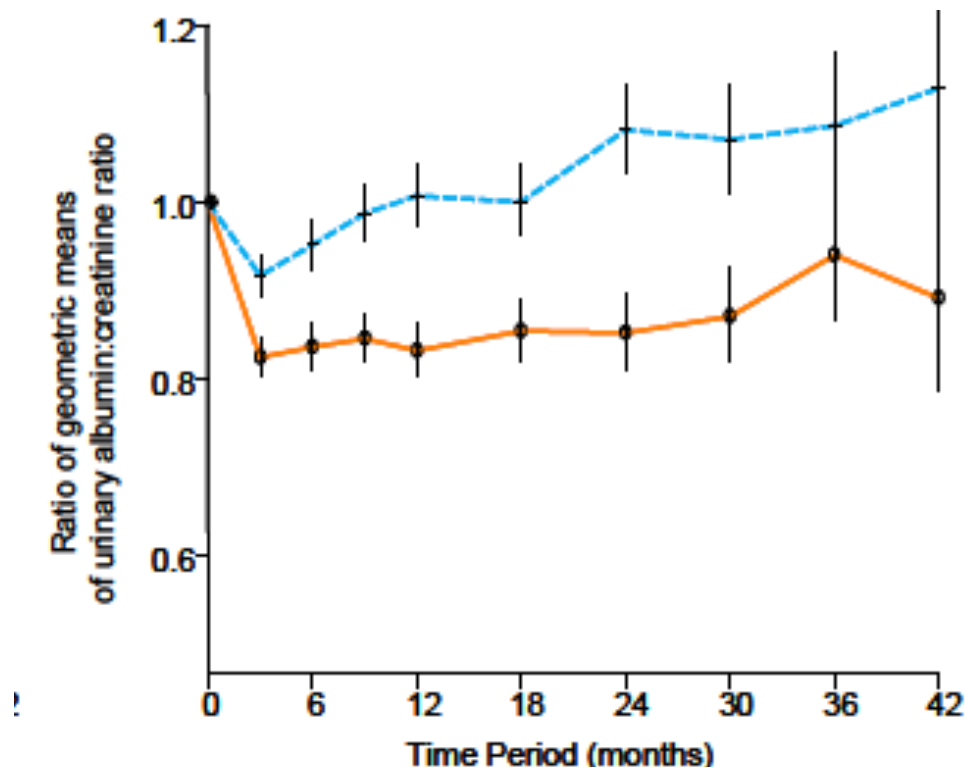


“This analysis assumes that a decrease in albuminuria of 40% had the same clinical significance than an increase of 90% !!!!!!!”

Cardiorenal End Points in a Trial of Aliskiren for Type 2 Diabetes

Hans-Henrik Parving, M.D., D.M.Sc., Barry M. Brenner, M.D., Ph.D.,
John J.V. McMurray, M.D., Dick de Zeeuw, M.D., Ph.D., Steven M. Haffner, M.D.,
Scott D. Solomon, M.D., Nish Chaturvedi, M.D., Frederik Persson, M.D.,
Akshay S. Desai, M.D., M.P.H., Maria Nicolaides, M.D., Alexia Richard, M.Sc.,
Zhihua Xiang, Ph.D., Patrick Brunel, M.D., and Marc A. Pfeffer, M.D., Ph.D.,
for the ALTITUDE Investigators*

The overall urinary albumin-to-creatinine ratio decreased more with aliskiren than with placebo (between-group difference, 14 percentage points; 95% CI, 11 to 17)



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Table 2. Prespecified Primary and Secondary Composite Outcomes and Deaths.*

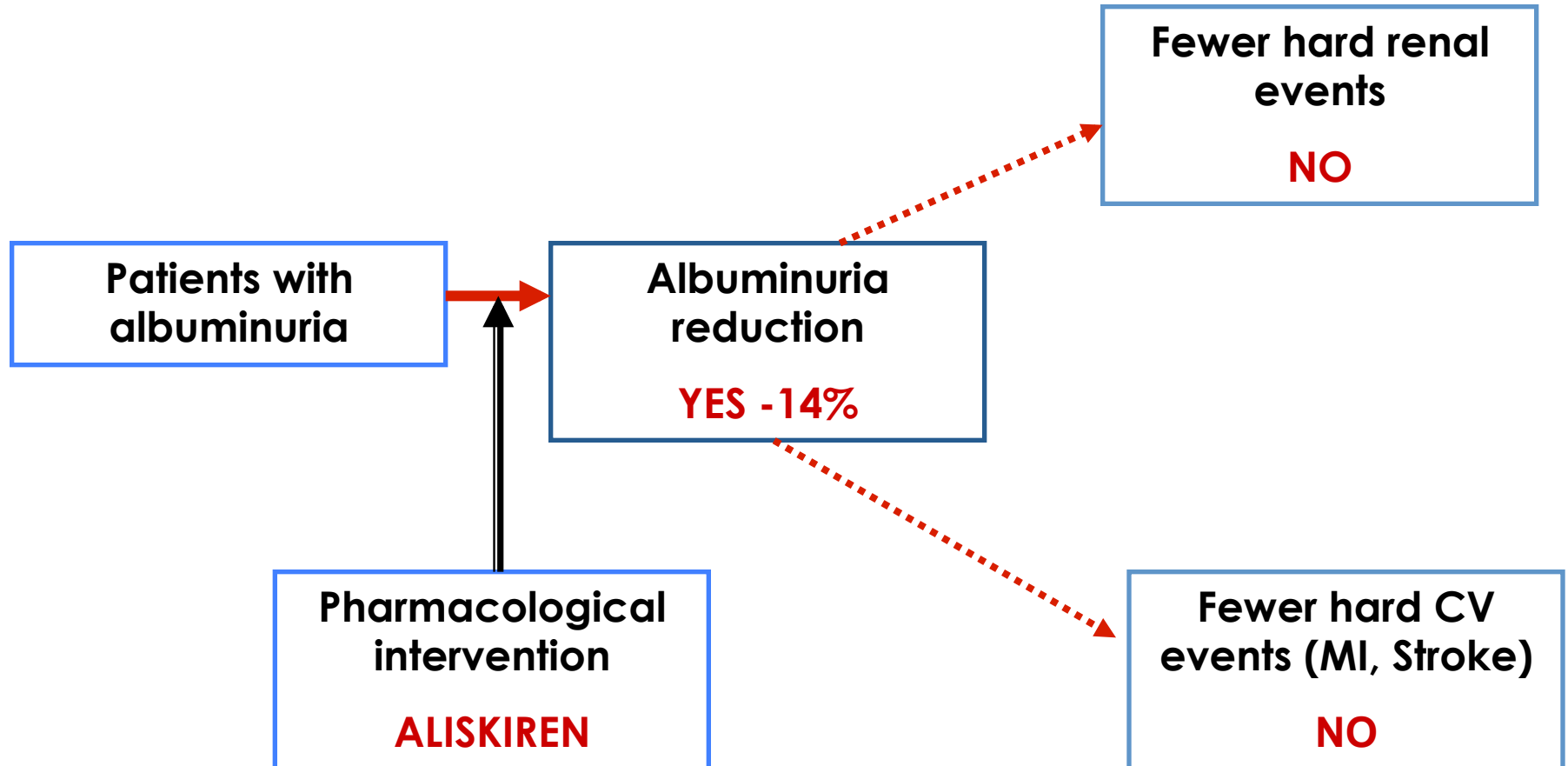
Outcome	Aliskiren (N = 4274) <i>no. of patients (%)</i>	Placebo (N = 4287) <i>no. of patients (%)</i>	Hazard Ratio (95% CI)	P Value†
Primary composite outcome	783 (18.3)	732 (17.1)	1.08 (0.98–1.20)	0.12
Death from cardiovascular causes	246 (5.8)	215 (5.0)	1.16 (0.96–1.39)	0.12
Cardiac arrest with resuscitation	19 (0.4)	8 (0.2)	2.40 (1.05–5.48)	0.04
Myocardial infarction (fatal or nonfatal)	147 (3.4)	142 (3.3)	1.04 (0.83–1.31)	0.72
Stroke (fatal or nonfatal)	147 (3.4)	122 (2.8)	1.22 (0.96–1.55)	0.11
Unplanned hospitalization for heart failure	205 (4.8)	219 (5.1)	0.95 (0.78–1.14)	0.56
ESRD, death attributable to kidney failure, or loss of kidney function‡	121 (2.8)	113 (2.6)	1.08 (0.84–1.40)	0.56
Doubling of baseline serum creatinine	210 (4.9)	217 (5.1)	0.97 (0.80–1.17)	0.75
Cardiovascular composite outcome	590 (13.8)	539 (12.6)	1.11 (0.99–1.25)	0.09
Renal composite outcome	257 (6.0)	251 (5.9)	1.03 (0.87–1.23)	0.74
Death from any cause	376 (8.8)	358 (8.4)	1.06 (0.92–1.23)	0.42

* A patient may have had multiple cardiovascular and renal events of different types. All composite outcomes reflect only the first occurrence of any of the components.

† P values have not been adjusted for multiple comparisons.

‡ Loss of kidney function was defined by the need for renal-replacement therapy with no dialysis or transplantation available or initiated. ESRD denotes end-stage renal disease.

ALTITUDE



SUMMARY

- The association between microalbuminuria and cardiovascular disease is probably explained by a common pathophysiologic process, such as endothelial dysfunction or chronic, low-grade inflammation.
- Numerous studies have demonstrated that regression of albuminuria per se **is not** a reliable surrogate end-point for CV or renal outcomes.
- Specific pharmacological approaches such as RAAS dual-blockade have demonstrated that targeting blindly albuminuria was a **candid and/or harmful concept**.

Tableau. Évolution de la microalbuminurie et des événements cardiovasculaires et rénaux selon diverses approches thérapeutiques

Essai	Type d'intervention	Effet sur l'albuminurie	Effet sur les événements rénaux majeurs	Effet sur les événements cardiovasculaires
ADVANCE	Traitement intensif de la glycémie	+	–	–
ADVANCE	Traitement intensif de la PA	+	–	+
IDNT	Irbésartan	+	+	–
VALUE	Valsartan	+	–	Surcroît d'infarctus
ASCEND	Avosentan	+	–	Surcroît d'événements
ACCOMPLISH	Amlodipine vs HCTZ	–	+	+
ORIENT	Olmésartan	+	–	–
ONTARGET	Double blocage vs simple blocage	+	–	–
ALTITUDE	Aliskirène + Valsartan vs Valsartan	+	–	–

Nowadays, there exists no definite rationale to recommend targeting microalbuminuria beyond and above blood pressure control in hypertensive patients in order to improve their prognosis.

11 000 000 d' hypertendus :

$$10,8 \text{ Euros} \times 11000000 = 110\,000\,000 \text{ Euros}$$

Pour quelles conséquences pratiques?

Mr Jean-Jacques M. 48 ans, chiffres élevés
dépistés en médecine du travail.

PA : 150/95 mmHg (90)

créat : 80 μ mol/l

glycémie 0.96 g/l

HDL : 0.46g/l LDL:1.40 g/l CT : 2.26 g/l

Tabac=0

Automesure : 144/90 mmHg

Mr Jean-Jacques M. 48 ans, chiffres élevés
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microalbuminurie -

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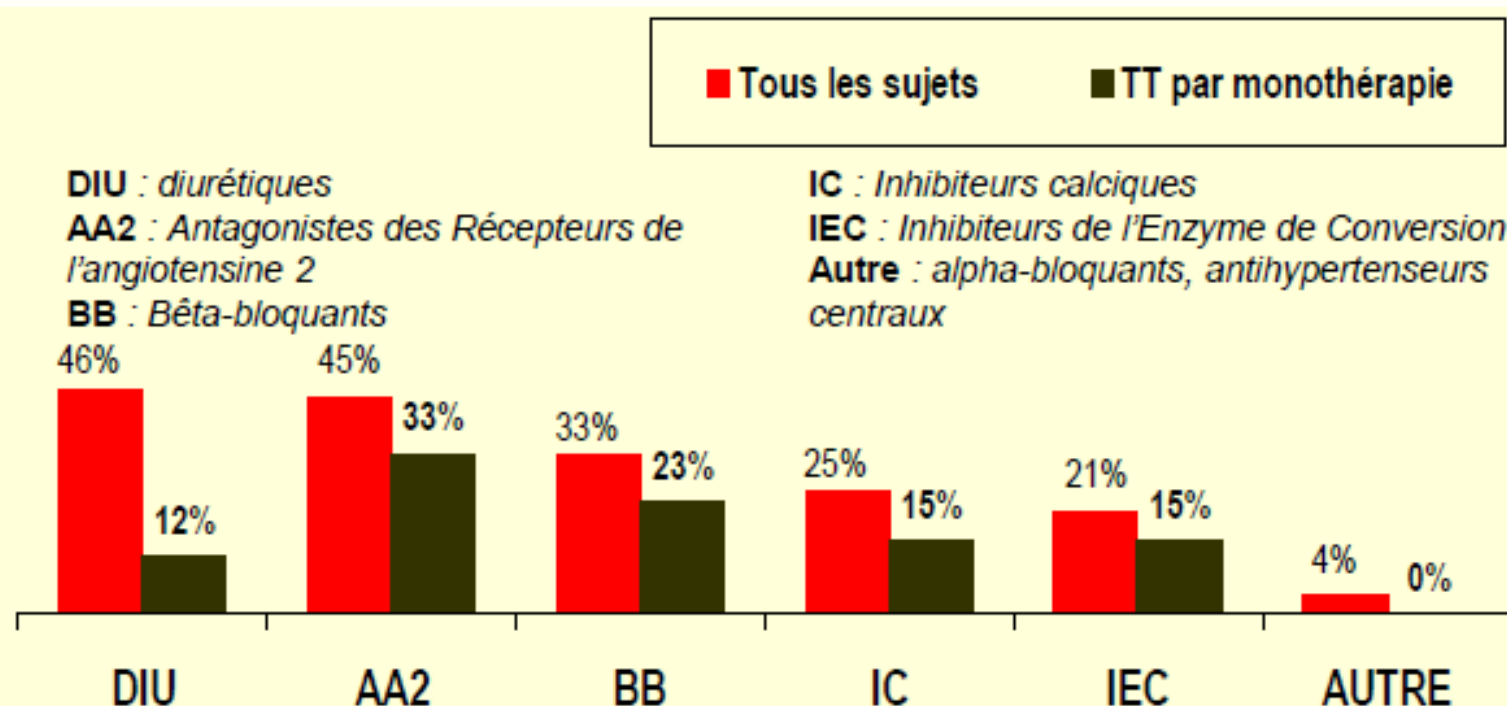
HDL : 0.46g/l LDL:1.40 g/l CT : 2.26 g/l

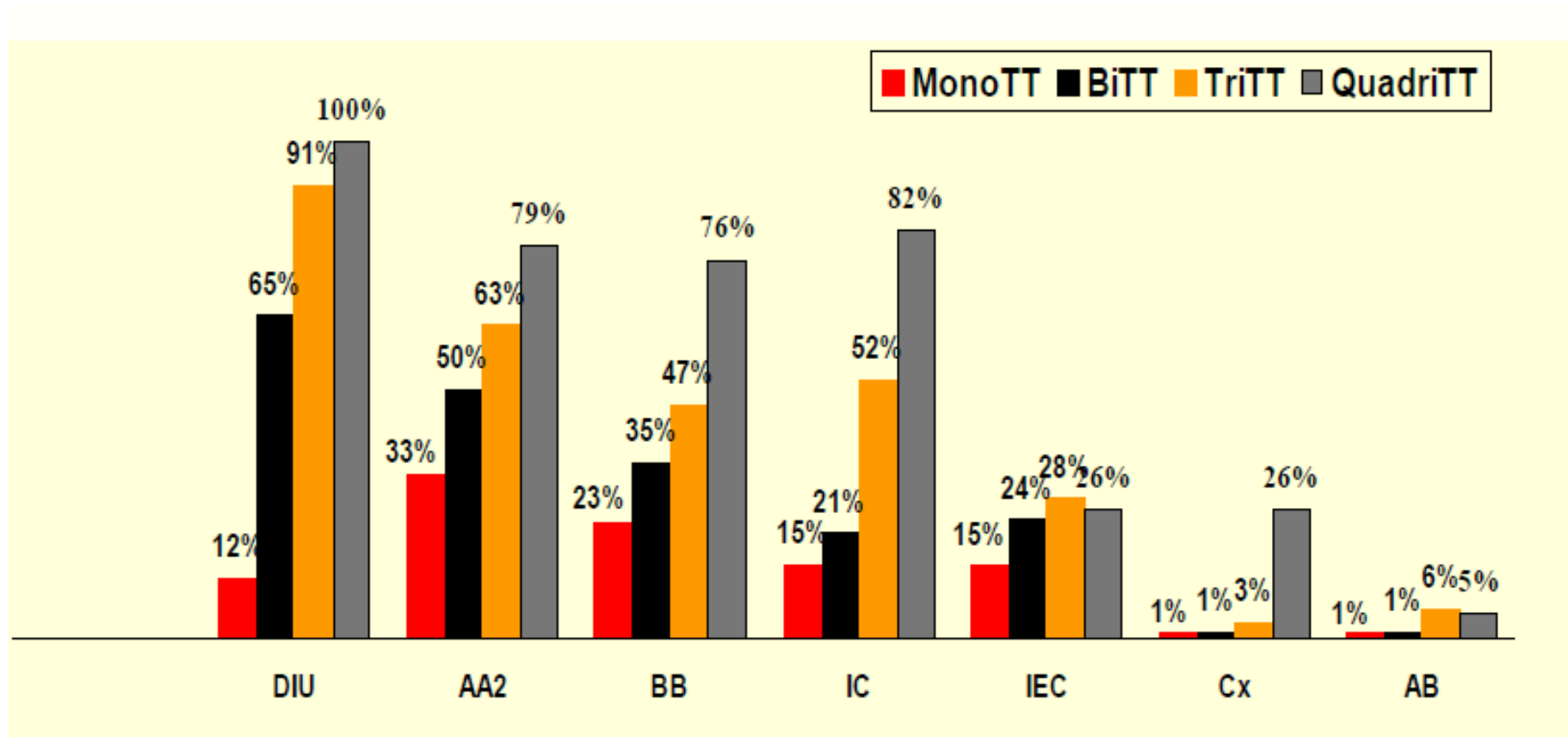
Tabac=0

Automesure : 144/90 mmHg

microalbuminurie +

Figure 1: Utilisation des anti-hypertenseurs en 2009. Analyse de l'utilisation des principes pharmacologiques.





Ma suggestion

- Bandelette urinaire pour tout le monde
- Microalbuminurie à ne faire que chez le diabétique équilibré

L'histoire

Mme M. Malienne 22 ans, admise par les urgences pour précordialgies d'effort le 1er juin 2007

Découverte d'une anémie ferriprive à 6.2 g/dl

Transfusée aux urgences et transférée dans le service

L'histoire

Antécédents

HTA traitée par Fludex, auparavant transitoirement traitée par Cozaar, stoppé pour intolérance. (Kaliémie sous Fludex: 3.2 mmol/l)

Métrorragies abondantes depuis 15 jours.

Avis gynéco : Fausse couche spontanée

L'histoire

En cours d'hospitalisation: BMI 20; signale un amaigrissement de 6 kg en 2 mois

- Confirmation d'une HTA permanente (160/80 mmHg), associée à une hypokaliémie persistante sous Monotilidien
- Découverte de glycémies modérément élevées (1.4 – 2.21 g/l) ; HbA1c à 6.5%

L'histoire

Planification d'un **bilan hormonal** à la recherche d'un hyperaldostéronisme

Et d'une **imagerie** à la recherche d'une cause rénovasculaire ou surrénale à l'HTA

Scanner réalisé le jour de la sortie

Rénine / Aldo couché debout

Sortie à J6 sous : Monotildiem 300LP ;
Diamicron30 LM 1 ; Tardyferon B9.

Consultation à 2 mois planifiée

Acte II

Retour inopiné de la patiente en consultation
fin juillet

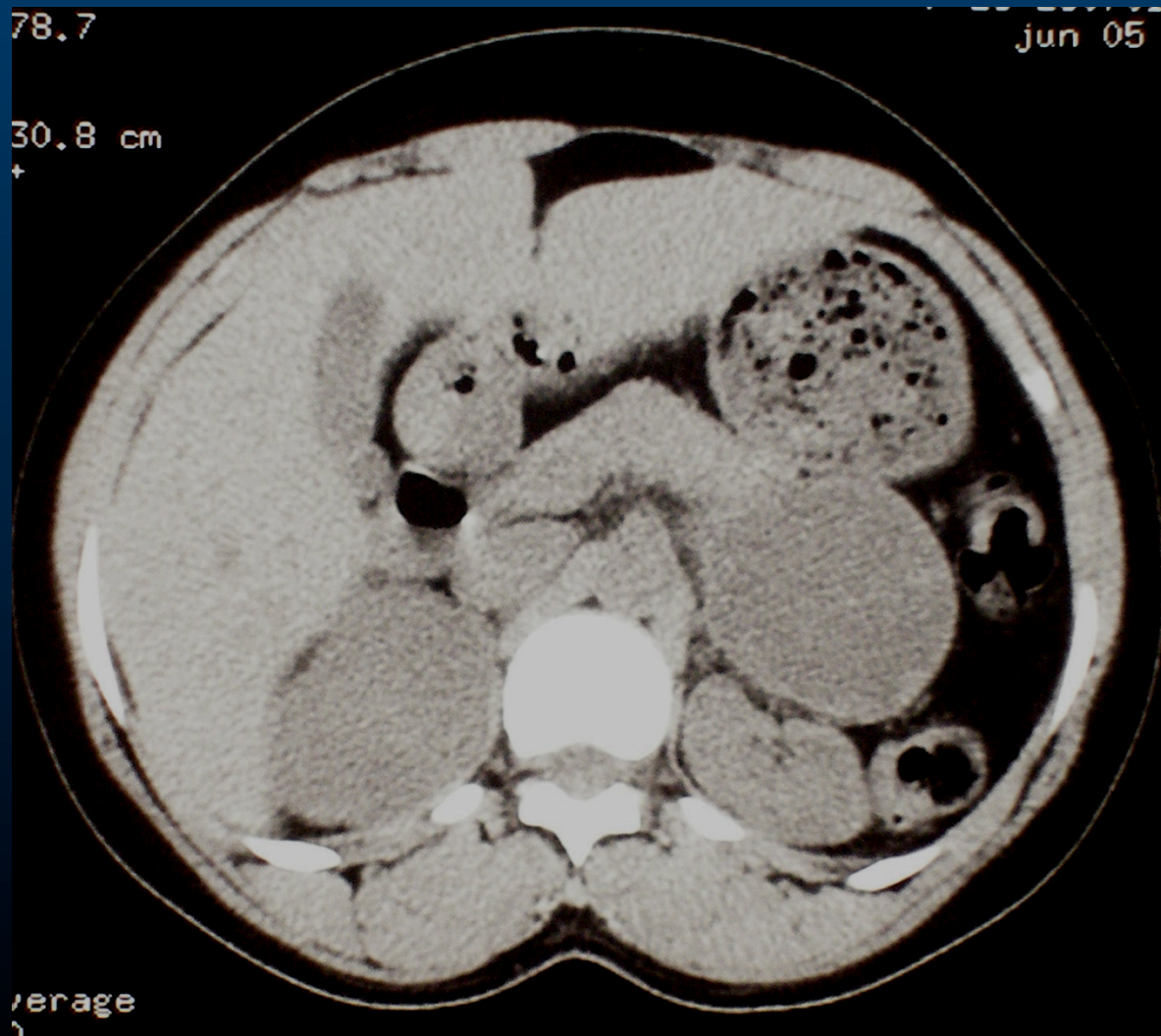
- « Je n' ai pas pris tous les médicaments »
- « Je crois que je suis enceinte »

Acte II

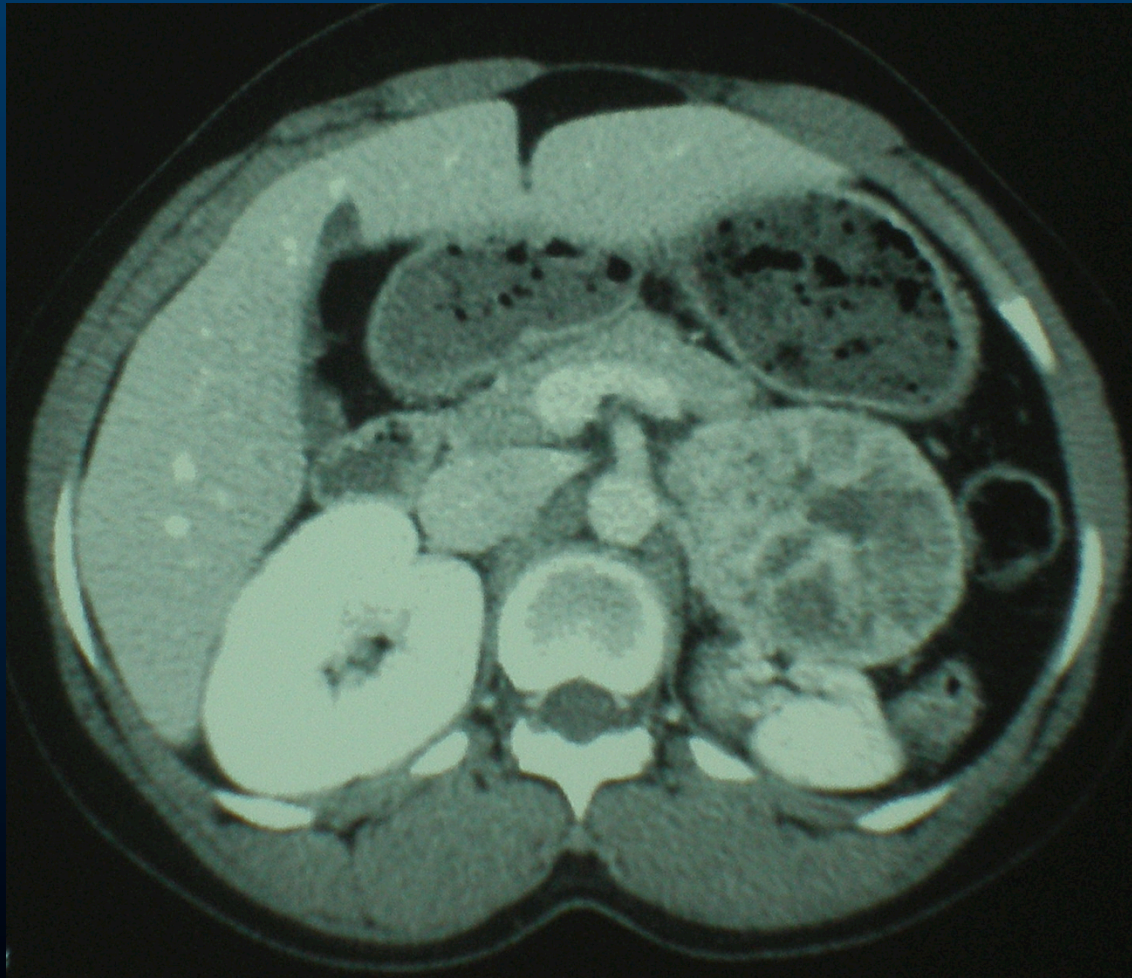
Synthèse des examens demandés en fin d'hospitalisation

- Renine (couché): **15** uU/ml (N: 5-47)
(debout): **99** uU/ml (N: 7-76)
- Aldostérone (couché): **313** pmol/L (N: 28-445)
(debout): **1582** pmol/L (N: 111-862)
- Exhumation de l'angio-scanner des artères rénales et surrénales

Angio-Scanner



Angio-Scanner



Tumeur surrénalienne solide , hétérogène, 7 cm, comprimant le pédicule rénal gauche; atrophie rénale homolatérale.

Ré-admission immédiate

Confirmation d'une grossesse en urgence

PA 160 / 100 (85) couchée ; PAS 120 mmHg
debout

HGT 1.45 g/l

Cs gynéco : Grossesse évolutive 6 semaines

Récapitulons...

1 femme de 22 ans

1 HTA précoce

1 diabète

1 grossesse

2 causes potentielles d' HTA

Acte III

Repos

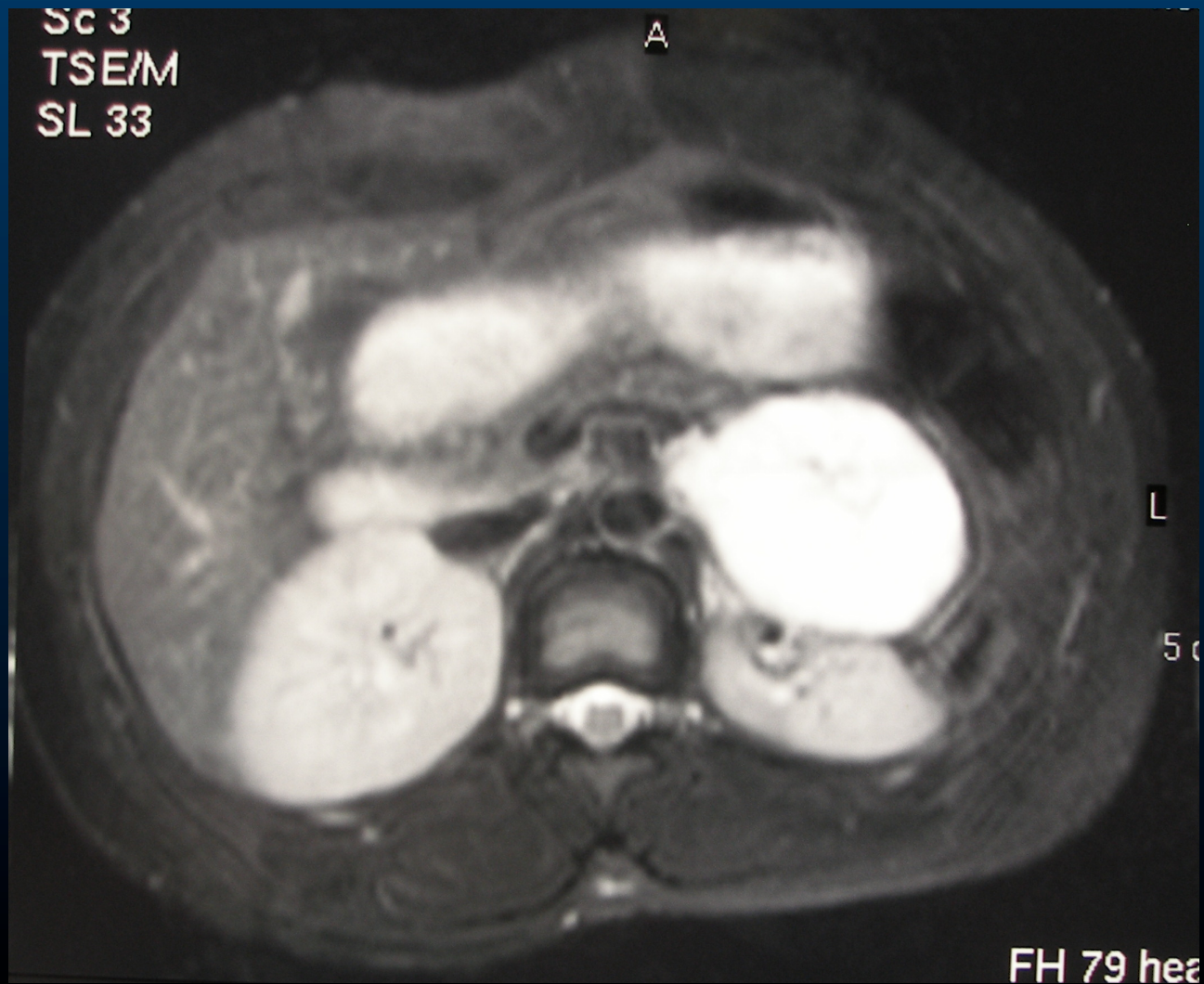
Remplissage IV initial

Introduction progressive d'alpha-bloquants
puis de bêta-bloquants

110 /60 mmHg (62) sous 6 mg de
Minipress et 120 mg d'Avlocardyl.

Bilan étiologique complémentaire

IRM abdomino-pelvienne



Normétadrénaline urinaire:

5837 nmol/24h (N<2100)

soit 948 nmol/mmol créat (N<280)

Métadrénaline et 3-méthoxytyramine normales

Chromogranine A: 655 µg/L (N<86,5)

Absence d'arguments cliniques ou biologiques
pour une endocrinopathie associée

Que faire ?

- 1 - ITG première, Surrénalectomie.
- 2 - Traitement médicamenteux, poursuite de la grossesse, et surrénalectomie post-partum
- 3 - Surrénalectomie et poursuite de la grossesse
- 4 – Dénervation en urgence

- Environ 200 cas isolés publiés
- Découverte d'un phéochromocytome au cours d'une grossesse : 1 / 50 000 grossesses
- Mortalité maternelle 25%, mortalité fœtale 55% en cas d'absence de diagnostic
 - Si diagnostiqué : Mortalité maternelle 3%, mortalité fœtale 15%

TRAITEMENT

- Indication chirurgicale?
 - Auparavant, surrénalectomie après accouchement
 - Entre 1988 et 97, sur 42 cas, 80 % succès de la surrénalectomie avant 24 SA.



Consensus actuel:

- <24SA: Surrénalectomie pendant la grossesse
- >24SA: Surrénalectomie après accouchement

- Avant 24 SA: SURRENALECTOMIE LAPAROSCOPIQUE
 - Surrénalectomie par laparoscopie: 1992 (Gagner)
 - 1ere surrénalectomie laparoscopique pendant une grossesse : 2000 (Demeure)
 - Supériorité de la laparoscopie en terme de pronostic foetal
 - Inocuité de la laparoscopie chez la femme enceinte

(Limitation de la pression intra-abdominale, monitoring du foetus)

CI : Suspicion de malignité ; taille > 6cms

PHEOCHROMOCYTOME ET GROSSESSE

REVUE DE LA LITTÉRATURE

Characteristic	Case report			
	Current case	Demeure et al ²	Martinez Brocca et al ³	Pace et al ⁴
Patient				
Age, yr	28	24	34	24
Pregnancy status	1st	1st	Not stated	1st
Time of diagnosis	1st trimester	1st trimester	1st trimester	1st trimester
Preoperative care				
Alpha-adrenergic blockade	Yes*	Yes	Yes	Yes
Tumour				
Side	Right	Right	Right	Left
Size, cm	2.2	3.2	2	6
Operation				
Gestational age, wk	16	18	20	13
Position	Lateral	Lateral	Lateral	Lateral
Approach	Transabdominal	Transabdominal	Transabdominal	Transabdominal
Operative time, min	108	240	165	140
Complications	None	None	None	None
Postoperative care				
Complications	None	None	None	None
Length of stay, d	2	4	Not available	3
Follow-up				
Normalization of BP	Yes	Yes	Yes	Yes
Biochemical normalization	Yes	Yes	Yes	Yes
Delivery	Term	Term	Term	Term
Health of infant	Healthy	Healthy	Healthy	Healthy

- Après 24 SA:
 - Poursuite du traitement médical
 - Césarienne dès maturité foetale
 - Surrénalectomie en post partum

Acte IV : Chirurgie

Programmée à 18 SA. (Prof Ph Wind, Avicenne)

Par voie laparoscopique (<120 min)

Suites péri-opératoires simples.

Consultation 8 nov 2007

PA : 110 /70 sans traitement ; HGT nle

Métanéphrines et chromogranine normalisées

Accouchement voie basse Avril 2008

A garder à l'esprit

Ce qui est exceptionnel peut survenir

HTA et hyperglycémie = un œil sur les surrénales

Le diagnostic de phéochromocytome nécessite un suivi à long terme (PA,Mnu,CGA)

Le circuit des examens et des dossiers, (même à Avicenne, dans le meilleur des services....) est PERFECTIBLE !!!!