Polykystose rénale autosomale dominante

Philippe Yale, M D
Le 12 mars 2018

Conflits d'intérêt

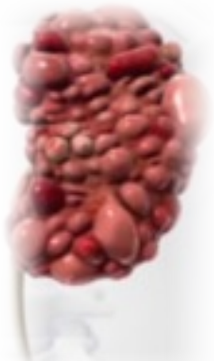
Otsuka

Tolvaptan

Janssen

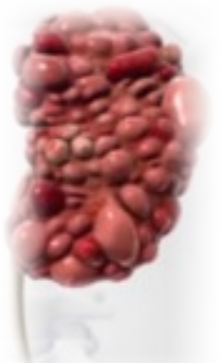
MERCK

SERVIER



Objectifs

- Reconnaître les différentes manifestations des complications de la polykystose rénale
- Évaluer les risques de progression de la maladie
- Citer les données probantes sur l'efficacité et l'innocuité des traitements publiés dans le consensus d'experts canadiens
- Donner des conseils pratiques sur la référence en néphrologie pour les patients atteints de polykystose rénale



Plan

Canadian Society of Nephrology/
Société canadienne de néphrologie
CSN/SCN

- Introduction sur la polykystose
- Évaluation diagnostique
- Traitement

Étiologies de l'IRC

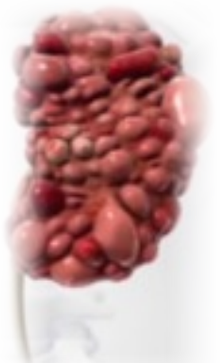
1. Néphropathie diabétique
2. Pathologies kystiques
3. Glomérulonéphrites
4. Néphropathie hypertensive

Étiologies de l'IRC

1. Néphropathie diabétique
2. Néphropathie hypertensive
3. Glomérulonéphrites
4. **Pathologies kystiques**

Épidémiologie

- Maladie génétique rénale la plus fréquente
- Atteint 1/500 à 1/1 000
- IRC terminale
  - ♂: 54 ans
  - ♀ : 58 ans
  - 10-15% des dialysés



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Original Research Article

Canadian Journal of Kidney Health and Disease
Volume 4: 1–12

DOI: 10.1177/2054358117695784
journals.sagepub.com/home/cjk
SAGE

Assessing Risk of Disease Progression and Pharmacological Management of Autosomal Dominant Polycystic Kidney Disease: A Canadian Expert Consensus

Dr Daniel Bichet

HÔPITAL DU SACRÉ-CŒUR DE MONTRÉAL
HSCM *Doués pour la vie*

Dr Ahsan Alam

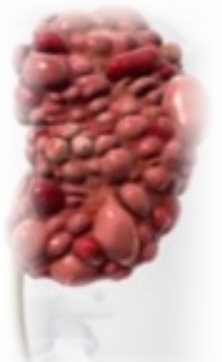
Centre universitaire de santé McGill
McGill University Health Centre

Dr Rolf Loertscher

Lakeshore

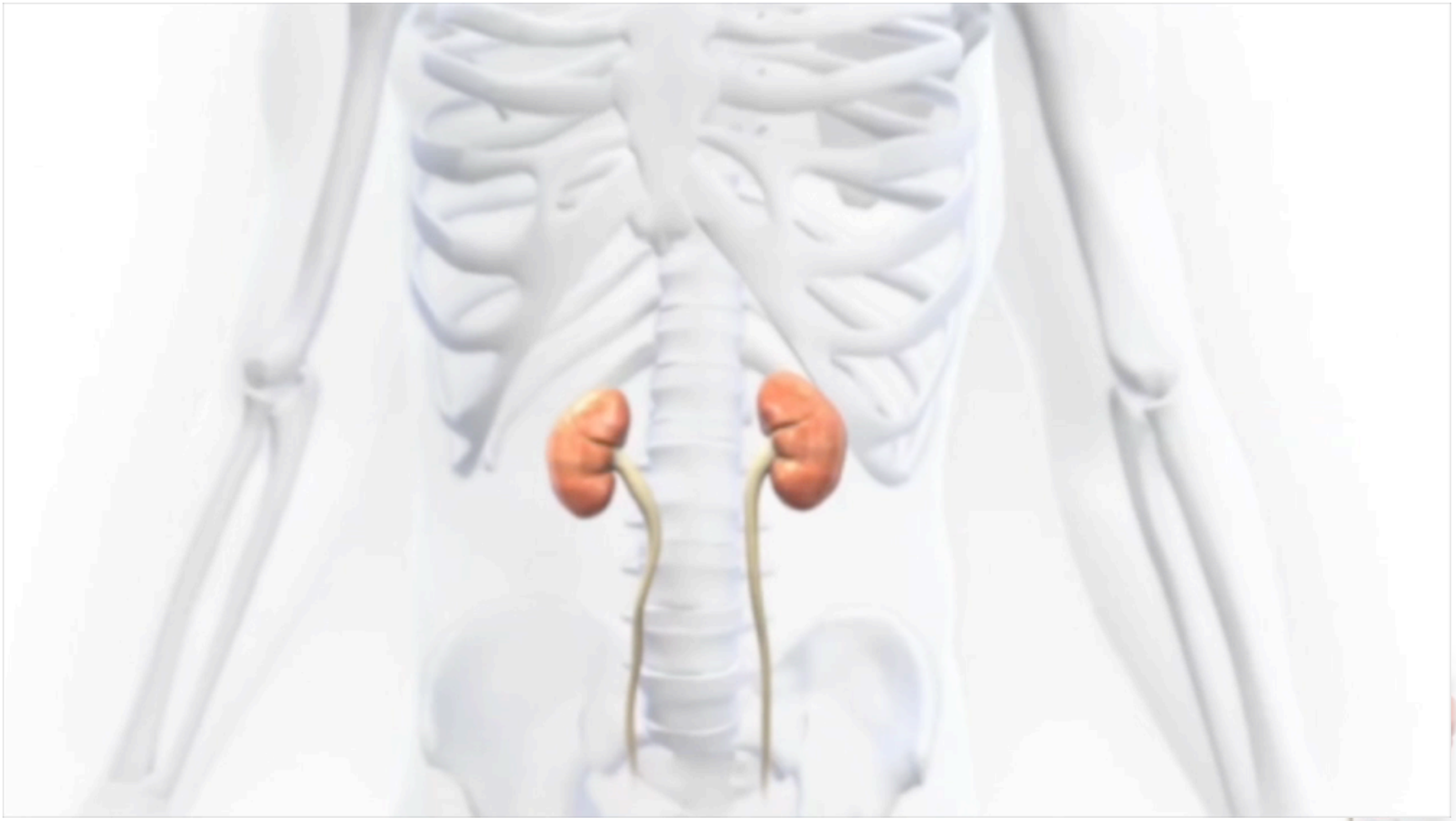
Pathophysiologie

- Mutation PKD
  - Polycystine
  - Perte de reconnaissance de polarité planaire → multiplication accélérée
  - Kyste séparé du tubule qui continue de croître et accumule du fluide
  - Prolifération surtout au tubule collecteur au niveau des cellules principales et dans les canaux biliaires intra-hépatiques
  - Croissance des kystes → ischémie du parenchyme → IRC

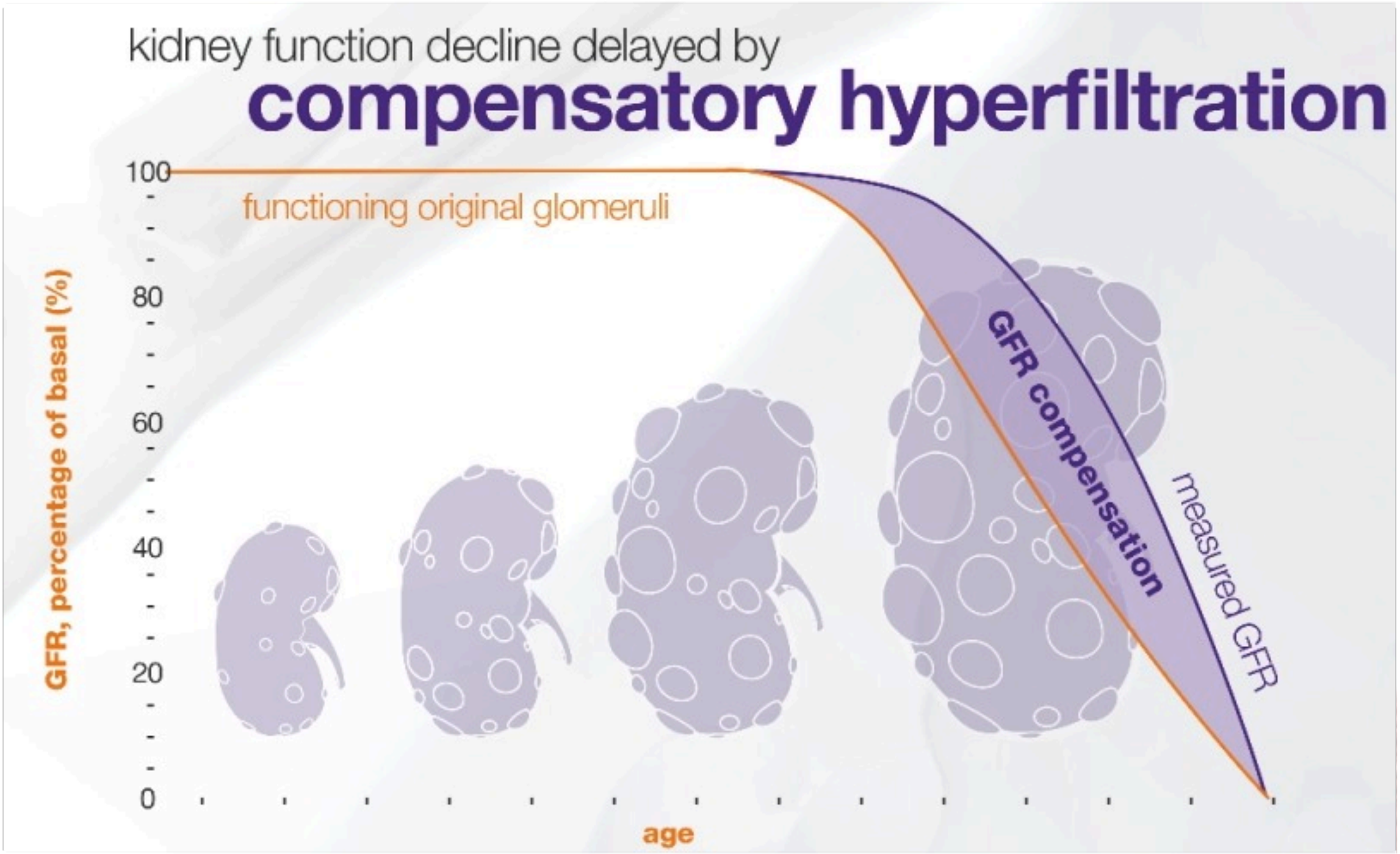


Pathophysiologie

Pathophysiologie



Pathophysiologie

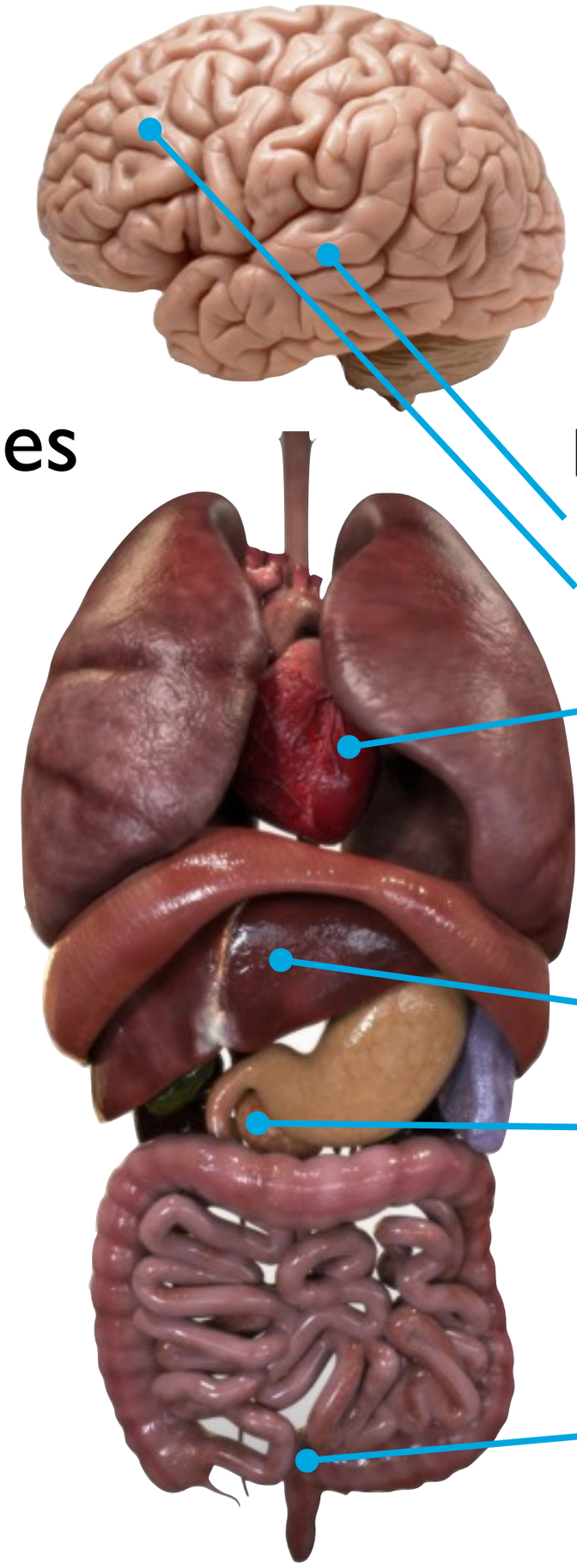


Pathophysiologie

- Gène PKD 1 (16p13.3): Polycystine 1
  - 90% des mutations
  - Plus de kystes plus tôt
  - IRC terminale vers 55 ans
  - 2 323 mutations connues
- Gène PKD 2 (4q21): Polycystine 2
  - 10% des mutations
  - Moins sévère
  - IRC terminale vers 79 ans
  - 278 mutations connues

Manifestations rénales

- Douleur
- Lithiases
- Saignements
- Kystes infectés
- HTA
- IRC



Manifestations extra-rénales

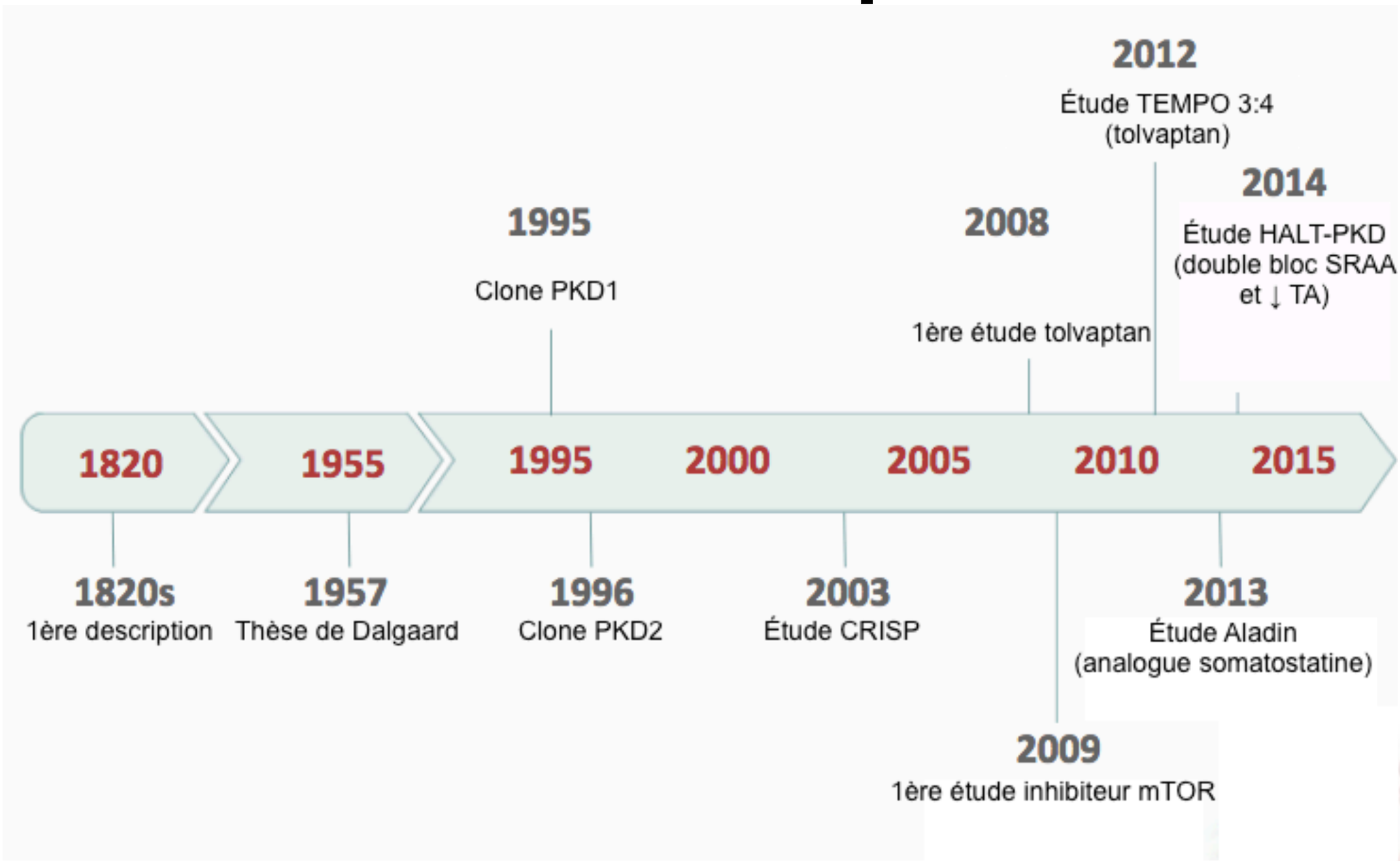
- Anévrysmes intracrâniens
- Kystes arachnoïdiens
- Prolapsus mitral, racine aortique
- Kystes hépatiques
- Kystes pancréatiques
- Kystes vésicules séminales

Historique

En quelle année fut décrite la polykystose rénale?

- Égypte antique
- Rome
- 19e siècle
- 1964

Historique



McFarlane et al. Programme éducatif, http://slideplayer.com/slide/9053726/

Diagnostic

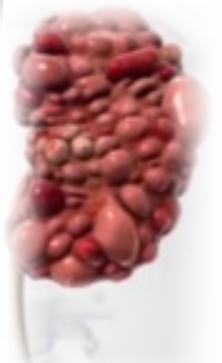
Diagnostic initial

Risque de progression

Traitement

Volume rénal total (VRT)

Classification



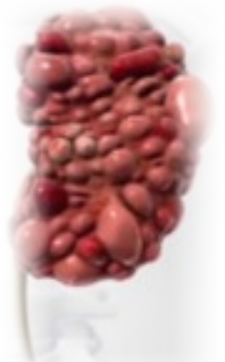
Diagnostic
Initial

Diagnostic initial

- Imagerie
  - Échographie: diagnostic initial
    - Innombrables kystes
    - Kystes hépatiques
  - Précision sur la taille: IRM / CT
- Histoire familiale

Si FHx +:

15-39 ans	≥ 3 kystes
40-59 ans	≥ 2 kystes / rein
≥ 60 ans	≥ 4 kystes / rein



Diagnostic
initial

Diagnostic initial

Quel est le volume normal d'un rein?

- 18 mL
- 120 mL
- 170 mL
- 415 mL

Diagnostic

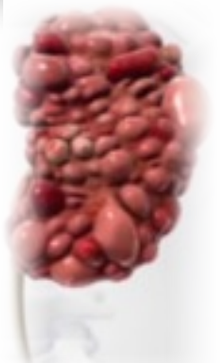
Diagnostic initial

Risque de progression

Traitement

Volume rénal total (VRT)

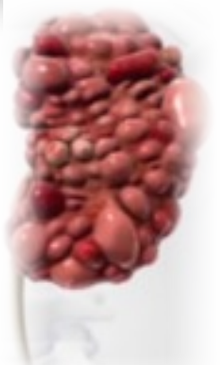
Classification



Diagnostic

Volume rénal total (VRT)

Risque de progression → Classification

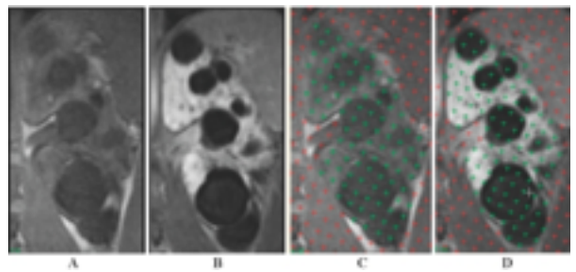


Diagnostic

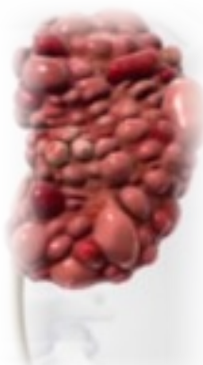
Évaluation du risque de progression

Risque de progression

- Classification
  - Clinique Mayo
    - Classe 1 ou 2 (risque faible)
    - Classe 1A à 1E



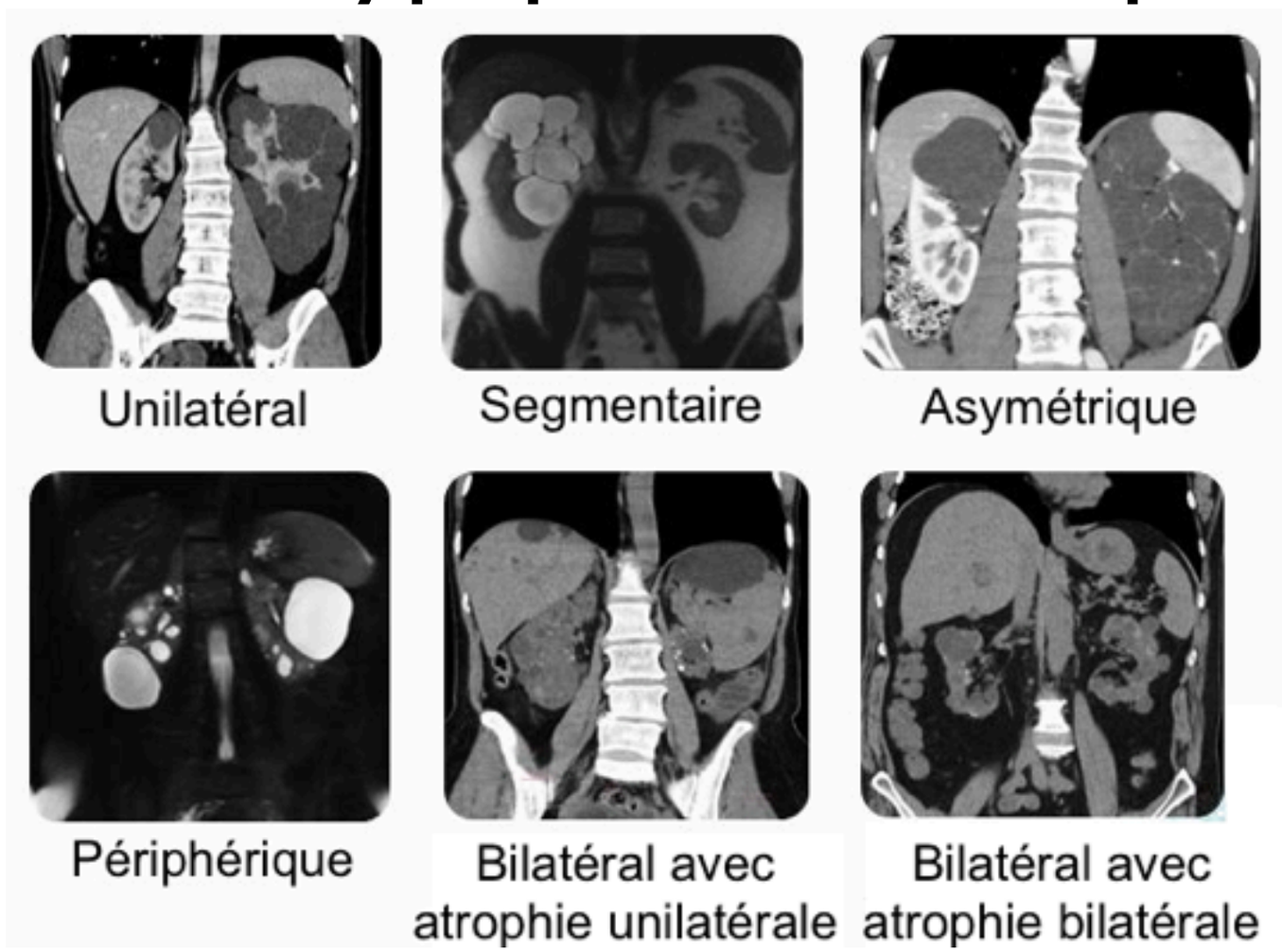
- Volume rénal total (VRT)
  - Stéréologie (gold) ou ellipsoïde (IRM > CT) (simple et équivalent): VRT > 750 mL
  - Écho: longueur > 16,5 cm ~ 750 mL

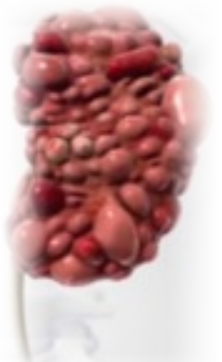


Diagnostic

Évaluation du risque de progression

- Classe I: typique: risque de progression
- Classe II: atypique: faible risque

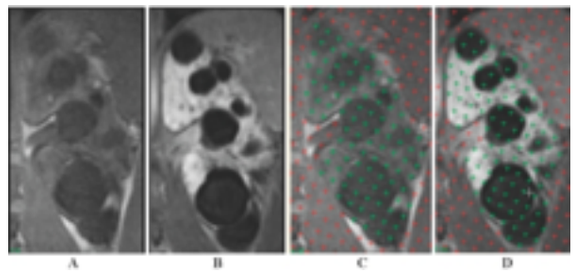




Diagnostic

Évaluation du risque de progression

- Classification
  - Clinique Mayo (figure)
    - Classe 1 ou 2 (risque faible)
    - Classe 1A à 1E



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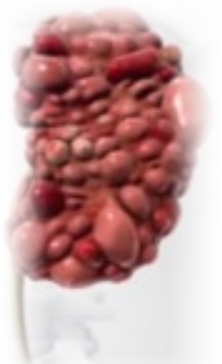
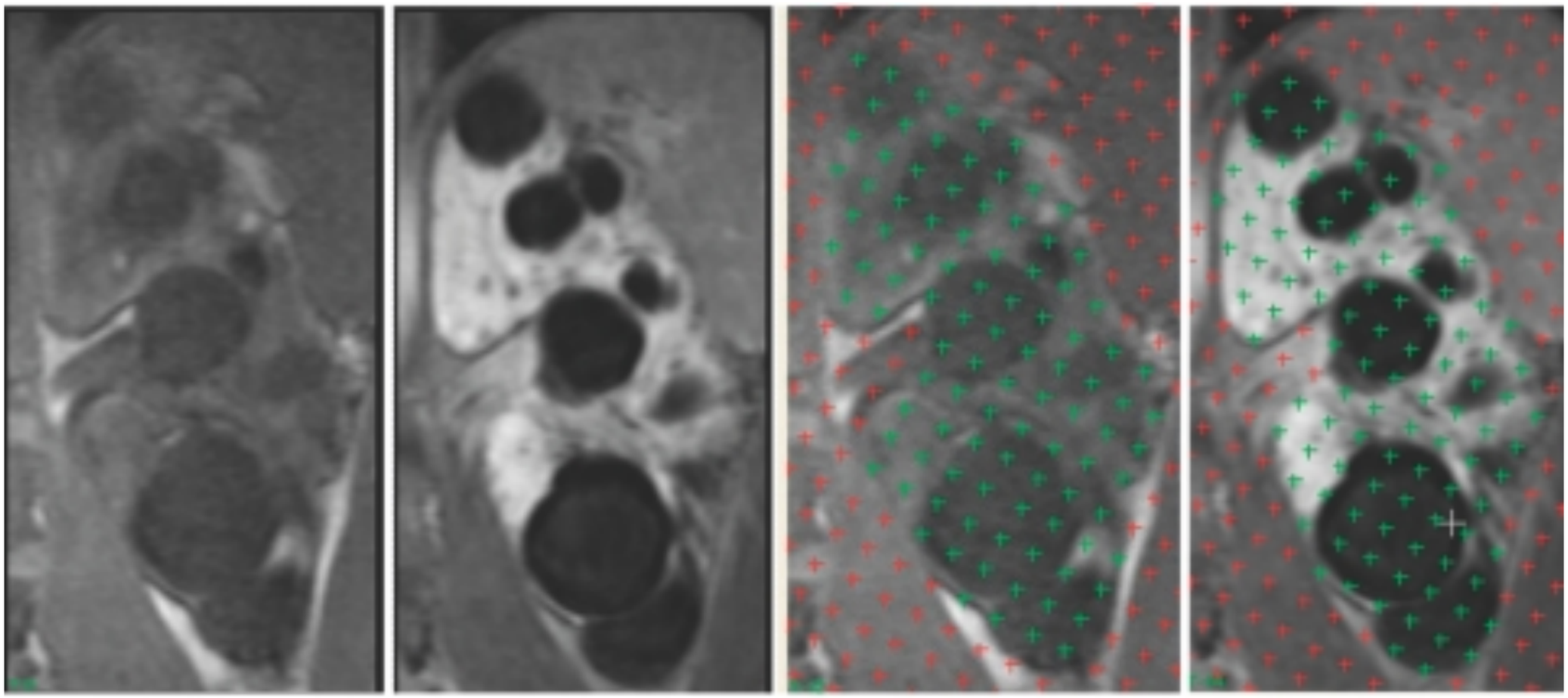


Diagnostic

Évaluation du risque de progression

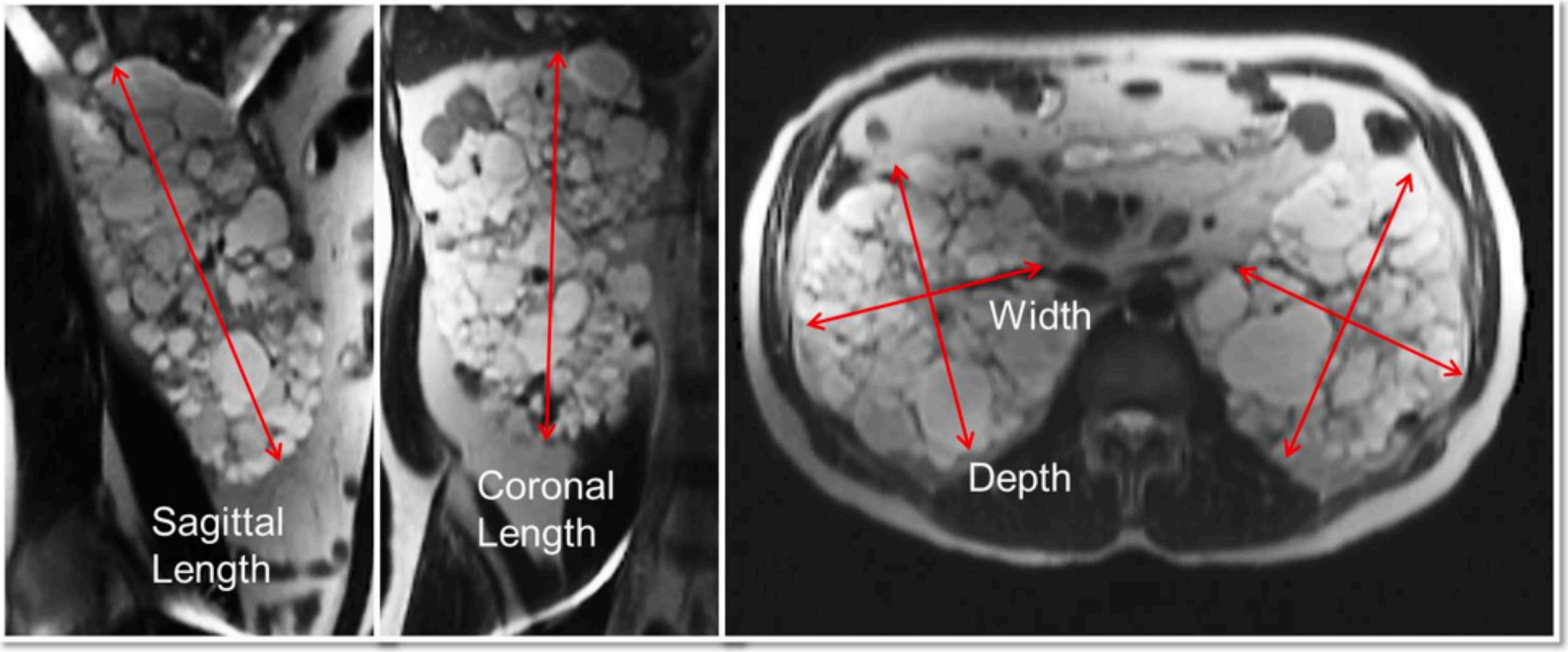


Stéréologie

http://www.mayo.edu/research/documents/pkd-center-adpkd-classification/doc-20094754

Diagnostic

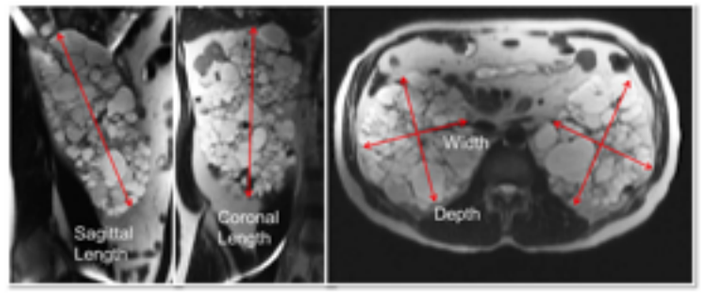
Évaluation du risque de progression



Ellipsoïde

http://www.mayo.edu/research/documents/pkd-center-adpkd-classification/doc-20094754

Diagnostic



Évaluation du risque de progression

1 Kidney Volume Calculator based on Ellipsoid equation (π/6xLxWxD) from MRI or CT image

Required Data Entry

Right Kidney		**Left Kidney**	
Sagittal Length (mm)		Sagittal Length (mm)	
Coronal Length (mm)		Coronal Length (mm)	
Width (mm)		Width (mm)	
Depth (mm)		Depth (mm)	

Calculated Results

Right Kidney Volume (mL) | **Left Kidney Volume (mL)**

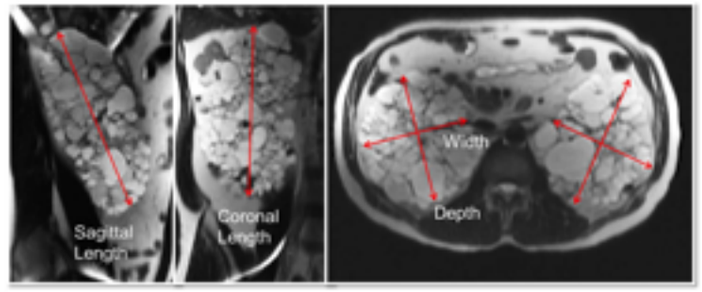
Total Kidney Volume (mL)

Clear All | Calculate Volumes

Ellipsoïde

http://www.mayo.edu/research/documents/pkd-center-adpkd-classification/doc-20094754

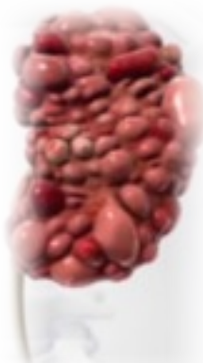
Diagnostic



Évaluation du risque de progression

2	ADPKD Classification using Kidney Volume Calculator
Required Data Entry Patient Height (m) Patient Age (years) Clear All	**Calculated Results** **Height Adjusted TKV (mL/m)** **ADPKD Classification** Calculate Classification

Ellipsoïde

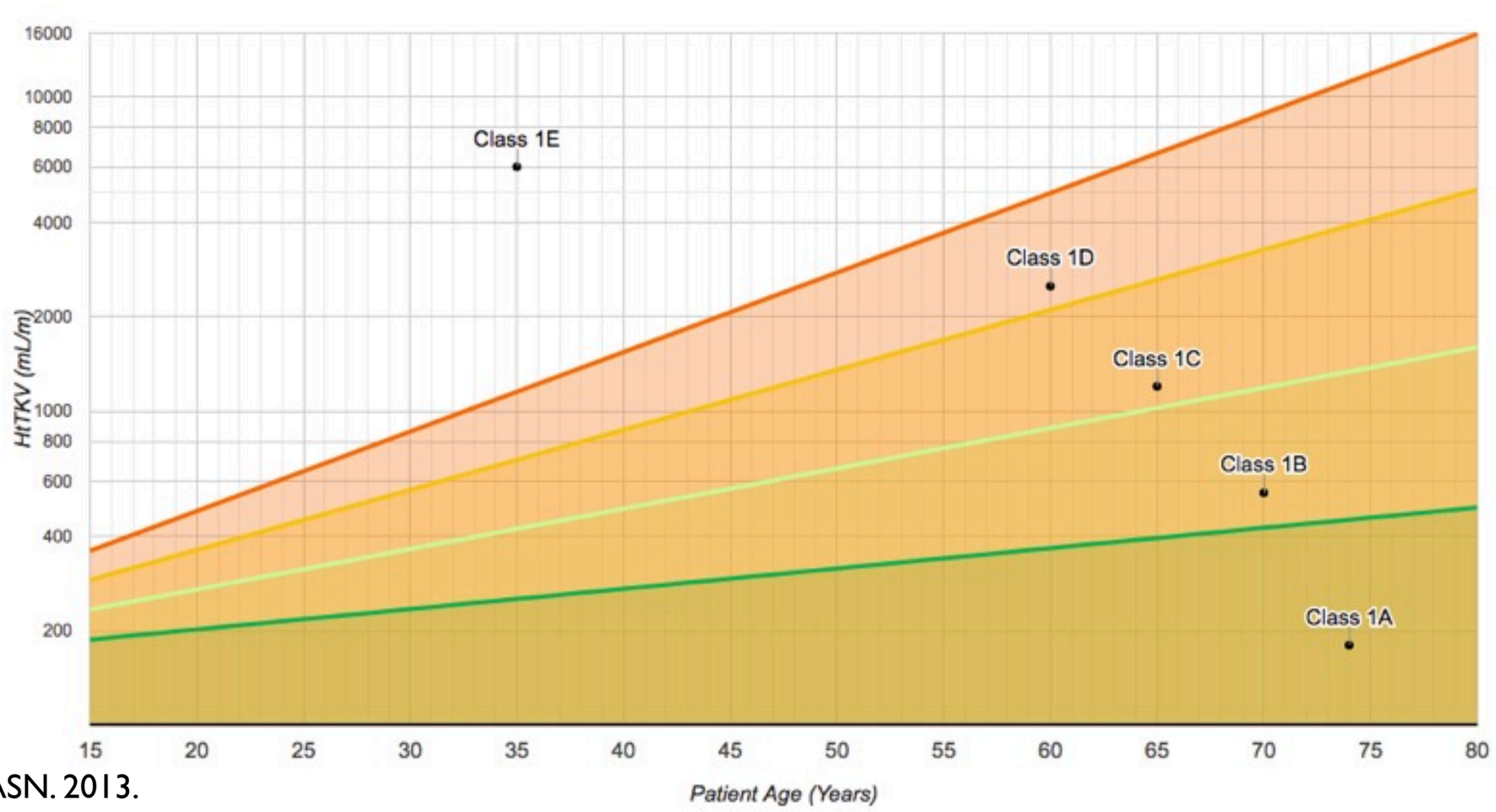


http://www.mayo.edu/research/documents/pkd-center-adpkd-classification/doc-20094754

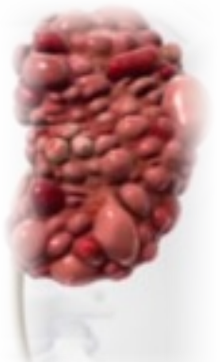
Diagnostic

Évaluation du risque de progression

- Classe I: typique: classification de Mayo



Irazabal et al. JASN. 2013.

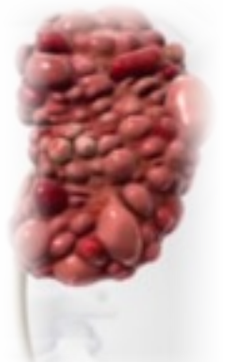


Diagnostic

Évaluation du risque de progression

- Classe I: typique: classification de Mayo

	↑ VRT/an
IA	< 1,5 %
IB	1,5 - 3 %
IC	3 - 4,5 %
ID	4,5 - 6 %
IE	> 6 %



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Diagnostic

Évaluation du risque de progression

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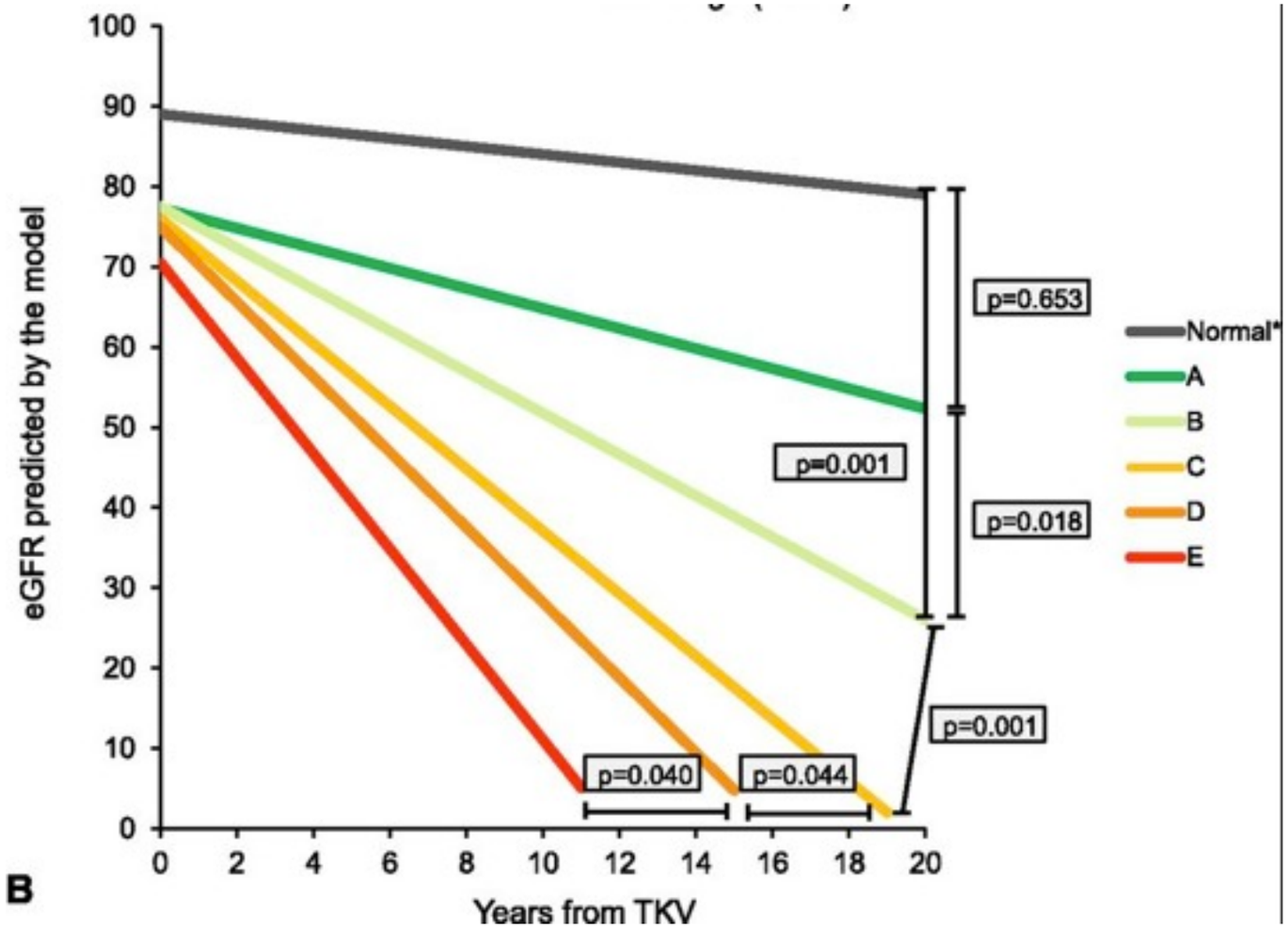
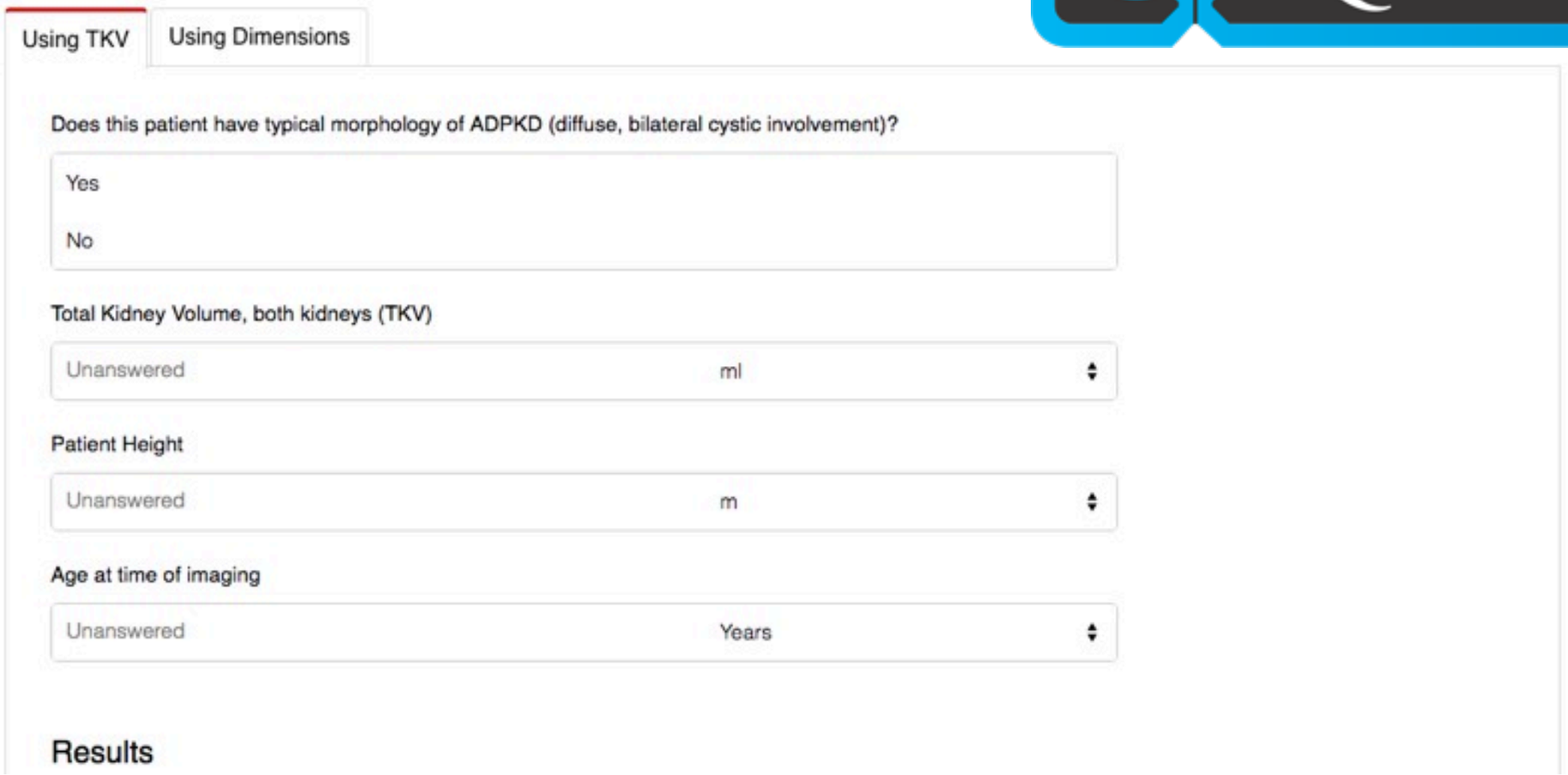


Irazabal et al. JASN. 2013.

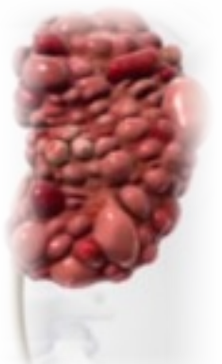
Diagnostic

Évaluation du risque de progression

- Outils en ligne



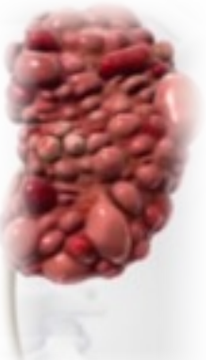
https://ukidney.com/nephrology-resources/adpkd-channel/mayo-adpkd-risk-tool#using-tkv



Diagnostic

Évaluation du risque de progression

- Exemple: Mme Tremblay
  - ♀ 32 ans, polykystose à l'écho
  - Mère polykystique, HD à 52 ans
  - 1 soeur polykystique, ø IRC à 3[illegible]
  - IRM:
    - Morphologie typique (classe 1)
  - Volume rénal total (ellipsoïde): 1281 mL



Diagnostic

Évaluation du risque de progression

Using TKV | Using Dimensions

Does this patient have typical morphology of ADPKD (diffuse, bilateral cystic involvement)?

Yes

No

Total Kidney Volume, both kidneys (TKV)

1281 ml

Patient Height

1.63 m

Age at time of imaging

32 Years

Diagnostic

Évaluation du risque de progression

Results

HtTKV

785.9 mL/m

Mayo Clinic Class

1D

Risk of Renal Progression

High risk, interventions to delay renal decline should be considered

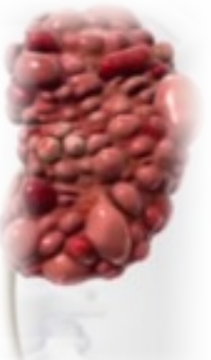
Estimated Frequency of ESRD at 10 years (from study cohort)

47.1%

Diagnostic

Évaluation du risque de progression

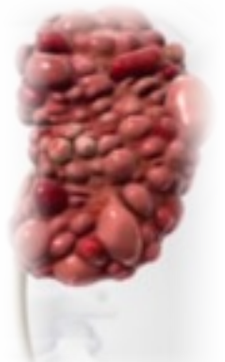
- Exemple: Mme Tremblay
  - ♀ 32 ans, polykystose à l'écho
  - Mère polykystique, HD à 52 ans
  - 1 soeur polykystique, ø IRC à 36 ans
  - IRM:
    - Morphologie typique (classe 1)
  - Volume rénal total (ellipsoïde): 1281 mL
  - Analyse
    - Sous-classe 1D
    - Risque d'IRCT à 10 ans: 47,1%



Polykystose autosomale dominante

Évaluation du risque de progression

- Imagerie sériée
  - Pas recommandé
  - Si VRT ↑ > 5% / an, haut risque



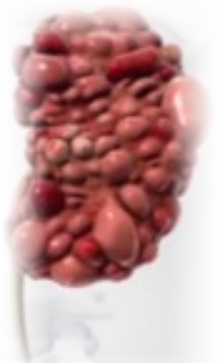
Polykystose autosomale dominante

Évaluation du risque de progression

- Autres facteurs

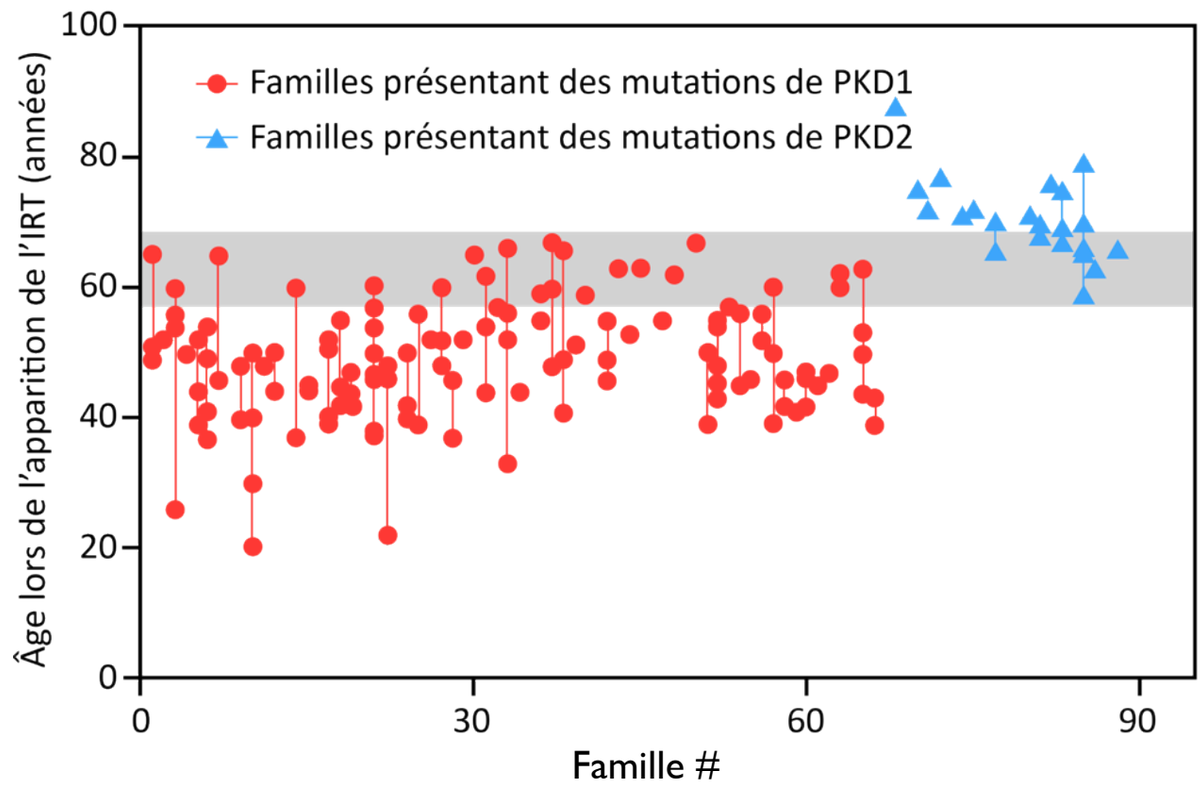
Table 5. The PROPKD Scoring System.

Factor	Points
Male	1
Hypertension before age 35 y	2
First urological event before age 35 y	2
PKD2 mutation	0
Nontruncating *PKD1* mutation	2
Truncating *PKD1* mutation	4



Rôle du dépistage génétique

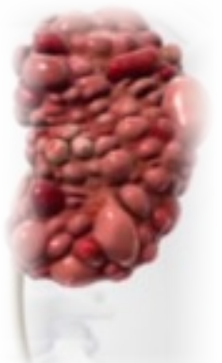
- Prédiction selon l'histoire familiale
  - 1 personne IRCT < 58 ans: PKD1
  - 1 personne IRCT > 68 ans: PKD 2



Barua et al. JASN. 2009.

Rôle du dépistage génétique

- Ne pas tester lorsque
  - L'imagerie est claire
  - L'imagerie familiale est claire
  - Manifestations extrarénales
- Envisager lorsque
  - Évaluation du donneur vivant
  - Présentation atypique et absence d'histoire familiale
  - Conseils prénataux



Canadian Society of Nephrology/
Société canadienne de néphrologie
CSN/SCN

Diagnostic
Résumé

- Référer en néphrologie afin d'établir le risque et l'indication de traiter
- Dépistage génétique
  - Non, sauf circonstances particulières
- Imagerie
  - Établir Classe typique (1) ou atypique (II)
  - Si classe I, établir le volume avec l'équation ellipsoïde (IRM, CT) ou longueur à l'écho
  - Répéter au maximum 1x/an
  - Établir risque de progression
    - Classification de Mayo
    - Gain volémique > 5%/an

Traitement

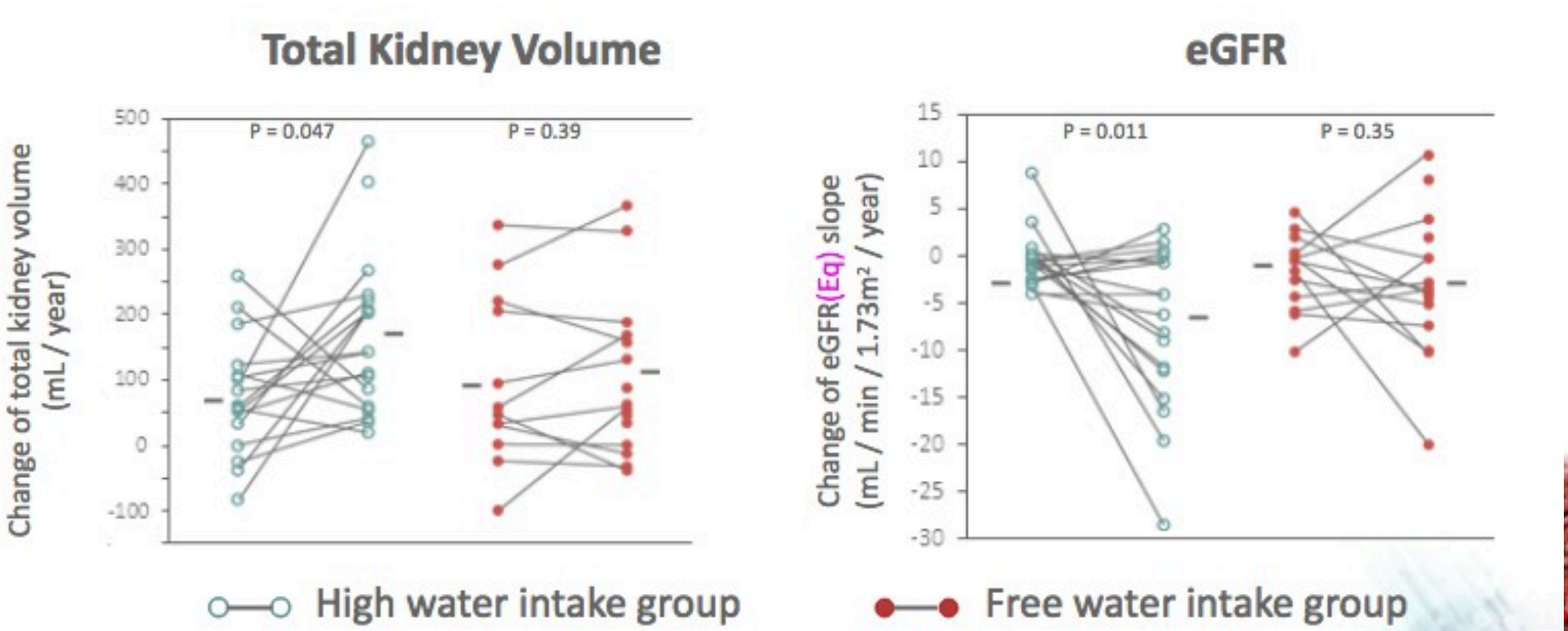
Concernant le traitement de la polykystose

- Il n'en existe aucun
- Le sirolimus permet de ralentir la progression
- Le tolvaptan permet de ralentir la progression
- Le tolvaptan permet de renverser la maladie

Traitement pharmacologique

Apport en eau

- Pas de bénéfice clair



Higashihara. NDT. 2014.

Traitement pharmacologique

Contrôle TA rigoureux

- Étude HALT-PKD A - 5 ans
  - < 50 ans, TFGe > 60 mL/min/1,73m^2, ø co-morbidité CV

	< 110/75	< 130/80
VRT	5,6%	6,5%
↓ Albuminurie	3,8%	2,5%
↓ TFGe	2,9	3

Shrier et al. NEJM. 2014.

Traitement pharmacologique

Contrôle TA rigoureux

- Étude HALT-PKD A - 5 ans
  - < 50 ans, TFGe > 60 mL/min/1,73m^2, ø co-morbidité CV

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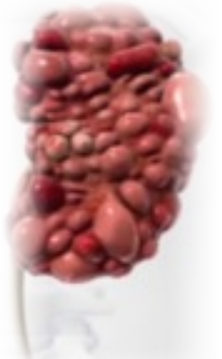
Shrier et al. NEJM. 2014.



Traitement pharmacologique

Contrôle TA rigoureux

- Étude HALT-PKD B - Lisinopril + (Telmisartan vs placebo)
  - < 50 ans, TFGe > 60 mL/min/1,73m^2, ø co-morbidité CV
- ø bénéfice

Traitement pharmacologique

Inhibiteurs mTOR

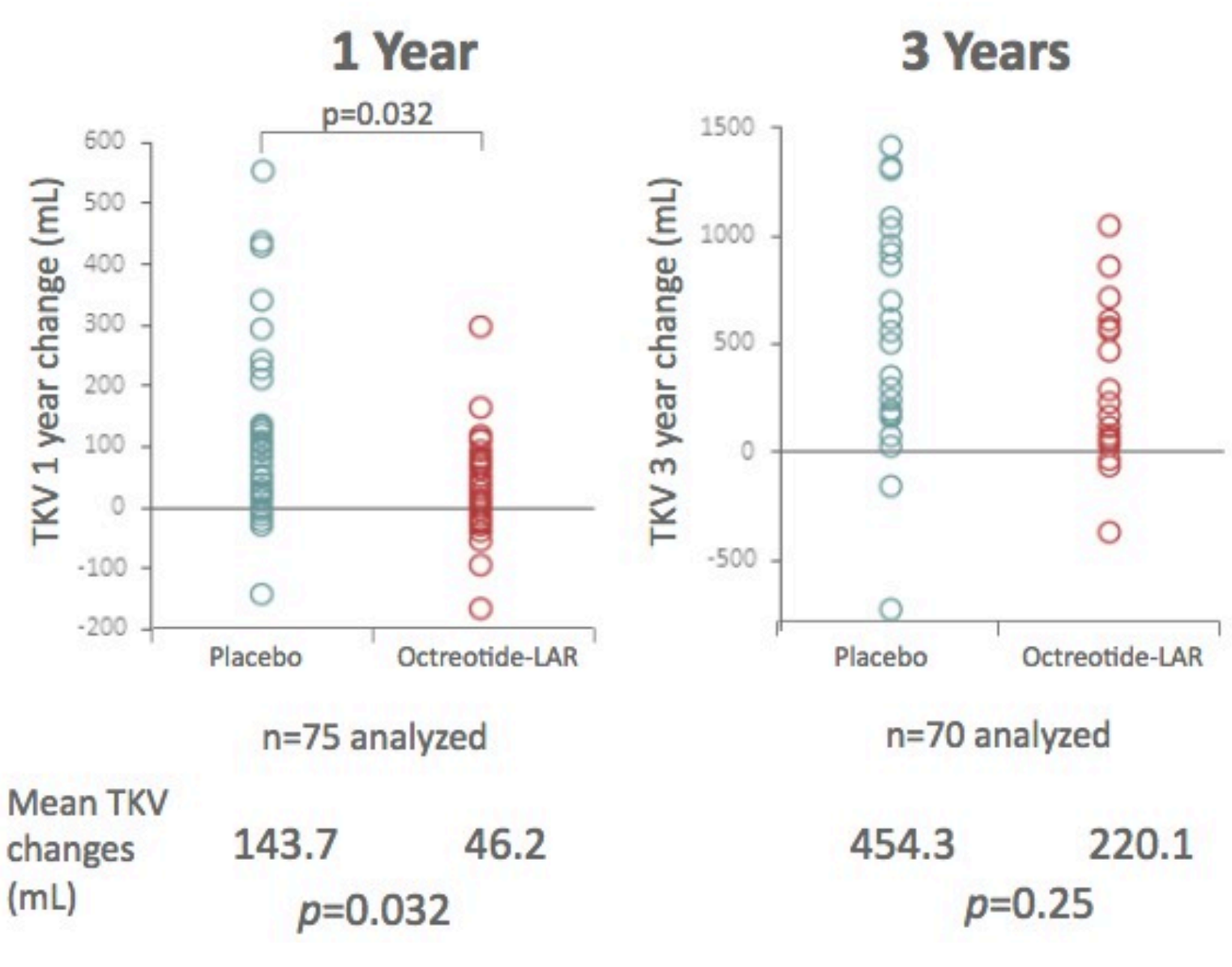
- Étude
  - mTOR fait croître kystes
  - À 18 mois, sirolimus sans effet sur VRT, TFGe
  - À 2 ans, everolimus sans effet sur VRT
    - Beaucoup de pertes au suivi
    - Étude trop courte?
    - Maladie trop avancée?

Liu et al. Transplant Proc. 2014.
Walz et al. NEJM. 2010.

Traitement pharmacologique

Analogues somatostatine

- Étude ALADIN: octréotide



Caroli et al. Lancet. 2013.

Traitement pharmacologique

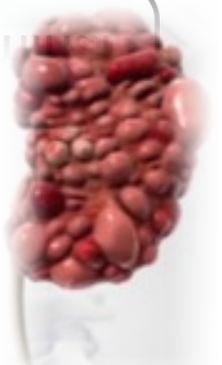
Tolvaptan

- Mécanisme

Bloc
- Transcription ADN
- Libération
- V_2R

AMPc

- Prolifération cellulaire kystes
- Sécrétion fluide endoluminal

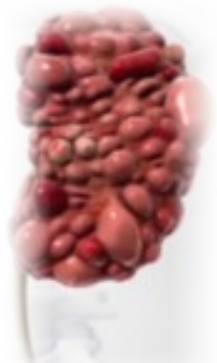


Traitement pharmacologique

Tolvaptan

- Usage
  - Grosse dose AM, petite dose 8h plus tard
  - Initiale: 45-15 mg
  - Cible: 90-30 mg (si toléré)
  - Boire
    - Polyurie

JINARC
tolvaptan

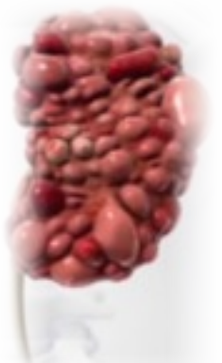


Étude TEMPO 3:4

Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes

- Phase III
- Distribution aléatoire
- Double insu
- 3 ans
- 1 145 patients
- Tolvaptan vs Placebo
  - Hydratation importante chez tous

Torres et al. NEJM. 2015.

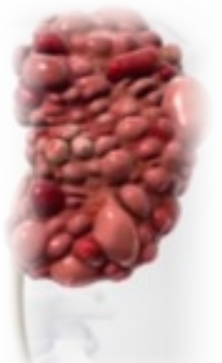


Étude TEMPO 3:4

Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes

- Phase III
- Distribution aléatoire
- Double insu
- 3 ans
- 1 145 patients
- Tolvaptan vs Placebo
  - Hydratation importante chez tous

Inclusion
18 - 50 ans
VRT > 750 mL (IRM)
Cockroft > 60 mL/min



Torres et al. NEJM. 2015.

Étude TEMPO 3:4

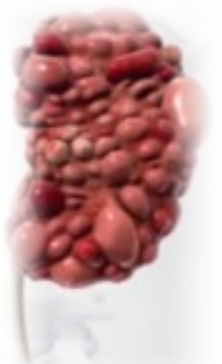
Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Tolvaptan (N = 961)	Placebo (N = 484)
Male sex — no. (%)	495 (51.5)	251 (51.9)
Age — yr	39±7	39±7
Race — no. (%)†		
White	810 (84.3)	408 (84.3)
Asian	121 (12.6)	62 (12.8)
Other	30 (3.1)	14 (2.9)
Stratification factor — no. (%)		
Hypertension	765 (79.6)	382 (78.9)
Estimated creatinine clearance <80 ml/min	242 (25.2)	130 (26.9)
Total kidney volume <1000 ml	197 (20.5)	101 (20.9)
Medical history — no. (%)		

Hypertension	765 (79.6)	382 (78.9)
Estimated creatinine clearance <80 ml/min	242 (25.2)	130 (26.9)
Total kidney volume <1000 ml	197 (20.5)	101 (20.9)
Medical history — no. (%)		
Hematuria	338 (35.2)	164 (33.9)
Kidney pain	496 (51.6)	239 (49.4)
Nephrolithiasis	187 (19.5)	109 (22.5)
Urinary tract infection	290 (30.2)	164 (33.9)
Anemia	105 (10.9)	48 (9.9)
Proteinuria	233 (24.2)	116 (24.0)
Current medication — no. (%)		
Angiotensin-converting–enzyme inhibitor	419 (43.6)	199 (41.1)
Angiotensin-receptor blocker	307 (31.9)	165 (34.1)
Angiotensin-converting–enzyme inhibitor, angiotensin-receptor blocker, or both	683 (71.1)	350 (72.3)
Beta-blocker	171 (17.8)	94 (19.4)
Calcium-channel blocker	180 (18.7)	104 (21.5)
Diuretic	32 (3.3)	14 (2.9)

Torres et al. NEJM. 2015.



Étude TEMPO 3:4

Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes

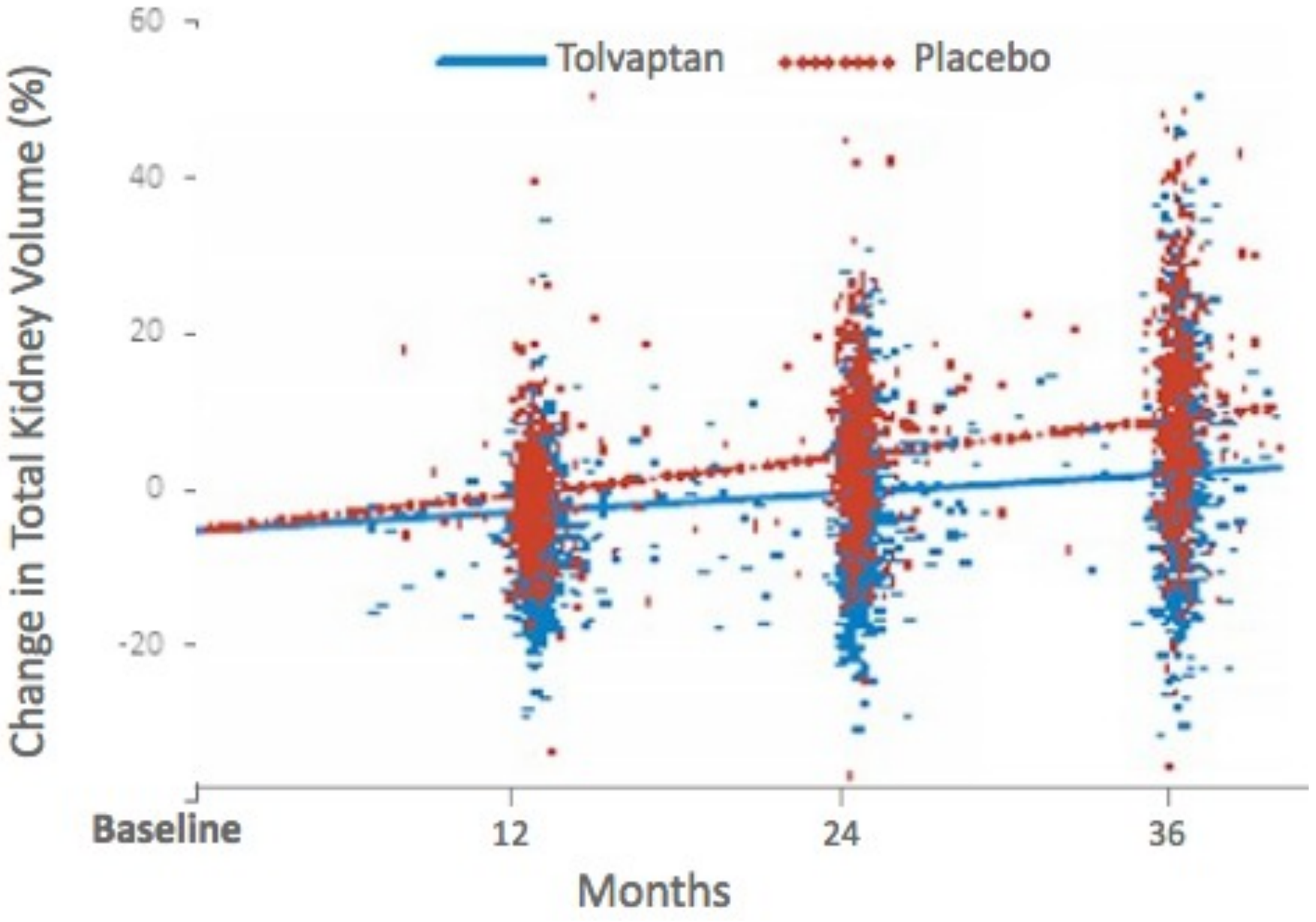
Table 1. (Continued.)

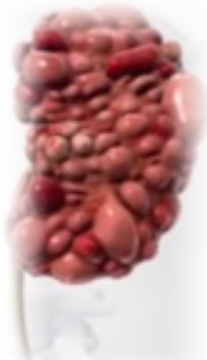
Characteristic	Tolvaptan (N = 961)	Placebo (N = 484)
Height — cm	173.5±10.4	173.6±7.8
Weight — kg	79±18	79±18
Blood pressure — mm Hg		
Systolic	128.6±13.5	128.3±13.5
Diastolic	82.5±9.9	82.5±9.3
Total kidney volume — ml	1705±921	1668±873
Height-adjusted total kidney volume — ml/m	979±515	958±483
Serum creatinine — mg/dl‡	1.05±0.30	1.04±0.32
Reciprocal of serum creatinine — $(mg/ml)^{-1}$	102.27±27.21	104.30±35.60
Estimated creatinine clearance — ml/min§	104.08±32.76	103.80±35.60
Estimated GFR — ml/min/1.73 m^2¶	81.35±21.02	82.14±22.73
Urinary albumin-to-creatinine ratio‖	7.2±14.3	8.6±21.7

Torres et al. NEJM. 2015.

Étude TEMPO 3:4

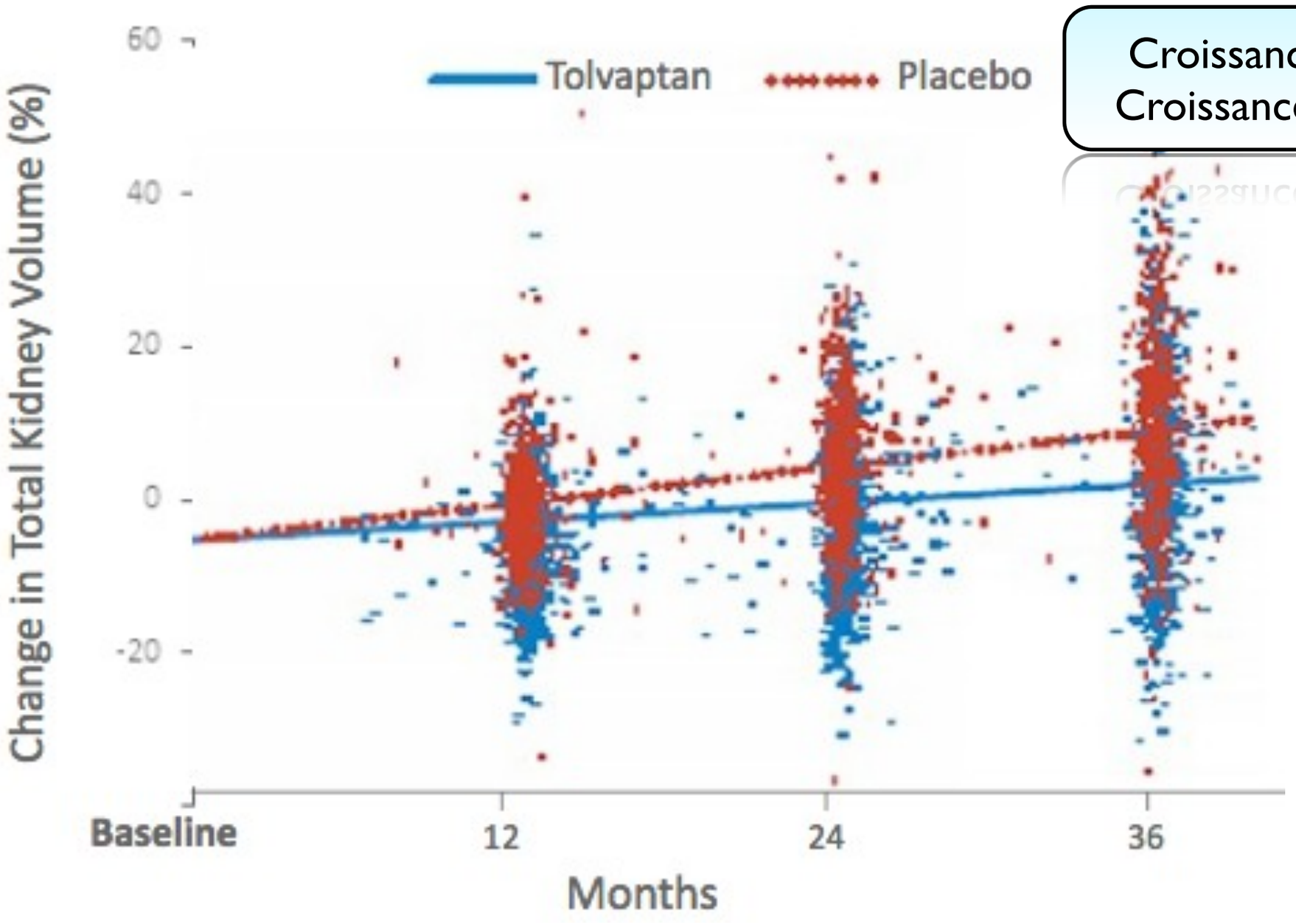
Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes



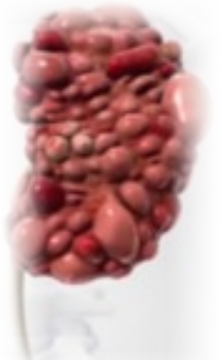


Étude TEMPO 3:4

Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes



Croissance placebo: 5,5%/an
Croissance tolvaptan: 2,8%/an

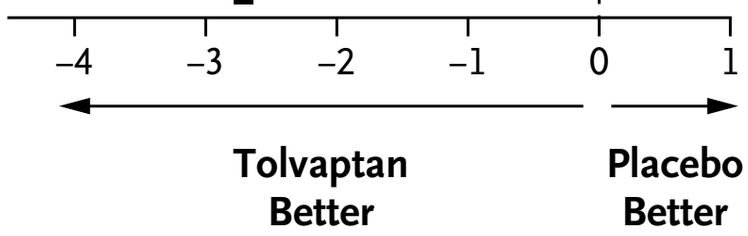


Étude TEMPO 3:4

Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes

B **Treatment Effect for Total Kidney Volume**

Subgroup	Absolute Treatment Effect	Relative Treatment Effect	Annual Slope		P Value
	Difference in annual slope (%/yr)	%	Tolvaptan %/yr	Placebo	
Sex					
Male		37.3	4.15	6.62	<0.001
Female		71.1	1.24	4.29	<0.001
Age					
<35 yr		28.0	4.37	6.06	0.02
≥35 yr		58.2	2.23	5.34	<0.001
Hypertension					
Yes		50.5	3.01	6.09	<0.001
No		51.2	1.62	3.32	0.008
Estimated creatinine clearance					
<80 ml/min		57.2	2.27	5.32	<0.001
≥80 ml/min		47.5	2.92	5.56	<0.001
Total kidney volume					
<1500 ml		48.8	2.24	4.37	<0.001
≥1500 ml		51.1	3.29	6.74	<0.001
All patients		49.2	2.80	5.51	<0.001



Étude TEMPO 3:4

Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes

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	Difference in annual slope (%/yr)	%	Tolvaptan %/yr	Placebo	
Sex					
Male		37.3	4.15	6.62	<0.001
Female		71.1	1.24	4.29	<0.001
Age					
<35 yr		28.0	4.37	6.06	0.02
≥35 yr		58.2	2.23	5.34	<0.001
Hypertension					
Yes		50.5	3.01	6.09	<0.001
No		51.2	1.62	3.32	0.008
Estimated creatinine clearance					
<80 ml/min		57.2	2.27	5.32	<0.001
≥80 ml/min		47.5	2.92	5.56	<0.001
Total kidney volume					
<1500 ml		48.8	2.24	4.37	<0.001
≥1500 ml		51.1	3.29	6.74	<0.001
All patients		49.2	2.80	5.51	<0.001

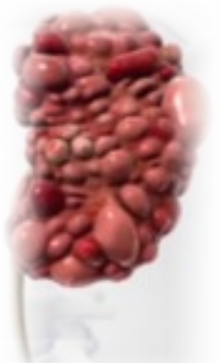
Étude TEMPO 3:4

Tolvaptan Efficacy and Safety in Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes

- Mieux lorsqu'on s'attarde aux IC-IE

Classe : N (%)	2: 42 (3,1)		1B: 96 (7,4)		1C: 474 (37)		1D: 441 (34)		1E: 220 (18)	
	VRT	DFGe	VRT	DFGe	VRT	DFGe	VRT	DFGe	VRT	DFGe
Placebo	2,48	-1,66	3,25	-2,10	5,12	-3,59	6,62	-3,89	7,75	-4,93
Tolvaptan	2,27	-1,34	1,23	-1,79	1,79	-2,32	3,03	-2,99	4,96	-3,46
Valeur p	0,88	0,75	0,023	0,64	<0,0001	<0,0001	<0,0001	0,007	<0,0001	<0,0001

- ↓ TFGe -2,7 vs -3,7



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	VRT	DFGe	VRT	DFGe	VRT	DFGe	VRT	DFGe	VRT	DFGe
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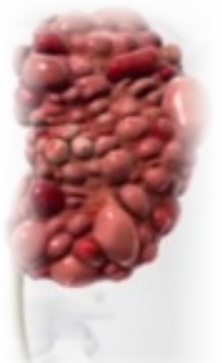
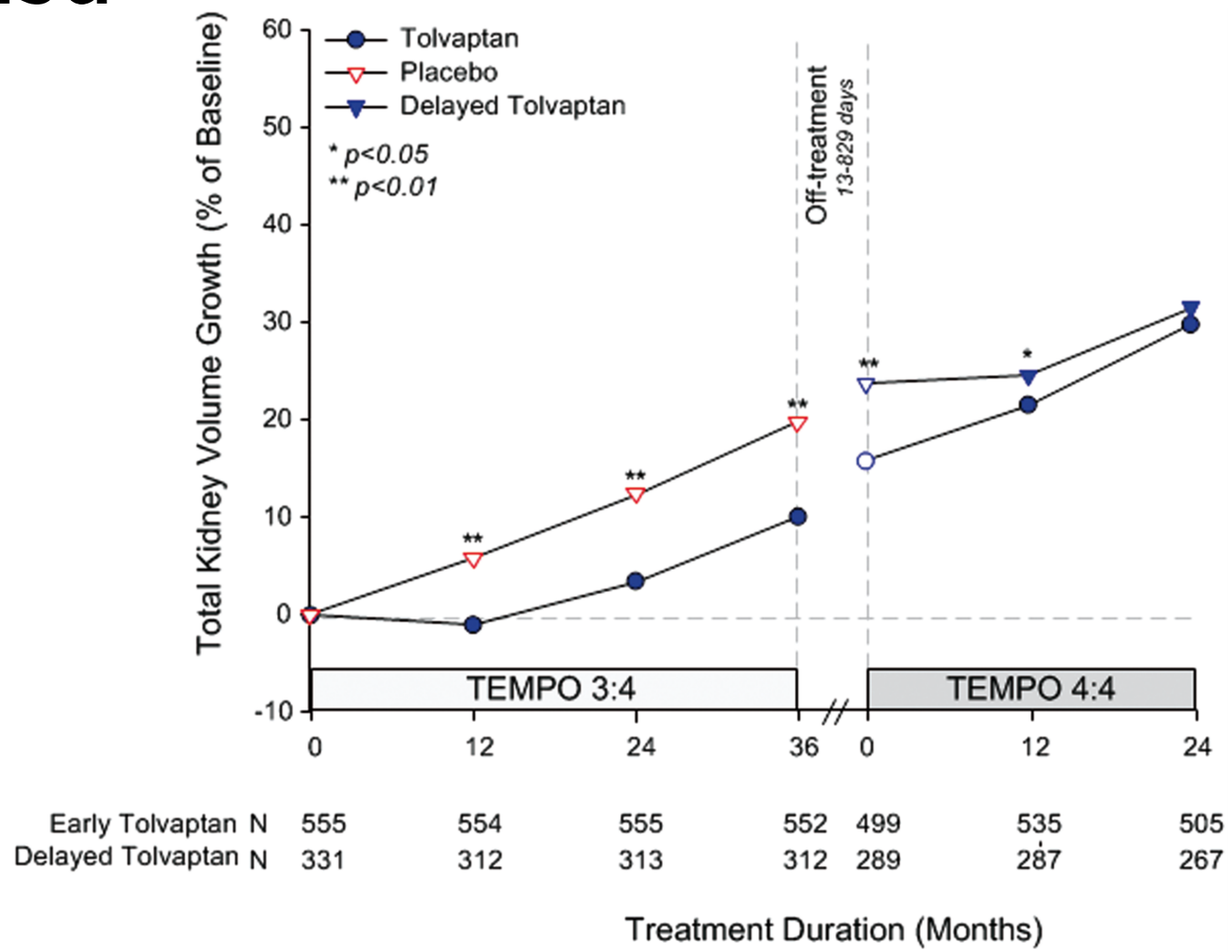
Valeur p	0,88	0,75	0,023	0,64	<0,0001	<0,0001	<0,0001	0,007	<0,0001	<0,0001

- ↓ TFGe -2,7 vs -3,7

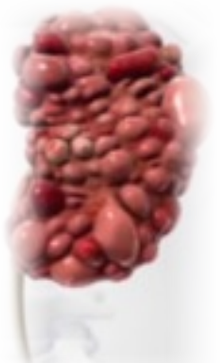


Étude TEMPO 4:4

- Prolongation de 2 ans de TEMPO 3:4
- ø insu



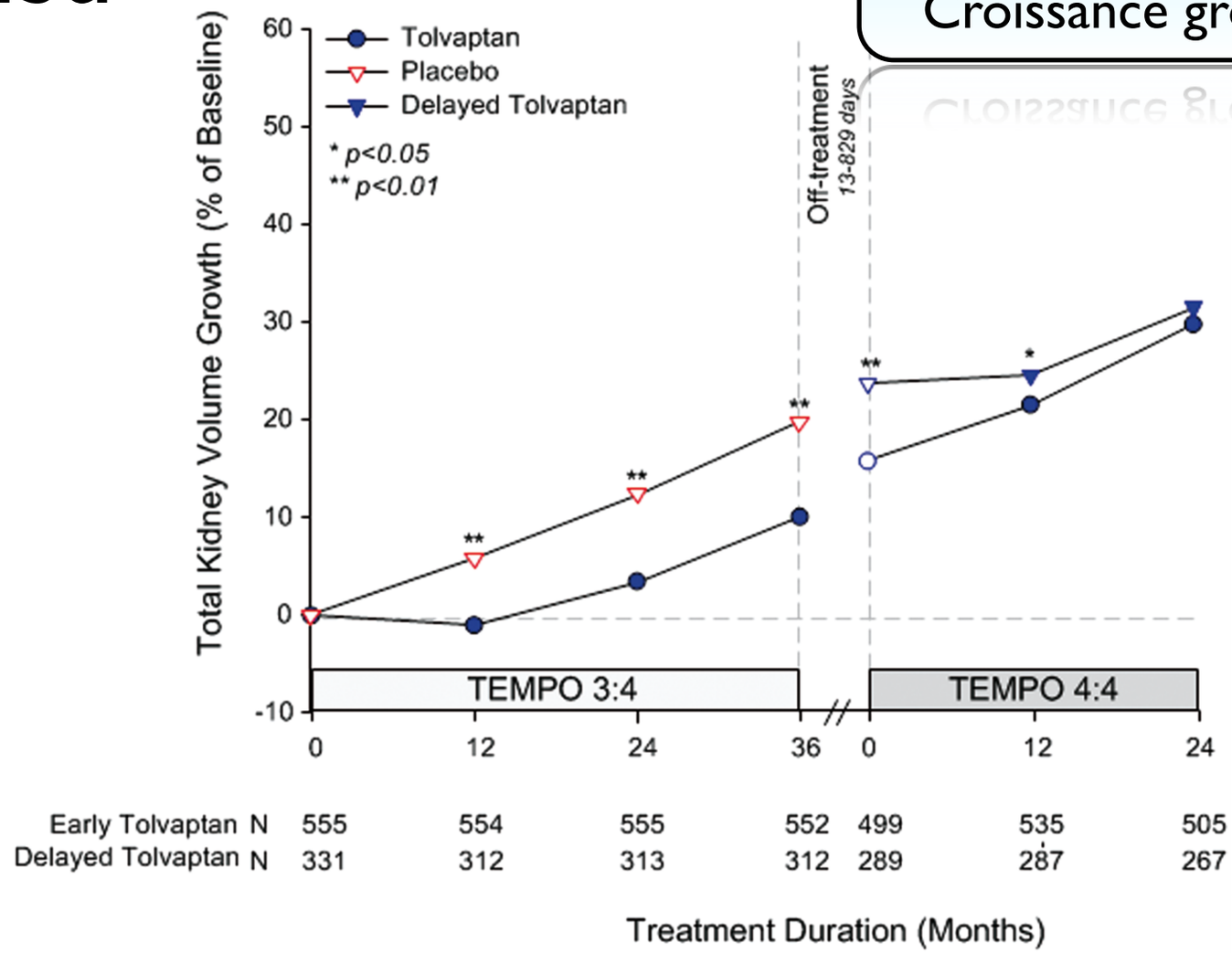
Torres et al. NDT. 2017.

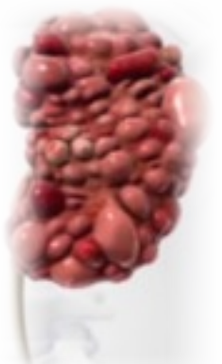


Étude TEMPO 4:4

- Prolongation de 2 ans de TEMPO 3:4
- ø insu

Croissance groupe tardif: 31,6%
Croissance groupe précoce: 29,9%





Torres et al. NDT. 2017.

ADPKD

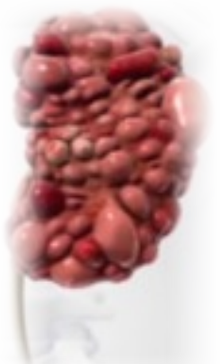
REPRISE

Étude REPRISE

Replicating Evidence of Preserved Renal Function: An Investigation of Tolvaptan Safety and Efficacy in ADPKD

- Objectifs
  - Confirmer le bénéfice de tolvaptan en IRC plus avancée
  - Confirmer l'innocuité hépatique du tolvaptan et la sécurité de la surveillance mensuelle

Torret et al. NEJM. 2017.



ADPKD

REPRISE

Inclusion

	TEMPO 3:4	REPRISE
Âge	18 - 50 ans	18 - 55 - ou - 56 - 66 avec TFGe 25-44 et déclin > 2mL/min/an
VRT	TKV > 750 mL	-
TFG	> 60 mL/min	25 - 65 mL/min
Issue 1°	VRT	TFGe

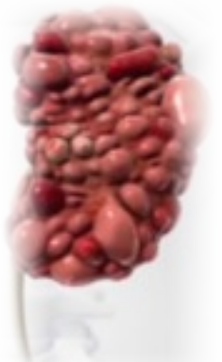
ADPKD

REPRISE

Résultats

Table 1. Demographic and Clinical Characteristics at Baseline and Safety Profile during the Single-Blind Tolvaptan Period.*

Characteristic	Tolvaptan Group (N = 683)	Placebo Group (N = 687)
Age — yr	47.3±8.2	47.2±8.2
Male sex — no. (%)	347 (50.8)	333 (48.5)
Height — cm	174±10	173±10
Weight — kg	84.6±19.9	81.6±19.3
Body-mass index	28.0±5.8	27.7±5.6
Race — no. (%)†		
White	626 (91.7)	632 (92.0)
Asian	22 (3.2)	19 (2.8)
Black	25 (3.7)	23 (3.3)
Other	10 (1.5)	13 (1.9)
Family history of polycystic kidney disease — no./total no. (%)	514/679 (75.7)	529/687 (77.0)
Blood pressure — mm Hg		
Systolic	129.3±13.8	129.9±14.5
Diastolic	82.1±9.6	82.6±9.7
Estimated GFR — ml/min/1.73 m^2‡	40.7±10.9	41.4±11.2
Chronic kidney disease stage — no./total no. (%)		
2	32/683 (4.7)	39/684 (5.7)
3a	209/683 (30.6)	202/684 (29.5)
3b	303/683 (44.4)	315/684 (46.1)
4	139/683 (20.4)	128/684 (18.7)
Hypertension — no. (%)§	634 (92.8)	640 (93.2)
Current use of RAAS inhibitor — no. (%)	595 (87.1)	581 (84.6)
History of kidney pain — no. (%)	338/675 (50.1)	344/679 (50.7)
Dose at end of single-blind tolvaptan period — no. (%)		
60 mg in morning and 30 mg in afternoon	118 (17.3)	124 (18.0)
90 mg in morning and 30 mg in afternoon	565 (82.7)	563 (82.0)



ADPKD

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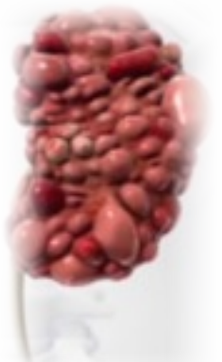
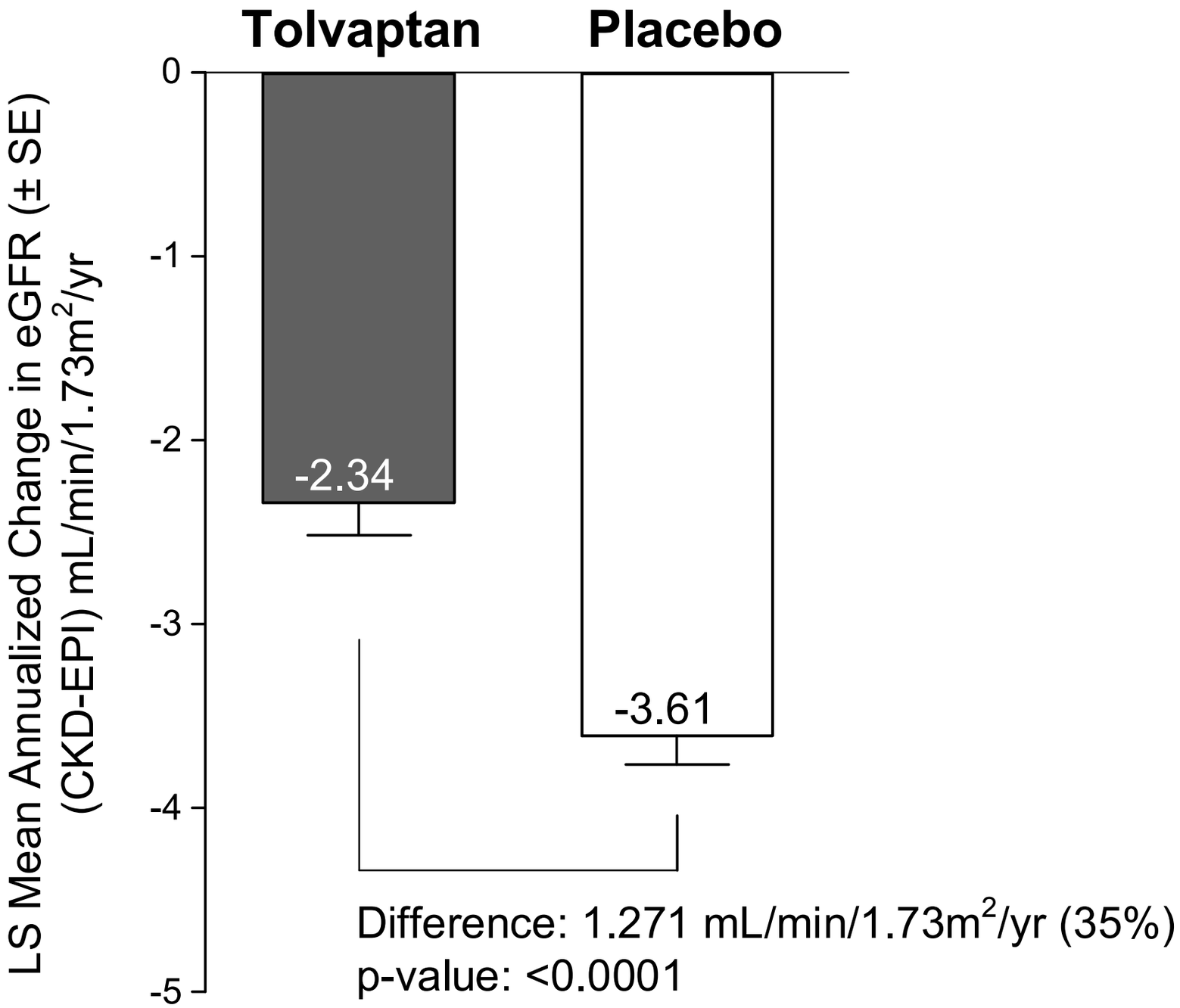
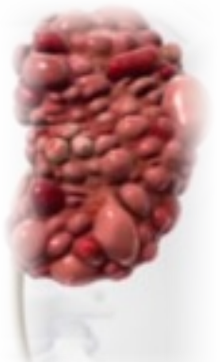


ADPKD

REPRISE

Résultats





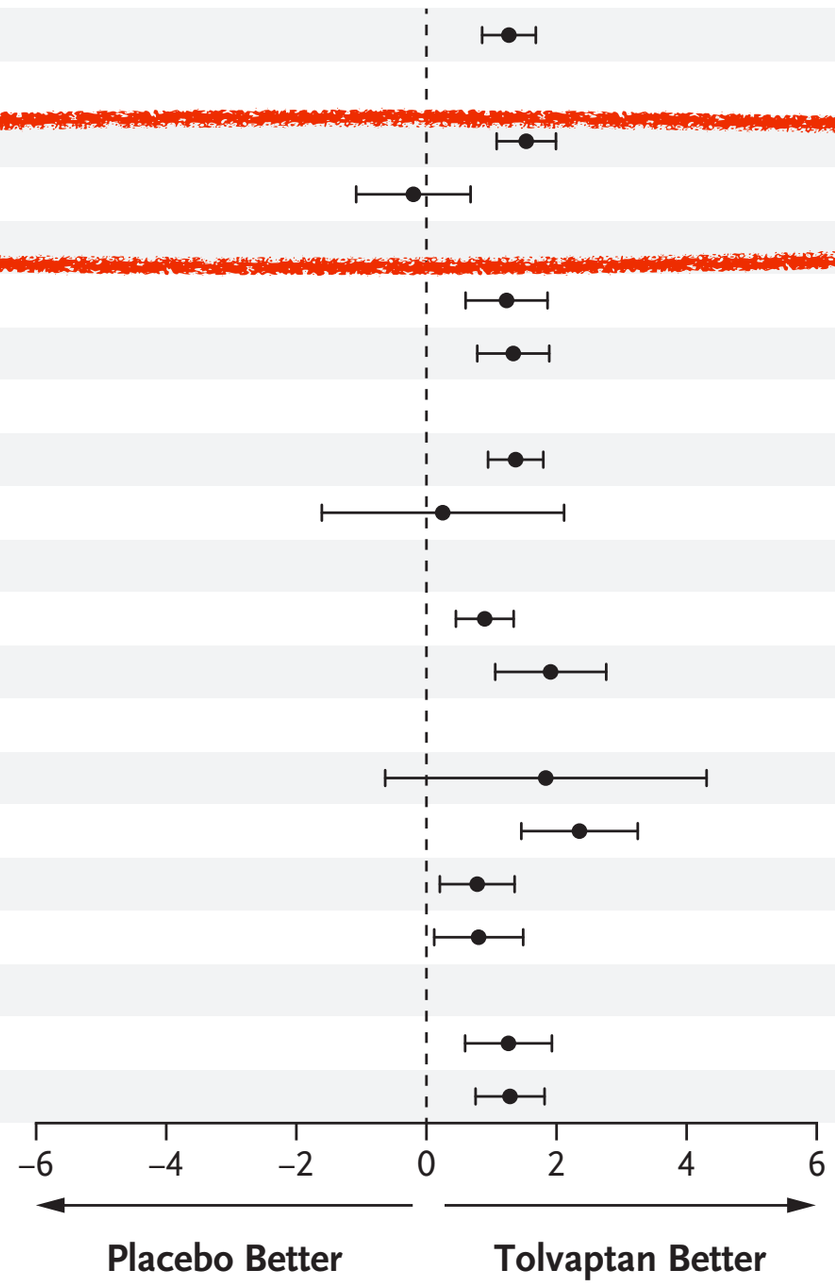
ADPKD

REPRISE

Résultats

A Subgroup Analyses

Subgroup	Tolvaptan	Placebo	Mean Estimated GFR Change (95% CI)	Difference	P Value
			Tolvaptan / Placebo		
	no. of patients		*ml/min/1.73 m²*		
All patients	668	663	−2.34 / −3.61	1.27	<0.001
Age					
≤55 yr	572	569	−3.07 / −4.60	1.54	<0.001
>55 yr	96	94	−2.54 / −2.34	−0.20	0.65
Sex					
Female	327	341	−2.89 / −4.13	1.23	<0.001
Male	341	322	−3.09 / −4.43	1.34	<0.001
Race					
White	614	610	−2.97 / −4.34	1.37	<0.001
Nonwhite	54	53	−3.29 / −3.54	0.25	0.79
Baseline estimated GFR					
≤45 ml/min/1.73 m²	432	423	−3.45 / −4.35	0.90	<0.001
>45 ml/min/1.73 m²	236	240	−2.20 / −4.11	1.91	<0.001
Chronic kidney disease stage					
2	31	38	−2.81 / −4.65	1.84	0.14
3a	206	196	−2.13 / −4.49	2.36	<0.001
3b	294	304	−3.20 / −3.99	0.78	0.008
4	137	125	−3.80 / −4.60	0.81	0.02
Geographic region					
United States	286	282	−2.88 / −4.14	1.26	<0.001
Other	382	381	−3.09 / −4.38	1.29	<0.001



ADPKD

REPRISE

Résultats

A Subgroup Analyses

Subgroup	Tolvaptan	Placebo	Mean Estimated GFR Change (95% CI)		Difference	P Value
			Tolvaptan	Placebo		
	no. of patients		*ml/min/1.73 m²*			
All patients	668	663	−2.34	−3.61	1.27	<0.001
Age						
≤55 yr	572	569	−3.07	−4.60	1.54	<0.001
>55 yr	96	94	−2.54	−2.34	−0.20	0.65
Sex						
Female	327	341	−2.89	−4.13	1.23	<0.001
Male	341	322	−3.09	−4.43	1.34	<0.001
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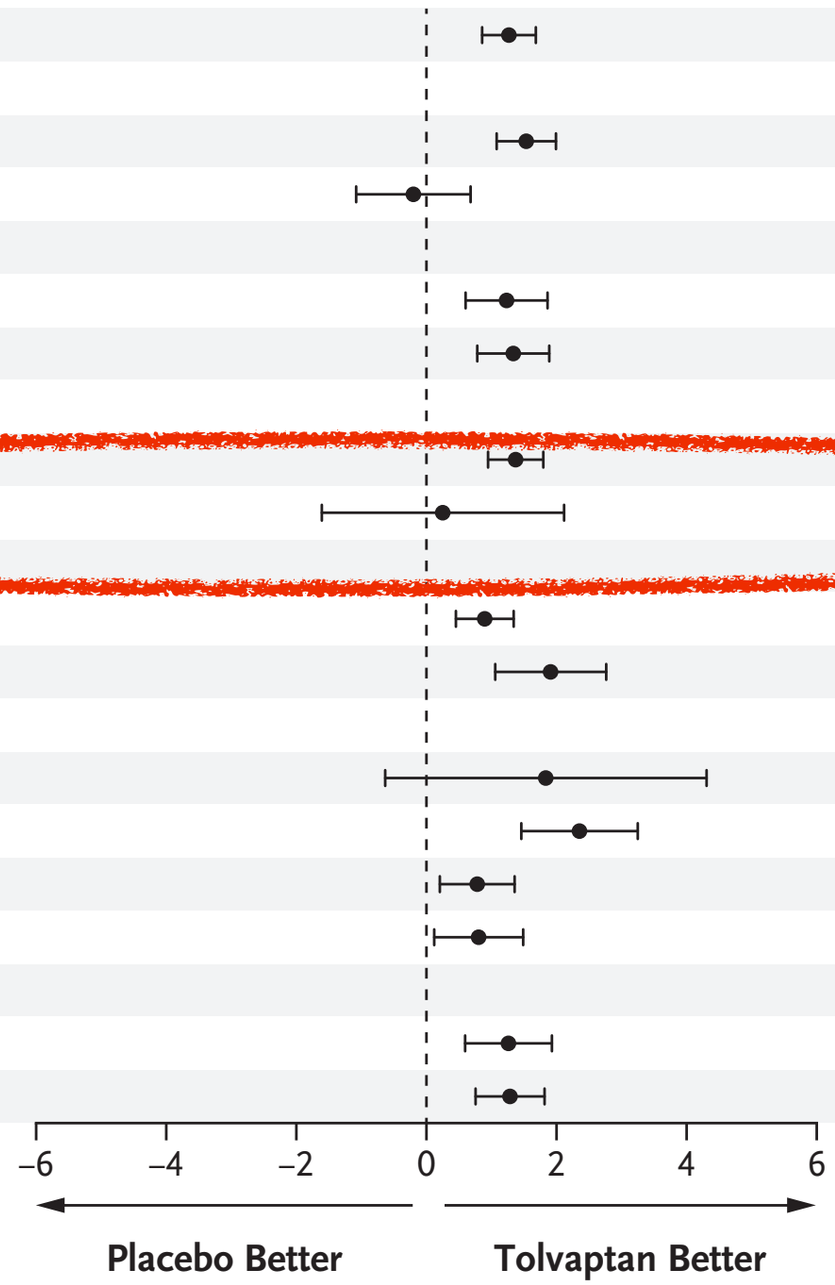

ADPKD

REPRISE

Résultats

A Subgroup Analyses

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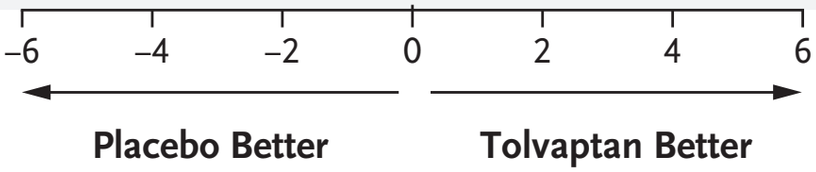
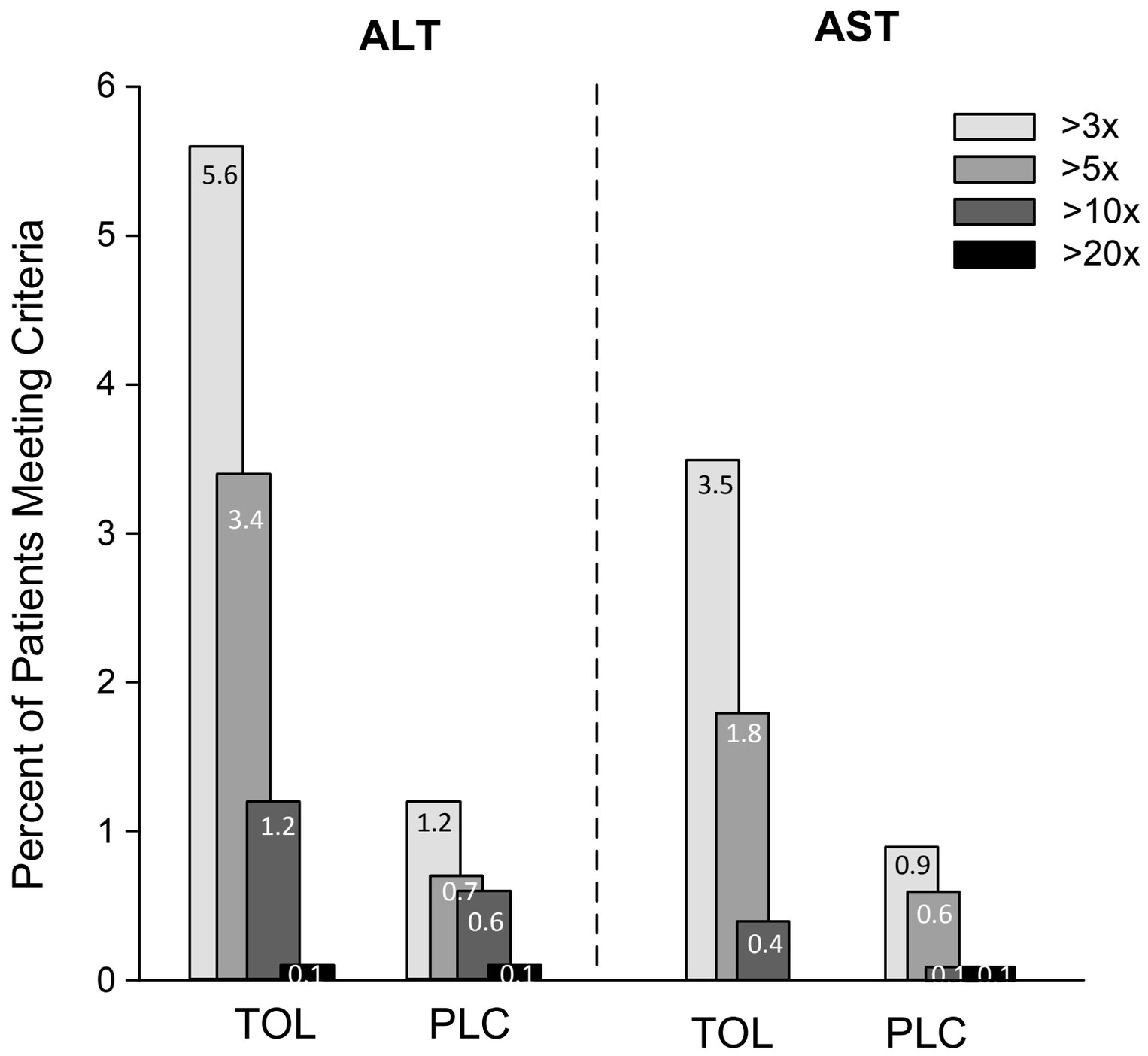


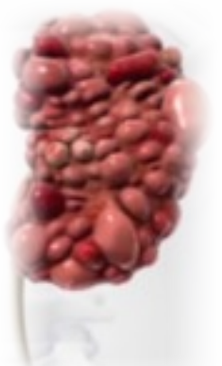
ADPKD

REPRISE

Résultats

Inocuité



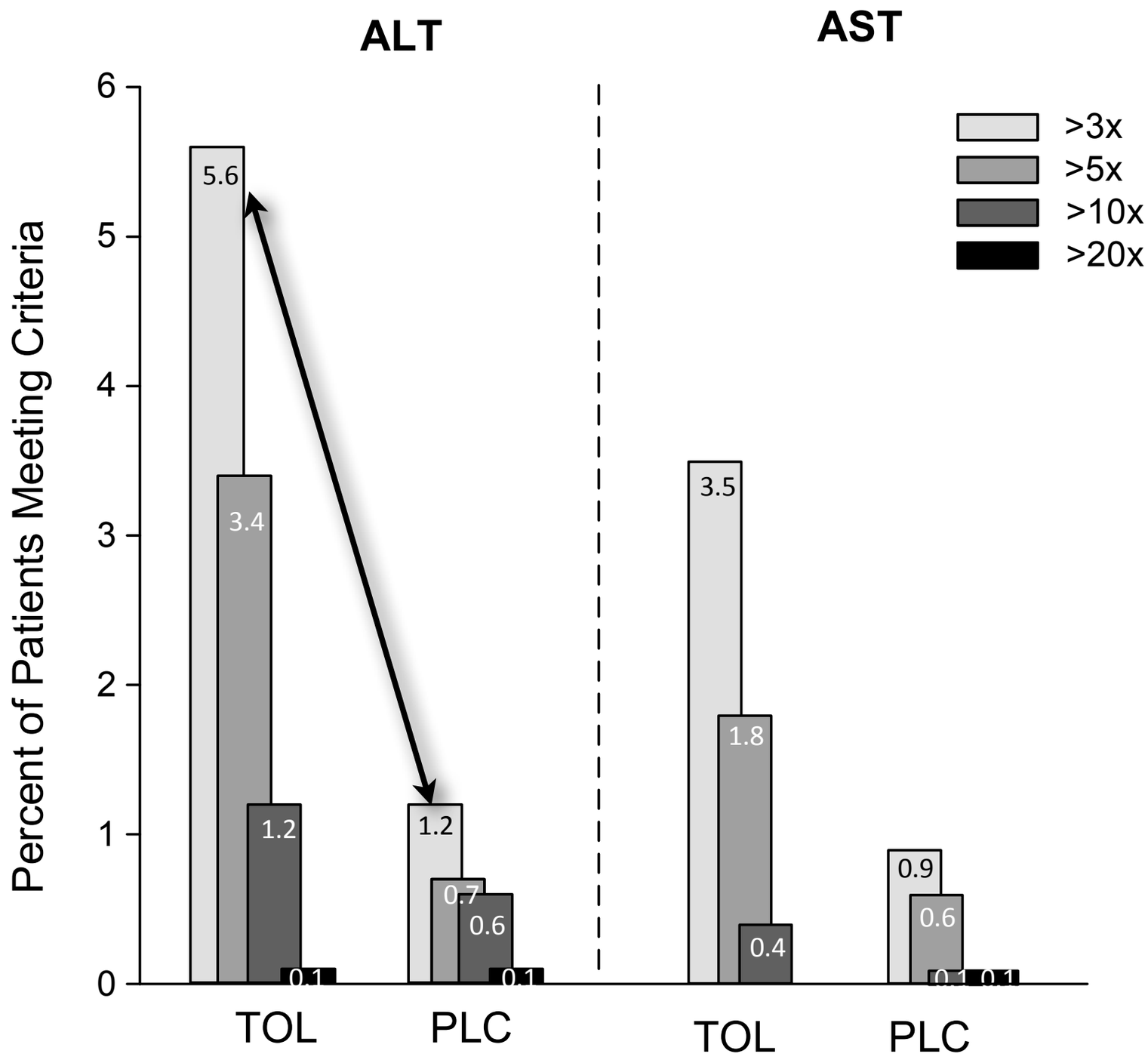


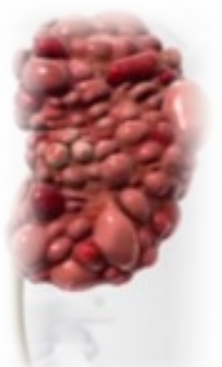
ADPKD

REPRISE

Résultats

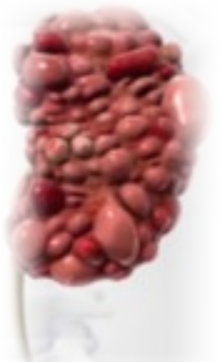
Inocuité





Résumé

- Étude prospective, randomisée, contrôlée, à double insu
- Portant sur des sujets avec IRC plus avancée et des sujets plus âgés
- Bénéfice à 1 an comparable à l'étude TEMPO 3:4
- Sécuritaire



Traitement

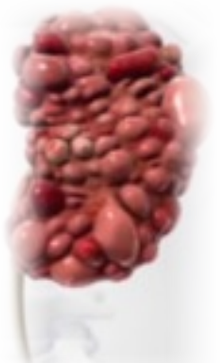
- Autres agents à l'étude
  - Triptolide
  - Bosutinib
  - PD98059
  - EKI-785
  - Sirolimus, everolimus
  - Roscovitine
  - Etanercept

Canadian Society of Nephrology/
Société canadienne de néphrologie
CSN/SCN

Traitement

Résumé

- Viser TA < 110/75 mm Hg (HALT-PKD)
  - Si < 50 ans et TFGe > 60 mL/min/1,73m^2 sans co-morbidité CV
    - Viser TA < 110/75 mm Hg
- Tolvaptan si (TEMPO 3:4)
  - 18-50 ans
  - Cockroft > 60 mL/min (CKD-EPI > 45 mL/min)
  - VRT > 750 mL (Écho longueur > 16,5 cm)
  - Mayo 1D et 1E (1C si autres facteurs de risque)



Conclusion

- Maladie autosomale dominante (PKD1 et PKD2) affectant ~ 0,1% des Canadiens
  - 4e cause d'IRC terminale
- Plusieurs manifestations rénales et extra-rénales
- Risque d'IRCT selon classification de Mayo
  - Outil de décision thérapeutique
- Traitement
  - Tolvaptan: étudié dans TEMPO et REPRISE
    - Gain de volume ralenti de 49% / 3 ans
    - Perte de TFGe ralentie de 1,3 mL/min/an p/r placebo
    - Sécuritaire: surveillance mensuelle du bilan hépatique