MECHANISMS OF RENAL FUNCTION DECLINE AND ESRD

Rémi Salomon
Necker Hospital, Paris, France

Amsterdam, June 17th 2016

Disclosure of Interests

- Alexion (registery, sponsored education)
- Raptor (expert witness, co-investigator)
- Oxthera (co-investigator)

(e.g. employment, consultancy, honoraria, stock ownership, sponsored education, research grant, educational grant, expert witness, other relevant funding, etc ...)

2. Management of renal function decline and ESRD

Q1. How can we optimize a cooperative approach of tertiary expert centers with local care centers, particularly in the patient transition from pediatric to adult care? How/when do we involve non-renal specialists to address extrarenal manifestations?

Q2. Are so-called "renoprotective drugs" dangerous in some rare kidney diseases, such as salt-wasting tubulopathies? Is the generally accepted wisdom in nephrology (such as use of ACE-inhibitors, avoidance of NSAID, etc.) applicable to specific rare diseases and at all levels of kidney function? Are most treatment targets (blood pressure, sodium, dietary protein, etc.) still applicable for this population?

Q3. How should one monitor for potential renal and extrarenal complications and if so, how frequently?

Q4. How can we help the patient and family to accept the chronic disease, live with it and manage it responsibly? Any specific issues related to compliance, monitoring, and follow-up?

Q5. How can we ensure equity of access to optimal care, including expensive drugs?

Q6. What is the optimal modality for dialysis? Does this vary by disorder?

Q7. What is the optimal timing for transplant and role/utility of pre-emptive transplantation? How can we better address the risk of disease recurrence post-transplant?

Q8. What are extrarenal issues in dialysis or transplant settings that call for particular management?

Q9. How can growth-related issues and treatment be optimally managed?

Overview

- 9 questions around management of renal function decline and CKD progression
- Impossible to consider the 150 different rare renal diseases (RRD)
- I choose some exemples
  - Our experience
  - The general perspective around RRD

- Cystinosis in adult
- *HNF1B* and autism
- Lowe syndrome/ haemorrhage
- Methylmalonic acidemia/ transplantation
- Growth hormone treatment

Q1. How can we optimize a cooperative approach of tertiary expert centers with local care centers, particularly in the patient transition from pediatric to adult care? How/when do we involve non-renal specialists to address extrarenal manifestations?

Patients with rare disease should be referred to tertiary centre at the time of diagnosis (or for diagnosis to be done) and regularly thereafter

Adult centre are in general not expert in rare diseases, in each centre it would be wise to have one referent nephrologist with a special interest in rare disease to take care of these patients

Once a year (or less depending on the situation) a multidisciplinary check-up can be organized during a single day including:

dietician, psychologist, dedicated nurse and the different specialits…

ORKiD FILIÈRE ORPHAN KIDNEY DISEASES

Le réseau de santé des maladies rénales rares de l'enfant et de l'adulte

KDIGO Controversies Conference on Common Elements in Uncommon Kidney Diseases

Acteurs de la filière

- Centre de référence
- Centre de compétences

2. Les première actions de la filières

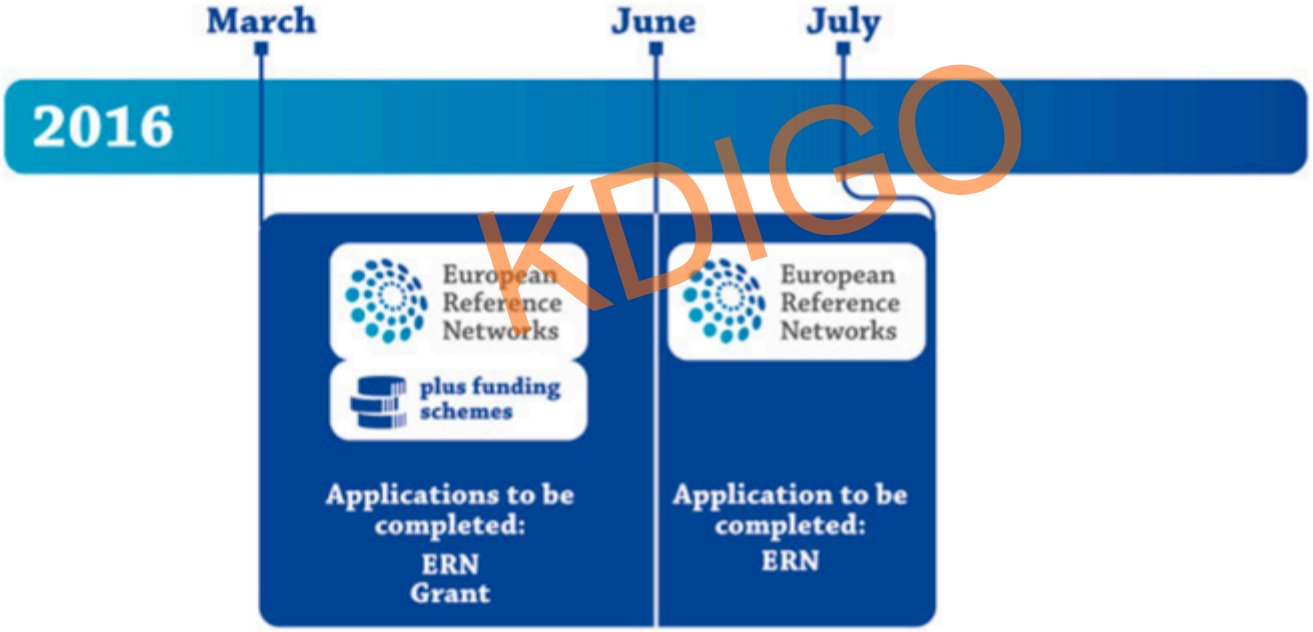
www.filiereorkid.com

European networks of reference for rare diseases

Browse the theme

- Introduction
- Definition of centre of reference in European countries
- Identifying and designating centres of reference at national level
- Identifying and designating European reference networks
- Diagnosis and care: how can centres of reference best serve rare disease patients?

RARE DISEASES



All topic

Go back to

Europe

Brows

Introdu

Definit

Identifying and designating centres of reference at national level

Identifying and designating European reference networks

Diagnosis and care: how can centres of reference best serve rare disease patients?

Transition from pediatric to adult care

Sensibilisation years before

See the adolescent alone during outpatient clinics

Common outpatient clinics (when possible) with both adult and pediatric nephrologists at the time of transition

Edit protocols for the care

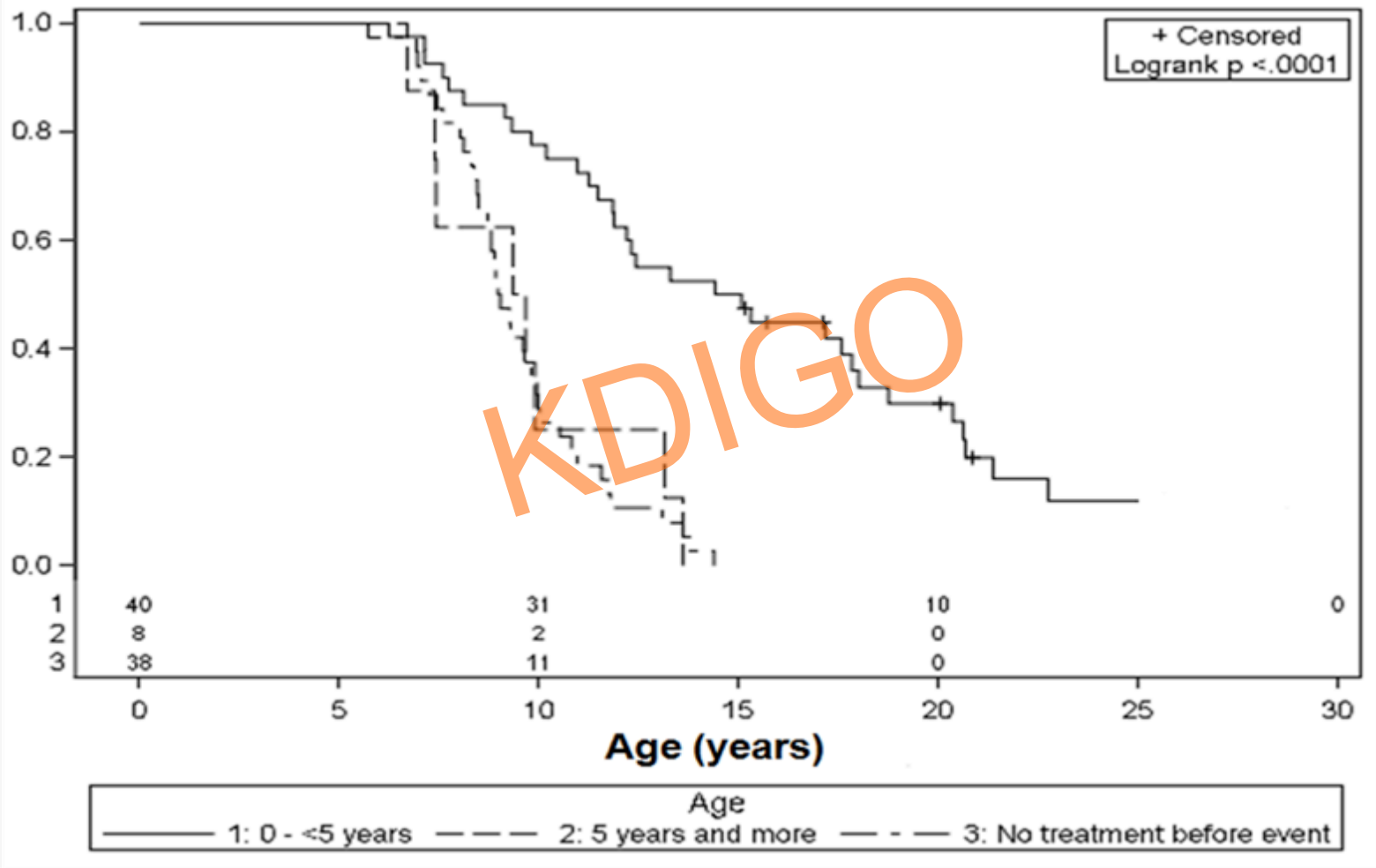
Keep talking with the adult nephrologists

Staff with A and P to discuss the cases

Everyone need to know and improve his knowledge about the complications that occur with ageing

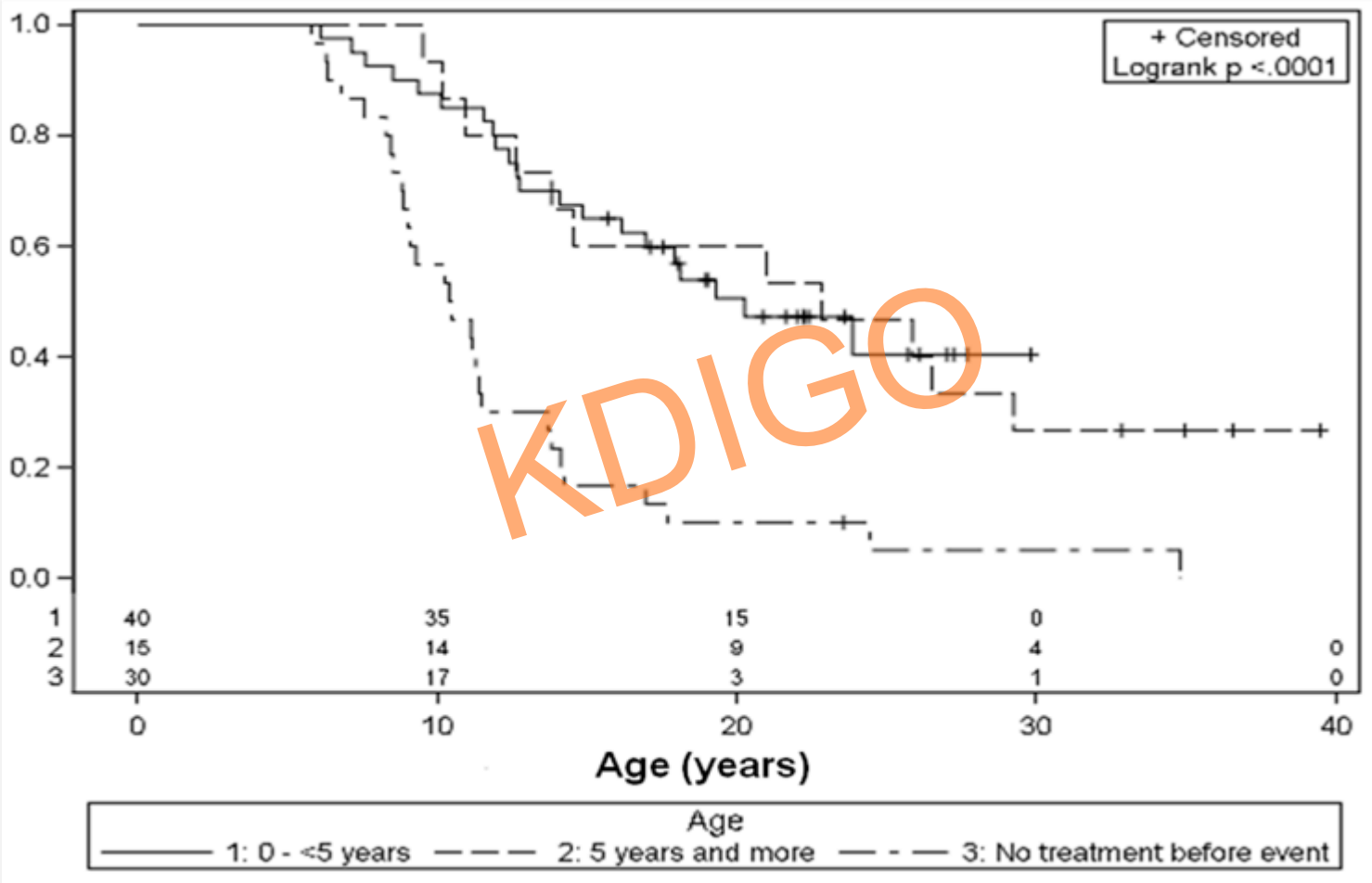
Ex: cystinosis

ESRD in cystinosis



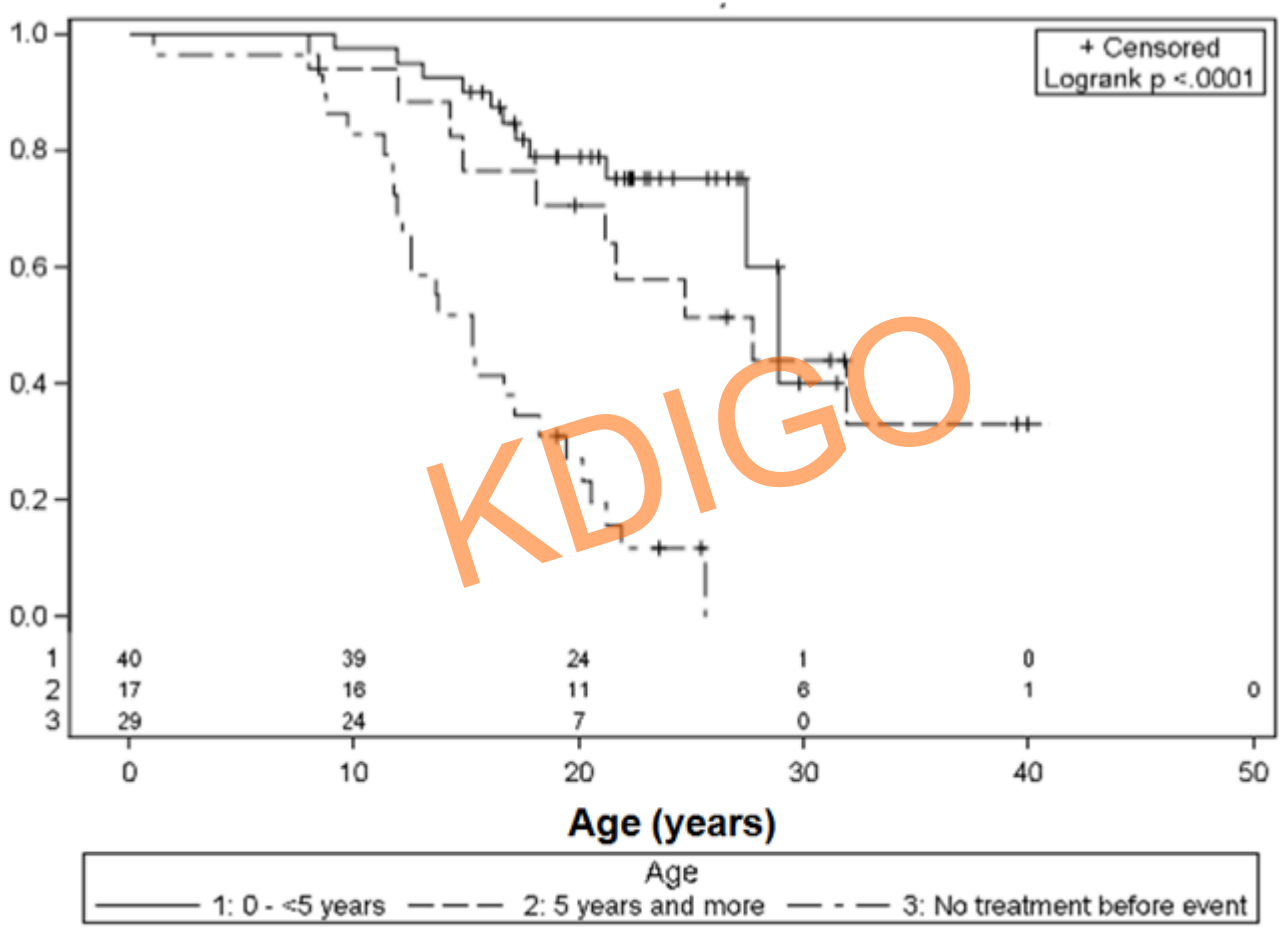
Brodin-Sartorius et coll, Kidney Int, 2011

Cystinosis: Hypothyroidism



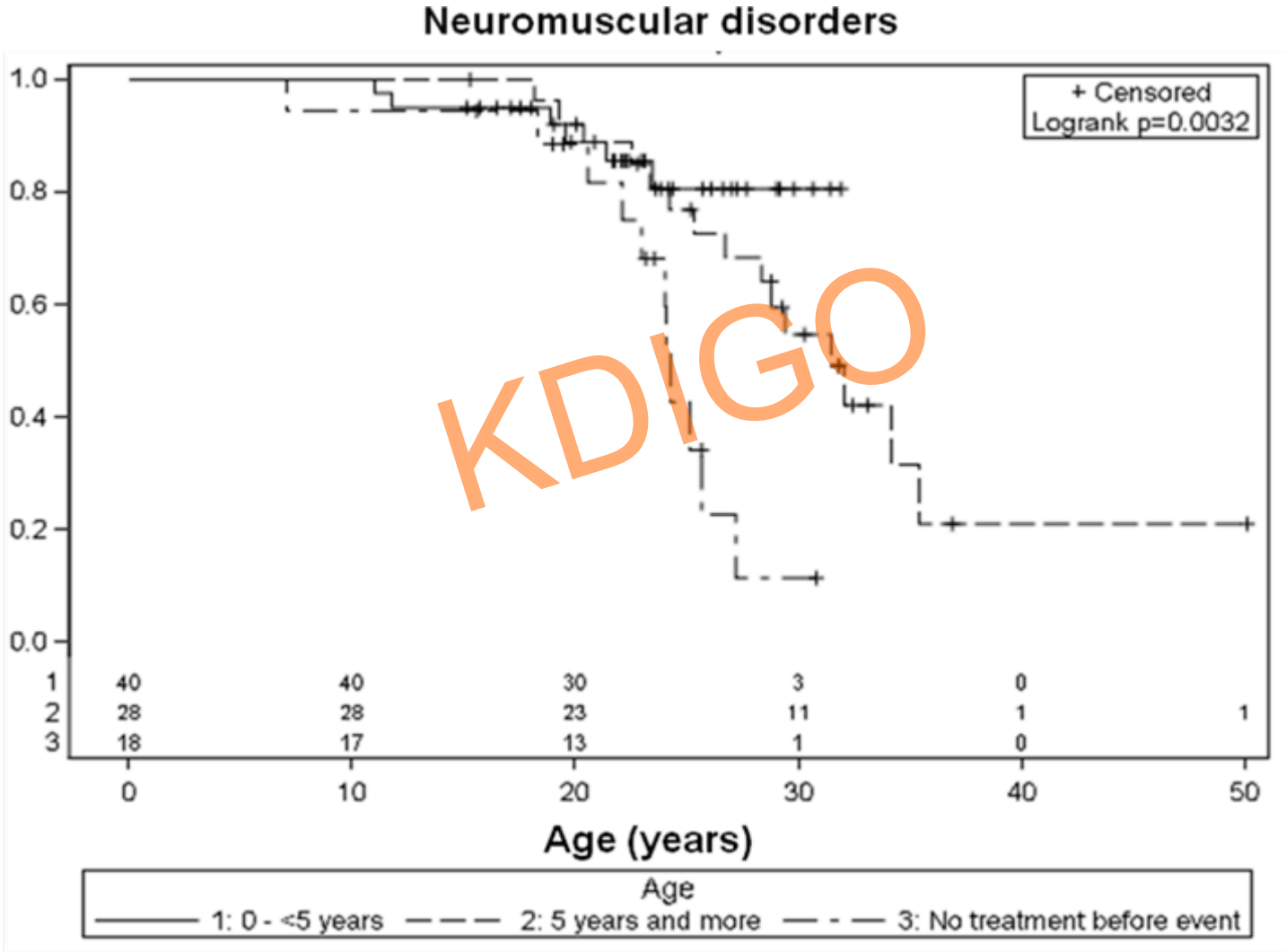
Brodin-Sartorius et coll, Kidney Int, 2011

Cystinosis: Diabetes



Brodin-Sartorius et coll, Kidney Int, 2011

Cystinosis: neuromuscular complications



Brodin-Sartorius et coll, Kidney Int, 2011

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Proximal tubulopathies, the albuminuria can be high but there is no evidence that blockade of the RAS is effective, moreover it can be dangerous and not tolerated if dehydration occurs

NSAID is effective in reducing the amount of urine in tubulopathies, some studies have addressed the question of their toxicity on the long term, what the follow-up should be ? DFG measurement ? renal biopsies ?

Avoid NSAID in tubulopathies in which the natural evolution is chronic renal failure (Dent, Lowe, nephronophtisis …)

Other renoprotective measures :

> blood pressure control under 50 perc

> protein limitation

> lipid and uricemia control

Q3. How should one monitor for potential renal and extrarenal complications and if so, how frequently?

It really depends on the disease and on specific situations, difficult to give general recommandations

....but we can list all the complications that can be encountered (if possible with their frequencies) and guidelines for the care

Some complications are not well known and deserve more collaborative studies

Ex ; Lowe and bleeding disorder, *TCF2* and autism (special comments on that)

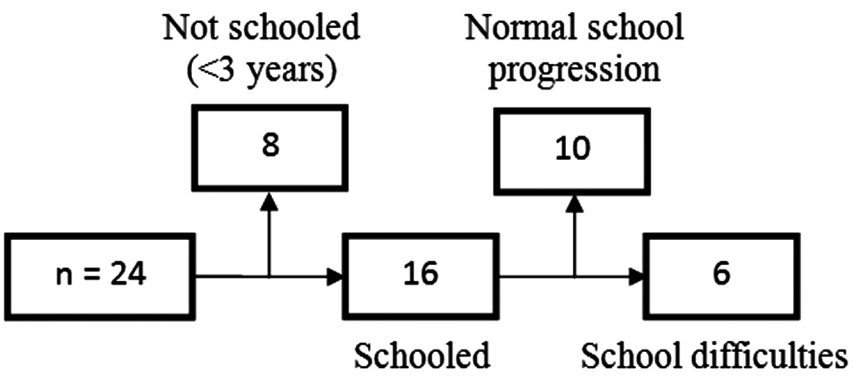
Renal cysts and diabetes with *HNF1B* mutation or deletion

- 37 patients de la cohorte HNF1B
  - Centres volontaires
  - Patients vus le temps de l'étude

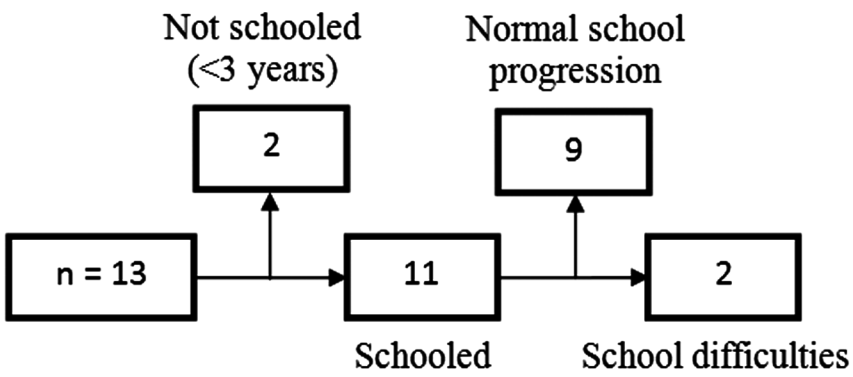
- Vérification de la microdélétion
- Evaluation neurolopsychologique
- Evaluation morphologique
- Comparaison mutation / délétion

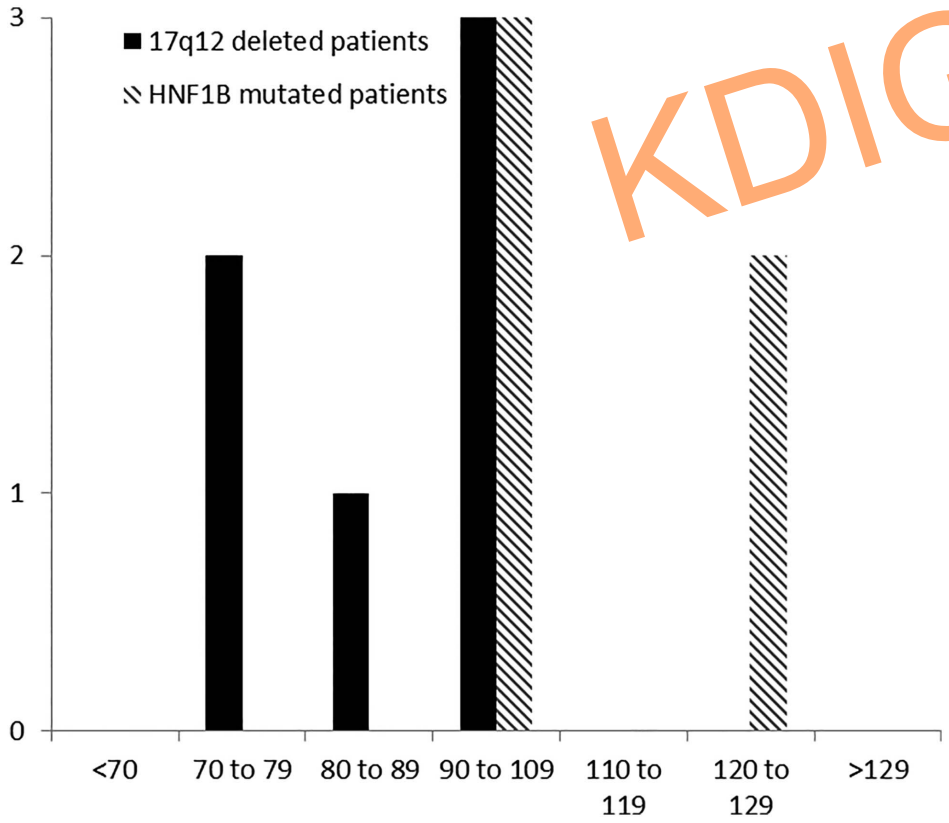
Laffargue, Arch Dis Child, 2015

HNF1B deletion



HNF1B point mutation

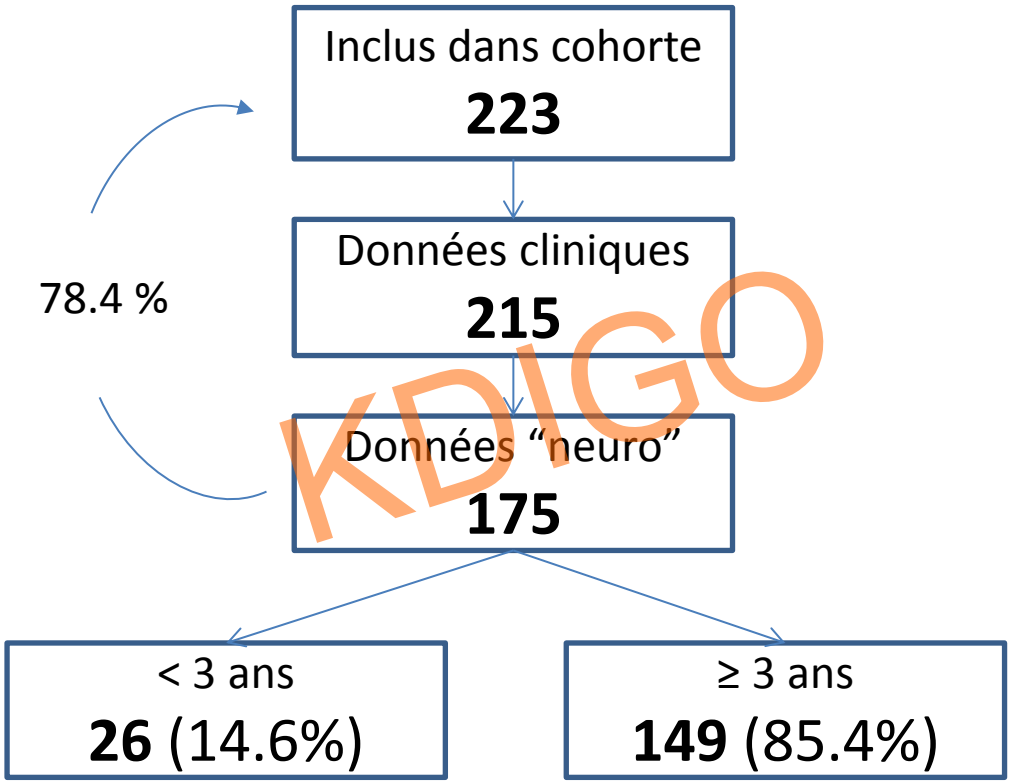




Intelligent quotient

Laffargue et al, Arch Dis Child 2015

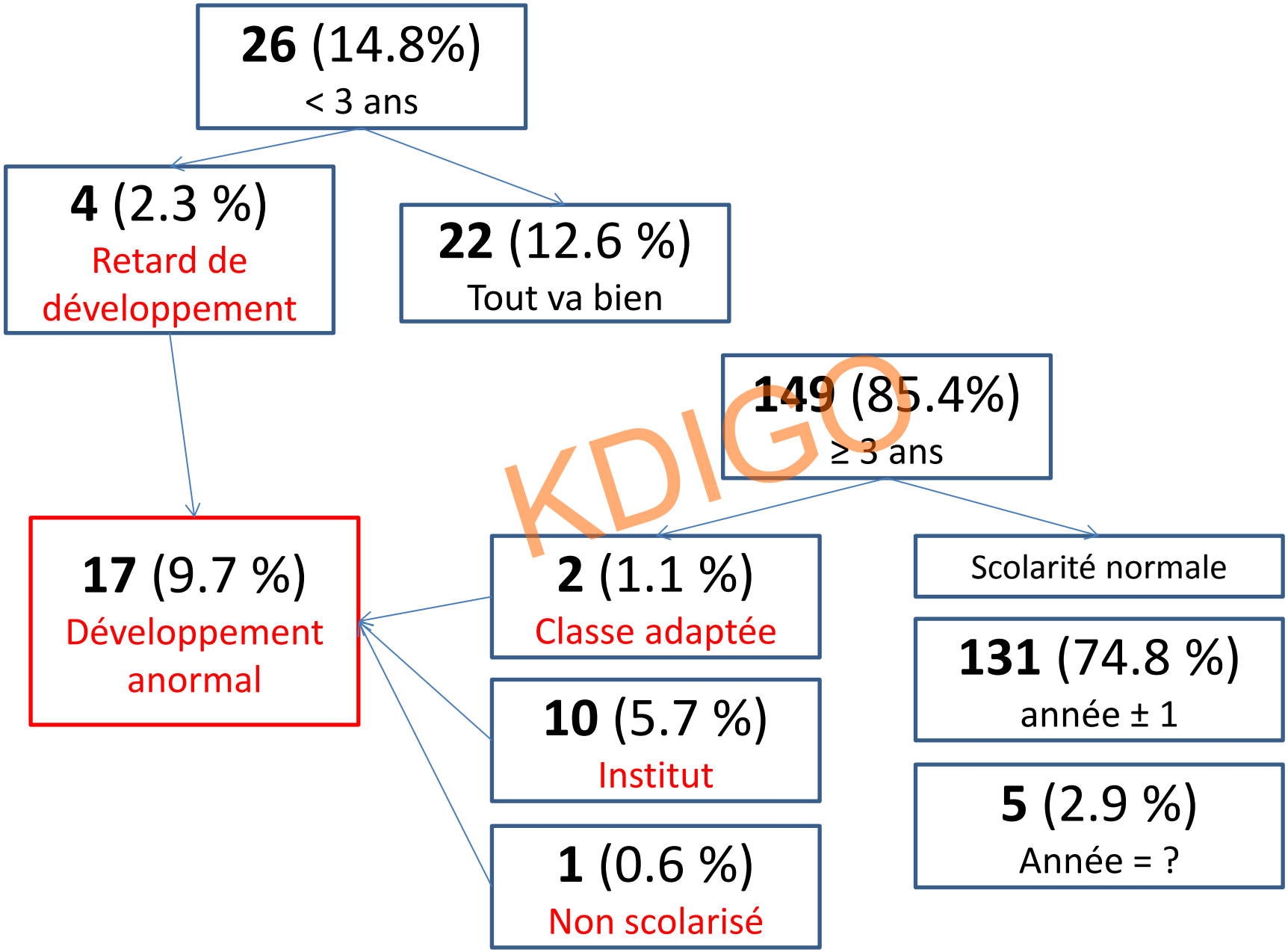
Population étudiée



Age moyen : 7.9 ans

Sex Ratio (M/F) : 1.49

V Guigonis (Limoges)
SoRare Ref Centre


26 (14.8%)
< 3 ans
4 (2.3 %)
Retard de développement
22 (12.6 %)
Tout va bien
149 (85.4%)
≥ 3 ans
17 (9.7 %)
Développement anormal
2 (1.1 %)
Classe adaptée
10 (5.7 %)
Institut
1 (0.6 %)
Non scolarisé
Scolarité normale
131 (74.8 %)
année ± 1
5 (2.9 %)
Année = ?
KDIGO

RCAD, *HNF1B* and autism spectrum disorders

- Do have to take into account this association as significant ?
- Do we have to consider it for prenatal diagnosis ?
- We have certainly to keep in mind this observation in the care
- Do we have to give this information to the families ?

Lowe syndrome : a «new » symptom

- Interest of the analysis of a large cohort

and

- Of digital database

French national Lowe Syndrome network

- Created in 2002 (GIS Maladies Rares, J. Lunardi and R. Salomon)
- 2004-2009: Reinforced by the National Plan for Rare Diseases and creation of Reference Centres
  - Diagnosis
  - Management
  - Epidemiological and clinical research
  - Information and communication
- Different projects including a clinical survey for LS
- Important role of the “ASL” = French LS parents association

ASL
Association française du Syndrome de Lowe

ASL

Association française du
Syndrome de Lowe

Accueil | L'association | La maladie | Conseil scientifique | Soutenir l'ASL | Contact | Connexion

art%3A10.1007%2Fs00467-015-3157-8.pdf

Disneyland Paris © 2014

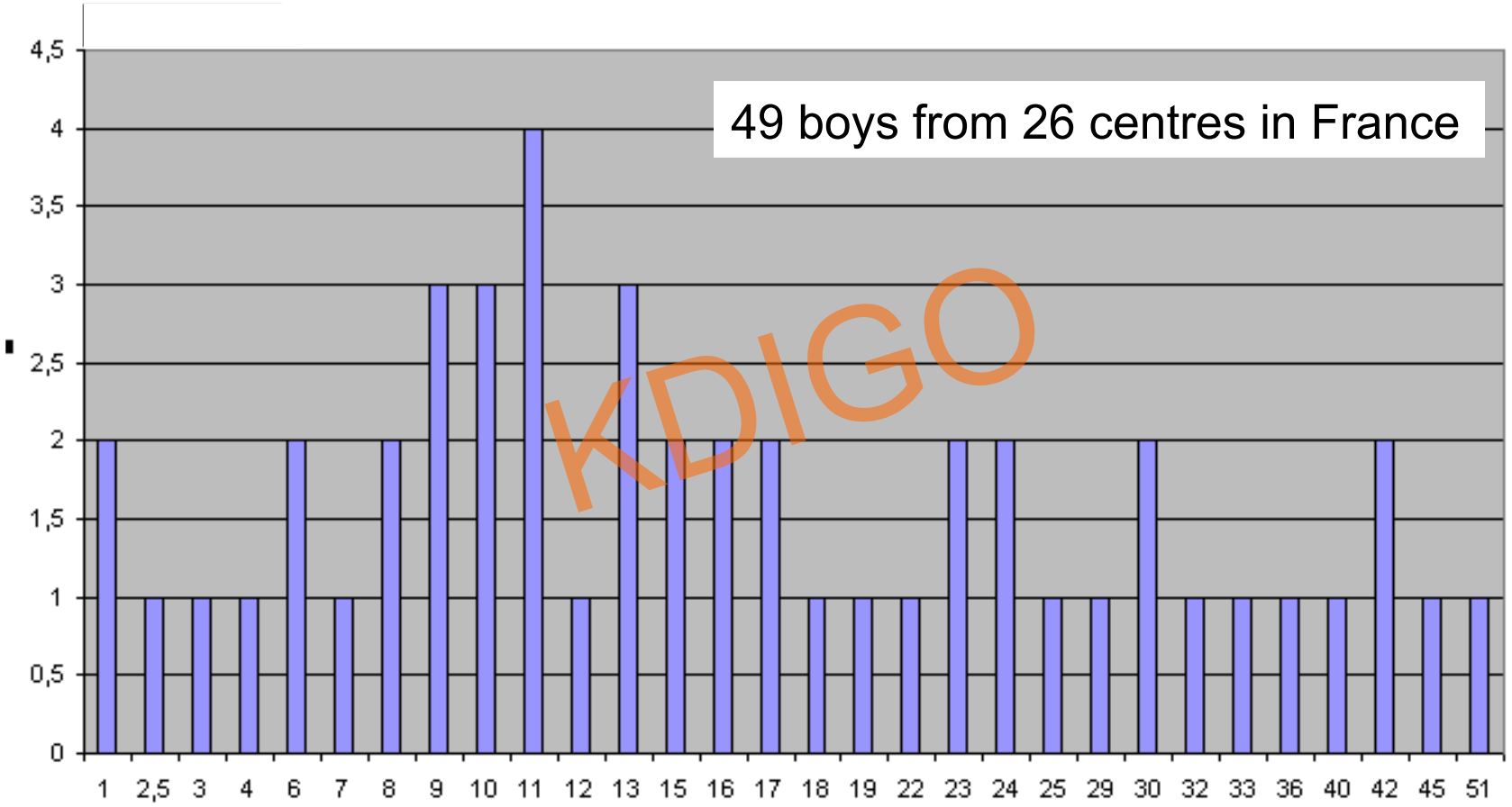
"Les 20 ans de l'association

Dr G Baujat
Genetic department
Necker, Paris

Lowe syndrome retrospective survey

- Retrospective multicentric review by one physician
- Genetic analysis of OCRL1 (J. Lunardi)
- Medical data: questionnaire
- Phone call to the families for some details (development, visual acuity, education)
- Phenotype-genotype correlations analysis

Lowe syndrome french cohort (2004-2009)



Average age: 18 years

Lowe syndrome
Renal manifestations

Constant tubular defect (“Fanconi”)

– Diagnosis: ≈ 12 months (26% < 1 m)

– Variable in severity and type ++

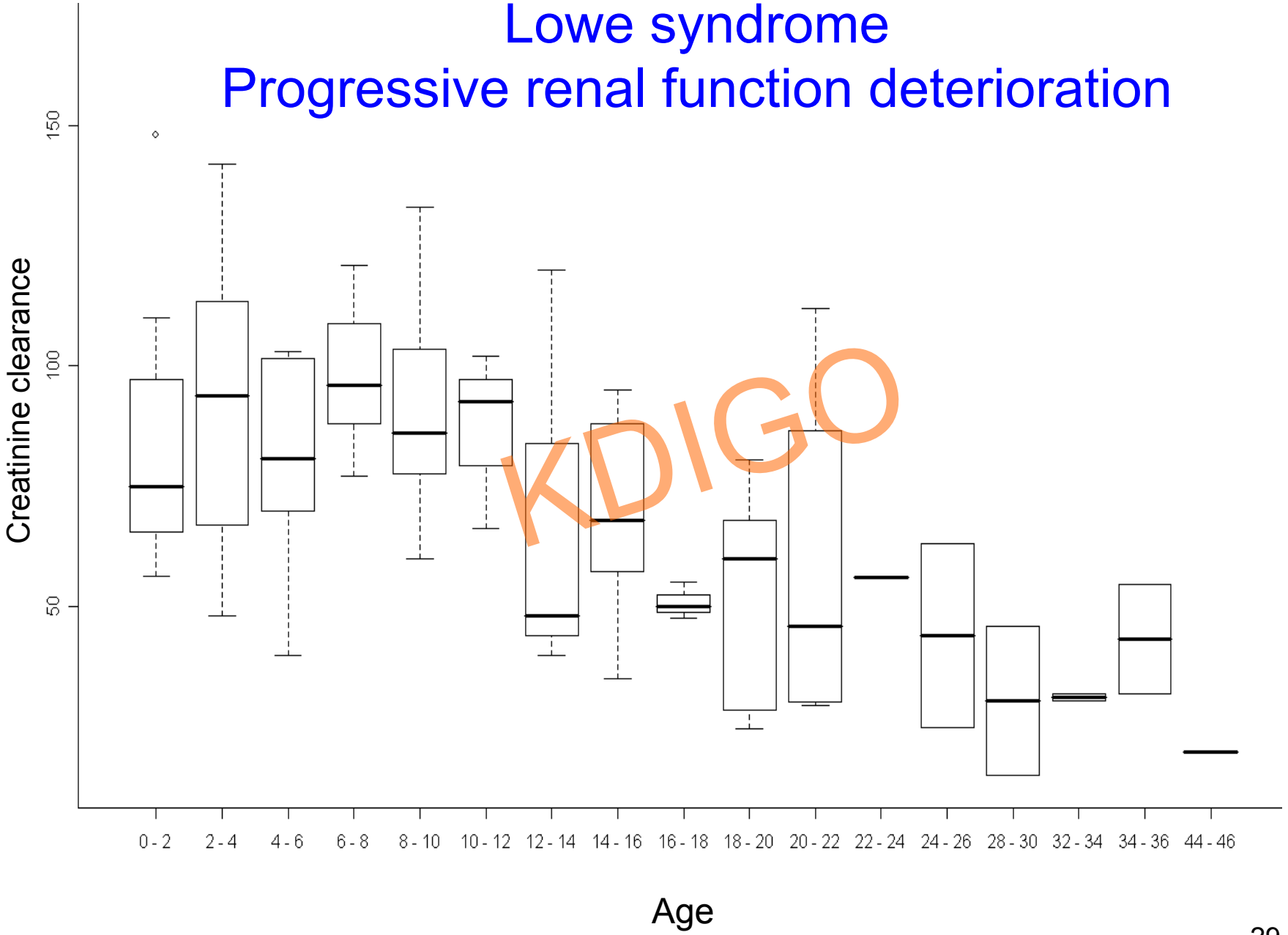
1/ acidosis : bicarbonate treatment: 80% (>3,4m)

2/ hypokalemia requiring oral K: 14%

3/ hyperphosphaturia and hypercalciuria 68%

- fractures 26% , rickets 40%
- néphrocalcinosis in 58 %

Lowe syndrome
Progressive renal function deterioration



Hematological complications

- Isolated microcytosis or microcytic anemia (without iron deficiency): 18

- Bleeding history: notification of 8 cases !
  - Haemorrhagic complications during or after surgery
    - Craniostenosis: 2
    - Scoliosis: 1
    - Cataract surgery: 1
    - Knee surgery: 1
    - Serious bleeding after tooth extraction: 4
  - But few haematoma/ epistaxis

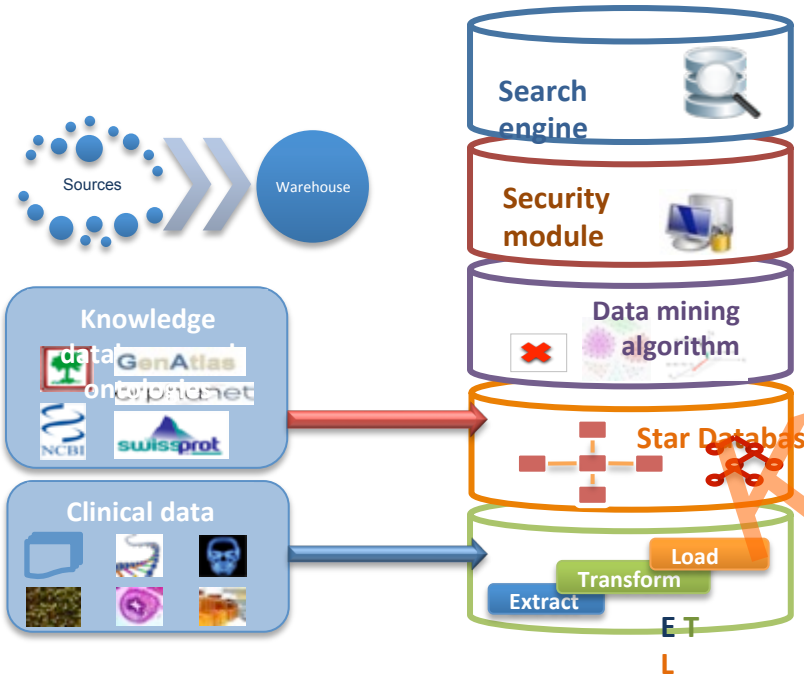
Preliminary study in 6 LS patients

Patient	Age (yr)	Previous Surgery	Bleeding	PFA-100 Closure Times		von Willebrand		Hb	Fib	Platelets
				EPI	ADP	Ag	VWF:RCo			
				85–165 s	71–118 s	50–150 %	50–150 %	>10.5 g/dL	2–4 g/L	>175 G/L
1	1	Eye	Yes	**181**	**135**	**279**	**216**	**10.2**	**8.2**	267
2	10	Neurologic & eye	Yes	**>300**	**166**	**305**	**199**	**9.8**	**5.1**	178
3	5	Eye	No	**195**	**126**	**295**	**275**	11.7	**5.2**	336
4	2	Eye	Yes	**197**	**128**	**251**	**200**	**10.1**	3.5	195
5	17	Tooth extraction	No	**>300**	**129**	**262**	**200**	11.7	4	**143**
6	14	Tooth extraction	Yes	**189**	**188**	**332**	**224**	11.3	2.9	**112**

>> Platelet dysfunction

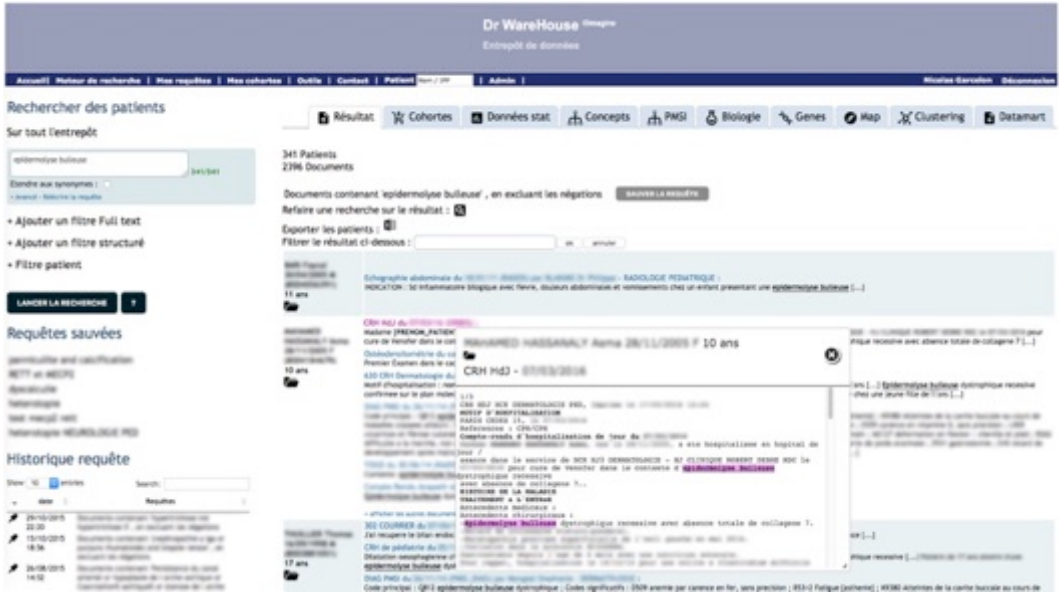
Lasne et al, Br J Haematol. 2010

Another way to increasen our knowledge on rare diseases : Biomedical Data Warehouse



Nicolas Garcelon
(Imagine Institute)

From Individual memory
to collective memory organized and sustainable



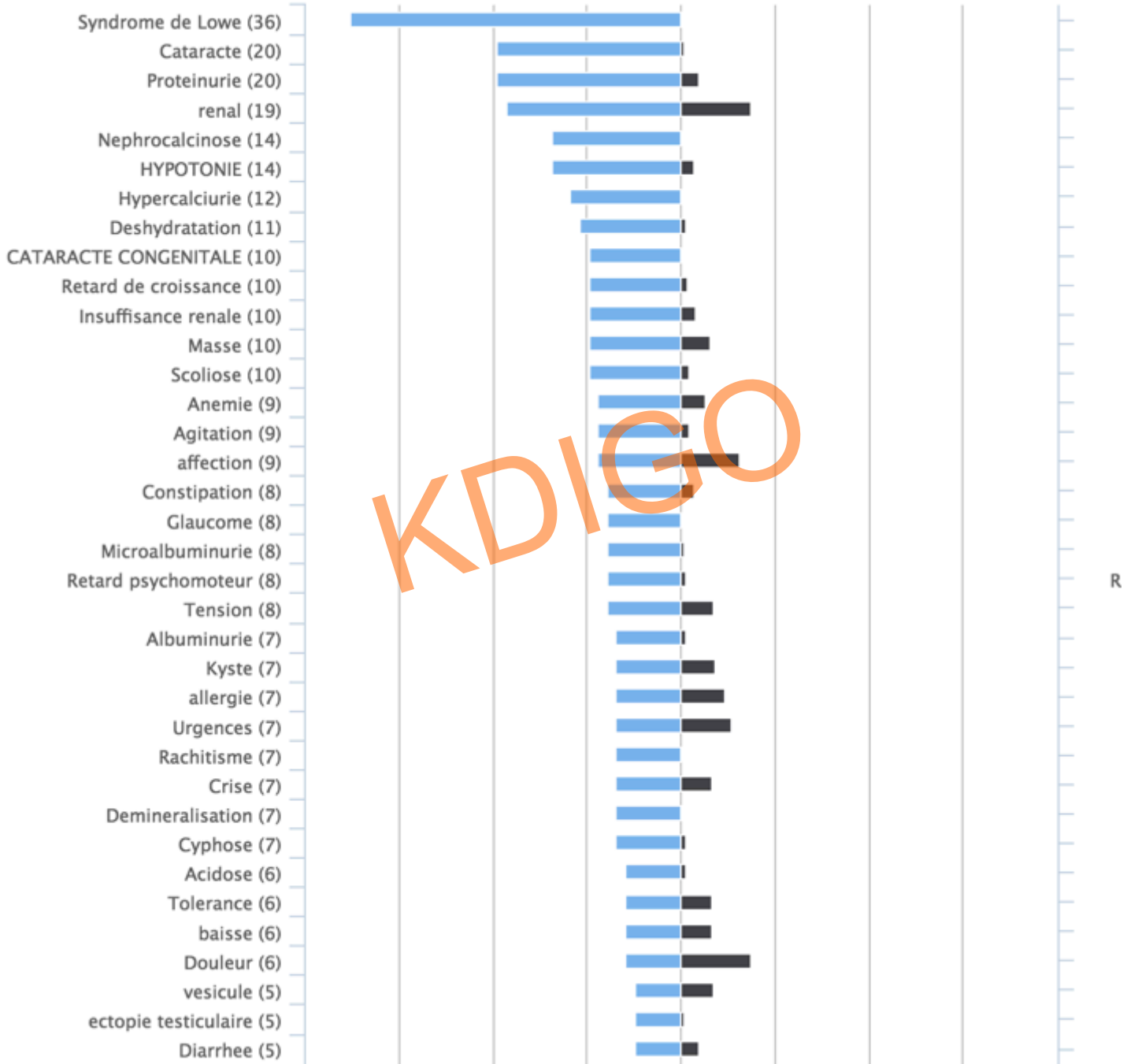
Necker –Enfants Malades Hospital since ≈ 2000 (essentially 2007)
Number of patients : 366 000 patients
Number of documents : 2 700 000 health records (free text)


Dr WareHouse ©Imagine
Entrepôt de données
Accueil | Moteur de recherche | Mes requêtes | Mes cohortes | Outils | Contact | Patient Nom / IPP |
Rémi Salomon Déconnex
Rechercher des patients
Sur tout l'entrepôt
lowe
41/41
Etendre aux synonymes :
+ Avancé - Réécrire la requête
+ Ajouter un filtre Full text
+ Ajouter un filtre structuré
+ Filtre patient
Résultat
Cohortes
Données stat
Concepts
PMSI
Biologie
Map
41 Patients
498 Documents
Documents contenant 'lowe' , en excluant les négations
SAUVER LA REQUÊTE
Refaire une recherche sur le résultat :
Exporter les patients :
Filtrer le résultat ci-dessous :
ok
annuler

Show 10 entries

Search:

Concepts	Nb patients	% résultat	% entrepôt	% resultat / entrepôt
Syndrome de Lowe	36	87.8	0	100
Cataracte	20	48.8	.9	.7
Proteinurie	20	48.8	4.7	.1
renal	19	46.3	18.6	0
Nephrocalcinose	14	34.1	.2	2.4
HYPOTONIE	14	34.1	3.5	.1
Hypercalciurie	12	29.3	.2	1.7
Deshydratation	11	26.8	1.1	.3


% patients dans le résultat / % patients dans entrepôt
Syndrome de Lowe (36)
Cataracte (20)
Proteinurie (20)
renal (19)
Nephrocalcinose (14)
HYPOTONIE (14)
Hypercalciurie (12)
Deshydratation (11)
CATARACTE CONGENITALE (10)
Retard de croissance (10)
Insuffisance renale (10)
Masse (10)
Scoliose (10)
Anemie (9)
Agitation (9)
affection (9)
Constipation (8)
Glaucome (8)
Microalbuminurie (8)
Retard psychomoteur (8)
Tension (8)
Albuminurie (7)
Kyste (7)
allergie (7)
Urgences (7)
Rachitisme (7)
Crise (7)
Demineralisation (7)
Cyphose (7)
Acidose (6)
Tolerance (6)
baisse (6)
Douleur (6)
vesicule (5)
ectopie testiculaire (5)
Diarrhee (5)
KDIGO
R

Show 10 entries

Concepts	Nb patients	% résultat	% entrepôt	% res
troubles de l'hemostase	5	12.2	.7	.2
hemorragie	3	7.3	9.9	0
Hemolyse	2	4.9	.9	.1
Hemophilie	1	2.4	.2	.2
Syndrome hemorragique	1	2.4	.9	0
hemolyse intra-vasculaire	1	2.4	0	4
troubles hemorragiques	1	2.4	1.6	0

Showing 1 to 7 of 7 entries (filtered from 415 total entries)

How can we help the patient and family to accept the chronic disease, live with it and manage it responsibly? Any specific issues related to compliance, monitoring, and follow-up?

Association of patients

Meeting with families and doctors and other professional implicated in the care

Explain the disease to the adolescent (or before)

Dedicated nurses

Psychologist, psychiatrist, psychomotrician ...

Documentation

Specific devices to improve compliance (telemedicine)

Q5. How can we ensure equity of access to optimal care, including expensive drugs?

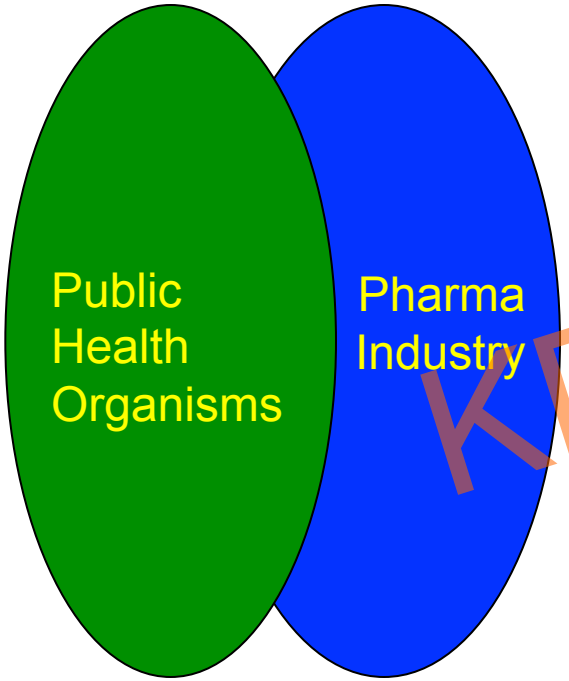
?

Disclosure of Interests

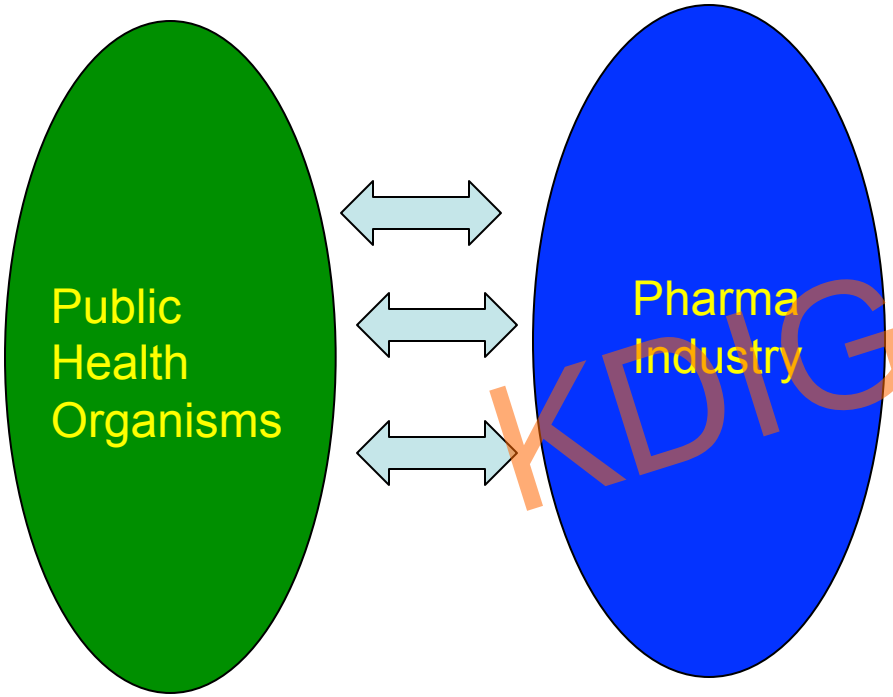
- Alexion (registery, sponsored education)
- Raptor (expert witness, co-investigator)
- Oxthera (co-investigator)

(e.g. employment, consultancy, honoraria, stock ownership, sponsored education, research grant, educational grant, expert witness, other relevant funding, etc ...)

Q5. How can we ensure equity of access to optimal care, including expensive drugs?



Q5. How can we ensure equity of access to optimal care, including expensive drugs?



More independent registries, clinical research programs…

KOL / pharma companies

…/…

Q6. What is the optimal modality for dialysis? Does this vary by disorder?

It depends on the disease

Specific question for hyperoxaluria, methylmalonic acidemia

The size of the patient

Probably PD when the child has severe mental retardation

But need a strong familial involvement (not always possible)

Q7. What is the optimal timing for transplant and role/utility of pre-emptive transplantation? How can we better address the risk of disease recurrence post-transplant?

Timing of transplantation:

Is transplantation always possible ? Acceptable ? Ethical issues...

If one consider that transplantation should not be done, what's about dialysis ?

Sustaining life or prolonging dying? Appropriate choice of conservative care for children in end-stage renal disease: an ethical framework

Janis M. Dionne · Lori d'Agincourt-Canning

Pediatr Nephrol 2014

Table 1 Summary recommendations[a] for shared decision-making regarding the withholding and withdrawing of dialysis in pediatric practice

Recommendation	Description
Recommendation 1	Develop a patient–physician relationship that promotes family-centered shared decision-making for all pediatric patients with AKI, CKD, and ESRD.
Recommendation 2	Fully inform patients with AKI, stage 4 or stage 5 CKD, or ESRD and their parents about the diagnosis, prognosis, and all appropriate treatment options. Inform children and adolescents in a developmentally appropriate manner, and if feasible, seek their assent about treatment decisions.
Recommendation 3	Facilitate informed decisions about dialysis for pediatric patients with AKI, CKD, or ESRD, discuss prognosis, potential complications, and quality of life with the patient, parents and/or legal guardian.
Recommendation 4	Establish a systematic due process approach for conflict resolution if disagreements occur about dialysis decisions. Use conflict resolution interventions when family members disagree with one another, when children disagree with their parents, when families disagree with the health care team, or when the health care team disagrees about initiating, not initiating, or withdrawing dialysis
Recommendation 5	Institute family-centered advance care planning for children and adolescents with AKI, CKD, and ESRD. The plan should establish treatment goals based on a child's medical condition and prognosis.
Recommendation 6	Forgo dialysis if initiating or continuing dialysis is deemed to be harmful, of no benefit, or merely prolongs a child's dying process. The decision to forgo dialysis must be made in consultation with the child's parents. Give children and adolescents the opportunity to participate in the decision to forgo dialysis to the extent that their developmental abilities and health status allow.
Recommendation 7	Consider forgoing dialysis in a patient with a terminal illness whose long-term prognosis is poor if the patient and family are in agreement with the physician that dialysis would not be of benefit or the burdens would outweigh the benefit.
Recommendation 8	Consider the use of a time-limited trial of dialysis in neonates, infants, children, and adolescents with AKI or ESRD to allow for the assessment of extent of recovery from an underlying disorder
Recommendation 9	Develop a palliative care plan for all pediatric patients with ESRD from the time of diagnosis and for children with AKI who forgo dialysis. The development of a palliative care plan is a continuation of the process of advance care planning and should be family-centered.

Q7. What is the optimal timing for transplant and role/utility of pre-emptive transplantation? How can we better address the risk of disease recurrence post-transplant?

Timing of transplantation:

Is transplantation always possible ? Acceptable ? Ethical issues...

If one consider that transplantation should not be done, what's about dialysis ?

Pre-emptive whenever possible and particularly if dialysis is hazardous or not efficient enough : MMA, hyperoxaluria

METHYL- MALONIC ACIDEMIA

Isoleucine

Valine

Méthionine
Thréonine
AGNIC..

Propionyl-CoA

Propionyl-CoA Carboxylase

B8 = Biotine

Acidurie propionique

D-méthylmalonyl-CoA

Méthylmalonyl-CoA racémase

L-méthylmalonyl-CoA

Méthylmalonyl-CoA mutase

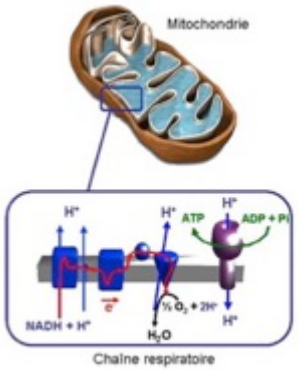
Acidurie méthylmalonique

Succinyl-CoA

B12 = Cobalamine

Cycle de Krebs

NADPH



Methylmalonic acidemia

- methylmalonyl-coenzyme A mutase deficiency
  - Mut 0 : no activity
  - Mut - : partial activity

- Presentation : coma (intoxication), acidocetosis, hyperammoniemia

- Treatment: low protein intake, carnitine, antibiotherapy to control intestinal flora

- Complications :
  - Neurological
  - Renal
  - Pancytopenia
  - Growth retardation

Renal disease

- Usual complication of the disease despite treatment
  - 47%
  - CRF at 6,5 years (1,5-18,6)
  - More earlier and severe with Mut 0
- Tubulo-interstitial nephritis
- Physiopathology :
  - direct toxicity of MMA on the tube
  - Mitochondrial dysfunction > apoptosis

Molecular Genetic and Metabolism 2009.

Indication of transplantation

- Objectives :
  - To improve the metabolic disorders (less decompensation)
  - Increase protein intake, better nutrition
  - Quality of life

- Transplantation :
  - Ubiquitary enzyme, liver +++ kidney + (18%)

  - Liver alone : decrease MMA but does not avoid renal insufficiency
  - Kidney alone : increase MMA excretion and bring the enzyme

Questions

- Which patient to be transplanted ?
- When ?
- K / L / L + K ?

- Our experience in Necker :
  - 5 K alone
  - 3 K + L
  - No L alone

MMA : kidney transplantation alone
Necker Experience

Renal transplantation in 4 patients with methylmalonic aciduria: A cell therapy for metabolic disease

A. Brassier [a], O. Boyer [b], V. Valayannopoulos [a], C. Ottolenghi [c], P. Krug [b], M.A. Cosson [a], G. Touati [a], J.B. Arnoux [a], V. Barbier [a], N. Bahi-Buisson [d], I. Desguerre [d], M. Charbit [b], J.F. Benoist [e], L. Dupic [f], Y. Aigrain [g], T. Blanc [g], R. Salomon [b], D. Rabier [c], G. Guest [b], P. de Lonlay [a], P. Niaudet [b,*]

Mol Genet and Metabol 2013

- Improvement of the metabolic disease (sMMA and uMMA↘)

But

- Modest augmentation of the protein intake (0,6 > 0,66 g/kg/j)
- Modest neurologic improvement but less decompensations

Treatment of Methylmalonic Acidemia by Liver or Combined Liver-Kidney Transplantation

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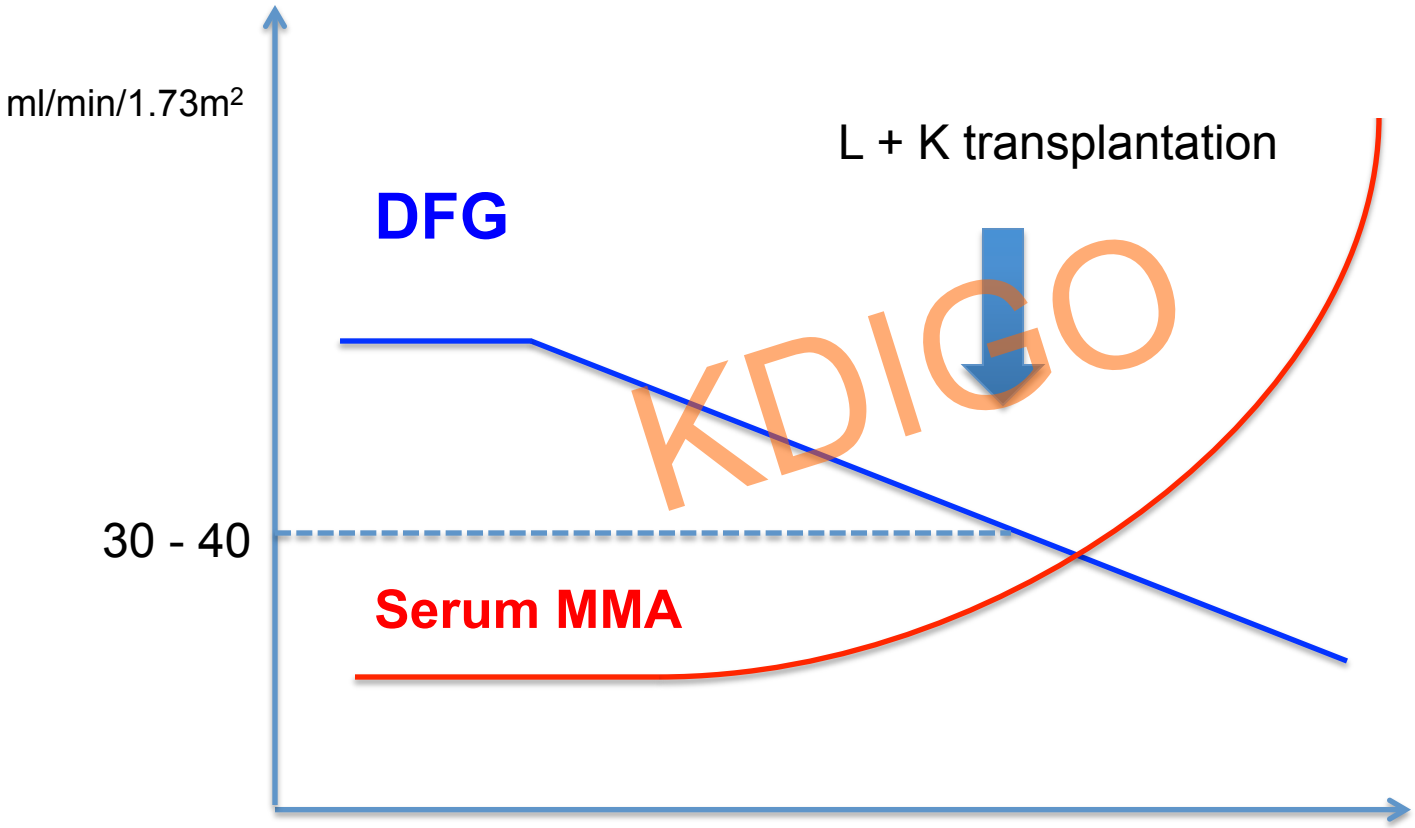
J Pediatr 2015

Lucile Packard Children's hospital, Standford, USA

6 liver Tr alone and 8 liver + kidney Tr

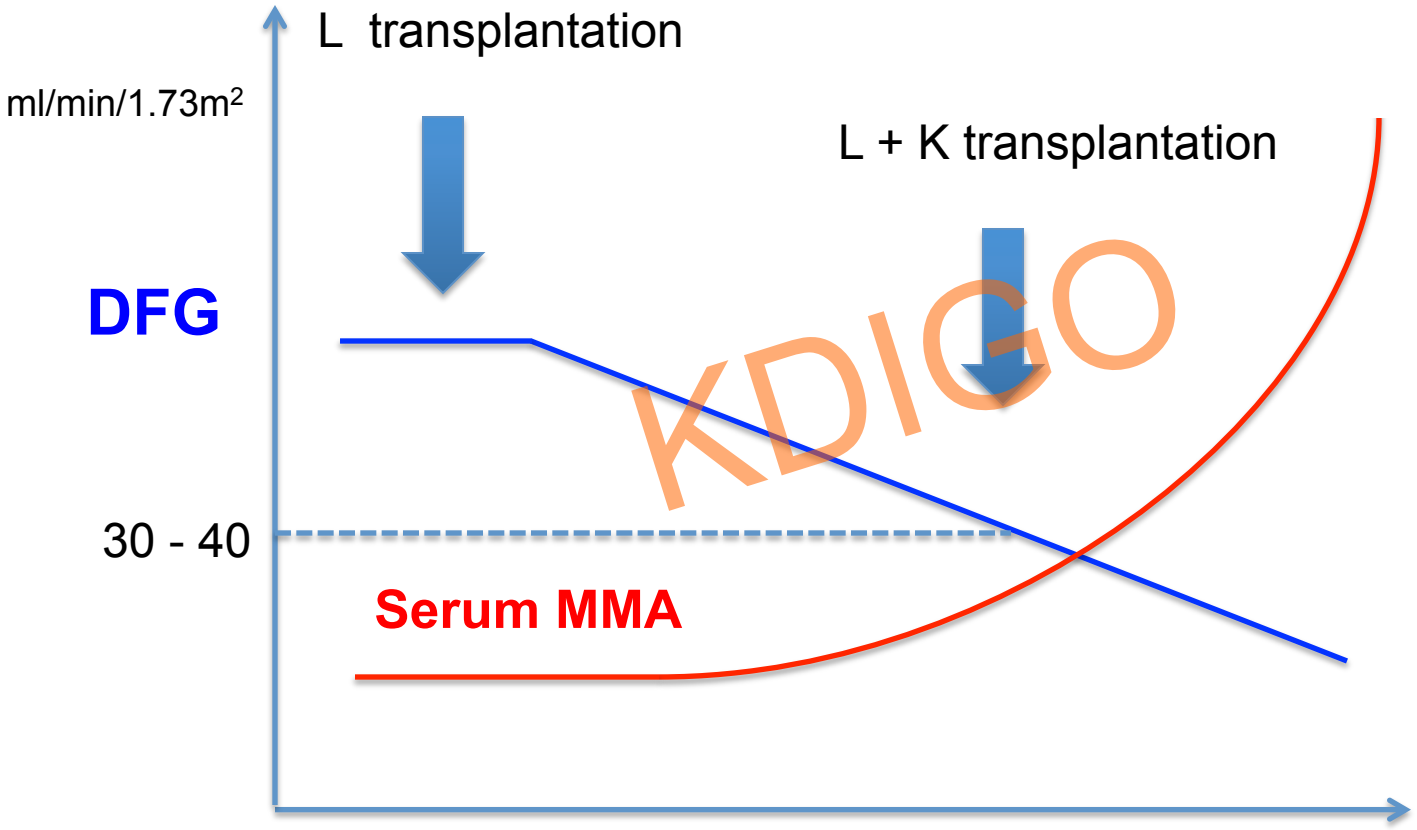
Table I. Demographic, diagnostic, and surgical data of patients (n = 14) who received LKT or LT at Lucile Packard Children's Hospital at Stanford between December 1997 and May 2012

Patient	Sex	Time of diagnosis	Identified by NBS	Diagnosis*	Age at Tx	Procedure	Graft	Long-term immunosuppression	Complications
1	M	Neonatal	no	Non-B12-responsive clinically	10 y 9 mo	LKT	Whole	Prednisone, tacrolimus	
2	M	Neonatal	no	fibroblast assay, mut^0	20 y 8 mo	LKT, bilateral nephrectomy	Whole	Prednisone, tacrolimus, sirolimus	1. Re-exploration, bleeding 2. Post-transplant diabetes mellitus and hypertension attributed to immunosuppressive regimen
3	M	Neonatal	no	Fibroblast assay, mut^0	5 y 11 mo	LKT, bilateral nephrectomy, splenectomy	Whole	Prednisone, tacrolimus, azathioprine	1. Spontaneous splenic rupture → splenectomy 2. Re-exploration, bleeding 3. Seizure POD12 (high tacrolimus level)
4	M	Neonatal	no	†	11 y 2 mo	LKT, right nephrectomy, splenectomy	Whole	Sirolimus	
5	F	Neonatal	yes	c.682C>T (p.R278X), c.1106 G>A (p.R369H)	3 y 3 mo	LT	Whole	Tacrolimus, mycophenolate	Mild acute rejection 4 weeks post-transplantation, received steroids
6‡	F	3 mo	no	c.322C>T (p.R108C)	15 y 4 mo	LKT	Whole	Prednisone, tacrolimus, mycophenolate	
7	F	Neonatal	yes	c.682C>T (p.R228X), c.581C>T (p.P194L)	11 mo	LT	Whole	Tacrolimus	
8	F	9 mo	no	c.572C>A (p.A191E)	17 y 6 mo	LKT, splenectomy	Whole	Tacrolimus, mycophenolate	Re-exploration, drainage of subphrenic abscess
9	M	Neonatal	no	c.349G>T (p.E117X), c.1038_1040 delTCT	8 y 10 mo	LKT	Whole	Tacrolimus, mycophenolate	Acute rejection 3 weeks post-transplant
10	M	2 y	no	Fibroblast assay, mut^0	16 y 1 mo	LKT	Whole	Prednisone, tacrolimus, mycophenolate	
11	F	Neonatal	yes	c.682C>T (p.R228X)	10 mo	LT	1. Whole 2. Whole	Tacrolimus	1st transplantation: Hepatic artery thrombosis POD5 → re-transplantation. 2nd transplantation: No complications
12§	F	Neonatal	yes	c.1399C>T (p.R467X)	1 y 1 mo	LT	Seg 2-4	Tacrolimus	Mild acute rejection POD10, received dose of steroids
13§	F	Neonatal	yes	c.1399C>T (p.R467X)	1 y 2 mo	LT	Seg 2-4	Tacrolimus	
14	F	Neonatal	yes	c.682C>T (c.R228X) p.A732WFSX3	1 y 8 mo	LT	Whole	Tacrolimus	


ml/min/1.73m2
L + K transplantation
DFG
KDIGO
30 - 40
Serum MMA

Transplantation in MMA

- Serum creatine is not a good marker of GFR (reduce muscle mass)
- Decline GFR can occur before the age of 10
- Dialysis does not eliminate MMA efficiently (PD or HD or both ?)
- KT alone might limits the occurrence of metabolic decompensations
- LKT when GFR around 30 – 40 ml/min/1.73m2
- LT alone before GFR decline is a good option (Standford's experience)
- What is the GFR decline after LT alone ?
- Which option when GFR 40 – 80 ?

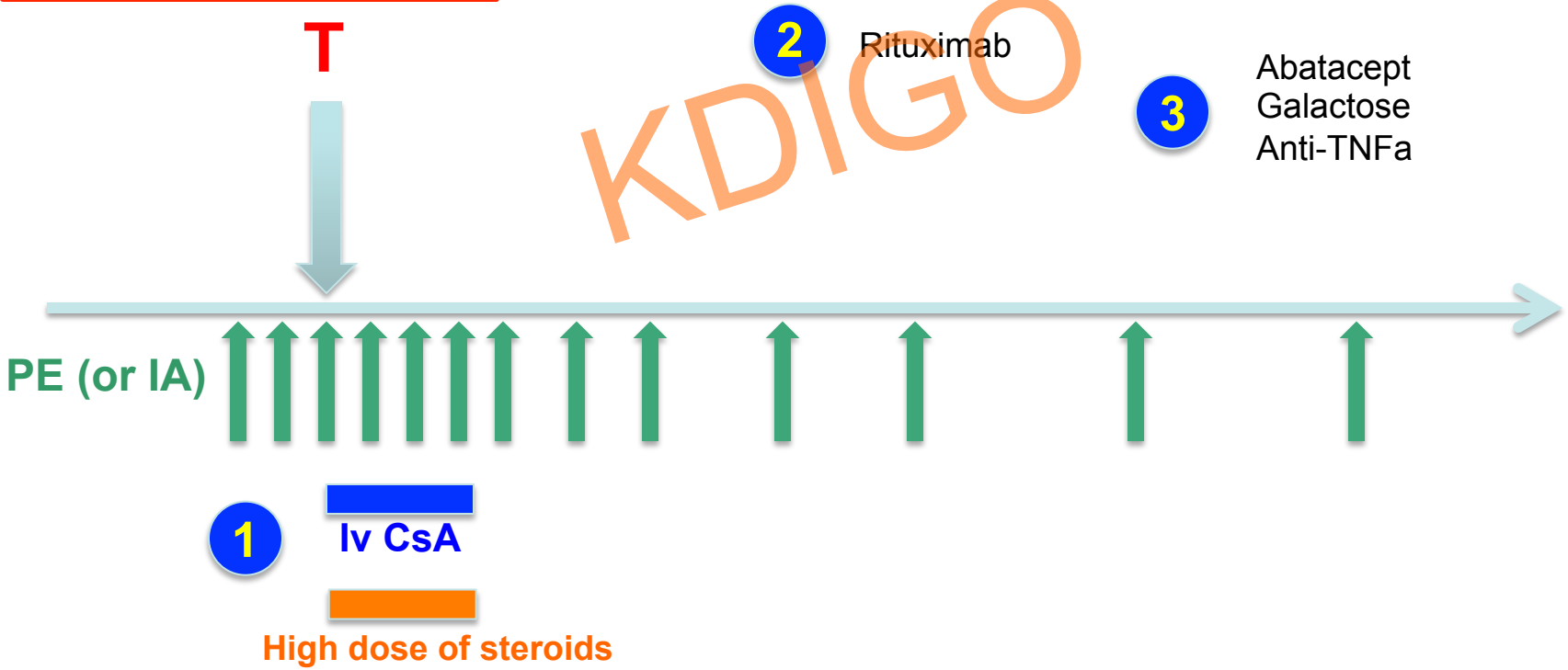

L transplantation
ml/min/1.73m2
L + K transplantation
DFG
KDIGO
30 - 40
Serum MMA

Q7. What is the optimal timing for transplant and role/utility of pre-emptive transplantation? How can we better address the risk of disease recurrence post-transplant?

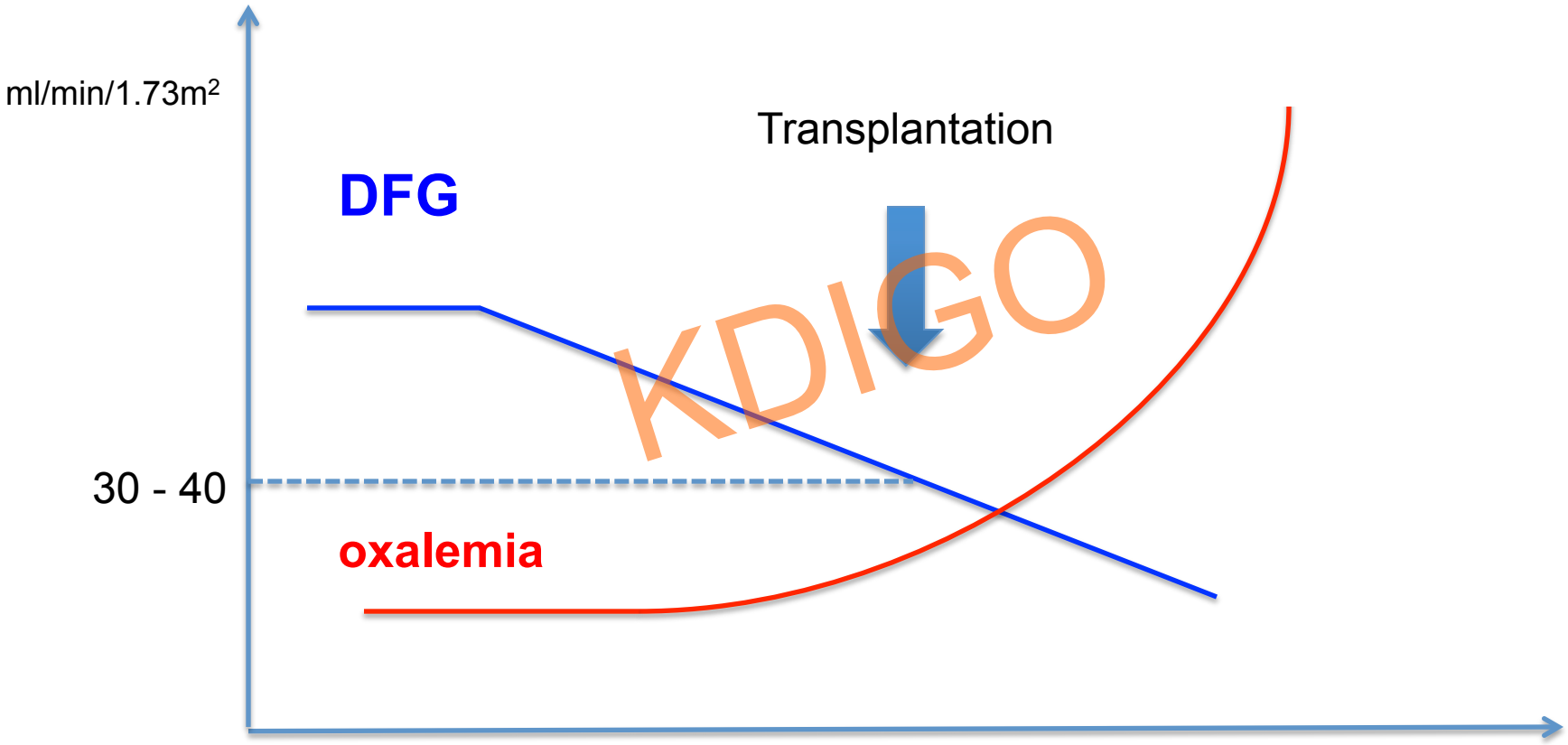
High risk of recurrence :

- Rapid occurence of ESRD
- Recurrence on first graft
- Intial steroid-sensitivity
- (Molecular signature)

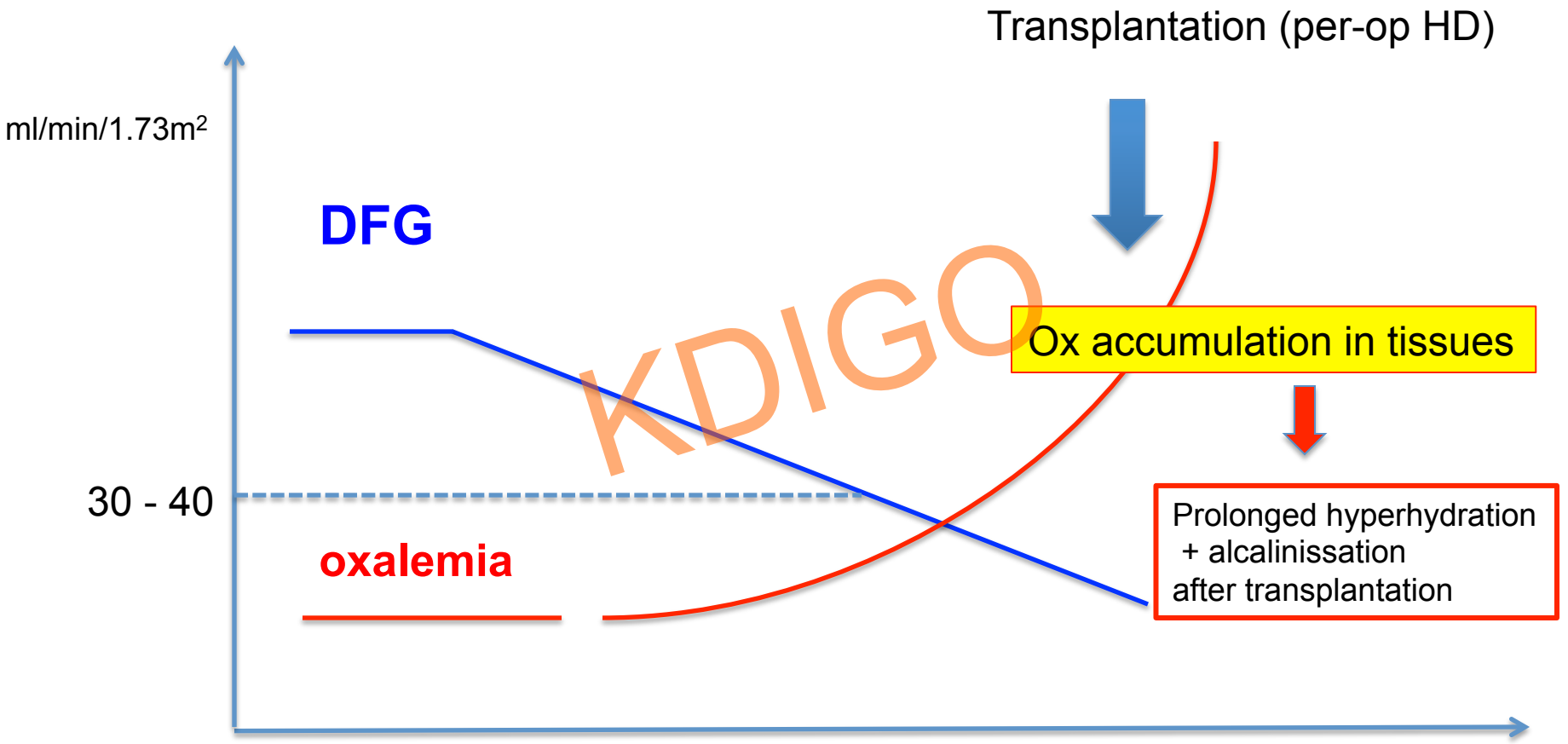
Recurrence in nephrotic syndrome



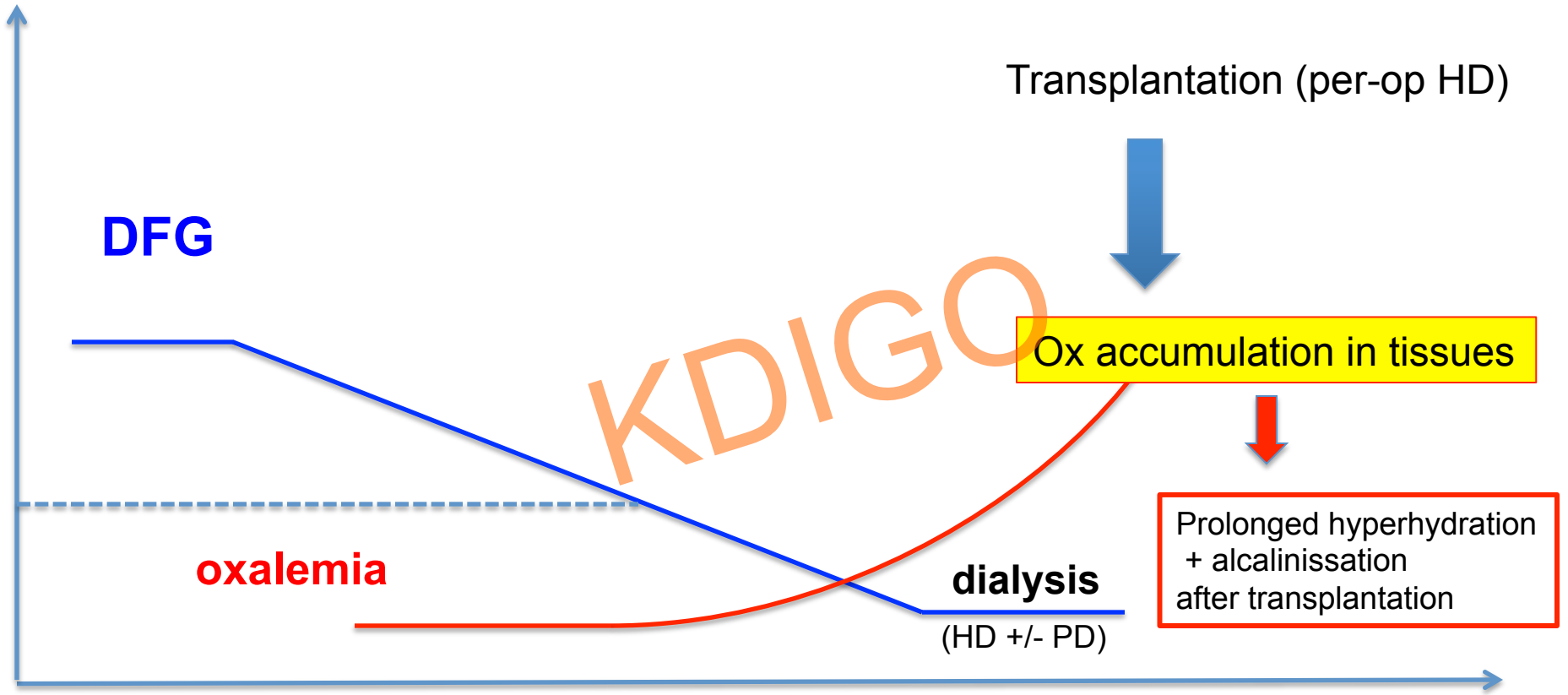
Transplantation in hyperoxaluria



Transplantation in hyperoxaluria



Transplantation in hyperoxaluria



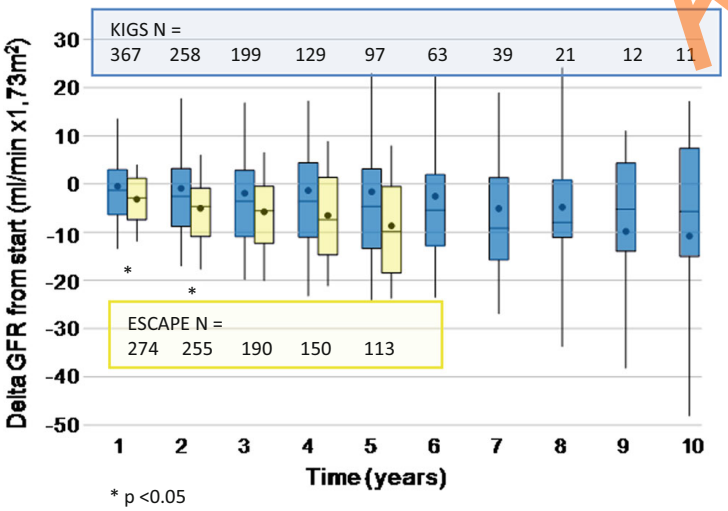
Q9. How can growth-related issues and treatment be optimally managed?

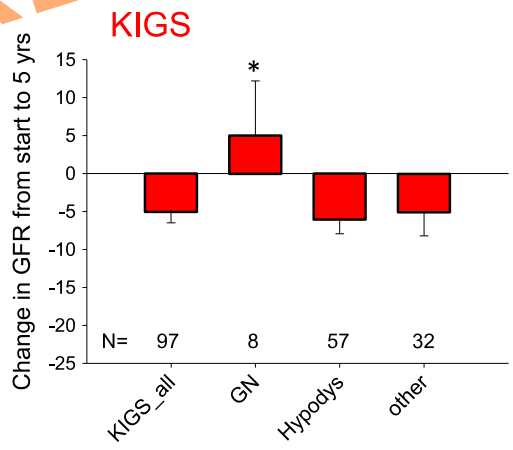
Pediatr Nephrol (2015) 30:2145–2151
DOI 10.1007/s00467-015-3157-8

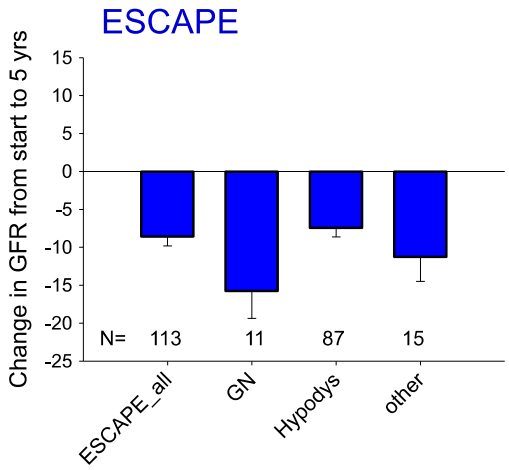
ORIGINAL ARTICLE

Long-term growth hormone treatment in short children with CKD does not accelerate decline of renal function: results from the KIGS registry and ESCAPE trial

Otto Mehls[1] · Anders Lindberg[2] · Dieter Haffner[3] · Franz Schaefer[1] · Elke Wühl[1] · for members of the German KIGS Board · ESCAPE Trial Group







Q9. How can growth-related issues and treatment be optimally managed?

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Advance Access publication 28 April 2015

Considerable variations in growth hormone policy and prescription in paediatric end-stage renal disease across European countries—a report from the ESPN/ERA-EDTA registry

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Table 3. Actual use of rGH and patients with short stature on dialysis

Country	% of rGH use	Eligibility according to short stature (height SDS less than −2)		Eligibility according to national criteria	
		% of patients eligible for rGH	% of eligible patients receiving rGH	% of patients eligible for rGH	% of eligible patients receiving rGH
Belgium	40.2	33.5	49.7	38.0	39.8
Czech Republic	22.2	42.0	16.7	42.0	16.7
Estonia	50.0	83.3	50.0	83.3	50.0
Greece	18.8				
Italy	20.5				
Lithuania[a]	6.8				
The Netherlands	31.0				
Portugal	22.6	49.7	29.5	33.5	23.2
FYR of Macedonia	33.3	44.4	50.0	15.6	0.0
Serbia	34.9	54.3	42.4	32.7	38.3
Slovenia	43.6	38.1	51.4	44.1	51.4
Spain	24.8	39.2	33.6	47.1	29.1
United Kingdom	11.6	53.8	15.9	47.0	15.5
Overall	21.7	45.9	26.0	30.1	24.1

In 21 out 28 countries GH is reimbursed
In 15, there is a national policy (and they are quite different)

Table 4. Actual use of rGH and patients with short stature on transplantation

Country	% of rGH use	Eligibility according to short stature (height SDS less than −2)		Eligibility according to national criteria	
		% of patients eligible for rGH	% of eligible patients receiving rGH	% of patients eligible for rGH	% of eligible patients receiving rGH
Belgium	19.9	51.9	29.3	38.9	22.8
Czech Republic	7.7	30.7	10.0	35.7	8.3
Estonia	0.0	20.0	0.0	38.9	0.0
Greece	6.5	48.4	13.3	48.7	11.1
Lithuania[a]	2.1	57.3	2.8	50.6	8.3
The Netherlands	4.0	25.6	6.0	28.8	10.4
Portugal	0.0	34.3	0.0	26.5	3.8
Serbia	4.6	40.8	9.6	35.4	9.5
Slovenia	0.0	53.6	0.0	46.5	0.0
Spain	8.3	29.4	13.7	39.8	9.2
United Kingdom	3.9	45.4	6.6	47.5	5.3
Overall	5.5	38.9	8.9	42.3	7.6

Thank you for your attention

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