Steroid Resistant Nephrotic Syndrome

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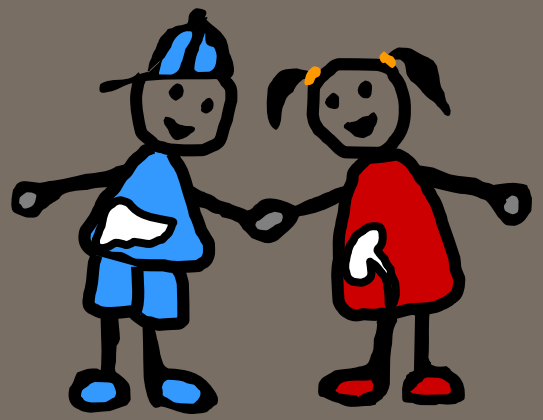


Third Cycle – Second IPNA-ESPN Junior Master Classes
Online, September 11-12, 2021

Conflict of Interest (COI)

- The **I**nternational **P**ediatric **N**ephrology **A**ssociation launched, organized, and funded the presented guideline initiative, which included travel and accommodation costs for the core group members. The funder had no influence on the content of the guideline.

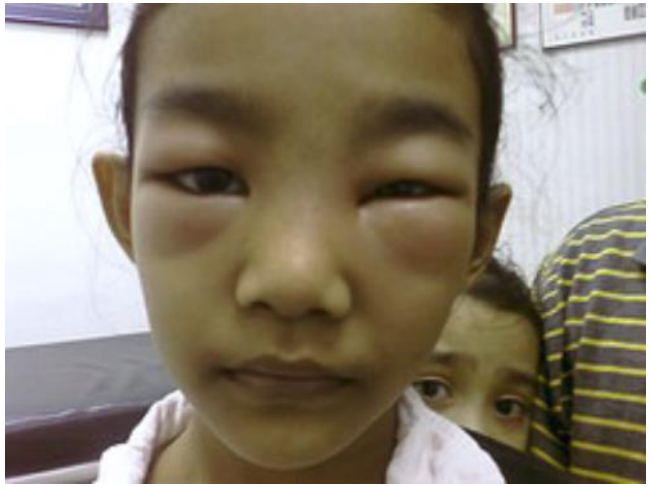
Idiopathic nephrotic syndrome in children

Steroid-sensitive NS
75-90%

Steroid-resistant NS
10-25%

Multiple Relapses
60-80%

ESKD and Renal Tx **30-70%**

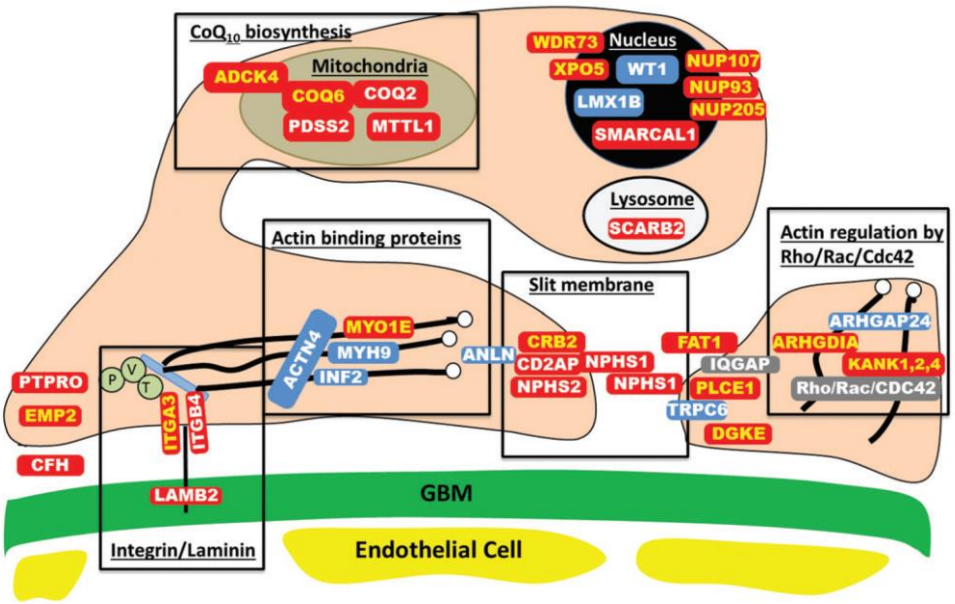


Courtesy of Marina Vivarelli

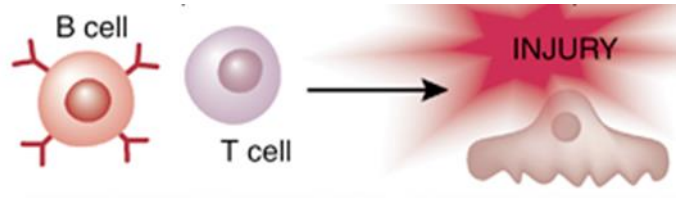
Steroid resistant nephrotic syndrome in children

Monogenic/familial

Immune-mediated



Lovric et al, Nephrol Dial Transpl 2016



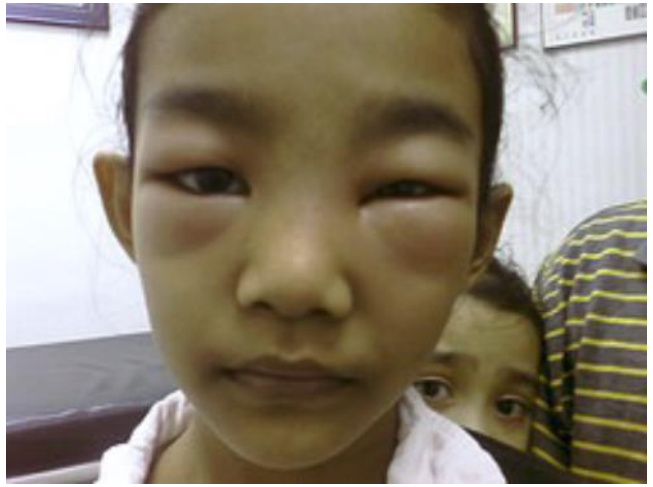


Table 1. Partial List of Proposed Humoral Mediators of Glomerular Permeability in Idiopathic Nephrotic Syndromes

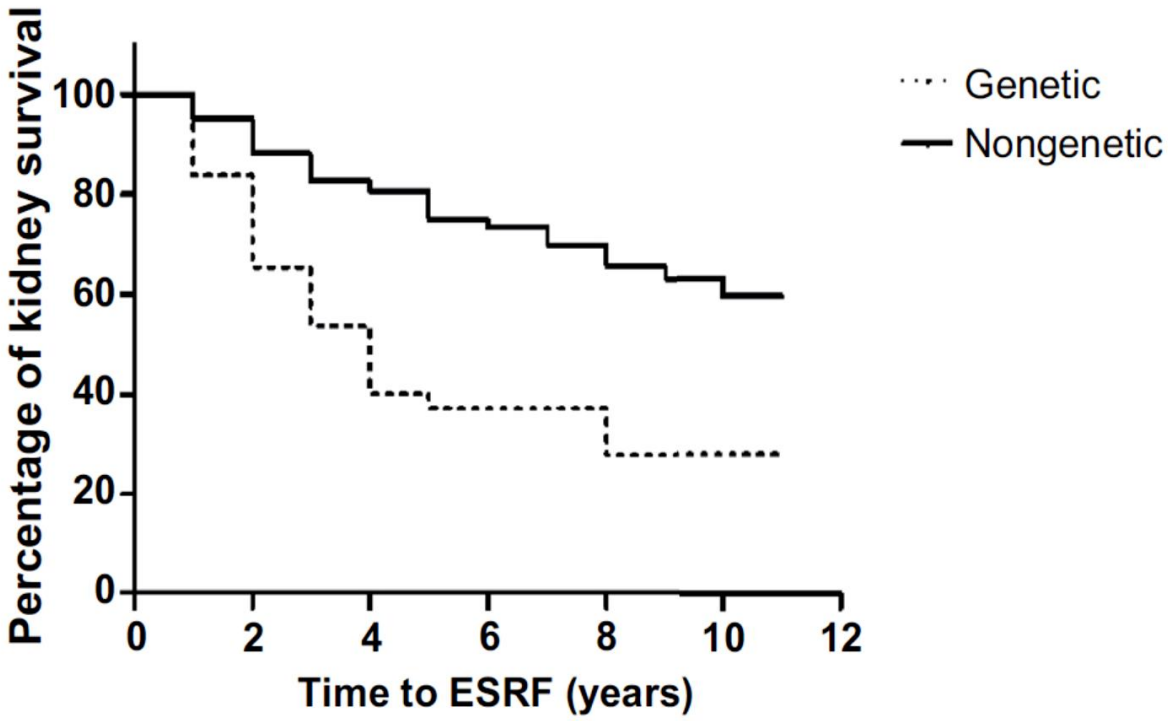
Candidate Factor	Major Findings	Example References
Permeability factors from T cells	Stimulation of T cells from nephrotic individuals releases substance(s) that induce vascular permeability in guinea pigs; secreted products of a T-cell hybridoma from MCD individual induces proteinuria when injected into rats	11, 22
Hemopexin	Present in normal and MCD plasma; proteinuria after injection into rats with decreased nephron expression in rat glomeruli	23-25
IL-13	Overexpression in rats produces features of nephrotic syndrome without histologic changes	26
CLC-1	Present in FSGS plasma; induces permeability in isolated glomeruli; decreases nephron expression ex vivo and in vitro	27
Angptl4	Induced in multiple rodent proteinuric models; podocyte transgenic rats develop proteinuria	27
suPAR	Induced in FSGS, but not MCD, patient sera; transgenic mice develop FSGS and proteinuria	6

Note: Other proposed mediators include vascular endothelial growth factor, heparinase, sialidase, and C-mip (intracellular protein).

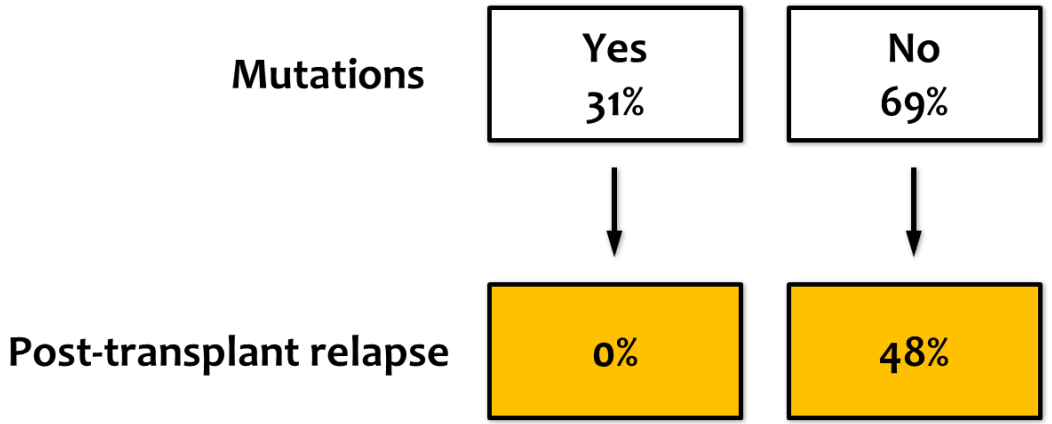
Courtesy of Marina Vivarelli

Parikh et al, AJKD 2011

Genetic *versus* Immune-mediated forms of primary SRNS



Bierzynska et al, Kidney Int 2017

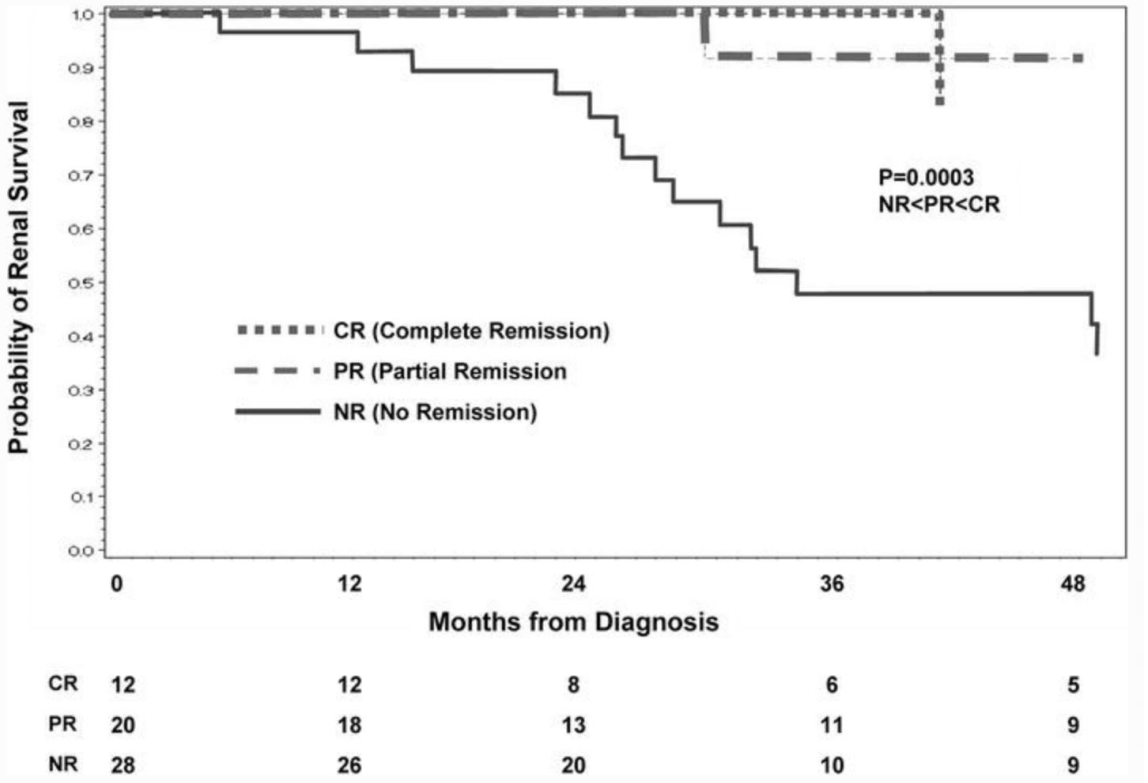


Adapted from Puckelwartz and Schnaper, Kidney Int 2017

Courtesy of Marina Vivarelli

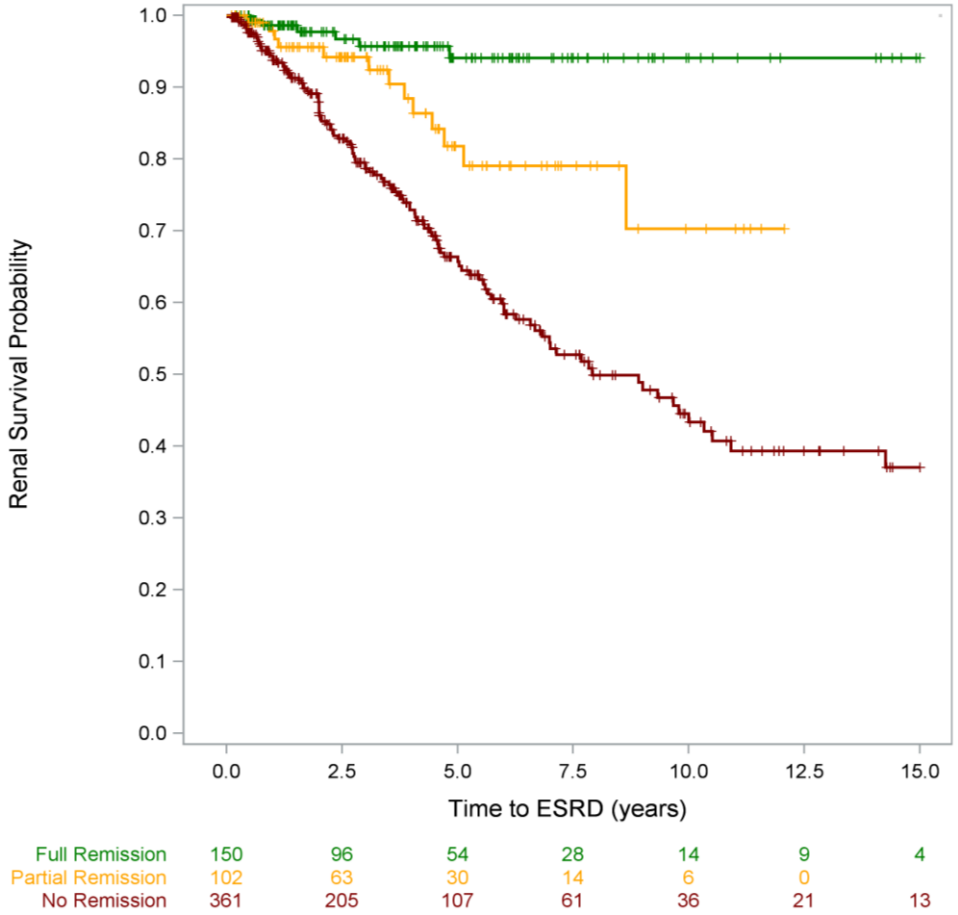
Why is it so important to achieve remission in SRNS?

Children (N=60)



Gipson et al., Ped. Nephrol 2006

Children (N=613)



Trautmann et al., JASN 2017

coordinated by the **IPNA Best Practices & Standards Commitee**

Pediatric Nephrology (2020) 35:1529–1561
https://doi.org/10.1007/s00467-020-04519-1

GUIDELINES

IPNA clinical practice recommendations for the diagnosis and management of children with steroid-resistant nephrotic syndrome

Agnes Trautmann[1] · Marina Vivarelli[2] · Susan Samuel[3] · Debbie Gipson[4] · Aditi Sinha[5] · Franz Schaefer[1] · Ng Kar Hui[6] · Olivia Boyer[7,8] · Moin A Saleem[9] · Luciana Feltran[10] · Janina Müller-Deile[11] · Jan Ulrich Becker[12] · Francisco Cano[13] · Hong Xu[14] · Yam Ngo Lim[15] · William Smoyer[16] · Ifeoma Anochie[17] · Koichi Nakanishi[18] · Elisabeth Hodson[19] · Dieter Haffner[20,21,22] · on behalf of the International Pediatric Nephrology Association

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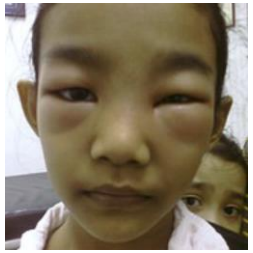
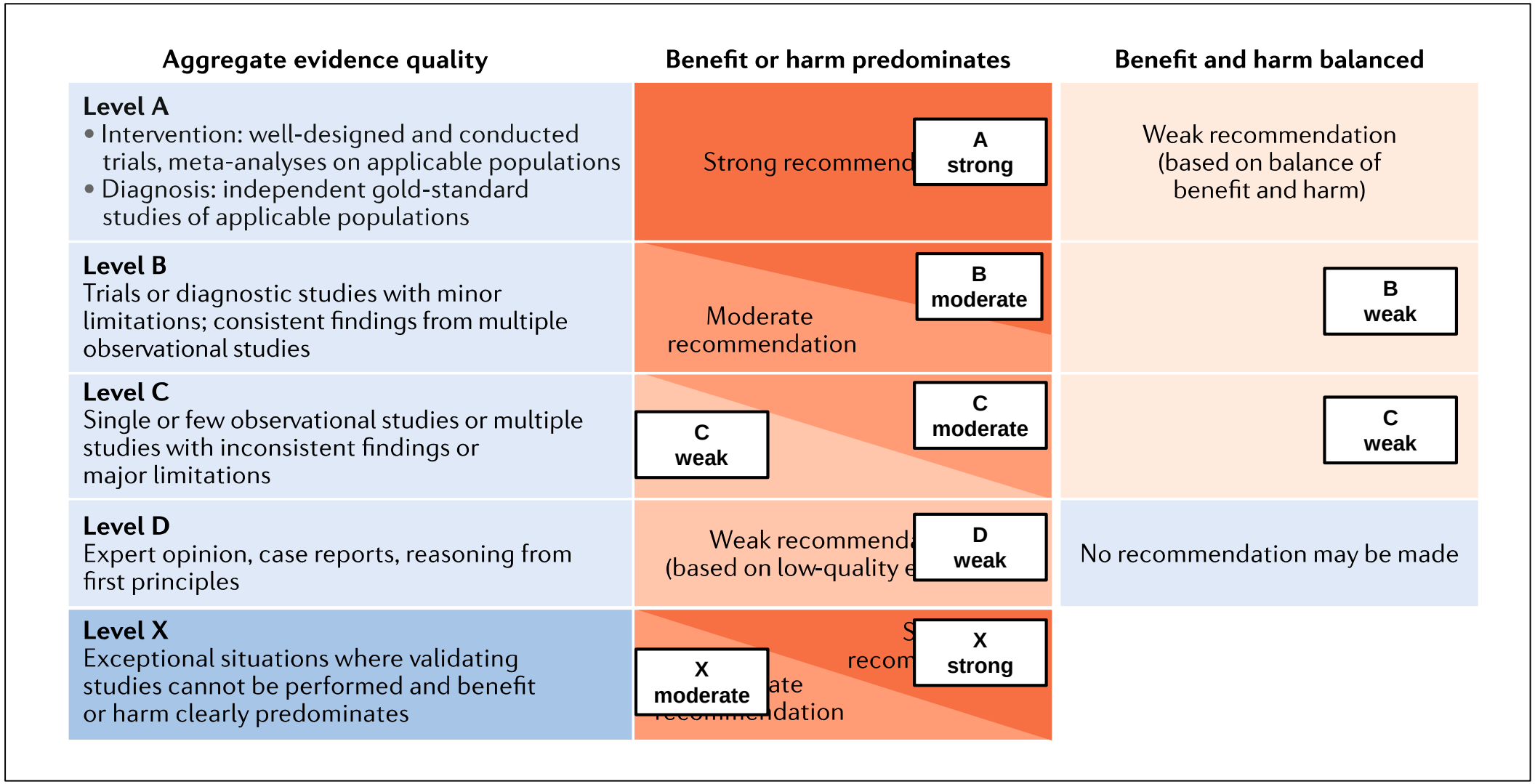
Guidelines on congenital nephrotic syndrome
Lipska et al. Eur J Hum Genet 2020
Boyer et al. Nat Rev Nephrol 2021

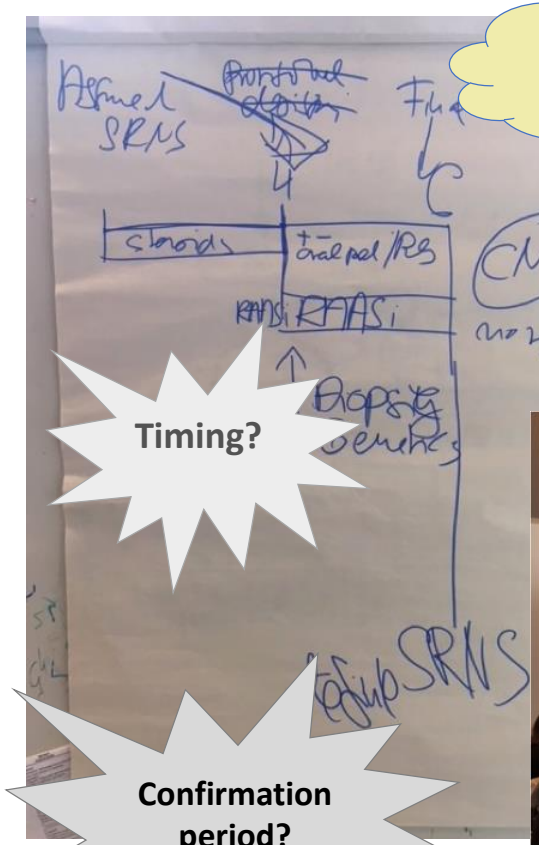


Methodology: **AAP Grading System**



AAP: American Academy of Pediatrics

Working on an algorithm for the SRNS management



Wording?

??

?

?

Different ressources?

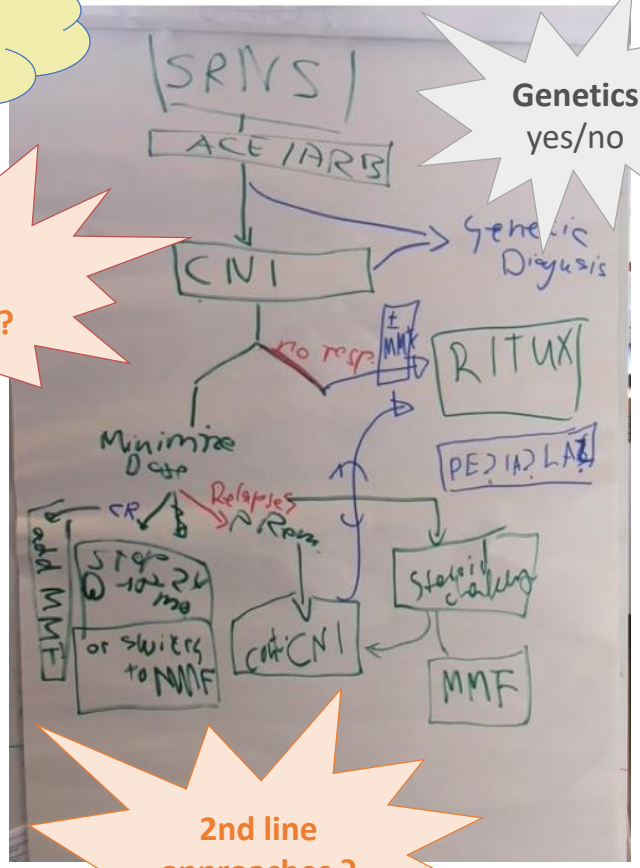
Definitions ???

Response evaluation ???

Timing?

1st line treatment?

Genetics yes/no

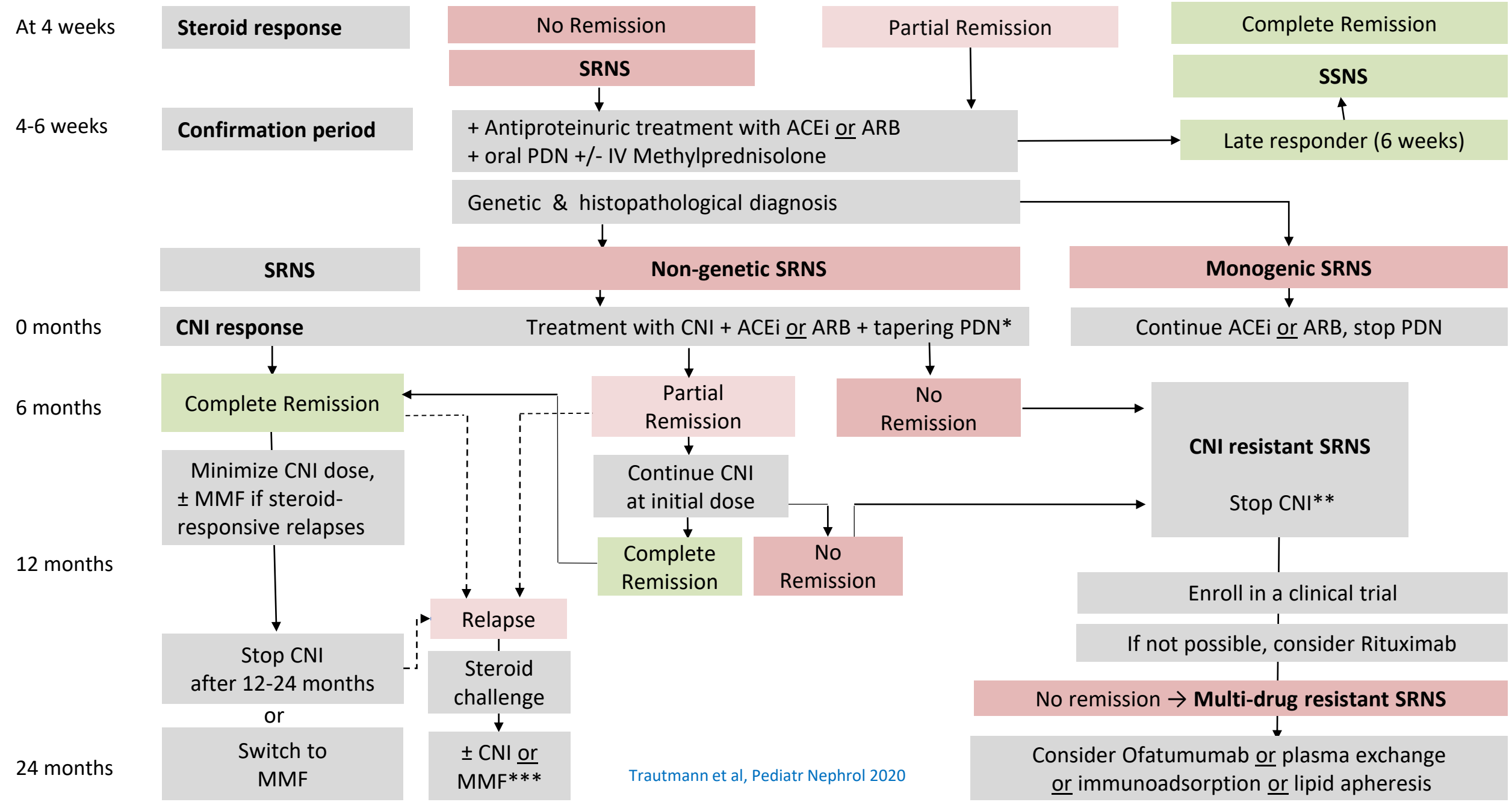


Confirmation period?

2nd line approaches ?

Evidence??

Onset of **Nephrotic Syndrome**: start of oral prednisolone at standard dose



Trautmann et al, Pediatr Nephrol 2020

Definition: **Nephrotic Syndrome**

Nephrotic-range proteinuria

UPCR ≥200 mg/mmol (2 mg/mg) in first morning void
or 24hr urine sample ≥1000 mg/m^2/day
corresponding to 3+ or 4+ by urine dipstick

+

Hypoalbuminemia
serum albumin <30 g/l

or

Edema when
serum albumin level is not available

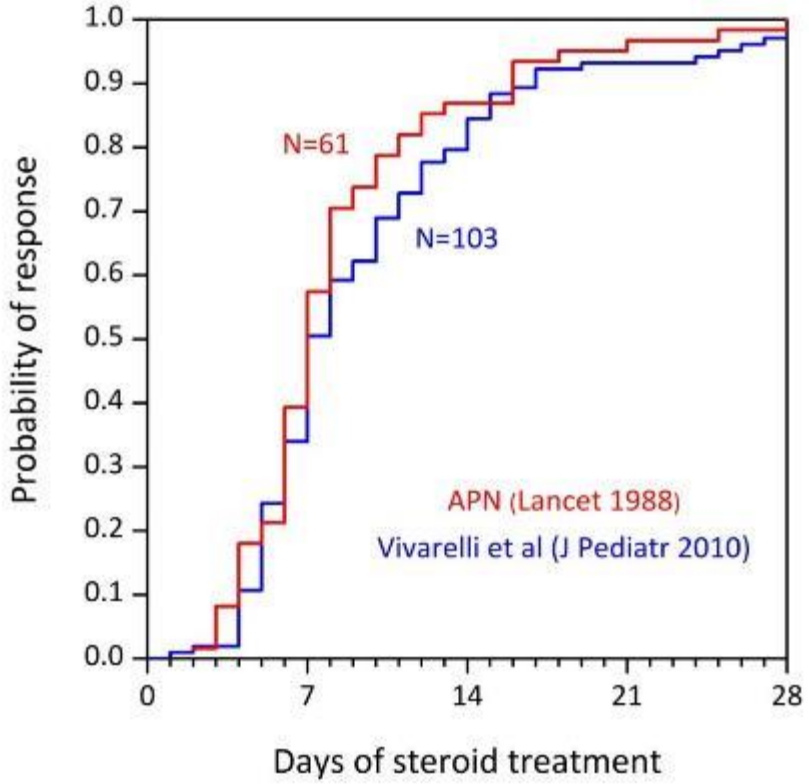
Nephrotic syndrome

Courtesy of Marina Vivarelli

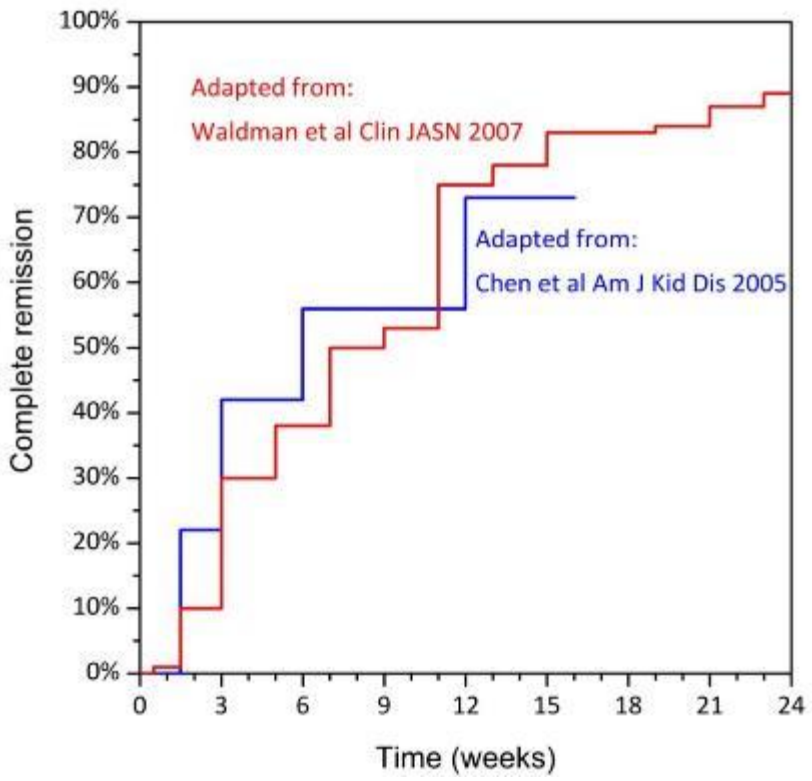
Trautmann et al, Pediatr Nephrol 2020

Most children who will respond to PDN do so within 4 weeks

Children



Adults



Courtesy of Francesco Emma

When should a child be labelled as having SRNS? Rationale for defining a “confirmation period”

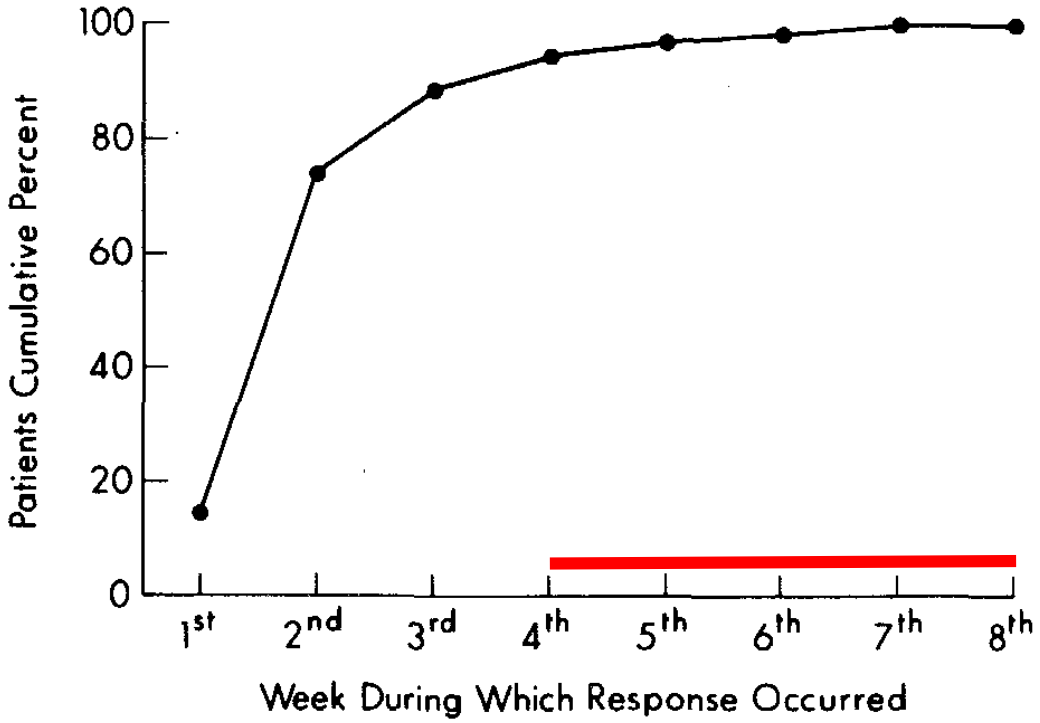


Figure. Cumulative distribution of time to response for initial responders.

International Study of Kidney Disease in Children. J Paediatr 1981

Definition: **SRNS versus SSNS**

Onset of **Nephrotic Syndrome**: start of oral prednisolone at standard dose (60 mg/m^2/day or 2 mg/kg/day), max. 60 mg/day

Steroid response	No Remission	Partial Remission	Complete Remission
At 4 weeks			

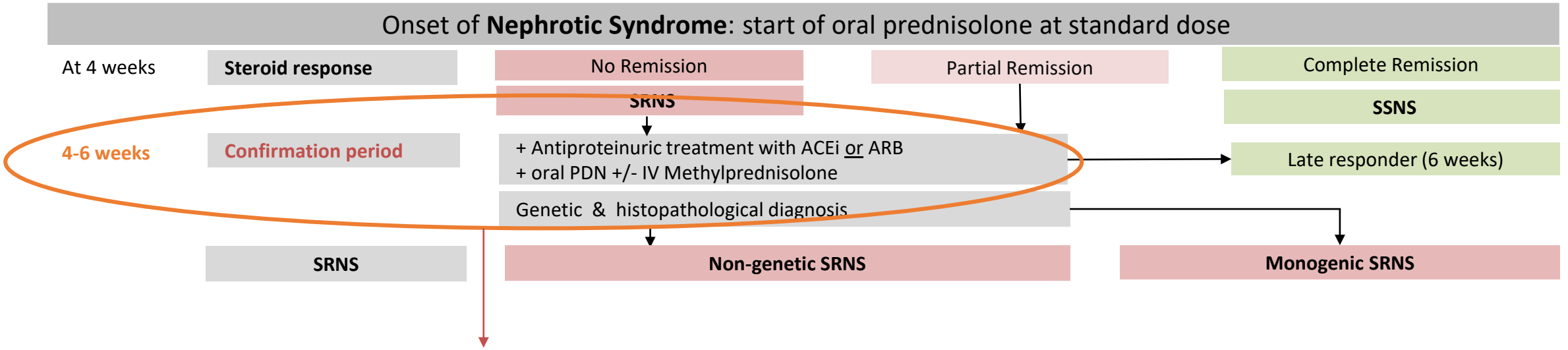
A strong

We recommend quantification of proteinuria by UPCR (based on first morning void or 24 hr urine sample) **at least once before defining a patient as SRNS and/or starting alternative immunosuppression**

No Remission	Partial Remission	Complete Remission
≥ 200 mg/mmol (≥ 2.0 mg/mg) or corresponding to 3+ or 4+ by urine dipstick	**> 20 but < 200 mg/mmol (> 0.2 but < 2.0 mg/mg) and,** if available, **serum albumin ≥ 30 g/l**	**≤ 20 mg/mmol (≤ 0.2 mg/mg)** or negative/ trace dipstick on ≥ 3 consecutive occasions
SRNS		**SSNS**
Lack of complete remission within 4 weeks of PDN		**Complete remission** within 4 weeks of PDN

Trautmann et al, Pediatr Nephrol 2020

Definition:
Confirmation Period for the Diagnosis of SRNS



We suggest using the confirmation period:

- To assess the response to further treatment with corticosteroids (daily oral prednisolone with/without 3 pulses of methylprednisolone) — **C** weak
- To initiate RAAS inhibitors (ACEi or ARB) as 1st line NON-immunosuppressive treatment. — **B** moderate
- To perform genetic testing and/or renal biopsy — **B** moderate

Trautmann et al, Pediatr Nephrol 2020

Initial workup:

- Assess fluid status
- Anthropometry: Height/weight/BMI in all, head circumference < 2 yrs age
- Assess pubertal stage (delayed puberty – Frasier syndrome?)
- Vaccination status
- Check for HBV, HCV, syphilis, varicella, HIV, TB in endemic areas before start of PDN
- Blood and urine work-up: CBC, eGFR, transaminases, urinalysis, thyroid, fasting glucose, blood lipids, baseline coagulation, C3 and C4, total IgGs
- Renal US
- Dietary assessment

A
strong

Trautmann et al, Pediatr Nephrol 2020

Work-up during CONFIRMATION PERIOD

Look for clues of cause

Secondary causes of SRNS: Parvovirus B19, CMV, Hepatitis B, HIV, malaria, sickle-cell disease, lymphoma, SLE

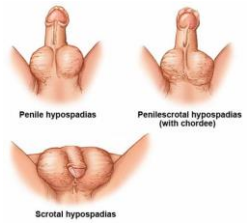
A strong

Genetic forms of SRNS:

- Family history: ask for consanguinity and for family cases of renal (hematuria, proteinuria, CKD of unknown origin) and extra-renal disease (deafness, nail/knee)
- Physical examination: search for extra-renal features (ambiguous genitalia, dysmorphic features, neurological examination, sight, hearing)

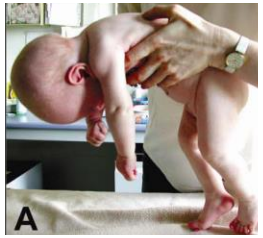
A strong

DDS/Frasier

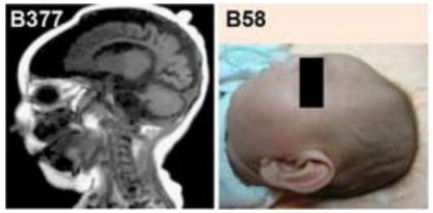


Pierson

Mitochondrial disease



Galloway Mowat



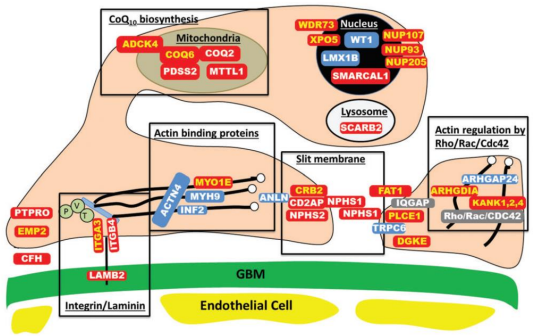
Guidelines on congenital nephrotic syndrome
Lipska et al. Eur J Hum Genet 2020
Boyer et al. Nat Rev Nephrol 2021

- If a genetic form of SRNS is suspected, performing urinalysis of siblings is suggested

C Moderate

Trautmann et al, Pediatr Nephrol 2020

SRNS in children

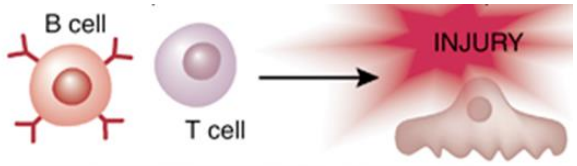


Monogenic

Structural anomalies of glomerular filtration barrier

Immune-mediated

Mixed T-/B-cell disorder
Circulating 'permeability' factor disease



Why is the differentiation genetic from non-genetic SRNS important?

- To provide specific treatment, when available
- To withdraw ineffective or harmful therapy
- To allow screening for dangerous co-morbidities
- To provide family counselling
- To provide an estimate of the risk of ESKD and post-transplant recurrence

Trautmann et al, Pediatr Nephrol 2020

When to perform genetic screening in SRNS?

B
moderate

In all patients with a diagnosis of primary SRNS,

EXCEPT in pts with secondary cause, in pts with initial steroid-sensitivity («secondary» SRNS)

C
weak

In low-resource settings, priority should be given to:

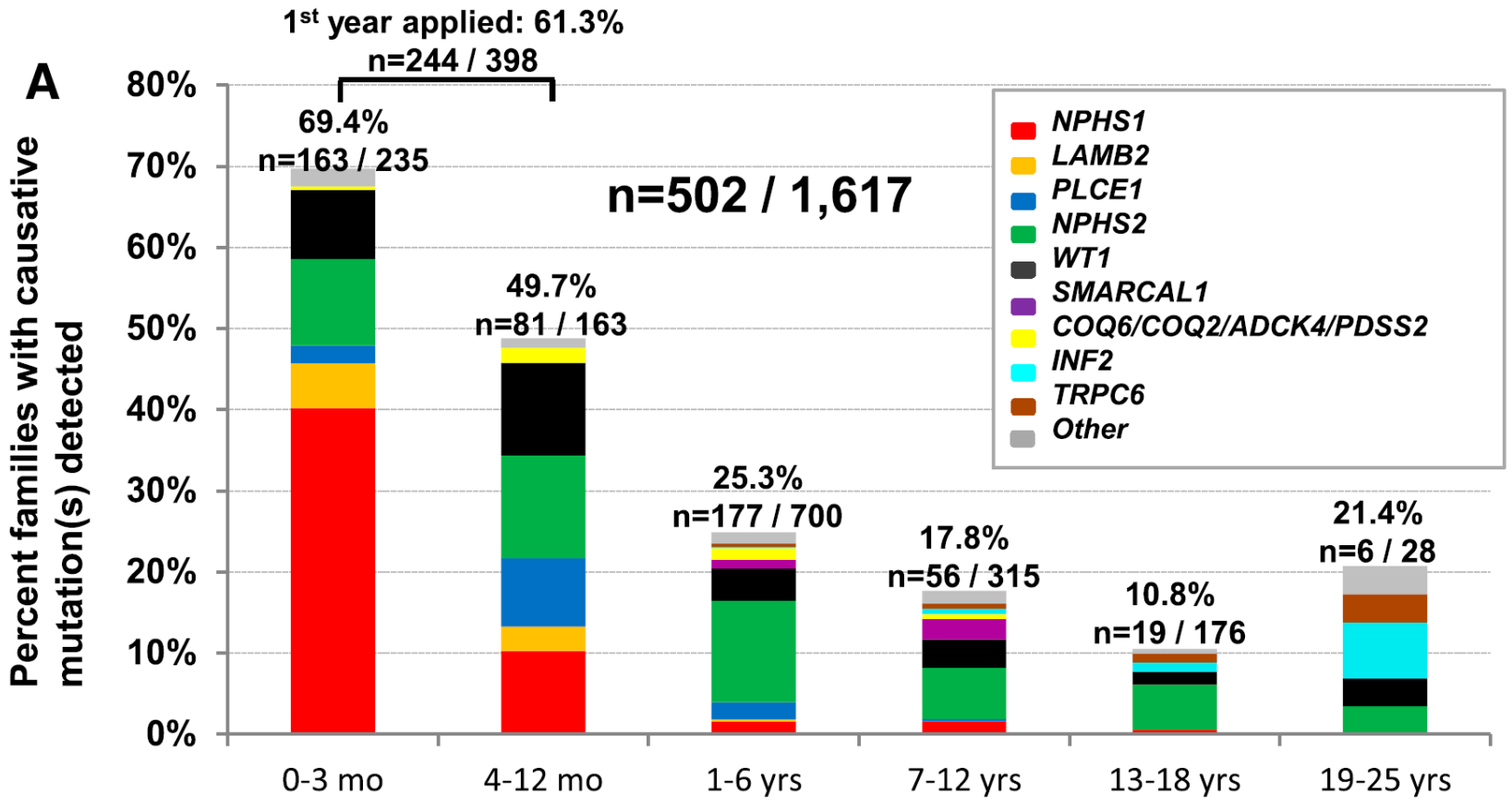
-familial forms

-children with extra-renal features, especially if very young

-pre-renal transplant

Trautmann et al, Pediatr Nephrol 2020

Frequency of genetic SRNS per age group



Sadowski et al, J Am Soc Nephrol 2015

How to perform genetic screening in SRNS?

Gene causing SRNS	Mode of inheritance	Total SRNS families with molecular diagnosis
NPHS2	AR	177 (9.93)
NPHS1	AR	131 (7.34)
WT1	AD	85 (4.77)
PLCE1	AR	37 (2.17)
LAMB2	AR	20 (1.12)
SMARCAL1	AR	16 (0.89)
INF2	AD	9 (0.5)
TRPC6	AD	9 (0.53)
COQ6	AR	8 (0.45)
ITGA3	AR	5 (0.28)
MYO1E	AR	5 (0.28)
CUBN	AR	5 (0.28)
COQ2	AR	4 (0.22)
LMX1B	AD	4 (0.22)
ADCK4	AR	3 (0.17)
DGKE	AR	2 (0.11)
PDSS2	AR	2 (0.11)
ARHGAP24	AD	1 (0.06)
ARHGDIA	AR	1 (0.06)
CFH	AR	1 (0.06)
ITGB4	AR	1 (0.06)
Total		526 (29.5)

21%

25%

30%

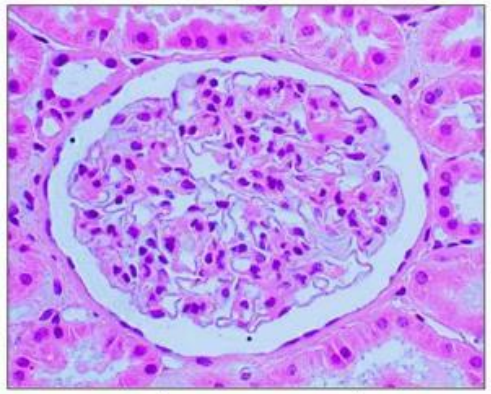
- NGS panel
- >80 SRNS causing genes (listed in Table 3)
- Genetic counseling

Lovric et al, Nephrol Dial Transpl 2016

Frequency of renal histology pictures in children with SRNS

25-40%

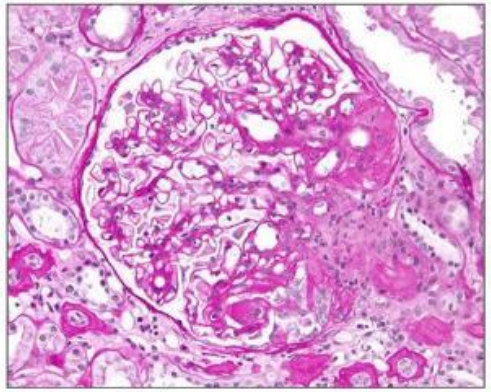
Minimal change disease
MCD



5 days post-transplant

35-55%

Focal segmental glomerulosclerosis
FSGS

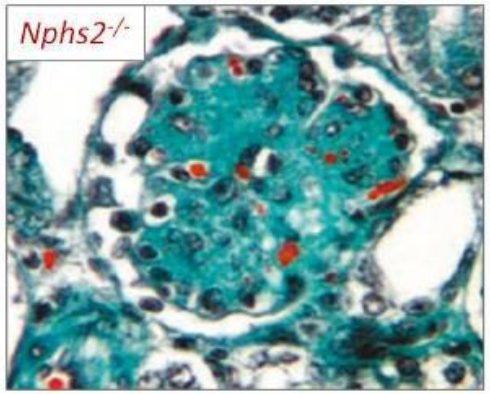


37 days post-transplant

Acute → *Chronic*

10-15%

Diffuse mesangial sclerosis
DMS



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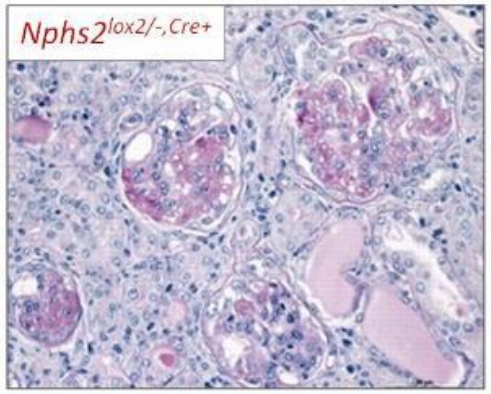


Early onset → *Late onset*

Roselli et al, Mol Cell Biol 2004 - Mollet et al, JASN 2009

20% other glomerular diseases: IgAN, IMN, Alport, C3G, SLE, TMA

modified from Tullus, Lancet Child Adolescent Health 2018

Courtesy of Marina Vivarelli

Why to perform a renal biopsy in SRNS?

- To exclude rare cases of other glomerular disorders presenting as SRNS (IgAN, IMN, Alport, C3G, SLE, TMA)
- To diagnose DMS
- To evaluate TI sclerosis and general status of kidney fibrosis
- Following CNIs, to assess for CNI-induced renal damage

Trautmann et al, Pediatr Nephrol 2020

When to perform a renal biopsy in SRNS?

In all patients with a diagnosis of primary SRNS,
EXCEPT in pts with secondary cause (infection/malignancy).

A
strong

In pts with a strong clinical suspicion of a genetic cause:
-familial forms
-children with extra-renal features, particularly of young age
PROVIDED genetic results are readily available,
genetic testing is suggested **before/instead** of a renal biopsy

D
weak

Trautmann et al, Pediatr Nephrol 2020

INITIAL MANAGEMENT

SUPPORTIVE MEASURES

- Balanced fluid intake
- Moderate sodium intake with a dietitian
- Loop diuretics in case of severe edema but lack of intravascular volume depletion

  ("overfilled patient")
- Addition of thiazides or potassium sparing diuretics (amilorid*/aldosterone) in case of refractory edema
- Albumin infusion in case of refractory edema and/or symptomatic hypovolemia or oliguria ("underfilled patient" - prolonged capillary refill time)

  20-25% albumin; 0.5-1 g/kg BW; ≧4h; add furosemide at the end

*epithelial sodium channel blocker

Trautmann et al, Pediatr Nephrol 2020

PREVENTION OF THROMBOSIS IN SRNS

Recommended: mobilizing patients, avoiding central venous lines

Not recommended: routine prophylactic anticoagulation

LMW heparin or oral anticoagulation prophylaxis and thrombophilic screening suggested if **positive family/personal history for thrombotic events or additional risk factors**:

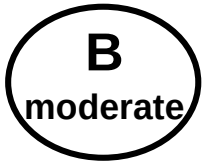
- central venous lines
- severe protracted hypoalbuminemia
- illness/infection with dehydration, immobilization

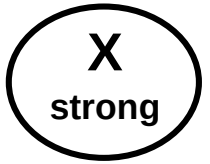
Trautmann et al, Pediatr Nephrol 2020

TREATMENT AT 4-6 WEEKS FROM ONSET IN SRNS

Glucocorticoids: i.v. methylprednisolone boli can be used, oral PDN is gradually tapered on alternate days and stopped in 6 months

RAAS inhibition: should be started of possible in all patients with EITHER an ACE-inhibitor OR an ARB.





- Aim for maximum tolerated dose (dosages are given in the manuscript)
- Caution if hyperkalemia, initial CKD, intravascular volume depletion
- Contraception necessary in fertile females

Trautmann et al, Pediatr Nephrol 2020

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- Aim for maximum tolerated dose (dosages are given in the manuscript)
- Caution if hyperkalemia, initial CKD, intravascular volume depletion
- Contraception necessary in fertile females

B
moderate

X
strong

CNI: should be started <u>after</u> receiving negative genetic tests results <u>or</u> during the confirmation period depending on its availability

B
Moderate

Trautmann et al, Pediatr Nephrol 2020

Non-genetic SRNS: Recommendation for 1st line IS treatment

- **CNI – cyclosporine A (CsA) or tacrolimus (TAC)** — B Moderate
- Suggest minimum treatment period of 6 months to determine response to CNI — B Weak
- Withhold or delay, if eGFR < 30 ml/min/1.73 m^2, AKI, uncontrolled hypertension — X strong

	CsA	TAC
Starting dose	3-5 mg/kg/day	0.1-0.2 mg/kg/day
Initial trough levels (tandem mass spectrometry)	80-120 ng/ml	4-8 ng/ml
Monitoring trough levels (refer to table 2)	**weekly** until steady state (4 weeks), then **every 1-3 mths** + serum creatinine as safety parameter	
Prevention	Adequate but minimal dosing of CNI, adapted by drug monitoring	
Side effects	Hypertension, nephrotoxicity, tremor, neurotoxicity, leg cramps, hypomagnesemia, interaction with other drugs	
	Hypertrichosis, gingival hyperplasia	Glucose intolerance, diabetes mellitus

B Weak

Co-intervention with Glucocorticoids

- We do not recommend prolonged (>6 months) routine treatment with prednisolone in conjunction with CNI and RAASi

C
Moderate

- We suggest tapering prednisolone treatment and discontinuing after 6 months

D
Weak

- Suggestion for tapering prednisolone after CNI initiation:

  40 mg/m^2 QOD for 4 weeks

  30 mg/m^2 QOD for 4 weeks

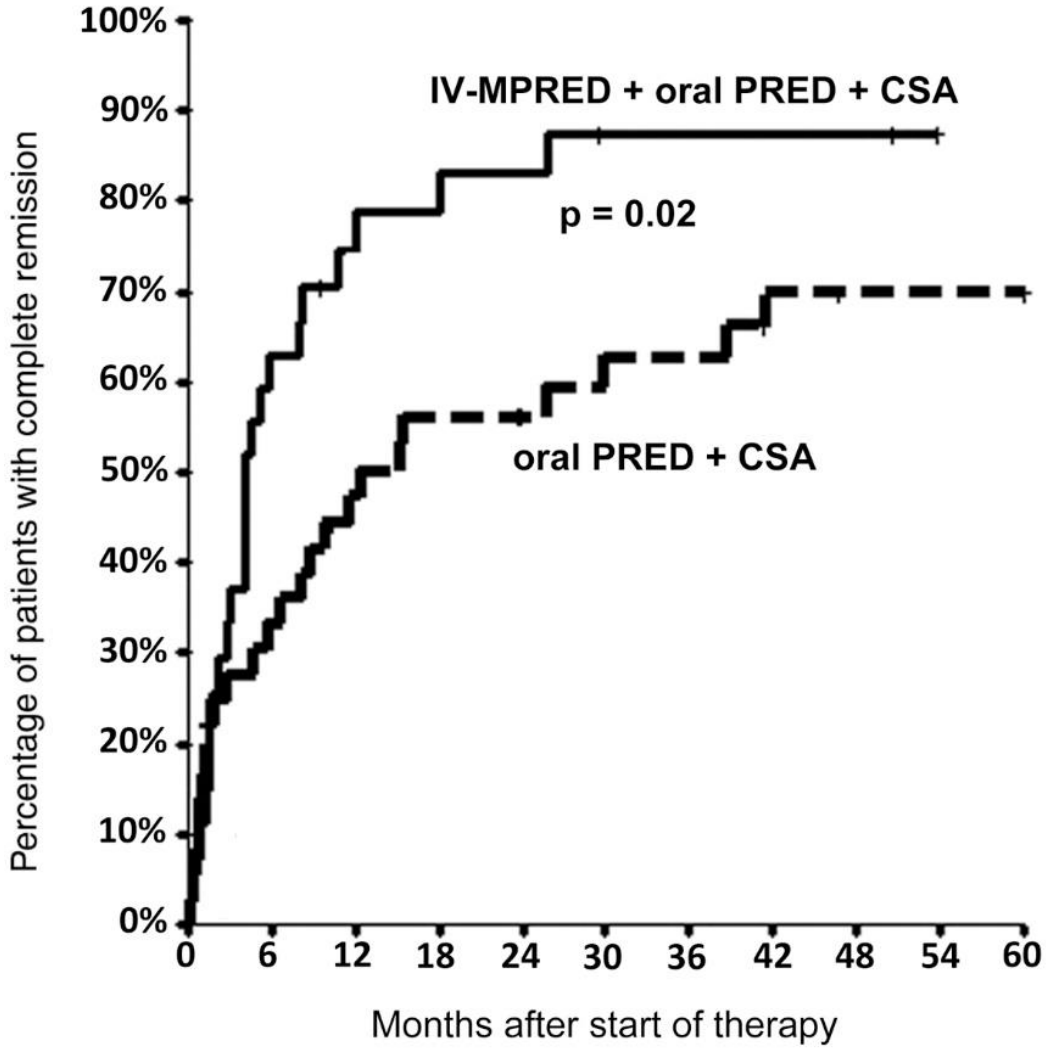
  20 mg/m^2 QOD for 4 weeks

  10 mg/m^2 QOD for 8 weeks, discontinuing thereafter

D
Weak

Trautmann et al, Pediatr Nephrol 2020

Over 50% of children with SRNS will respond to a CNI



It can take a looong time.

However:

- Need to avoid unnecessary toxicity in non-responders
- Opportunity to try other therapeutic options

Ehrich et al, Nephrol Dial Transpl 2007

Courtesy of Marina Vivarelli

CNI-Response at 6 months: **Complete Remission**

CNI response + **ACEi or ARB** + **Tapering prednisolone and discontinue at 6 months**

6 mths — Complete Remission

AIM: Maintain remission and avoid nephrotoxicity and side effects

Minimize CNI dose, ± MMF if steroid- resp. relapses

Reduce CNI dosages to the lowest dosage required to maintain remission.

C weak

12 mths

Stop CNI after 12-24 months

Consider discontinuation of CNIs after 12-24 months

C weak

or

24 mths — Switch to MMF

Alternatively, consider conversion to MMF to maintain remission

C weak

Trautmann et al, Pediatr Nephrol 2020

Relapses

	Relapse on CNI/ IS	Relapse post withdrawal of CNI/ IS
CNI	C Moderate • Adherence to CNI • Monitoring trough levels • Adequate trough levels	• Re-starting CNI/ the immunosuppression agent preventing relapses before • Monitoring trough levels D Weak
Steroid challenge	C Weak • Oral prednisolone 60 mg/m^2 daily until remission is achieved or for a maximum period of 4 weeks • subsequent tapering of prednisolone	

Complete remission
-> steroid sensitive relapse

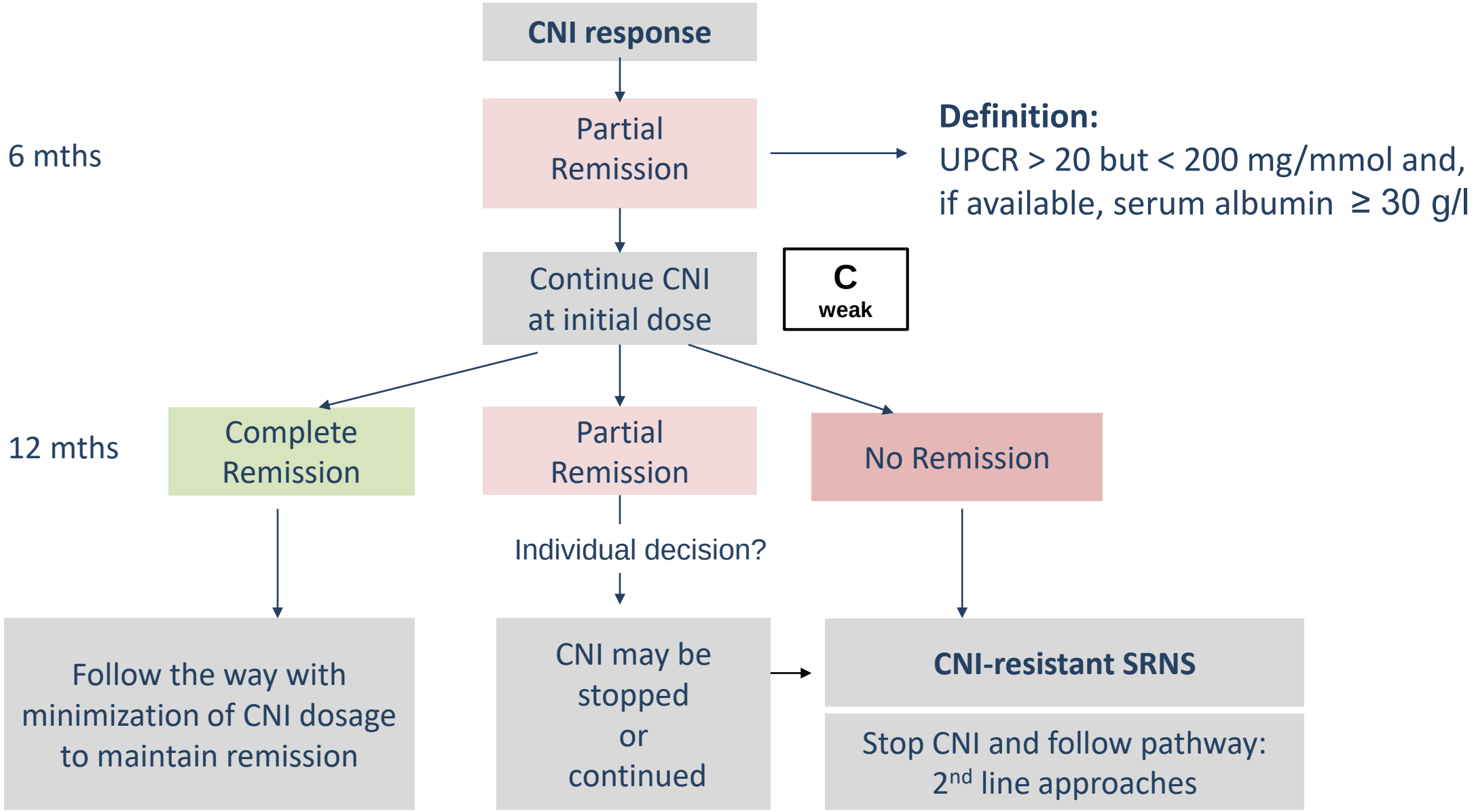
Consider use of MMF to maintain remission
C Weak

No response within 4 weeks
Frequent relapses
Side effect of medications

Follow the refractory SRNS protocol („second-line approaches“)

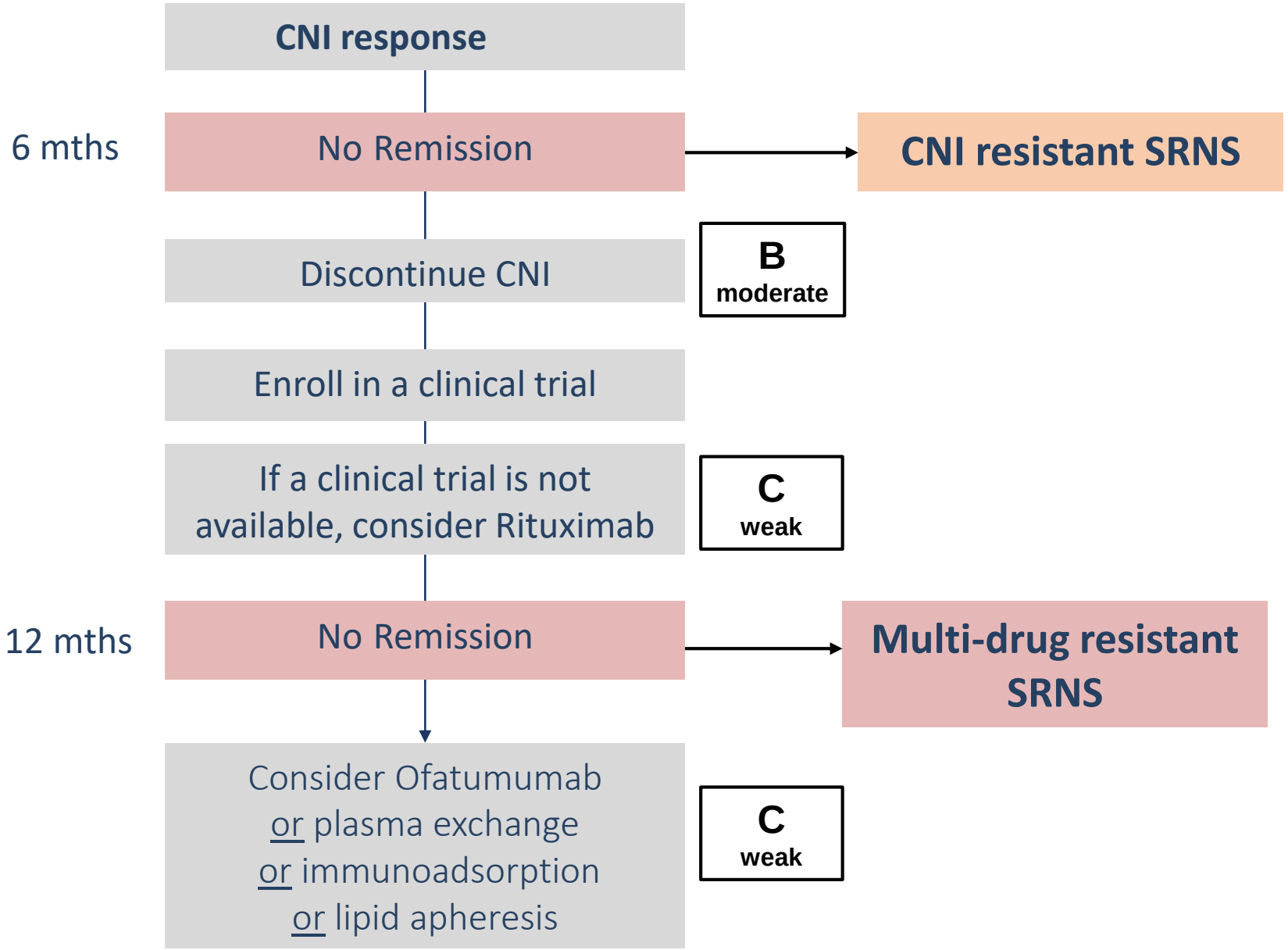
Trautmann et al, Pediatr Nephrol 2020

CNI-Response: **Partial Remission**



Trautmann et al, Pediatr Nephrol 2020

CNI-Response: **No Remission -> 2nd line approaches**



Absence of at least partial response to CNI after 6 months of treatment at adequate doses and/or levels

Absence of complete remission after 12 months of treatment with **2 mechanistically distinct steroid-sparing agents** at standard doses

Trautmann et al, Pediatr Nephrol 2020

Rituximab

- **Evaluate potential contraindications** before commencing rituximab:
  Screening in case of clinical suspicion and endemic background for:
  tuberculosis: chest X-ray, skin or blood test.
  Hepatitis B: HBs-Ag serology in case of elevated liver enzymes,
  JC-virus: spinal fluid examination in case of neurological symptoms

X strong

- **Administration:** 1-2 rituximab infusions at a dose of 375 mg/m^2 usually within 2 wks
- **Pre-medication:** antihistamine, paracetamol

C Weak

- **Monitoring:** Aiming for a reduction of the CD19 cell count < 5/µl or < 1%.
- **Antibiotic prophylaxis:** cotrimoxazole for a period of 3 up to 6 months depending on B cell recovery and immunosuppressive co-medication

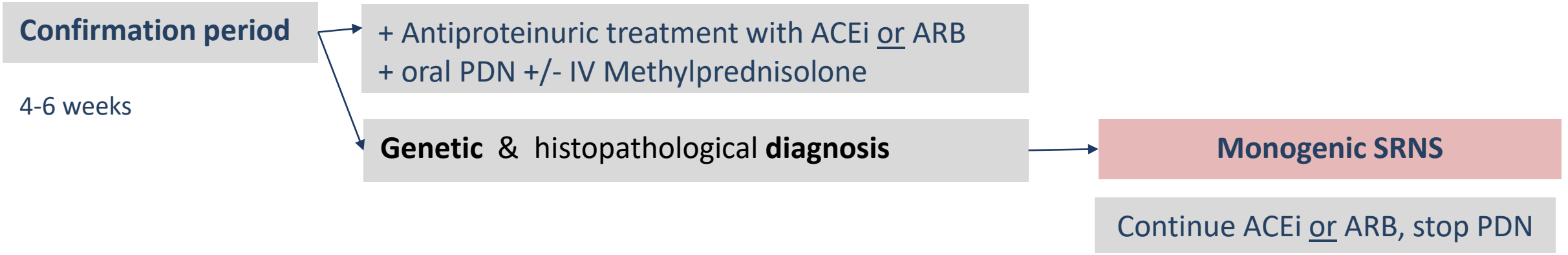
C Weak

- **Hypogammaglobulinemia:** Immunoglobulin substitution not routinely, however, be considered in cases of low serum IgG AND recurrent/ and or severe infections

D Weak

Trautmann et al, Pediatr Nephrol 2020

Genetic SRNS



- We recommend that **screening for all known podocytopathy genes be offered** to enable decisions on further immunosuppression.

X
strong

- We recommend **withholding CNI and stopping prednisolone treatment** in patients with **monogenic form** of SRNS.

B
moderate

- If genetic results are not available at the end of the confirmation period, we suggest to start treatment with CNI and to re-assess after receiving genetic results.

Trautmann et al, Pediatr Nephrol 2020

Withdrawal of immunosuppressive agents?

Monogenic SRNS

- Specific treatments?
- Extrarenal symptoms?
- Comorbidities?

Partial/ complete remission on IS??

- **Review pathogenicity of genetic variant**
- Duration of response?
- **Benefit-risk assessment:** benefits of remission vs. potential risks/harms of IS?
- **Parental counseling**

A strong

A strong

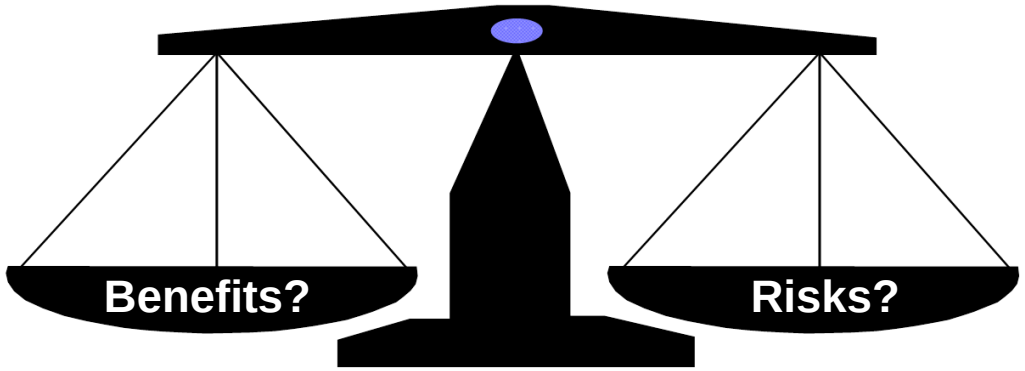
Non-responsive, non-genetic patients
Multidrug-resistant SRNS

- Discontinue ineffective treatment
- Continue non-immunosuppressive management
- Parental counseling

X strong

Explore available options for novel therapies being assessed in clinical trials?

X strong



Trautmann et al, Pediatr Nephrol 2020

Management of children with ESKD
- Preparation for 1st Transplantation -

- We recommend **kidney transplant be offered to children with ESKD** secondary to SRNS **regardless of genetic or non-genetic cause** of SRNS.

B
Moderate

- We recommend that the **anticipated recurrence risk** after kidney transplantation **should be discussed with the family** in renal replacement therapy planning.

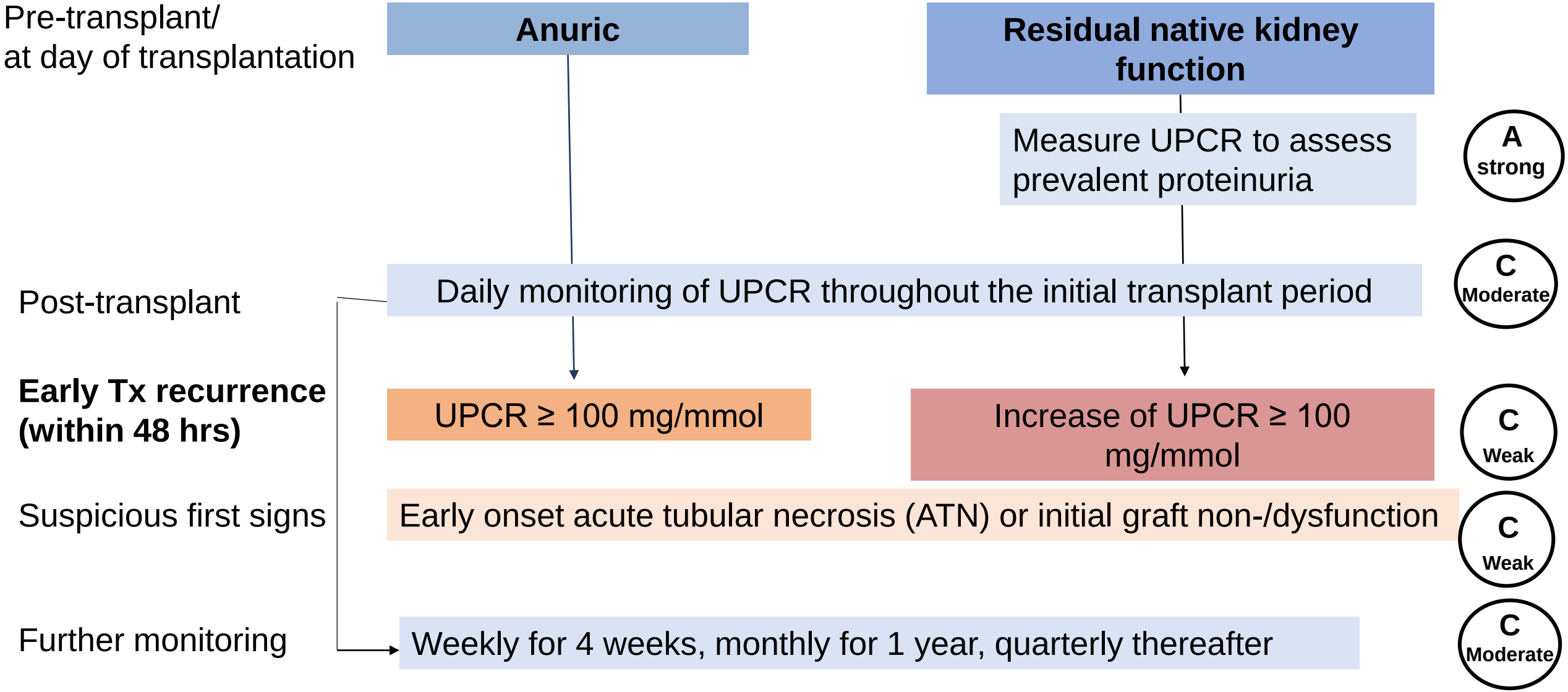
A
strong

- If **transplant will occur before resolution of NS** in the setting of ESKD, we suggest **considering medical or surgical nephrectomies** prior to transplantation.

D
Weak

Trautmann et al, Pediatr Nephrol 2020

Surveillance for post-transplant recurrence



Allograft biopsy?

We suggest that an allograft biopsy

is **not required to diagnose rapid recurrence of NS**,

B
Moderate

but allograft biopsy **is recommended for the exclusion of differential diagnosis** in the setting of

B
Moderate

- subnephrotic proteinuria
- delayed graft function
- recurrence after 48h
- late recurrence (≥ 3 months post-transplant): assessment including electron microscopy, infection, donor-specific antibodies serologies

Trautmann et al, Pediatr Nephrol 2020

Prevention of post-transplant recurrence

1st renal transplantation:

- There is **insufficient evidence** to recommend intervention strategies for the prevention of recurrence in children undergoing a **first** kidney transplant

?

2nd renal transplantation:

- We suggest **prophylactic plasmapheresis or immunoadsorption or lipid apheresis and perioperative rituximab** for use in children with a history of allograft loss due to **NS recurrence in a prior transplant**

C
Weak

Trautmann et al, Pediatr Nephrol 2020

Treatment of post-transplant recurrence

- We recommend implementing NS recurrence-specific therapy **as soon as possible** after diagnosis is established

X
strong

- **Suggested treatment strategies**
  - increasing doses of CNI
  - intravenous MPDN pulses
  - and/or plasmapheresis (or immunoadsorption)
  - with or without rituximab

C
Weak

- We suggest **initiating RAASi** when **no complete remission** is achieved following recurrence targeted therapy.

C
Weak

Trautmann et al, Pediatr Nephrol 2020

Key Points

SRNS

- accounts for 10-25% of cases with NS
- has a high risk for ESKD (30-70%) and
  post-transplant recurrence (50%)
- is associated with a high disease & treatment associated comorbidity

Differentiation between genetic and non-genetic forms matters

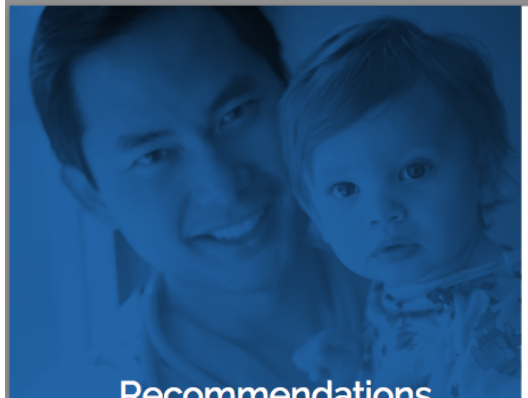
Aims: - Remission and preservation of kidney function
- Avoidance of severe side effects

Cornerstones of treatment: RAASi +/- CNI (non-genetic forms)

Global Distribution of the IPNA-CPR for SRNS

- **Open Access Publication** in **Pediatric Nephrology** (May 2020)
- **Open access translation** into the 16 different languages:

  Arabic, Chinese, **English, French**, **German, Greek. Hebrow, Italian,** Japanese, Korean, **Portugese, Russian, Slovenia, Spanish, Ukrainan, Turkish** and other under preparation (available www.theipna.org)
- **Webinars:** IPNA & ERKNet-/ESPN Webinars (November 2020, June 2021...)
- **Presentations at:**
  - **IPNA workshop & teaching courses**
  - **IPNA Regional Societies meetings & teaching courses**
  - **International Conferences:** WCN 2021, ERA/EDTA 2021.....
- **Elearning** – e.g. Elearning case SRNS in ERKNet schedule
- **Patient education material** (in 10 different languages, available www.theipna.org)

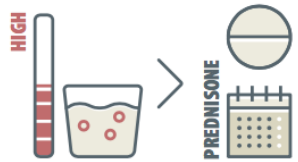


Recommendations from the International Pediatric Nephrology Association for the Diagnosis and Management of Children with Steroid-Resistant Nephrotic Syndrome (SRNS)

NEPHCURE® Kidney International
Saving Kidneys • Saving Lives

Patient material created with support from Nephcure Kidney International

1 Diagnosis

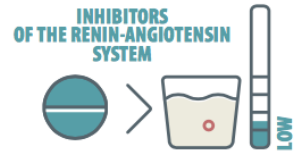


Steroid-resistant nephrotic syndrome (SRNS) is the persistence of protein in the urine after 4 weeks of treatment with prednisone/prednisolone. It can lead to decreased kidney function and/or kidney failure.

Genetic testing and a kidney biopsy should be considered in all children with SRNS without a clearly identified cause.

Genetic causes are identified in up to 1/3 of children. If a genetic cause is identified, medications that act on the immune system are not effective and should be discontinued.

2 Treatment



Use of medications that decrease the amount of protein in the urine and protect the kidneys are recommended once the diagnosis of SRNS is confirmed.

Once the diagnosis of SRNS is confirmed, treatment with cyclosporine or tacrolimus (or alternatives) for at least 6 months, should be started. If there is no response after 6 months, they should be discontinued. Medications to manage chronic kidney disease may be used.

Kidney transplant is recommended to all children who reach kidney failure, recognizing that there is a risk of recurrence of nephrotic syndrome in the new kidney. Removal of one or both kidneys in a patient may be needed prior to transplantation.

3 General measures

Encourage physical activity and healthy nutrition. Excessive salt intake should be avoided.

Routine vaccinations including the annual flu shot should be given. Live virus vaccines require caution in children taking immunosuppressive medications. Speak with your doctor before vaccinations.

Different medications may be needed to compensate the loss of proteins in the urine (hormones, vitamins, calcium).

IPNA International Pediatric Nephrology Association
GREAT CARE FOR LITTLE KIDNEYS. EVERYWHERE

Visit IPNA: www.theipna.org
Freely accessible at the IPNA website: www.theipna.org/resources/guidelines

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