

Efficacy of Calcineurin Inhibitor in Children With Steroid-Resistant Nephrotic Syndrome

1/ #Tweeetorial alert!!

Hey, #medtwitter #Nephtwitter, Calcineurin inhibitors (CNIs) may stabilize podocyte actin cytoskeleton, potentially remitting nephrotic syndrome; however, large-scale studies on CNI efficacy in steroid-resistant (SRNS) cases are limited.

1/a Skytorial alert!!

Hey, #medsky #Nephsky, Calcineurin inhibitors (CNIs) may stabilise podocyte actin cytoskeleton, potentially remitting nephrotic syndrome; however, large-scale studies on CNI efficacy in steroid-resistant (SRNS) cases are limited.

1b/ Our author is Abdul Qader@@md_abdulqader83 (pediatric nephrologist).



Our topic: Efficacy of CNI's in children with steroid-resistant nephrotic syndrome.

Article link- [https://www.kireports.org/article/S2468-0249\(25\)00481-4/fulltext](https://www.kireports.org/article/S2468-0249(25)00481-4/fulltext)

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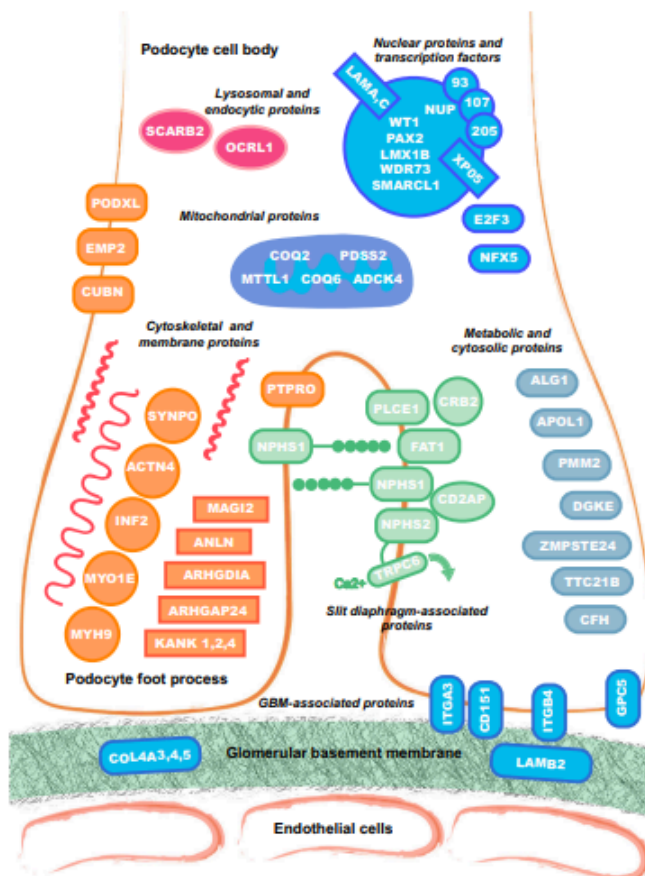
2/ SRNS is observed in approximately 10-15% of childhood nephrotic syndrome cases. What percentage of these SRNS cases are linked to pathogenic variants within podocyte-related genes?

- a) 35%
- b) 55%
- c) 30%
- d) 25%

3/C, approximately 30% of cases are caused by [pathogenic variations](#) linked to podocyte-related genes.

Here is a nice figure that summarises the [genetic mutations associated with SRNS](#).

Fig. 1 Genetic mutations associated with steroid-resistant nephrotic syndrome (SRNS) grouped according to location and function within the glomerular filtration barrier. For full names of proteins encoded by genes, please refer to Table 1



4/ Patient cohort ~

N = 278 (19 countries)

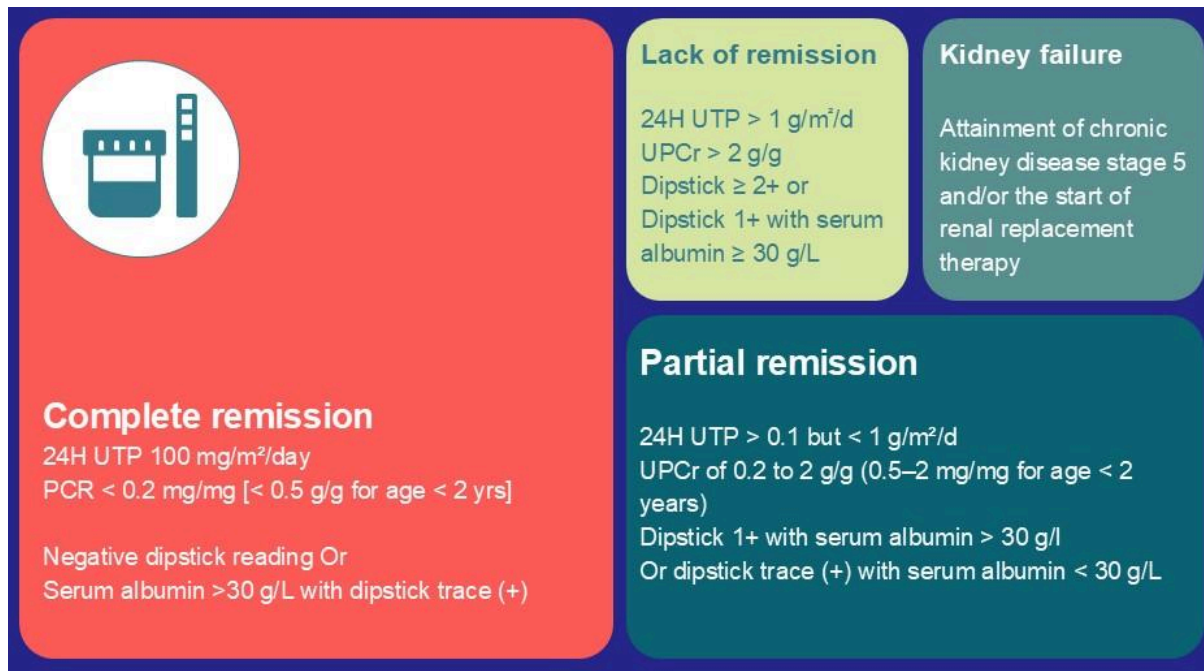
Age- 3months to 19 years at disease onset

Confirmed SRNS

Documented genetic status

Received CNI as first-line SRNS therapy within 3y of disease onset

5/ #Remission definitions



6/ Results:

Proven genetic disease = 59/278 (21.2%)

Genetic SRNS at onset =

- 1) Milder initial presentation
- 2) Less oedema & higher serum albumin
- 3) Higher FSGS

Compared to non-genetic SRNS

Progression to kidney failure => More often in genetic SRNS

6a/ CNI treatment

CNI was started 2.3m (1.5-5) after disease onset

Co-treatment with

- ▶ Steroids (96.8%)
- ▶ RAAS antagonists (81.3%)
- ▶ MMF in the later course (20.1%)*

*[less frequently in genetic (22.8% vs 10.2%)]

6b/ Cyclosporine A (CsA) Vs Tacrolimus (Tac)

- ▶ CsA [203/278] dose 4.6(3.6-5.5) mg/Kg/d [Trough 89 (67-119)]
- ▶ Tac (n=16) dose 0.12 (0.09-0.20) mg/kg/d [Trough 5.6 (4.3-6.9)]

📅 CNIs for 1.7y in nongenetic SRNS & for 0.7y in genetic SRNS

7a/ CNI in Non-genetic SRNS

First 6mos, steady 📉 Proteinuria 84%(80-87%)

CR 54.8% (n= 91, in 1st yr)

Cumulative incidence of CR [45% 1yr to 57%2yr]

🕒 Time to CR 4.5m (1.8-7.6)

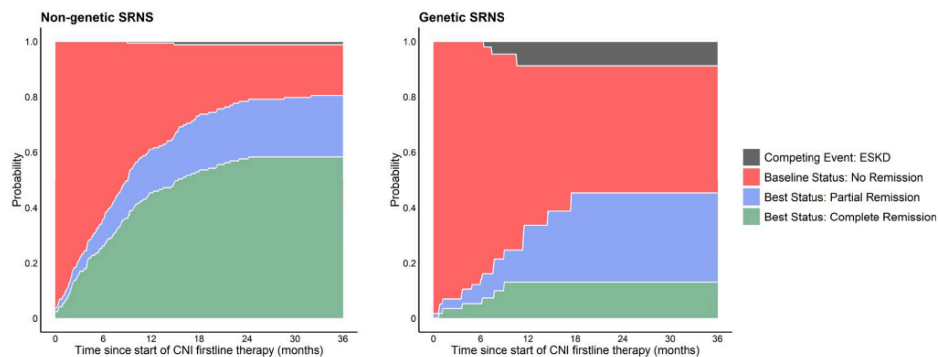


Figure 1. Cumulative incidence of best remission status and kidney failure during CNI treatment (competing risk analysis), stratified by etiology of disease. CNI, calcineurin inhibitor; ESKD, end-stage kidney disease; SRNS, steroid-resistant nephrotic syndrome.

7b/ Relapse (non-genetic)

👉 Breakthrough proteinuria in 67 after 7m (3.7-14.2)

📈 Cumulative relapse risk after CNI discontinuation

📅 1y = 40%

📅 4y = 64% (Fig. 3)

👶 Relapsing patients were younger [7.7 vs 10.6 years]

8/ Partial remission (Non-genetic)

Partial remission = 43/219 (19.6%)

👉 Nephrotic range proteinuria = 19/43 (44%) while on CNI treatment.

👥 Negative genetic testing but familial disease (24/176; 13.6%) = [CNI responsiveness: CR = (12/ 24 (50%), PR = 7(29.2%) & CNI resistant = 5 (20.8%)]

9/ Genetic SRNS (N=59)

After CNI,

Proteinuria ↓ in 60% (6m)

Returned to baseline 9-12 m

Cumulative CR 13% (7%–22%) within 5m

Remission sustained in 2/6**

PR in 11 (18.6%) on CNI + RAAS (8/11)

**A biallelic COQ6 pathogenic variant, remained in remission on coenzyme Q10 therapy) [CNI stopped after 7m]

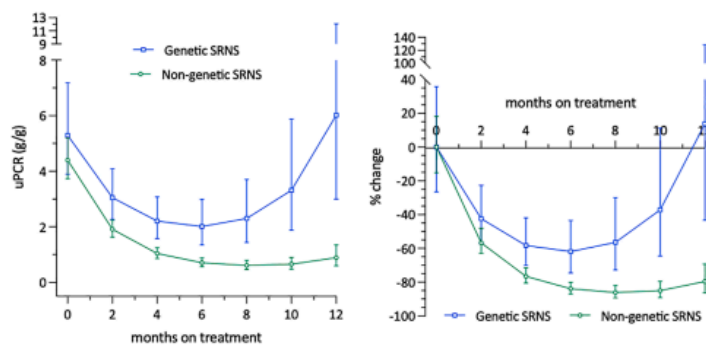


Figure 5. Absolute and relative uPCR change during first year of CNI therapy, stratified by SRNS etiology. CNI, calcineurin inhibitor; SRNS, steroid-resistant nephrotic syndrome; uPCR, urinary protein-to-creatinine ratio.

10/ CNI response in non-genetic

▶ Age at onset [Inversely related to CR within 1y]

👉 Age 1-6y= 2x as likely to achieve CR as adolescents [HR 2.14; 95% CI 1.06-4.31; $P < 0.05$]

Likelihood of CR ~ inversely related to time of RAAS coadmin (HR 0.99; 95% CI 0.98-0.99; $P < 0.005$)]

11/Long-term kidney outcome

Long term outcome

Nongenetic SRNS with preserved renal function

85% at 5y (95% CI: 80%–91%)

80% at 10y (73%–87%)

77% at 15y(68%–86 %)

Nongenetic SRNS (CR on CNI) an excellent kidney survival

- 👉 97% (92%–100%) 10-year
- 👉 42% (28%– 63%) in CNI-resistant patients ($P < 0.0001$)

Genetic disease 📌 risk of Kidney failure, with kidney survival

- 📌 58% (45%–76%) at 5y
- 📌 42% (28%–64%) at 10y
- 📌 35% (20%–61%) at 15y

Or,

11/a Long-term outcome

Nongenetic SRNS with preserved renal function

▶ 85% at 5y (95% CI: 80%–91%)

▶ 80% at 10y (73%–87%)

▶ 77% at 15y(68%–86 %)

Nongenetic SRNS (CR on CNI) 👉 an excellent kidney survival

👉 97% (92%–100%) 10-year

👉 42% (28%– 63%) in CNI-resistant patients ($P < 0.0001$)

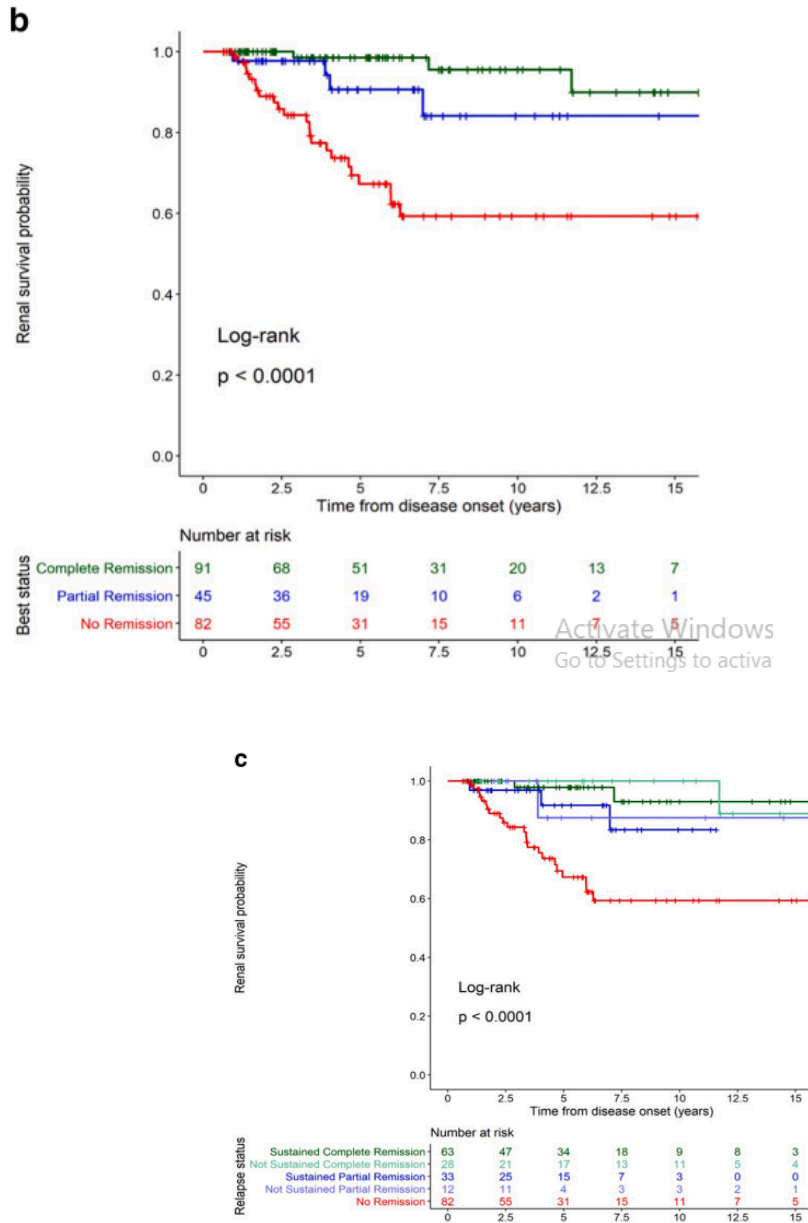


Figure 4. Long-term kidney survival of patients with SRNS treated with CNI. (a) Kidney survival by disease etiology (genetic, red vs. nongenetic, blue). (b) Kidney survival of patients with nongenetic SRNS stratified by best remission status achieved during first treatment year (full remission: green, partial remission: blue, no remission: red). (c) Kidney survival in patients with nongenetic SRNS subgrouped by persistence of remission status (sustained: dark blue green; nonsustained: bright blue/green). CNI, calcineurin inhibitor; SRNS, steroid-resistant nephrotic syndrome.

11 b/ Long term outcome in genetic disease

Genetic disease  risk of Kidney failure, with kidney survival

🎯 58% (45%–76%) at 5y

🎯 42% (28%–64%) at 10y

🎯 35% (20%–61%) at 15y

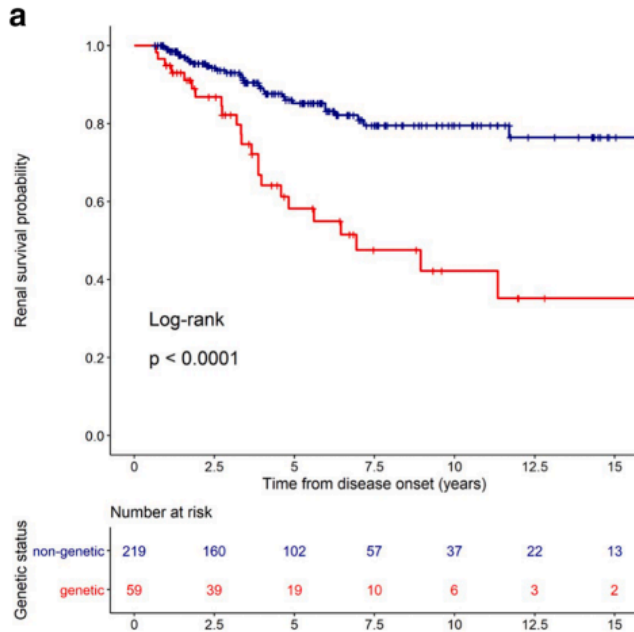


Fig-a: kidney survival by disease aetiology (Genetic, red Vs non-genetic, blue).

12/ Factors influencing long-term kidney survival

✓ The persistence of CR (Minor)

- ⊖ Patient age & kidney function at onset
- ⊖ Time to remission
- ⊖ Duration of remission
- ⊖ No of relapses on treatment
- ⊖ Duration of RAAS Rx

⚡ FSGS raises KF risk, but not if CNI-responsive(multivariate analysis).

15/ This tweetorial is brought to you by @md_abdulqader83 on behalf of @Klreports.
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