# Tabellen en Figuren

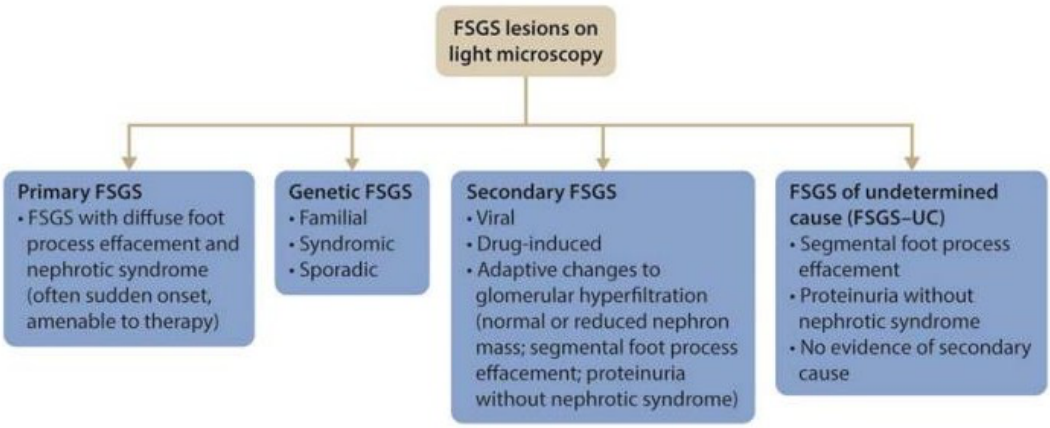


**Figure 49 | Proposed classification of FSGS.** FSGS, focal segmental glomerulosclerosis.

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| **Complete remission** |
| Reduction of proteinuria to <0.3 g/d or PCR <300 mg/g (or <30 mg/mmol), stable serum creatinine and serum albumin >3.5 g/dl (or 35 g/l) |
| **Partial remission** |
| Reduction of proteinuria to 0.3–3.5 g/d or PCR 300–3500 mg/g (or 30–350 mg/mmol) and a decrease >50% from baseline |
| **Relapse** |
| Proteinuria >3.5 g/d or PCR >3500 mg/g (or 350 mg/mmol) after complete remission has been achieved or an increase in proteinuria by >50% during partial remission |
| **Steroid-resistant FSGS** |
| Persistence of proteinuria >3.5 g/d or PCR >3500 mg/g (or 350 mg/mmol) with <50% reduction from baseline despite prednisone 1 mg/kg/d or 2 mg/kg every other day for at least 16 weeks |
| **Steroid-dependent FSGS** |
| Relapse occurring during or within 2 weeks of completing glucocorticoid therapy |
| **CNI-resistant FSGS** |
| Persistence of proteinuria >3.5 g/d or PCR >3500 mg/g (or 350 mg/mmol) with <50% reduction from baseline despite cyclosporine treatment at trough levels of 100–175 ng/ml (83–146 nmol/l) or tacrolimus treatment at trough levels of 5–10 ng/ml (6–12 nmol/l) for 4–6 months |
| **CNI-dependent FSGS** |
| Relapse occurring during or within 2 weeks of completing cyclosporine or tacrolimus therapy for >12 months |

**Figure 50 | Definition of remission, relapse, resistance, and dependence for FSGS.** CNI, calcineurin inhibitors; FSGS, focal segmental glomerulosclerosis; PCR, protein–creatinine ratio.

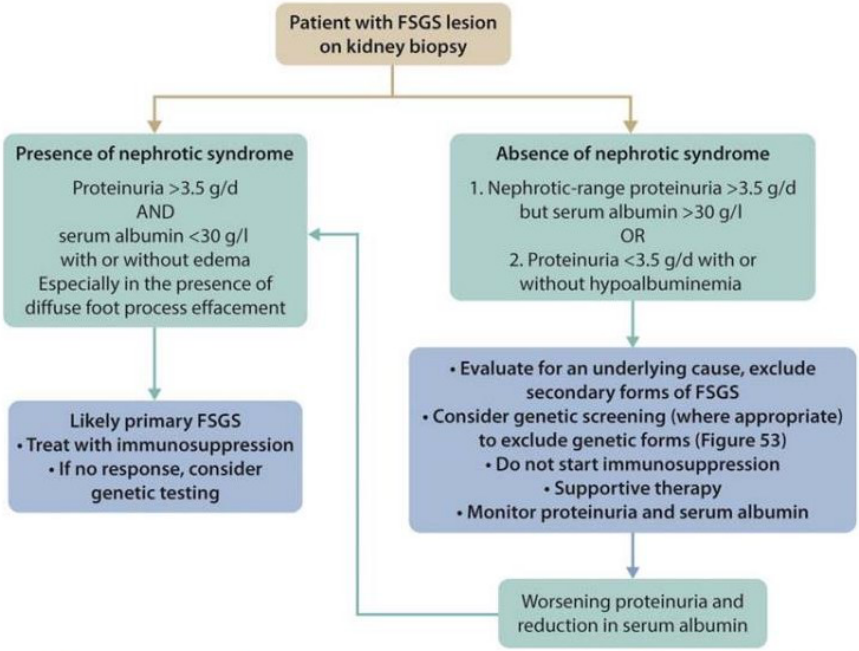


**Figure 51 | Evaluation of a patient with FSGS lesion on the kidney biopsy and no evidence of other glomerular pathology.** FSGS, focal segmental glomerulosclerosis.

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|---|---|
| **Secondary to alterations of glomerular epithelial cells** | |
| **Viral infections** | HIV (established)<br>CMV (probably)<br>Parvovirus B19, EBV, HCV (possibly)<br>Hemophagocytic syndrome (possibly)<br>SARS-COV-2 (with *APOL1* risk genotype) |
| **Drug-induced** | Direct-acting antiviral therapy<br>mTOR inhibitors, CNIs<br>Anthracyclines<br>Heroin (adulterants)<br>Lithium<br>Interferon<br>Anabolic steroids<br>NSAIDs |
| **Secondary to adaptive changes with glomerular hypertension** | |
| **Reduced nephron number** | Reflux nephropathy<br>Renal dysplasia<br>Oligomeganephronia<br>Sickle cell disease<br>Age-related FSGS |
| **Normal nephron number** | Obesity-related glomerulopathy<br>Primary glomerular diseases<br>Systemic conditions, e.g., diabetic nephropathy, hypertensive nephrosclerosis |

**Figure 52 | Causes of secondary FSGS.** *APOL1*, apolipoprotein L1; CMV, cytomegalovirus; CNI, calcineurin inhibitor; EBV, Epstein-Barr virus; FSGS, focal segmental glomerulosclerosis; HCV, hepatitis C virus; HIV, human immunodeficiency virus; mTOR, mammalian target of rapamycin; NSAID, nonsteroidal anti-inflammatory drug; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

| Genetic forms of FSGS | |
|---|---|
| **Genetic mutations of podocyte and glomerular basement membrane proteins** | • Familial<br>• Sporadic<br>• Syndromic |
| **Considerations for genetic testing in adults with FSGS** | |
| • When there is a strong family history and/or clinical features suggestive of a syndromal disease<br>• Aiding in diagnosis, especially if the clinical features are not representative of a particular disease phenotype<br>• Limiting immunosuppression exposure, especially in situations where patients appear to be resistant to treatment<br>• Determining the risk of recurrent disease in kidney transplantation<br>• Allowing for risk assessment in living-related kidney donor candidate, or where there is a high suspicion for *APOL1* risk variants<br>• Aiding in prenatal diagnosis | |

**Figure 53 | Utility of genetic testing in patients with FSGS.** *APOL1*, apolipoprotein-L1; FSGS, focal segmental glomerulosclerosis.

| Treatment | Dose and duration |
|---|---|
| **Glucocorticoids** | **Starting dose:**<br>• High-dose glucocorticoid therapy with prednisone at daily single dose of 1 mg/kg (maximum 80 mg) or alternate-day dose of 2 mg/kg (maximum 120 mg) |
| | **High-dose glucocorticoid treatment duration:**<br>• Continue high-dose glucocorticoid therapy for at least 4 weeks and until complete remission is achieved, or a maximum of 16 weeks, whichever is earlier<br>• Patients who are likely to remit will show some degree of proteinuria reduction before 16 weeks of high-dose treatment<br>• It may not be necessary to persist with high-dose glucocorticoid therapy until 16 weeks if the proteinuria is persistent and unremitting, especially in patients who are experiencing side effects |
| | **Glucocorticoid tapering:**<br>• If complete remission is achieved rapidly, continue high-dose glucocorticoid treatment for 2 weeks or after the disappearance of proteinuria, whichever is longer. Reduce prednisone by 5 mg every 1–2 weeks to complete a total duration of 6 months<br>• If partial remission is achieved within 8 to 12 weeks of high-dose glucocorticoid treatment, continue until 16 weeks to ascertain whether further reduction of proteinuria and complete remission may occur. Thereafter, reduce the dose of prednisone by 5 mg every 1–2 weeks to complete a total duration of 6 months<br>• If the patient proves to be steroid-resistant or develops significant toxicities, glucocorticoids should be rapidly tapered as tolerated and treatment with alternative immunosuppression like a CNI should be considered |
| **Calcineurin inhibitors*** | **Starting dose:**<br>• Cyclosporine 3–5 mg/kg/d in 2 divided doses OR tacrolimus 0.05–0.1 mg/kg/d in 2 divided doses<br>• Target trough levels could be measured to minimize nephrotoxicity<br>• Cyclosporine target trough level: 100–175 ng/ml (83–146 nmol/l)<br>• Tacrolimus target trough level: 5–10 ng/ml (6–12 nmol/l) |
| | **Treatment duration for determining CNI efficacy:**<br>• Cyclosporine or tacrolimus should be continued at doses achieving target trough level for at least 4–6 months, before considering the patient to be resistant to CNI treatment |
| | **Total CNI treatment duration:**<br>• In patients with partial or complete remissions, cyclosporine or tacrolimus should be continued at doses achieving target trough level for at least 12 months to minimize relapses<br>• The dose of cyclosporine or tacrolimus can be slowly tapered over a course of 6–12 months as tolerated |

**Figure 54 | Initial treatment of primary FSGS.** *The CNI, while often used twice daily, may be dosed once a day, depending on individual formulations. Blood levels of CNIs do not provide information on intracellular levels. The target ranges for CNIs have been based on the transplant literature. The KDIGO Work Group acknowledges that targets for glomerular diseases are not known. Most clinicians check these levels to verify adherence and avoid CNI toxicity. At present, the most reasonable dosing of a CNI may be to titrate in the individual patient to obtain the desired effect on proteinuria, balancing dose escalation against serum creatinine and reducing the dose if serum creatinine increases but does not plateau or increases over 30% of baseline. If the serum creatinine level does not fall after dose reduction, the CNI should be discontinued. CNI, calcineurin inhibitor; FSGS, focal segmental glomerulosclerosis.

| Treatment | Dose and duration |
|---|---|
| Calcineurin inhibitors* | **Starting dose:**<br>• Cyclosporine 3–5 mg/kg/d in 2 divided doses OR tacrolimus 0.05–0.1 mg/kg/d in 2 divided doses<br>• Target trough levels could be measured to minimize nephrotoxicity<br>• Cyclosporine target trough level: 100–175 ng/ml (83–146 nmol/l)<br>• Tacrolimus target trough level: 5–10 ng/ml (6–12 nmol/l) |
| | **Treatment duration for determining CNI efficacy:**<br>• Cyclosporine or tacrolimus should be continued at doses achieving target trough level for at least 6 months, before considering the patient to be resistant to CNI treatment |
| | **Total CNI treatment duration:**<br>• In patients with partial or complete remissions, cyclosporine or tacrolimus should be continued at doses achieving target trough level for at least 12 months to minimize relapses<br>• The dose of cyclosporine or tacrolimus can be slowly tapered over a course of 6–12 months as tolerated<br>• Consider discontinuing cyclosporine or tacrolimus if the eGFR continues to decline to <30 ml/min per 1.73 $m^2$ |
| Inability to tolerate or contraindications to calcineurin inhibitors | • Lack of quality evidence for any specific alternative agents<br>• Mycophenolate mofetil and high-dose dexamethasone, rituximab, and ACTH have been considered<br>• Treatment will need to be personalized and is dependent on availability of drugs and resources, as well as the benefits of further treatment and risks of adverse effects of immunosuppression<br>• Patients should be referred to specialized centers with the appropriate expertise, and should be evaluated on the appropriate use of alternative treatment agents or to discontinue further immunosuppression |

**Figure 55 | Treatment of glucocorticoid-resistant primary FSGS.** *The CNI, while often used twice daily, may be dosed once a day, depending on individual formulations. Blood levels of CNI do not provide information on intracellular levels. The target ranges for CNIs have been based on the transplant literature. The KDIGO Work Group acknowledges that targets for glomerular diseases are not known. Most clinicians check these levels to verify adherence and avoid CNI toxicity. At present, the most reasonable dosing of a CNI may be to titrate in the individual patient to obtain the desired effect on proteinuria, balancing dose escalation against serum creatinine and reducing the dose if serum creatinine increases but does not plateau or increases over 30% of baseline. If the serum creatinine level does not fall after dose reduction the CNI should be discontinued. ACTH, adrenocorticotropic hormone; CNI, calcineurin inhibitors; eGFR, estimated glomerular filtration rate.

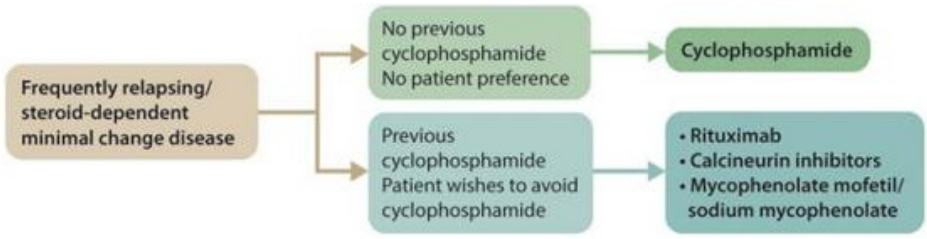


**Figure 47 | Treatment of FR/SD MCD in adults.** The choice of medication should be based on physician and patient preference. FR/SD, frequently relapsing/steroid-dependent.