EXTRACORPOREAL NEPHROLOGY GROUP [ECNG]

POST TRANSPLANT FSGS

DR VILESH VALSALAN

CONSULTANT NEPHROLOGIST AND TRANSPLANT PHYSICIAN

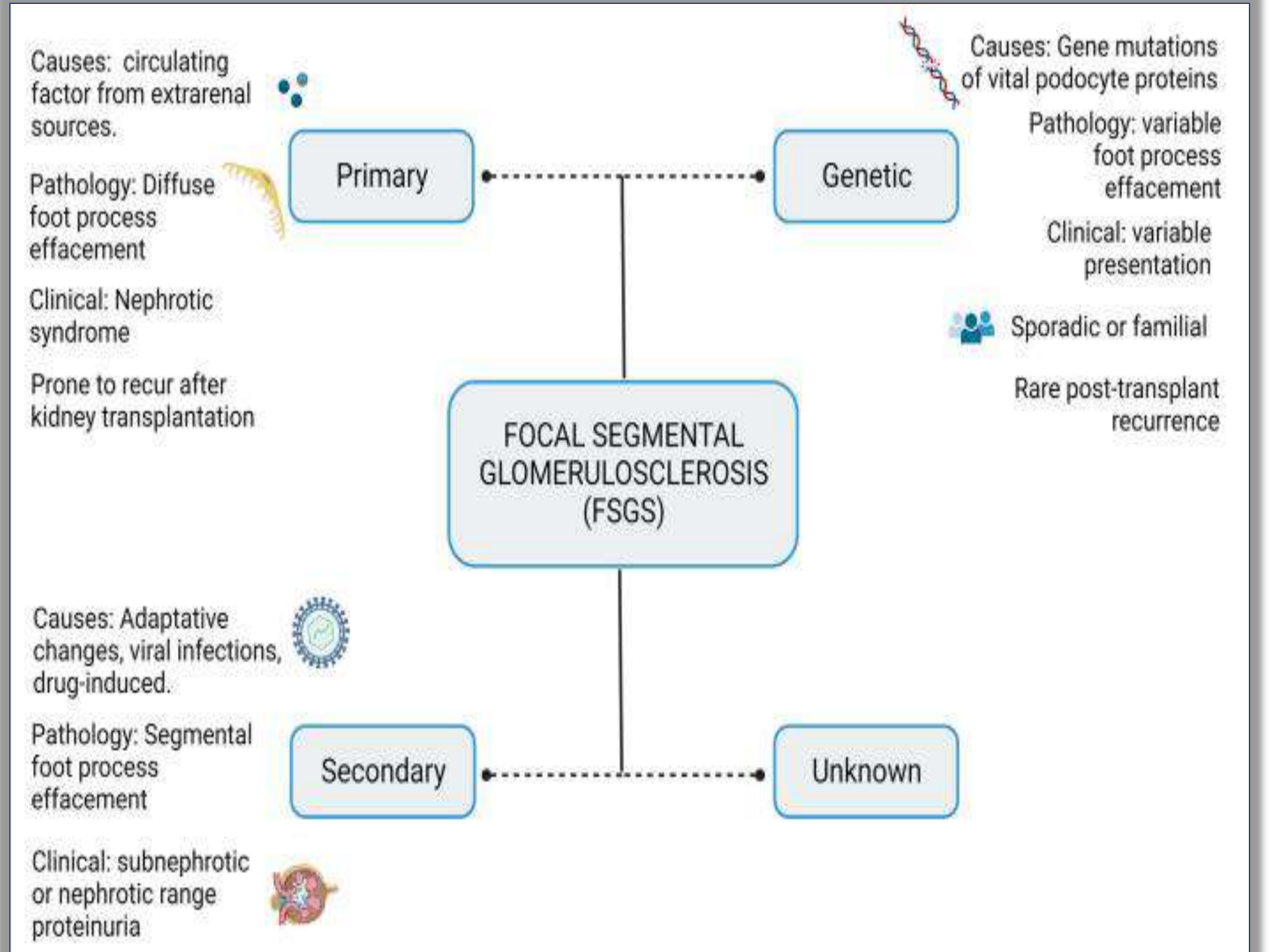
ACADEMIC CORDINATOR - ECNG

INTRODUCTION

- Hoyer et al first described rFSGS in 1972.
- Incidence: Primary FSGS recurs in roughly 30% to 50% of first-time kidney transplants, and jumps drastically to **50% to 80%** in subsequent transplants.
- Recurrent FSGS often manifests within hours to days after surgery.

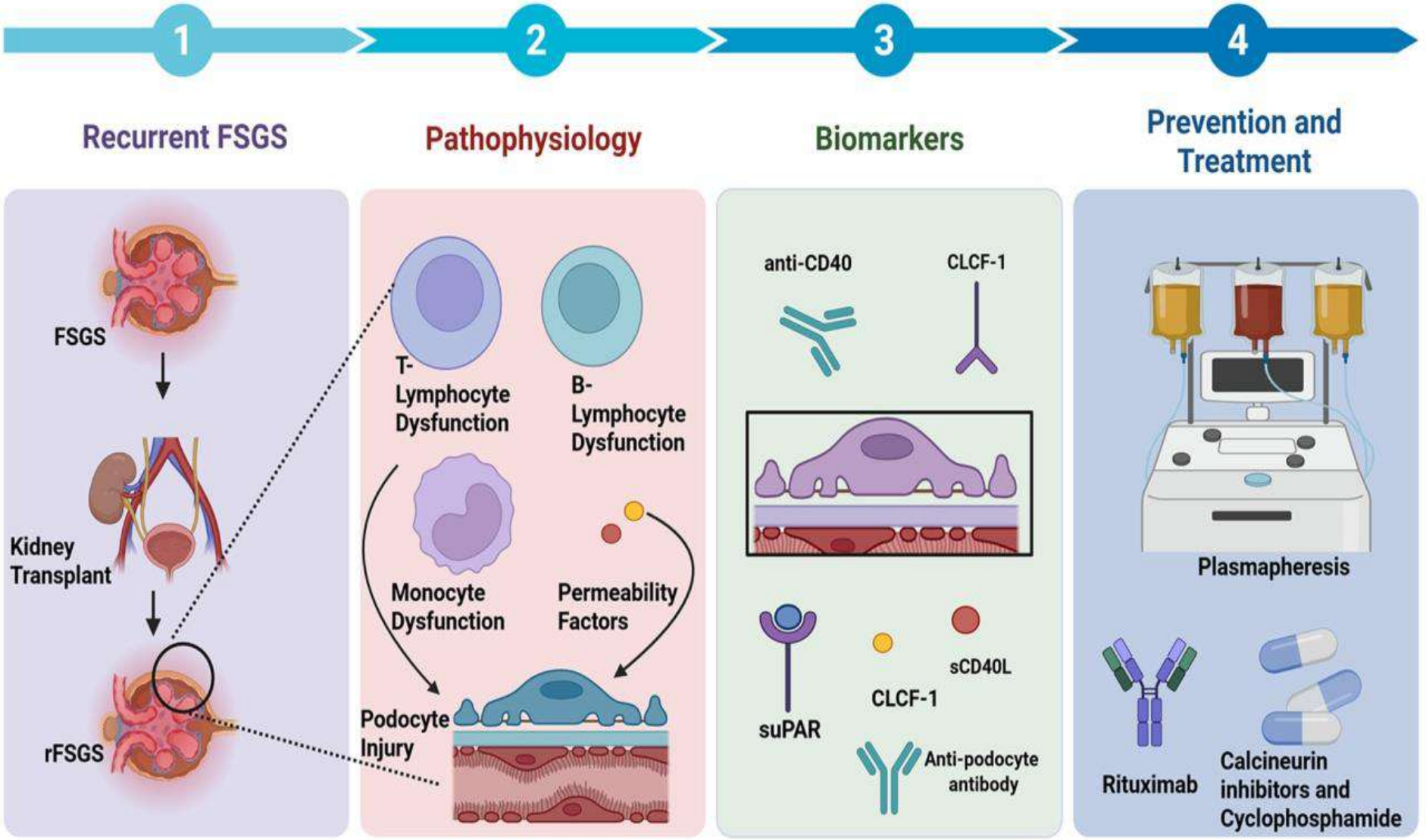
- Risk factors: Childhood onset, white race , malignant FSGS - rapid progression and recurrence of FSGS in prior transplant.
- Clinical Features: Nephrotic syndrome within weeks after transplantation. Also, can have hematuria, hypertension, and AKI.

- Prognosis: 20% of transplant recipients experience recurrence-related graft loss after 5-10 years.

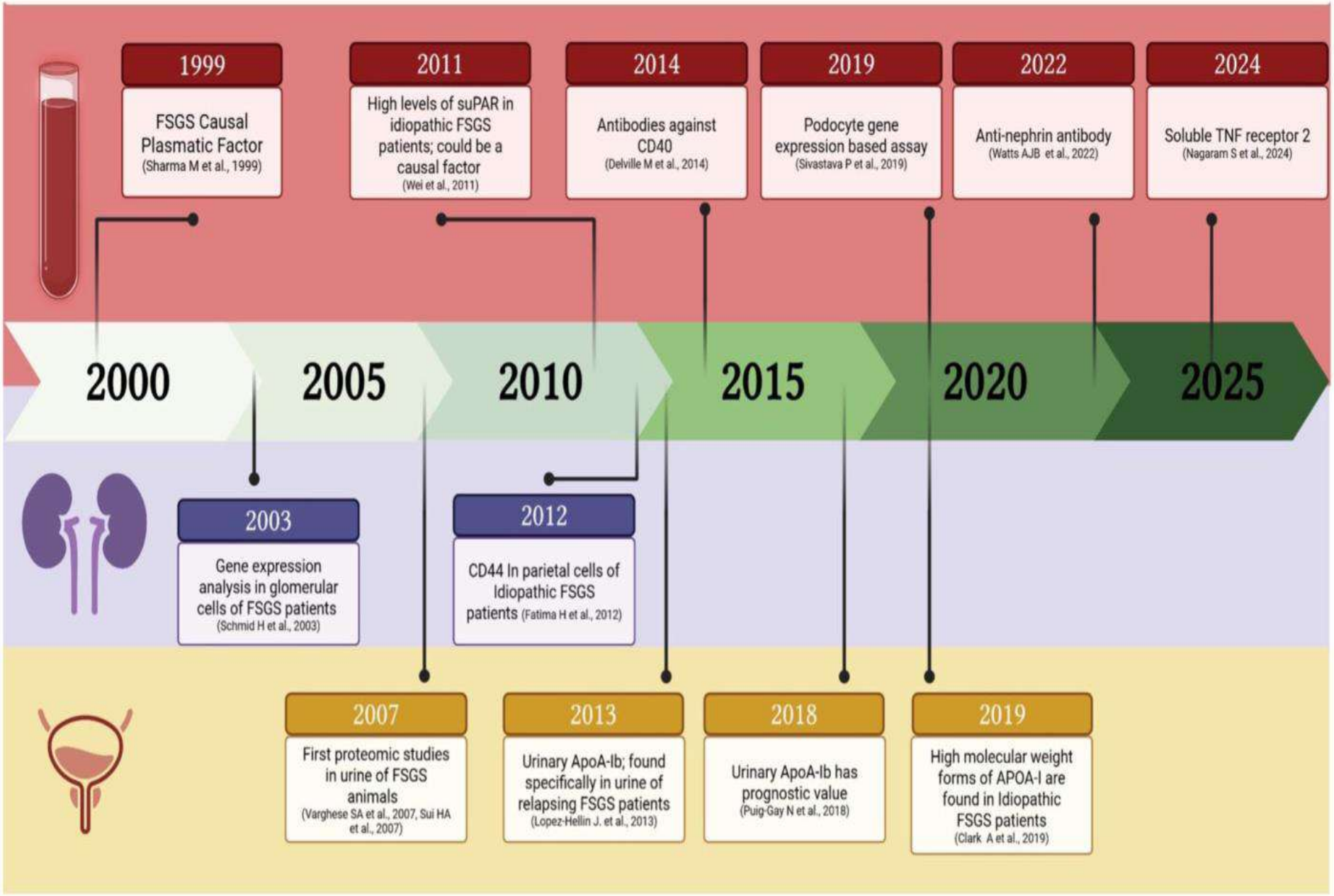

Causes: circulating factor from extrarenal sources.
Pathology: Diffuse foot process effacement
Clinical: Nephrotic syndrome
Prone to recur after kidney transplantation
Primary
Genetic
Causes: Gene mutations of vital podocyte proteins
Pathology: variable foot process effacement
Clinical: variable presentation
Sporadic or familial
Rare post-transplant recurrence
FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS)
Causes: Adaptative changes, viral infections, drug-induced.
Pathology: Segmental foot process effacement
Clinical: subnephrotic or nephrotic range proteinuria
Secondary
Unknown

	pFSGS	sFSGS
Pathogenesis	Presumed circulating permeability factor causing primary podocyte injury	Adaptive, genetic, viral, drug-induced, or other identifiable causes
Clinical presentation	Abrupt onset of nephrotic syndrome	Gradual proteinuria; nephrotic syndrome less common
Proteinuria	Usually nephrotic range (>3.5 g/day)	Variable; often subnephrotic initially
Serum albumin	Markedly reduced	Often normal or mildly reduced
Edema	Prominent	Mild or absent
Kidney function at presentation	May be preserved initially	Often associated with chronic kidney disease
Light microscopy	FSGS lesions; may show tip variant	FSGS lesions with chronic adaptive changes
Electron microscopy	Diffuse foot process effacement (>80%)	Segmental foot process effacement (<50%, often patchy) and no ischaemic changes in non sclerotic glomeruli
Response to immunosuppression	Frequently responsive	Generally poor; immunosuppression usually not indicated
Recurrence after transplant	High (30–60% in first graft)	Rare unless underlying cause persists

Recurrence of Focal Segmental Glomerulosclerosis: An Updated Review of Pathophysiology, Biomarkers, and Therapeutic Strategies



EVOLUTION OF BIOMARKERS IN DIAGNOSIS OF PRIMARY FSGS



Genetic testing

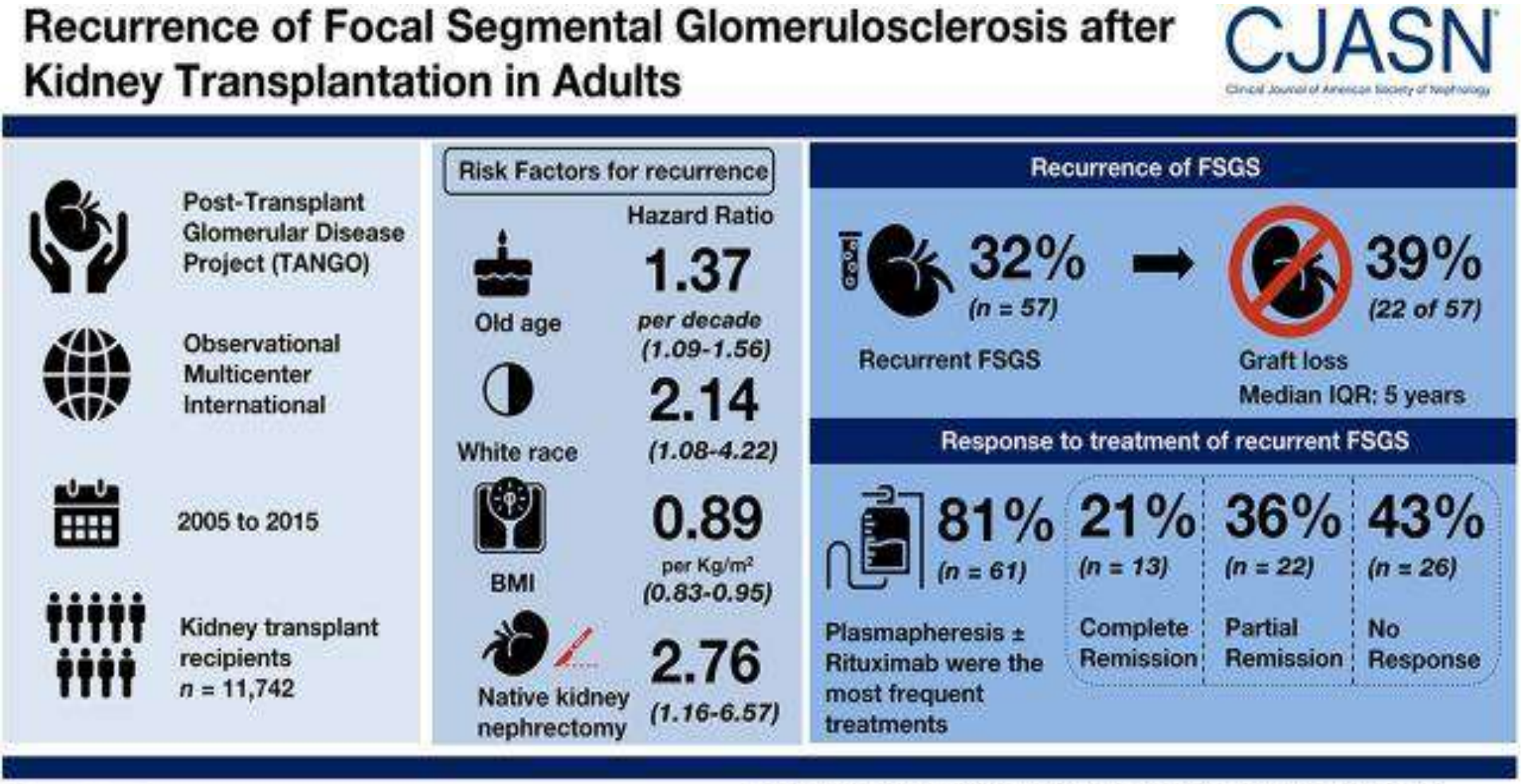
Indication

- steroid-resistant nephrotic syndrome
- onset in childhood or early adulthood
- familial FSGS
- syndromic features
- unexplained FSGS
- living related donor

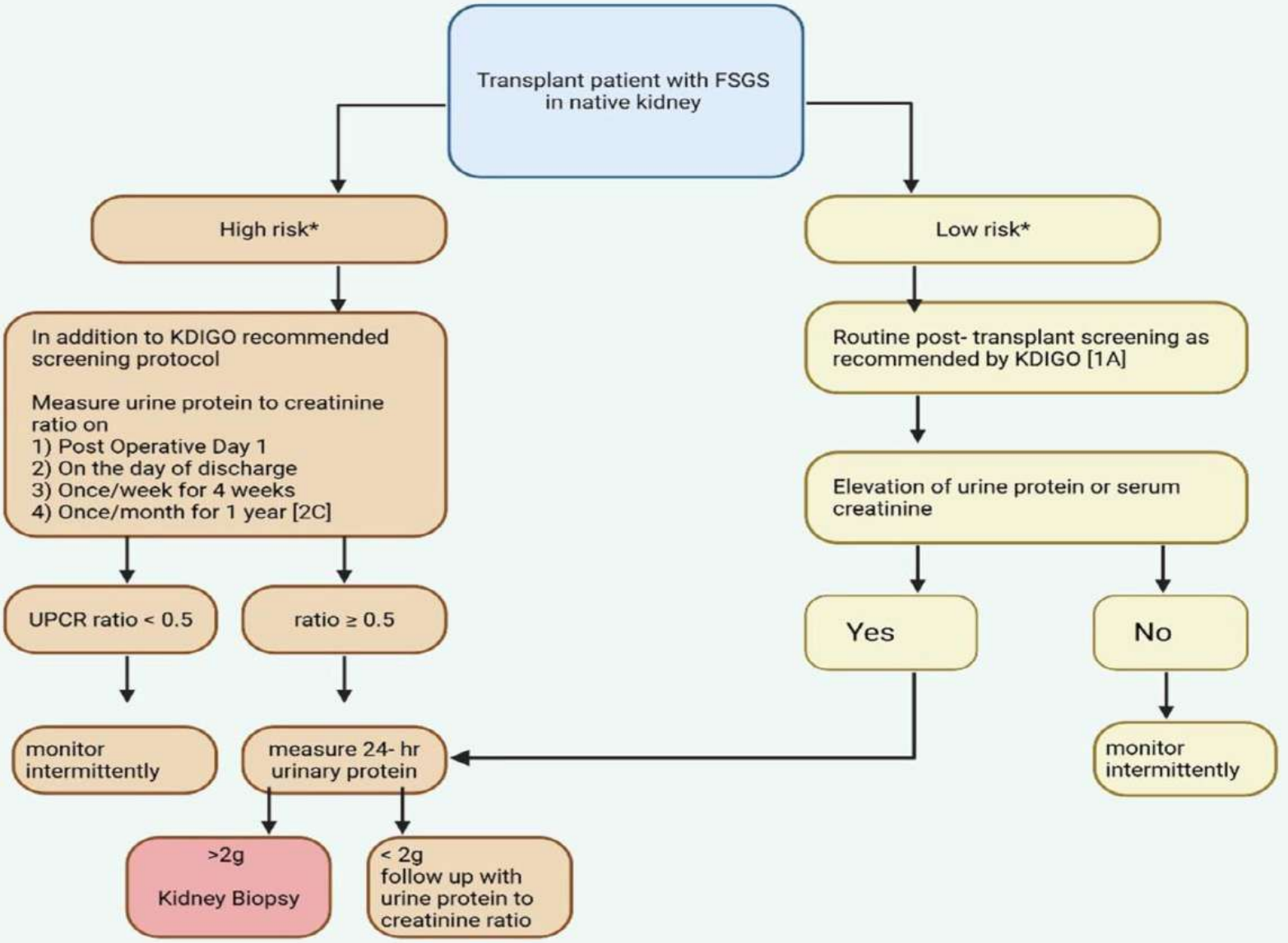
Helps in

- predicts recurrence risk(less recurrence)
- distinguishes genetic from primary FSGS
- avoids unnecessary immunosuppression
- guides donor selection
- identifies APOL1-associated disease
- improves genetic counseling and family sc

TANGO PROJECT



Post-Transplant Monitoring In FSGS



rFSGS Prevention, Monitoring & Treatment

RISK STRATIFICATION

- Genetic testing in young adults
- Circulating factors; Anti nephrin antibody, Anti CD40, FAST panel
- Prior graft loss= High risk
- Demographic risks

PREVENTION

- **Prophylactic plasmapheresis (PP):**
  - Ohta et al.,2001: recurrence **33% vs 87%**
  - Not recommended for routine prophylaxis (2C)
- **Prophylactic rituximab:**
  - No significant reduction in recurrence rates
  - Improved response to subsequent therapies (2D)

MONITORING

- **High-risk**: urine protein/ creatinine (day 1, discharge, weekly x 4montly x 4 monthly x12)
- if ≥0.5 -24h proteinuria
- >2g/day - biopsy
- low risk : routine KDIGO follow-up

TREATMENT

- **Plasmapheresis (PP):**
  - Daily ×3, then 3×/week ×2 weeks (1B)
  - Exchange 1−1.5 plasma volumes (1B)
  - Following initial therapy, proteinuria should be assessed, and the need for additional sessions should be determined by patient response (1B)
- **Calcineurin inhibitors (cyclosporine) + high-dose steroids:**
  - Combined with PP improves remission
  - If incomplete response → **Rituximab** 375 mg/m² weekly ×4 (2C)
    - Hold PP for 48 hours post-infusion
    - Useful in PP dependence/intolerance
- **Rituximab:**
  - Park et al. (2014); Israel study (2014−2023)
  - Useful in PP-dependent or refractory patients; enabled sustained remission in pediatric cohort
  - Also considered for PP/IA contraindications or PP dependence (2C)
  - Dose: 375 mg/m² weekly ×4; hold PP for 48 hrs post-dose (1A)
- **Immunoadsorption (IA):**
  - For relapse after PP or PP intolerance
  - Regimen: daily ×1 week → alternate days ×2 weeks → biweekly ×2 weeks (2C)
- **Cyclophosphamide + PP (children):**
  - Restrepo et al 2022 : 88% long-term remission
  - Temporary switch from MMF

SUPPORTIVE THERAPY

- ACEi / ARB for HTN (2B)
- Avoid routine triple therapy (2C)

NEWER THERAPIES

- **Novel anti CD20 antibodies**
  - Ofatumumab (limited to case reports)
  - Combination of obinutuzumab and daratumumab in multidrug resistant MCD –future options for rFSGS
- **Anti–tumor necrosis factor-a**
  - Infliximab or etarnecept along with high dose steroids
- **Mesenchymal stem cells**
  - In a PLEX dependent case, used as 6doses divided into 3 cycles of 2 infusions(1x 106 cells /kg/dose) then 3rdand 7^{th} month
  - Paracrine effect, modulating microenviornmentor stimulating native kidney stem cells