Considering the early proactive switch from a CNI to an mTOR-inhibitor (Case: Male, age 34)

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Patient details

Name	**Mr. B.I.B.**
DOB	**12 January 1975 (34yo)**
ESRD	**Membranous GN – Grade V**
	Tt. steroids + cyclophosphamide
Other history	**Hypertension (145/90 mmHg)**
	ACEi + ARB
	BMI: 24 (W: 73 Kg)
Transplant	**Pre-emptive kidney transplant (Sept 2007)**
	Living related donor (mother): 72yo – GFR 84 mL/min – no proteinuria – MGUS – normal BP
	BMI 20 (W: 52 Kg)

How do you consider this kidney transplant?

1. **Optimal**
2. **Sub-optimal**
3. **Non-useful for transplantation**

If you consider non-useful for transplant (exclude donor) the main reason is?

1. **Age of the donor**
2. **Presence of MGUS**
3. **Discordance between donor-recipient (BMI/Weight)**

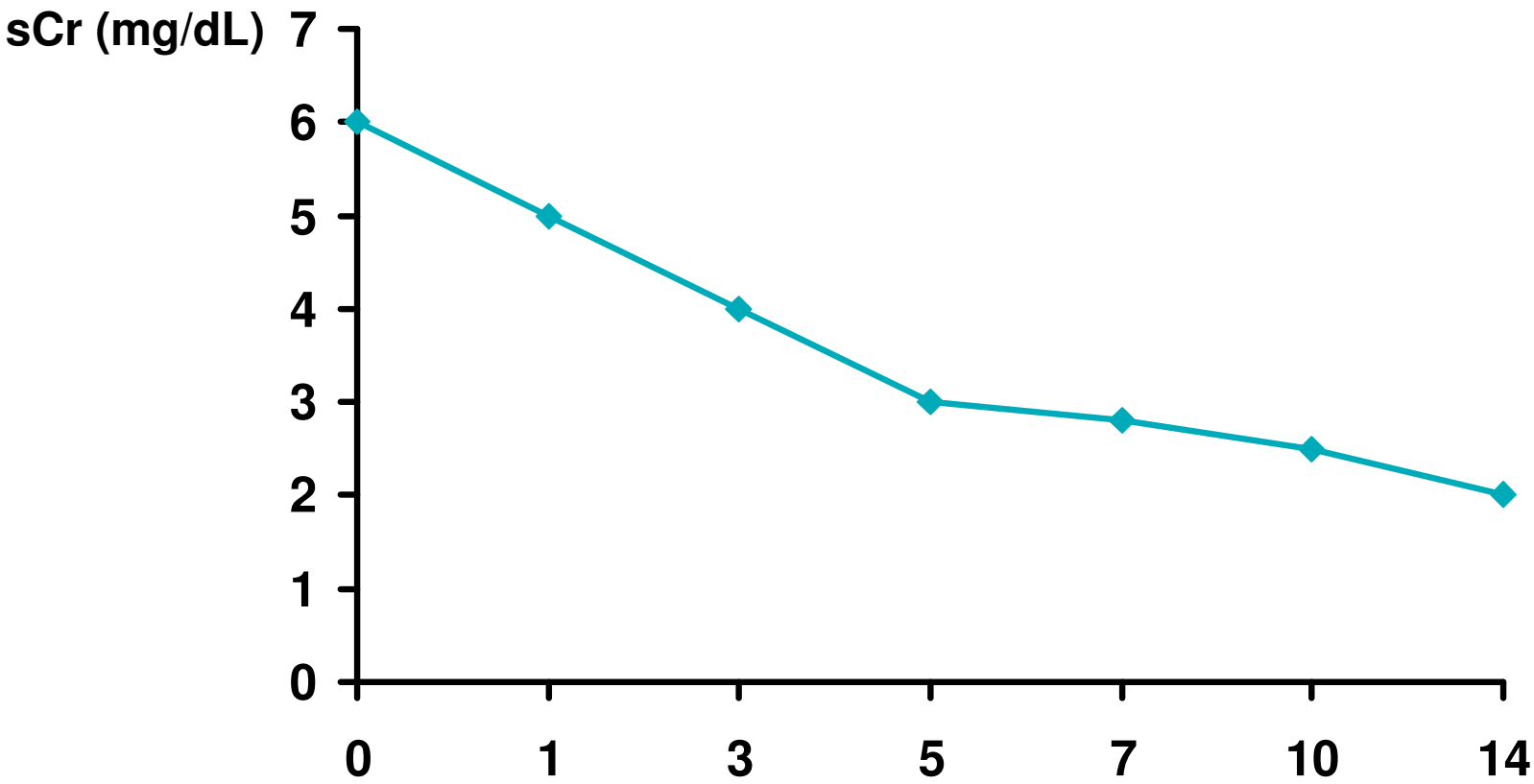
If you consider valid for transplantation, which will be your proposal initial immunosuppressive therapy?

1. **Tac + MMF + steroids without induction**
2. **Tac + MMF + steroids with induction**
3. **CNI-free therapy (mTORi + MMF + steroids + induction)**
4. **Steroid-free therapy with Induction**

Initial immunosuppression

- **Induction therapy**
  - **Basiliximab: 20 mg day 0 and 4**
- **Tacrolimus 0.1 mg/kg pre-op and then 0.1 mg/kg bid; target level 6-10 ng/mL**
- **MMF 1 g pre-op, then 1g bid**
- **Methylprednisolone: 500 mg pre-op, gradually reduced, reaching 15 mg by day 15, then 5mg by 4 weeks post transplant.**

Clinical course post-transplant



No acute rejection

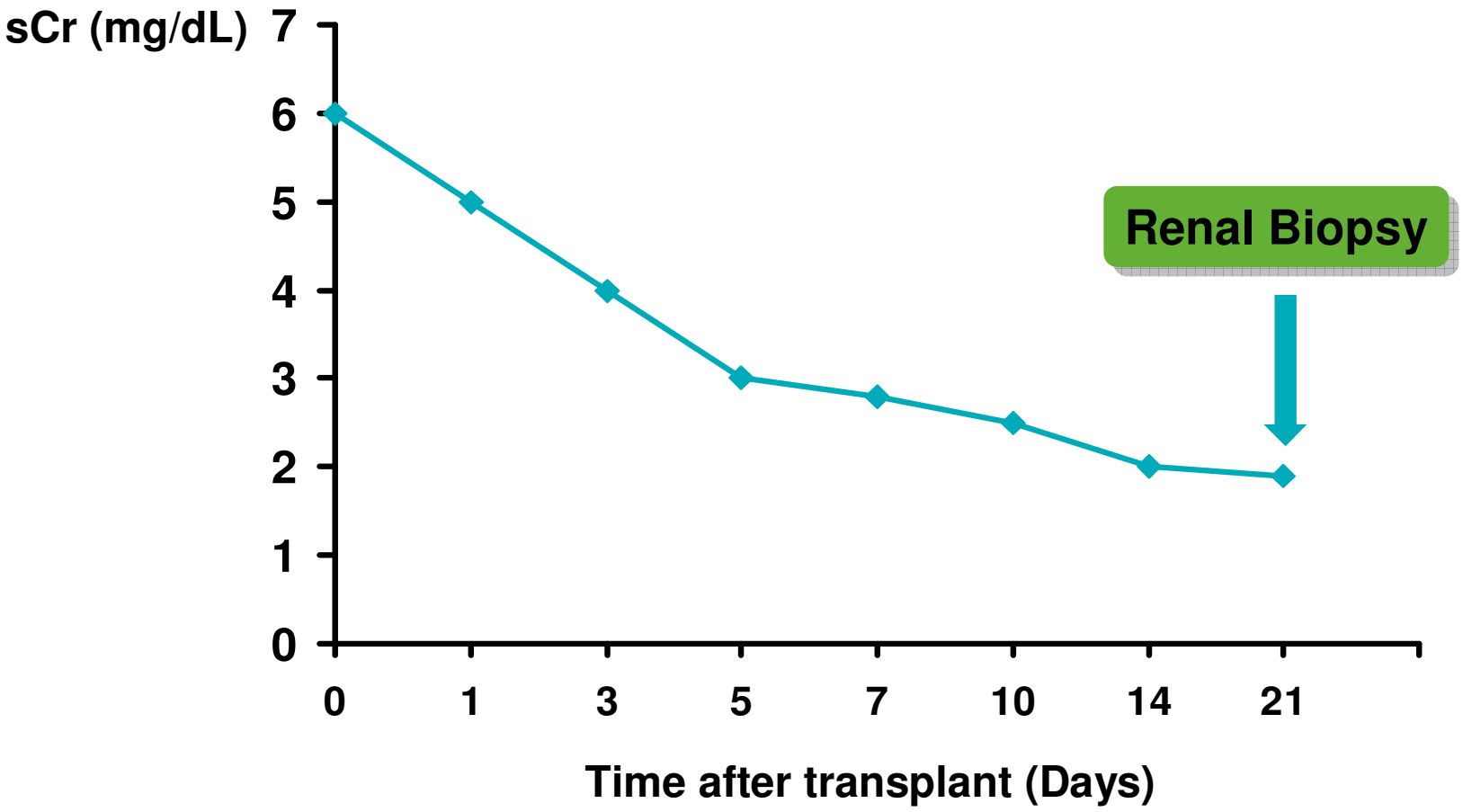
How do you consider the follow-up of this transplant?

1. **Normal, as expected**
2. **Excellent, as non-expected**
3. **Negative**

Would you consider performing a renal biopsy at that time?

1. **NO, because the F/U was good**
2. **YES, to exclude subclinical acute rejection**
3. **YES, because renal function is suboptimal**

Clinical course post-transplant



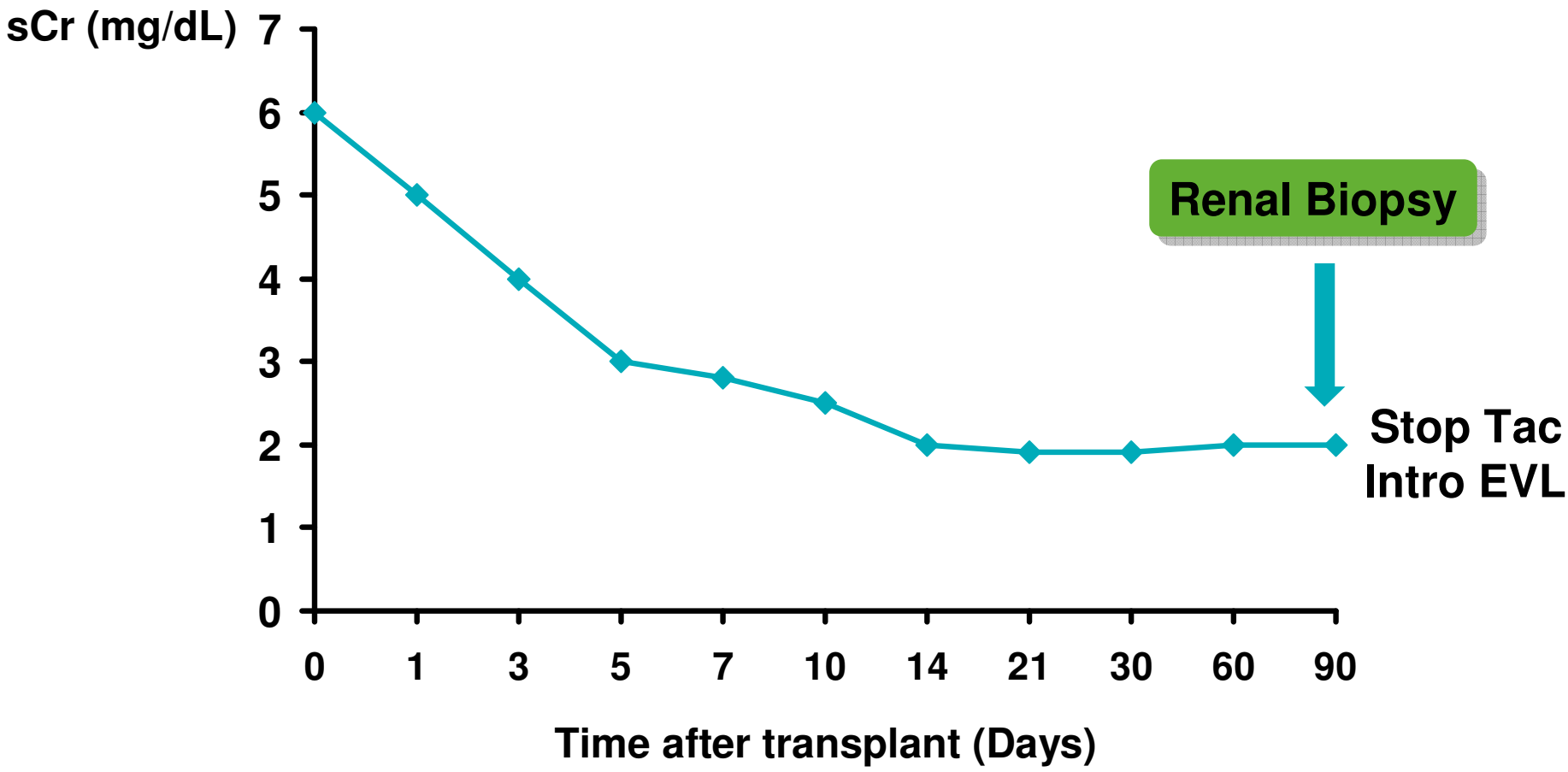
Progress (at 3 months)

- **Good initial graft function**
- **Stable renal function at 2 and 3 months**
  - GFR 46 mL/min
  - Serum creatinine 1.9 - 2.2 mg/dL
  - Proteinuria 145 mg/day
- **Immunosuppressive therapy:**
  - Prednisone 5 mg/day
  - MMF 500 mg bid
  - Tac 2.5 mg bid (BL: 4-6 ng/mL)
- **Hypertensive (145/90 mmHg): ACEi/CCB/BB**
- **Normal lipids**

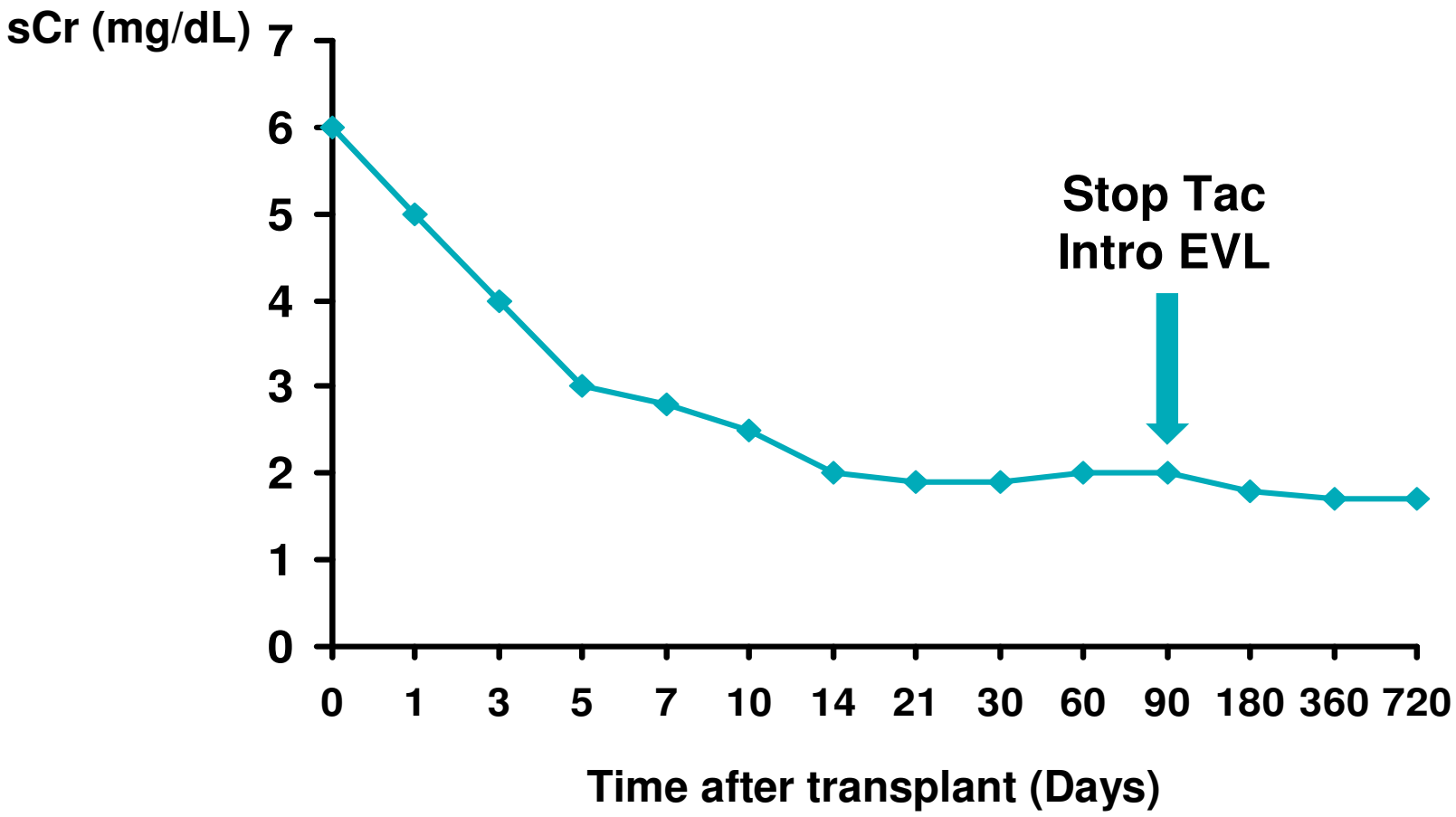
3 months – what would you do in terms of immunosuppression?

1. Make no changes (F/U is good)
2. Progressively eliminate steroids
3. Discontinue tacrolimus and introduce mTORi
4. Undertake protocol biopsy and then decide what action to take

Clinical course post-transplant



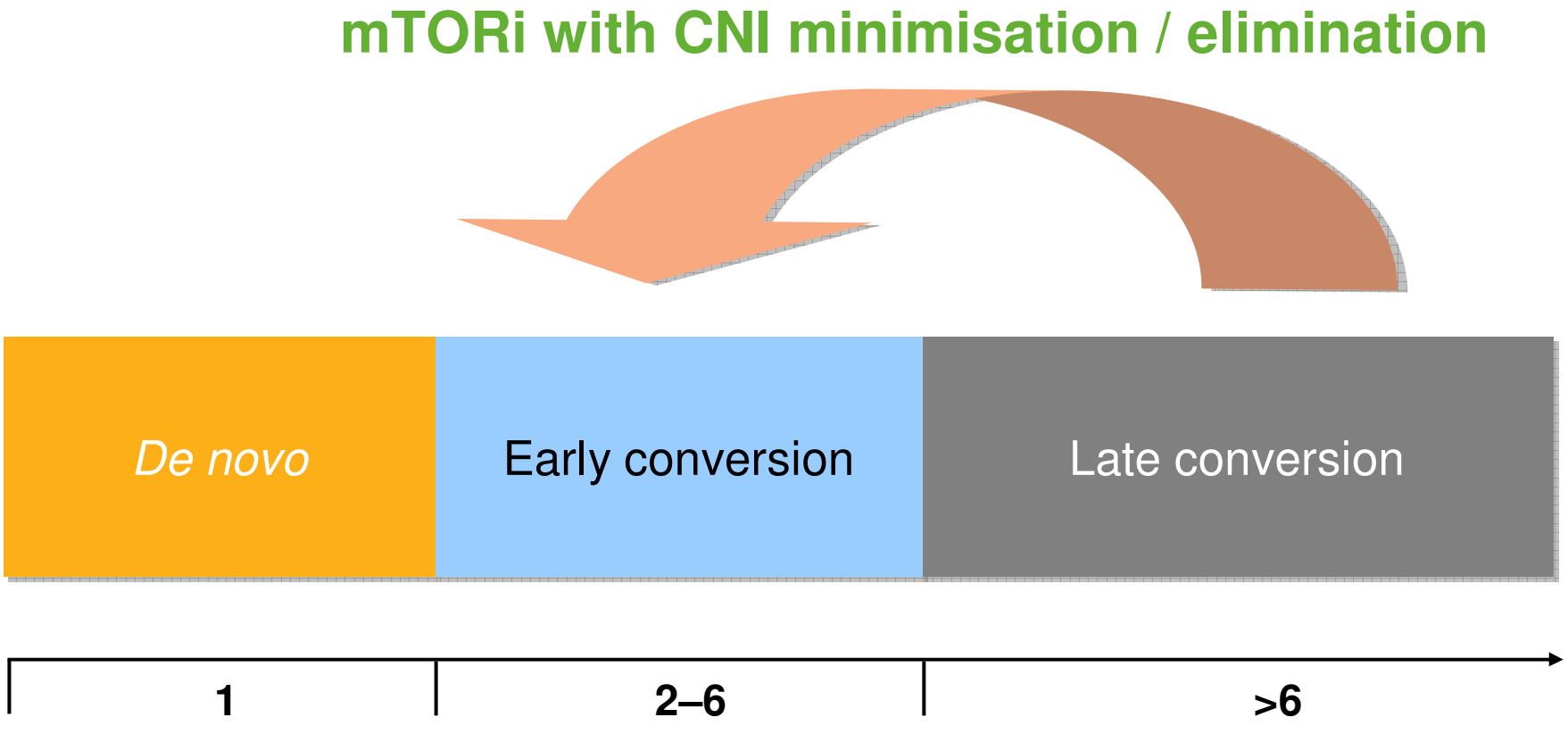
Clinical course post-transplant



Progress (at 2.5 years)

- **Stable renal function**
  - GFR 50-55 mL/min
  - Serum creatinine 1.7 – 1.9 mg/dL
  - Proteinuria 175 mg/day
- **Immunosuppressive therapy:**
  - Prednisone 2.5 mg/d
  - MMF 500 mg bid
  - EVL 1,5 mg /12h (5-8 ng/mL)
- **Hypertension (125/75 mmHg): ARB**
- **Lipids are normal: Atorvastatin (20 mg/day)**

mTORi: Strategies in renal transplantation



PSI, proliferation signal inhibitor; CNI, calcineurin inhibitor

Considering the total avoidance of CNIs using mTOR-inhibitor therapy (Case: Female, age 32)

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Clinical case

- A 32yo female affected of Membrano-Proliferative Glomerulonephritis
- ESRD – 1987 – submitted to kidney transplant – living donor (Father)
- CsA + Aza + Prednisone
- Correct follow-up – good recovery renal function - stable
- 2004: Increased serum creatinine
  - Renal biopsy: CAN grade II (CNI toxicity)
- sCr: 2 mg/dL – Proteinuria 750 mg/24h
- 2005: Late conversion from CsA to Sirolimus (2 mg.d)
- Accepted tolerance – NO severe AE

Clinical case

- Progressive deterioration of renal function – increase sCr
- 7/2008: sCr 4 mg/dL – CrCl 18 mL/min
- Immunosuppressive therapy: sirolimus (6-8 ng/ml) + Aza
- Consider a new kidney transplantation – living donor (mother)
- Mother: 72yo – good health conditions – BP normal – sCr 0.8 mg/dL – GFR 79 mL/min (RFR 15%) –
  NO contraindication
- Immunosuppressive therapy: ???
- Mother 72yo ??
- Pre-emptive transplantation ??

Clinical case

- Oct.2008: Second renal transplantation (living donor – mother)
- Therapy: Simulect + MPA + Pred + sirolimus (low doses)
- Surgery: OK – NO problems
- Good recovery of renal function – sCr 1.5 mg/dL (2 weeks)
- Sirolimus (2-3 mg.d): 6-9 ng/ml – MPA 500 mg/8h – Steroids
- Oct.10: Stable – good renal function (sCr 1.1 mg/dL) (GFR 55 mL/min) – good control of BP