

Practical Conversion to Advagraf® from Cyclosporine or Immediate release Tacrolimus

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Learning Objectives

- • Identify appropriate candidates for conversion
- • Understand pharmacokinetic differences
- • Perform practical conversion safely
- • Monitor patients after conversion
- • Apply available evidence in daily practice



Why Are We Discussing Conversion?

- • One-year graft survival >90%
- • Late rejection
- • dnDSA formation
- • Chronic allograft injury
- • Medication non-adherence
- Can regimen simplification improve long-term outcomes?



The Adherence Problem

- • Missed evening doses
- • Complex medication schedules
- • Pill fatigue

- Consequences:
 - • Underexposure
 - • Rejection
 - • dnDSA
 - • Graft loss



Evolution of Tacrolimus Formulations

- Prograf[®] (BID)
- ↓
- Advagraf[®] (OD)
- ↓
- Envarsus XR[®]

- Same active drug, different delivery technology



Pharmacokinetic Profile

	Prograf	Advagraf
• Dosing	BID	OD
• Absorption	Faster	Slower
• Peak	Higher	Lower
• AUC	Similar	Similar



Ideal Candidate

- ✓ Stable graft function
- ✓ >6 months post-transplant
- ✓ Adherence concerns
- ✓ High IPV



Patients Requiring Caution

- • Recent rejection
- • Unstable kidney function
- • Highly sensitized patients



IR Tacrolimus Conversion

- 1:1 conversion
- 1 mg BID → 2 mg OD
- 2 mg BID → 4 mg OD
- 3 mg BID → 6 mg OD



Therapeutic Drug Monitoring

- Day 0: Conversion
- Day 3–7: Trough
- Week 2: Repeat trough
- Month 1: Clinical review



Clinical Case 1

- 45-year-old male
- 4 years post-transplant
- Tacrolimus 2 mg BID
- Frequently misses evening dose



Why Convert from Cyclosporine?

- • Hypertension
- • Dyslipidemia
- • Cosmetic adverse effects
- • Simplification



Cyclosporine Conversion

- Stop Cyclosporine
- → Start Advagraf next morning
- → Early TDM
- → Dose adjustment



Initial Dose Selection

- 0.1–0.2 mg/kg/day
- 40:1 cyclosporin/tacrolimus ratio
- Depends on risk, time from transplant, concomitant drugs, center practice



Clinical Case 2

- 60-year-old female
- 8 years post-transplant
- Cyclosporine regimen
- New hypertension



- Causes:
 - • Non-adherence
 - • Drug interactions
 - • Food interactions
 - • Genetics



Why Does IPV Matter?

- • Acute rejection
- • dnDSA formation
- • Chronic injury
- • Worse graft survival



Can Once-Daily Tacrolimus Help?

- ✓ Reduced missed doses
- ✓ Better adherence
- ✓ Reduced behavioral variability



Drug Interactions

- Increase: Voriconazole, Posaconazole, Clarithromycin, Diltiazem
- Decrease: Rifampicin, Carbamazepine, Phenytoin
- Attention to MFM dosage

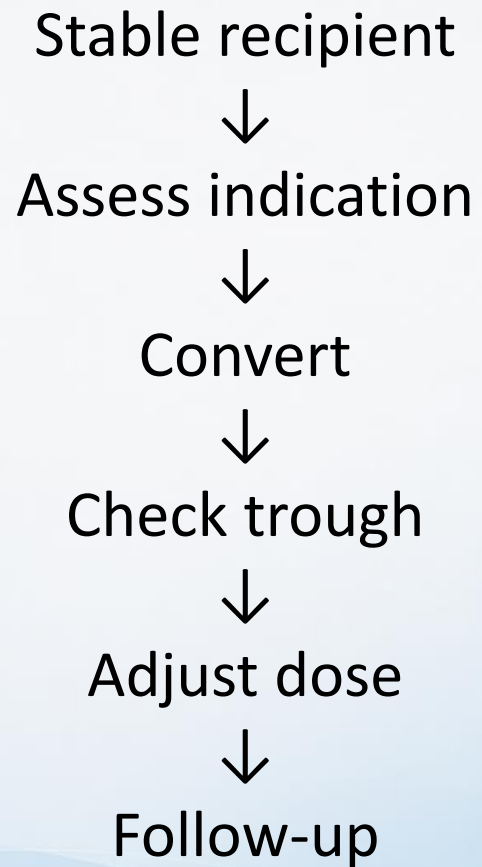


Common Pitfalls

- ✘ No trough monitoring
- ✘ Assuming equivalence
- ✘ Ignoring interactions



Practical Algorithm



Take Home Messages

- 1. Advagraf simplifies immunosuppression
- 2. IR Tacrolimus conversion is usually 1:1
- 3. TDM is essential
- 4. Adherence is the major advantage



References

- Caillard 2016
- Shuker 2016
- Barraclough 2011
- KDIGO
- EMA Advagraf SmPC

