Renal Function in Liver Transplant Recipients Receiving Basiliximab Induction to Delay Tacrolimus Initiation

Melina Braly, PharmD
PGY-1 Pharmacy Practice Resident
Mayo Clinic in Florida
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Disclosure

• I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation

Objectives

• Explain renal dysfunction in patients with end-stage liver disease (ESLD) and post-transplantation.
• Describe immunosuppression (IS) for liver transplantation.
• Illustrate how calcineurin inhibitors (CNIs) may cause renal dysfunction.
• Describe alternative methods to reduce calcineurin inhibitor exposure.
• Explain role of basiliximab in liver transplant.

Renal Dysfunction in ESLD and Post-Transplantation

• Incidence difficult to estimate due to:
  – Rapid changes in patient health status
  – Inaccuracy of renal labs
• Causes include:
  – Cirrhosis-induced circulatory changes
  – Comorbid diseases
  – Medications
• Associated with poor outcomes and increased mortality

Immunosuppression (IS) in Liver Transplant

• Calcineurin Inhibitors
  – Tacrolimus, Cyclosporine
• Anti-Metabolite Agents
  – Mycophenolate, Azathioprine
• Corticosteroids
  – Methylprednisolone, Prednisone

Calcineurin Inhibitors

• Medications: Tacrolimus, Cyclosporine
• Mechanism:
Calcineurin Inhibitors

- Adverse Drug Effects:
  - Nephrotoxicity
  - Neurotoxicity
  - Hypertension
  - Post-Transplant Diabetes
  - Hyperlipidemia
  - Abnormal hair growth

- Monitoring:
  - Trough Levels

Antimetabolite Agents

- Medications: Mycophenolate (MMF), Azathioprine
- Mechanism: Interfere with DNA synthesis and prevents B- and T-cell proliferation
- Adverse Drug Effects:
  - Anemia
  - Thrombocytopenia
  - Neutropenia
  - Nausea
  - Diarrhea

Corticosteroids

- Medications: Methylprednisolone, prednisone
- Mechanism: Nuclear factors that increase transcription of anti-inflammatory proteins
- Adverse Drug Effects:
  - Hyperglycemia
  - Osteoporosis
  - Increased risk of infection
  - Mood disturbances
  - Insomnia
  - Fluid retention
  - Hypertension

Calcineurin Inhibitors: Nephrotoxicity

- Mechanism:
  - Reduced GFR
  - Acute Toxicity
  - Chronic Toxicity

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Reducing CNI Exposure

• Maximize other immunosuppressive agents
  – Lower trough goal

• Delay CNI initiation
  – Basiliximab

Basiliximab

• Mechanism: Interleukin-2 (IL-2) receptor antagonist
  – Targets activated T cells and decreases activation and proliferation of T cells

• Indication: Induction therapy for transplants
  – Delays CNI initiation

• Adverse Drug Reactions: well tolerated

• Cost per dose (AWP): $3244.57 (20mg vial)

Mayo Clinic Transplant Protocol

• Renal dysfunction: SCr >1.5 mcg/ml or CrCl< 40ml/min

• Basiliximab (20mg) scheduled for POD 0 and 4
  – Standard IS initiated (MMF + steroids)

• Tacrolimus may be initiated by POD 4 or earlier depending on renal function

Literature

• Benefit of basiliximab remains unclear

• Trials excluded patients with renal dysfunction

• Conclusions have varied

• No studies have looked at one dose of basiliximab with tacrolimus against two doses of basiliximab with delayed tacrolimus therapy

Research Purpose

• Compare renal function one year post liver transplant between
  – Patients whose therapy included 2 doses of basiliximab on POD 0 and 4
  – Patients who did not receive a second dose of basiliximab on day 4 post-transplantation and instead began a CNI sooner than POD 4

Summary

• Renal dysfunction increases morbidity and mortality pre- and post-transplantation

• CNIs can cause renal dysfunction

• Induction therapy or reduced trough goals of CNIs may be used to decrease renal dysfunction

• Current study assesses renal function 1-year post-transplant to evaluate effect of basiliximab induction
Resources

- Factory: Hospira, Inc. [product manufacturer].

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Melina Braley, PharmD
PGY-1 Pharmacy Practice Resident
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