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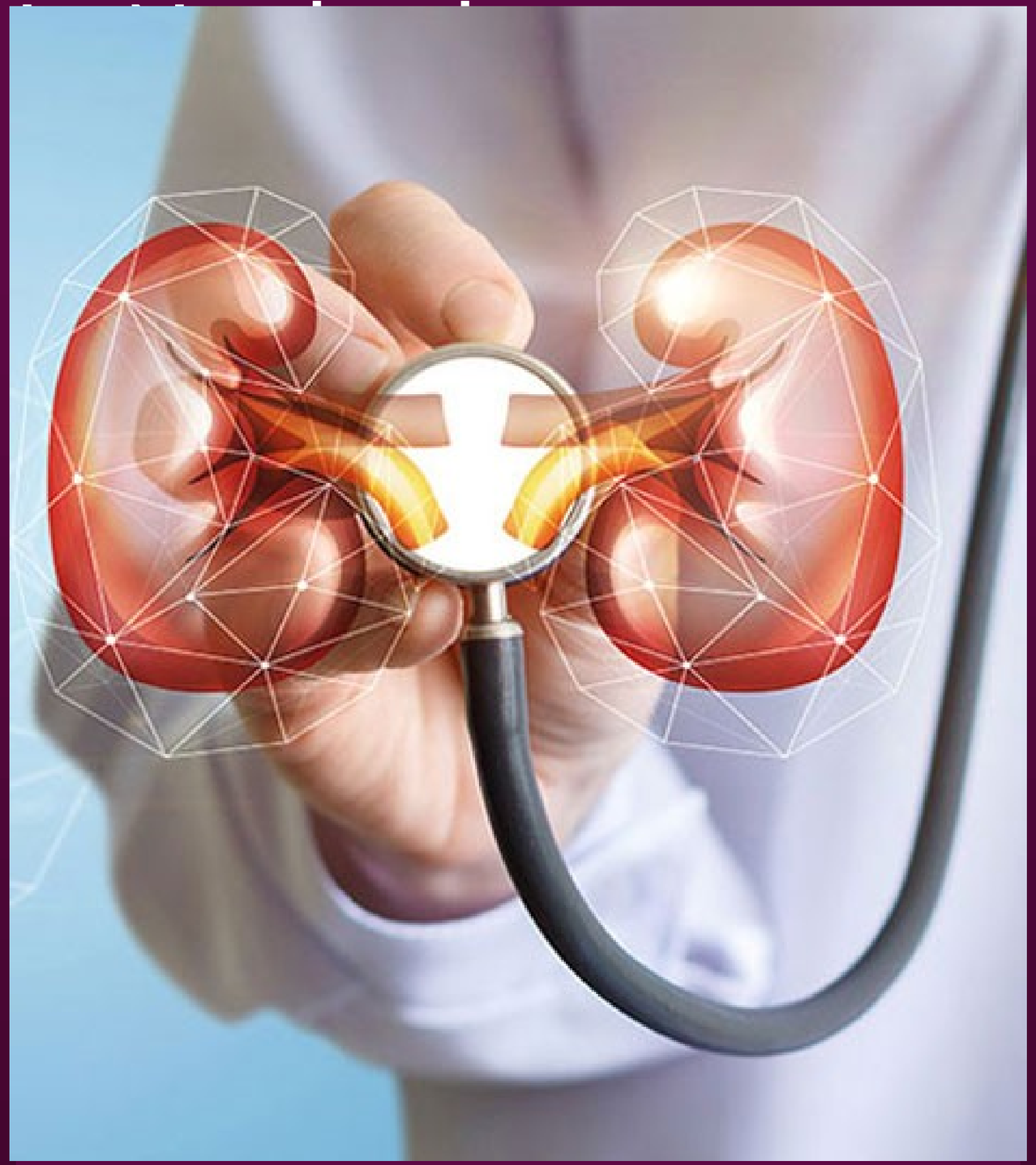
An RPG Company

Azathioprine Compendium



Azoran® 75

Azathioprine 75 mg Tablets

Azoran® 25

Azathioprine 25 mg Tablets

Azoran® 50

Azathioprine 50 mg Tablets

EXECUTIVE SUMMARY

AZATHIOPRINE IN NEPHROLOGY

- First study comparing CsA, MMF and AZA on long-term LN maintenance therapy showed that all treatments had similar efficacy in achieving and maintaining CRR, despite more severe baseline clinical features in patients treated with CsA.
- This long-term examination, although limited by small numbers, found little evidence for the superiority of MMF over AZA.
- Similar outcomes were obtained with PRED plus AZA or CsA treatments. Either therapeutic strategy could be used according to the particular characteristics of each patient. Triple immunosuppression was beneficial in patients with liver failure at onset.

AZA: Azathioprine,
IBD: Inflammatory Bowel diseases,
MP: Mercaptopurine,
OR: Overall Response,
MTX: Methotrexate,
AD: Atopic Dermatitis,
ANCA: Antineutrophil cytoplasmic antibodies,
TPMT: Thiopurine methyltransferase,
MMF: Mycophenolate Mofetil,
ASyS: antisynthetase syndrome,
SNVs: Systemic necrotizing vasculitides,
EGPA: Eosinophilic Granulomatosis with Polyangiitis,
LN: Lupus Nephritis,
CsA: cyclosporine
CRR: Complete Renal Remission, prednisone (PRED)

AZATHIOPRINE IN NEPHROLOGY

CLINICAL TRIALS

RANDOMIZED CONTROLLED TRIALS

CASE STUDY

Clinical Trials

Multicentric study comparing cyclosporine, mycophenolate mofetil and azathioprine in the maintenance therapy of lupus nephritis: 8 years follow up

Lorenza Maria Argolini.et.al.

Journal of Nephrology (2020)

Background and Aims

The ideal long-term maintenance therapy of Lupus Nephritis (LN) is still a matter of debate. The present study was aimed at comparing the efficacy/safety profile of cyclosporine (CsA), mycophenolate mofetil (MMF) and azathioprine (AZA) in long-term maintenance therapy of LN.

Method

We performed a retrospective study of patients with biopsy-proven active LN. After induction therapy, all patients received maintenance therapy with CsA, MMF or AZA based on medical decision. Primary endpoint was complete renal remission (CRR) after 8 years (defined as proteinuria < 0.5 g/24 h, eGFR > 60 ml/min/1.73 mq); secondary endpoints were: CRR after 1 year, renal and extrarenal flares, progression of chronic kidney disease (CKD stage 3 or above) and side-effects.

Result

Out of 106 patients, 34 received CsA, 36 MMF and 36 AZA. Clinical and histological characteristics at start of induction therapy were comparable among groups. At start of maintenance therapy, CsA patients had significantly higher proteinuria (P = 0.004) or nephrotic syndrome (P = 0.024) and significantly lower CRR (23.5% vs 55.5% on MMF and 41.7% on AZA, P = 0.024). At one year, CRR was similar in the three groups (79.4% on CsA, 63.8% on MMF, 58.3% on AZA, P = 0.2). At 8 years, the primary endpoint was achieved by 79.4% of CsA vs 83.3% of MMF and 77.8% of AZA patients (P = 0.83); 24 h proteinuria, serum creatinine, eGFR were similar. CKD stage 3 or above developed in 8.8% of CsA, in 8.3% of MMF and in 8.3% of AZA patients (P = 0.92). Flares-free survival curves and incidence of side-effects were not different.

Conclusion

This is the first study comparing CsA, MMF and AZA on long-term LN maintenance therapy. All treatments had similar efficacy in achieving and maintaining CRR, despite more severe baseline clinical features in patients treated with CsA.

https://pubmed.ncbi.nlm.nih.gov/25757867/A

RCT'S

Mycophenolate versus Azathioprine for Kidney Transplantation A 15-Year Follow-Up of a Randomized Trial

Clayton, Philip A.et.al.

Transplantation: July 27, 2012 - Volume 94 - Issue 2

Background and Aims

The use of mycophenolate mofetil (MMF) is associated with less acute rejection than azathioprine (AZA) early after kidney transplantation. However, the long-term impact of MMF versus AZA is less well studied.

Method

The Tricontinental Mycophenolate Mofetil Renal Transplantation Study was a double-blind randomized placebo-controlled trial of MMF versus AZA, together with cyclosporine and steroids, first reported in 1996. We analyzed the long-term outcomes of the Australian cohort of patients enrolled in this study using follow-up data from the Australia and New Zealand Dialysis and Transplant Registry. Patient and graft survival, cancer incidence, and estimated kidney function were compared on an intention-to-treat basis.

Result

A total of 133 Australian patients participated in the study: 45 were randomized to AZA, 44 were randomized to MMF 2 g/d, and 44 were randomized to MMF 3 g/d. Baseline characteristics were similar between the groups. Median follow-up was 13.8 years, during which there were 97 graft failures, 75 deaths, and 1 lost to follow-up. There were no statistically significant differences between the groups in long-term patient or graft survival, cancer incidence, or kidney function. Death-censored graft survival was best in the group with 3 g/d MMF and worst in the group with 2 g/d MMF. By 5 years, 42% of the MMF group had switched permanently to AZA, whereas crossover from AZA to MMF was rare.

Conclusion

This long-term examination, although limited by small numbers, found little evidence for the superiority of MMF over AZA.

https://pubmed.ncbi.nlm.nih.gov/22728292/

AZATHIOPRINE IN NEPHROLOGY

RCT'S

Autoimmune Hepatitis in Children: Prednisone plus Azathioprine versus Cyclosporine: A Randomized Trial

Cuarterolo.et.al.

Journal of Pediatric Gastroenterology and Nutrition: September 2020 - Volume 71 - Issue 3

Background and Aims

The aim of this study was to find the outcome and adverse effects of 2 initial treatments in children with autoimmune hepatitis, prednisone (PRED) plus azathioprine (AZA) versus cyclosporine (CsA).

Method

Between December 2008 and February 2012, 50 consecutive patients were centrally randomized to 1 of 2 treatment arms. Group 1: PRED was indicated at a dose of 1 to 2 mg · kg-1 · day-1 (up to 60 mg/day) and AZA at a dose of 1 to 2 mg · kg-1 · day-1. Group 2: CsA was administered at a dose of 4 mg · kg-1 · day-1 orally divided into 2 doses. After remission, all patients were given a combination of PRED at 0.3 to 0.5 mg · kg-1 · day-1 and AZA at 1 to 2 mg · kg-1 · day-1. Children presenting liver failure were placed on a triple immunosuppressive regimen if this condition persisted after 1 week of treatment, after liver function normalization they were switched back to their initial scheme.

Result

A total of 26 patients received PRED-AZA and 24 CsA. Both treatments showed similar initial results in effectiveness and safety, although remission was achieved earlier with PRED-AZA: 8.6 versus CsA: 13.6 weeks ($P < 0.0081$). All children recovered liver function in a mean time of 32 ± 26 days. Cushingoid syndrome was more frequently observed with PRED-AZA ($P < 0.001$) and gingival hypertrophy with CsA ($P < 0.001$). A significant increase in body mass index was observed in all patients from initial treatment to remission, being greater with PRED-AZA.

Conclusion

Similar outcomes were obtained with PRED plus AZA or CsA treatments. Either therapeutic strategy could be used according to the particular characteristics of each patient. Triple immunosuppression was beneficial in patients with liver failure at onset.

https://pubmed.ncbi.nlm.nih.gov/32520828/

Case Study

Azathioprine-Induced Tubulo-Interstitial Nephritis in Graft Kidney Transplant

Salima Al-Alawi.et.al.

Trends in Transplant, 2020 Volume 13: 2-3

Abstract

Kidney Transplant is the gold standard care for end-stage kidney disease (ESKD). Immunosuppression has a central role to maintain the graft function and its survival. Despite newer agents, still old agents such as azathioprine is still used by many clinicians at various places world-wide. However, hypersensitivity reactions, such as tubulointerstitial nephritis, can occur after starting these medications. There can be many causes of tubulointerstitial nephritis; drugs, infections and autoimmune diseases e.g.: sarcoidosis, systemic lupus erythematous and Sjogren's syndrome.

We report a case of acute interstitial nephritis after introduction of azathioprine in a kidney transplant recipient. A young female with a living related kidney transplant on triple immunosuppression medication consisting of prednisolone, tacrolimus and mycophenolate mofetil, expressed her desire to conceive eight months after her wedding.

Accordingly, mycophenolate mofetil was replaced by azathioprine. In subsequent visits it was observed that her graft kidney function was deteriorating progressively. All possible causes which could contribute to graft function deterioration were evaluated and a graft biopsy was performed.

The biopsy showed moderate interstitial inflammatory infiltrate rich in eosinophils with no evidence of cellular or antibody mediated rejection. It was successfully treated by stopping azathioprine and starting high dose oral prednisolone. Deterioration of kidney function in kidney transplant patients, who are put on azathioprine, should raise the suspicion of tubulointerstitial nephritis as a differential diagnosis

https://www.oatext.com/azathioprine-induced-tubulo-interstitial-nephritis-in-graft-kidney-transplant.php

NOTE