First-Line Azathioprine- Allopurinol Without Metabolite Monitoring Is an Effective and Safe Long-Term Therapy for IBD

Introduction

The number of IBD patients experiencing a beneficial response from the first-line, low-cost immunosuppressive azathioprine (AZA) is too low due to high rates of adverse events. Co-administration with allopurinol has been reported to improve tolerability and might be an option as first-line therapy.

Methods

The long-term efficacy, side-effects and safety of low-dose azathioprine with allopurinol (LDAA) was compared with AZA monotherapy (AZAm) in thiopurine-naïve IBD patients unguided by metabolite levels. Medical records of patients (identified from pharmacy dispensing records and an IBD database) were reviewed retrospectively. The primary outcome ‘clinical benefit’ was defined as: ongoing use of therapy without initiation of steroids, biologics or IBD-surgery. Secondary outcomes included disease activity scores, endoscopic findings, withdrawal of concomitant therapy (including steroids), CRP and adverse events.

Results

166 LDAA and 118 AZAm patients (≥ 90% having active disease) were included with a median follow-up of 25 and 27 months, respectively. Clinical benefit was higher in the LDAA cohort at both 6 months (74% vs 53%, p=0.0004) and 12 months (54% vs 37%, p=0.01). The overall median duration of beneficial response since commencement of therapy was 17 months (95%-CI 9 – 25) for LDAA therapy compared to 6 months (95%-CI 1 – 11) for AZAm. The lower efficacy of AZAm was explained by the median dose tolerated of 1.83 mg/kg (73% of most effective dose) and high percentage (45%) of patients discontinuing due to intolerance. Although elevated liver function tests and leukopenia were relatively commonly observed in the LDAA cohort, they only led to treatment withdrawal in 2% for both. Increasing allopurinol dosage from 100 to 200 – 300 mg/day significantly lowered liver enzymes in the majority (83%) of patients who had developed hepatotoxicity on LDAA.

Conclusions

Optimisation of AZA therapy for IBD is mandatory as poor outcomes were observed in our AZAm cohort. LDAA without metabolite monitoring should be considered standard first-line immunosuppressive therapy, as we demonstrated a safe and effective profile in the long-term.