THERAPEUTIC DRUG MONITORING OF TNFα INHIBITORS IN INFLAMMATORY BOWEL DISEASE: EVIDENCE FROM A REAL WORLD SETTING

Capoulas M[1], Loba A[1], Barroso A[1], Santos M[1], Santos C[1], Gomes MV[2], Andreozzi V[2], Félix J[2]

1. Pharmaceutical Services, Hospital Beatriz Angelo, Loures, Lisboa; 2. Exigo Consultores, Lisboa, Portugal

INTRODUCTION / OBJECTIVES

Biologics have become the mainstay for Inflammatory Bowel Disease (IBD) however these drugs often require dose escalation to maintain effectiveness. Optimizing drug response in IBD often requires dose escalation [1]. Therapeutic drug monitoring (TDM), whereby measurements of anti-TNFα drug levels and antibodies against TNFα-inhibitors are used to tailor therapy, is recommended to guide the IBD management, as it is associated with lower risk of treatment failure compared to empiric dose adjustment [2].

This study aimed to characterise therapeutic drug monitoring of the TNFα-inhibitor adalimumab in patients diagnosed with IBD.

METHODS

This was a retrospective observational study, with data collection from medical and pharmaceutical records. Inclusion criteria comprised patients with IBD diagnosis, on maintenance therapy with adalimumab, between 2014 and 2019, in a general Portuguese hospital.

Main outcomes analysed included:

- dose escalations,
- therapy discontinuations,
- TDM.

Statistical analysis included description of continuous variables with measures of central tendency and dispersion. Categorical variables were described through frequency distribution. All statistical analyses were conducted in R 3.6®.

RESULTS

A total of 40 patients met inclusion criteria, who had a mean age (standard deviation [SD]) of 39.6 (16.2) years and half were female (50.0%). The majority of patients had Crohn's Disease (90.0%), while the remaining 10.0% had Ulcerative Colitis.

Further patient characteristics are depicted in Table 1.

Table 1 Sociodemographic and clinical patients characteristics

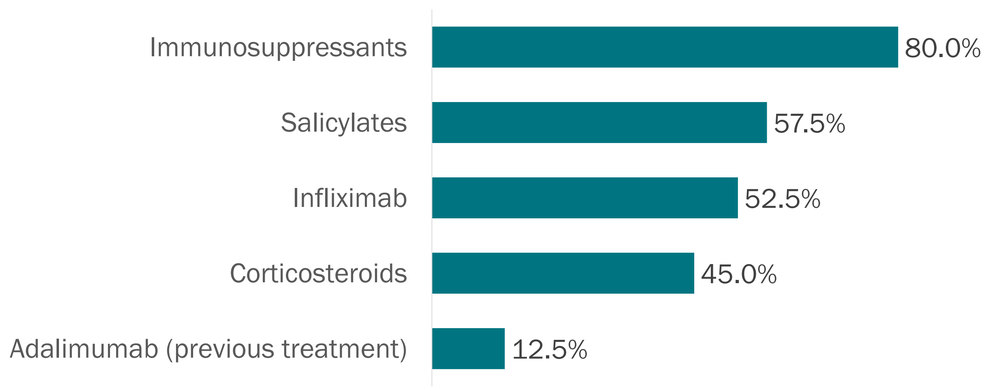
Patient characteristics	n	%|SD
Female	20	50.0%
Age in years (mean)	39.6	16.2
Weight in kg (mean)	66.7	15.7
Pathology		
Crohn's disease	36	90.0%
Ulcerative colitis	4	10.0%
Smoking status		
Non smoker	16	40.0%
Smoker	6	15.0%
Former smoker	4	10.0%
Unknown	14	35.0%

SD: standard deviation

Median time on therapy with adalimumab was 25.1 months. Adalimumab was more frequently administered as a fourth-line therapy for IBD (32.5%), including both conventional and biological treatment.

Most patients had been previously treated with immunosuppressants (80.0%), salicylates (57.5%), infliximab (52.5%) and corticosteroids (45.0%) (Figure 1). Also 12.5% of patients had been treated with adalimumab in a previous therapeutic lines (Figure 1).

Figure 1 Treatments administered prior to adalimumab (n=40)

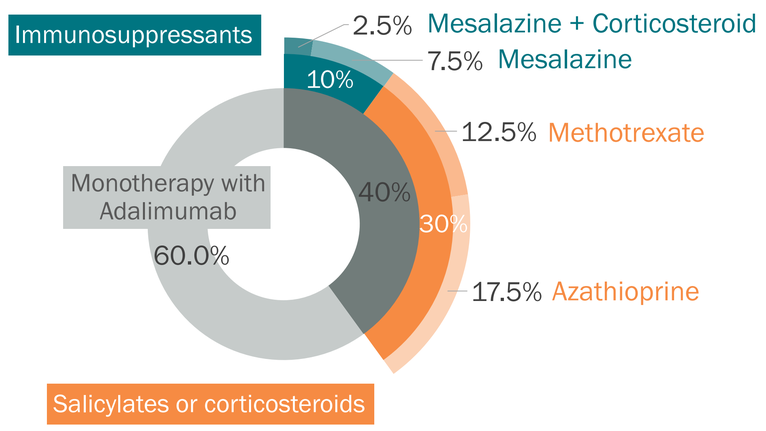


Legend: Corticosteroids: budesonide and hydrocortisone; Immunosuppressants: azathioprine, 6-mercaptopurine and methotrexate; Salicylates: mesalazine and sulfasalazine

RESULTS (cont.)

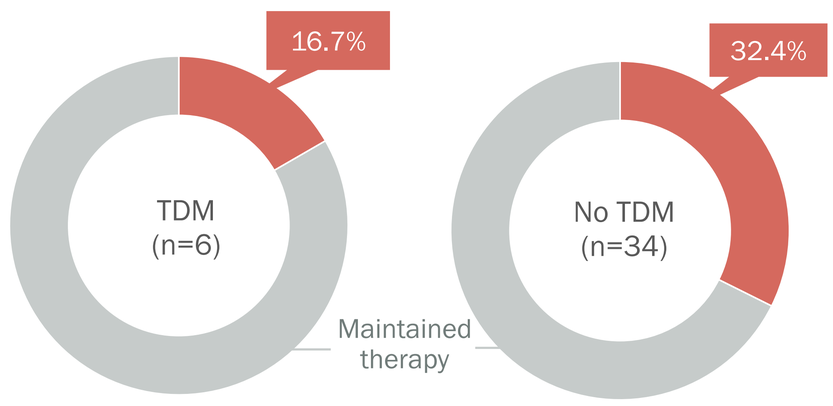
The majority of patients were under treatment with adalimumab in monotherapy. Notwithstanding, still 40.0% of patients had concomitant therapy: 30.0% with immunosuppressants and the remaining with salicylates and/or corticosteroids (10.0%) (Figure 2).

Figure 2 Treatment regimen in current line with adalimumab



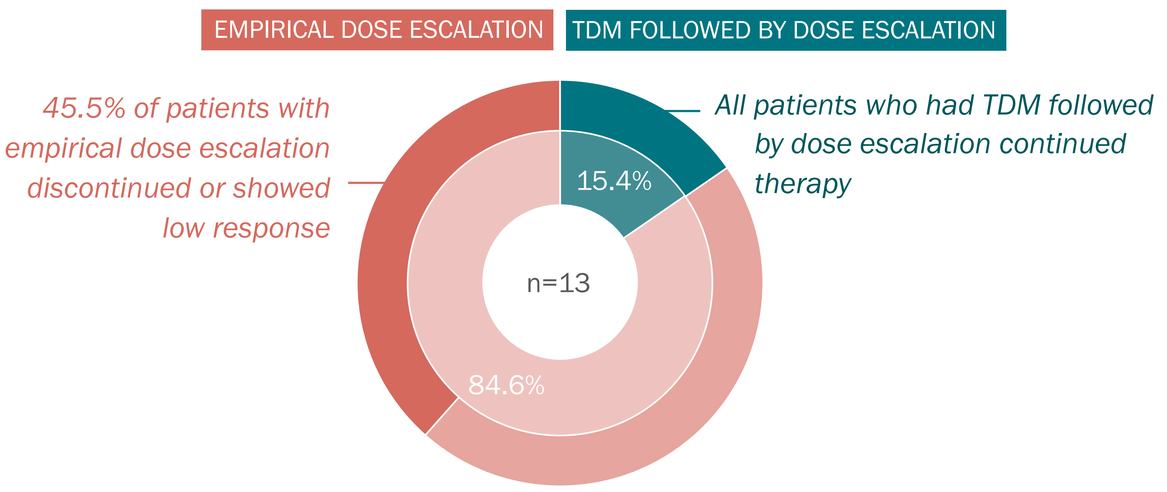
Few patients had TDM (15.0%), nonetheless discontinuation was much less frequent in this cohort of patients (16.7%), when compared to patients without TDM (32.4%) (Figure 3).

Figure 3 Treatment discontinuation in patients with TDM and without TDM



During follow-up, 13 patients (32.5%) had dose escalation. In most cases dose escalation was performed empirically (84.6%), while TDM was only performed in 15.4%. Until the end of follow-up, all patients who had TDM followed by dose escalation continued therapy, whereas 45.5% of patients with empirical dose escalation either discontinued or showed low response (Figure 4).

Figure 4 Empirical vs. TDM based dose escalation



CONCLUSION

This study showed that TDM of adalimumab lead to a lower proportion of discontinuations or low response in Inflammatory Bowel Disease treatment. Although TDM is still performed in a minority of patients, its use should be encouraged in real-world context for Inflammatory Bowel Disease.

The use of therapeutic drug monitoring should be encouraged to optimize real-world disease management, which is in accordance with recently published studies [2].

REFERENCES: [1] Rupniewska, E., et al., *Systematic Literature Review of Real-World Evidence on Persistence, Switching, and Dose Escalation with Biologics in Inflammatory Bowel Disease in the United States.* Value in Health, 2018. 21: p. S87-S88. [2] Papamichael, K. and A.S. Cheifetz, *Therapeutic drug monitoring in inflammatory bowel disease: for every patient and every drug?* Curr Opin Gastroenterol, 2019. 35(4): p. 302-310.

https://www.eahp.eu/25-6ER-010