Efficacy of Ustekinumab intensification and re-induction in Crohn's disease patients with insufficient or loss of response

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Introduction

Ustekinumab (UST) has proven to be an efficient maintenance therapy for moderate to severe **Crohn's disease** (CD). However, a significant percentage of patients treated with subcutaneous maintenance UST experience a **secondary loss of response (LOR) or partial response**.

We evaluated the clinical, biological and endoscopic response to **UST optimization** including:

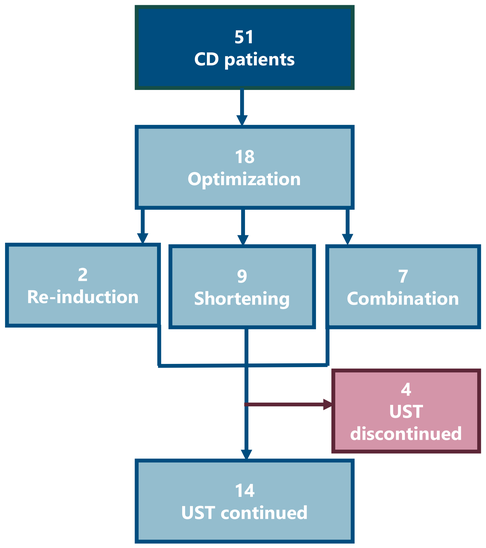
1. Re-induction: intravenous UST at a dose of 6 mg/kg
2. Shortening of the dosage interval: mainly every 4 weeks
3. Combination (1+2)

Methods

A retrospective, single-center study was performed including patients with CD who were treated with **maintenance UST** and received either IV **re-induction and/or shortening of the dosage interval** for a partial response or LOR. The **clinical and endoscopic response** was based on the physician's assessment. A **biological response** was defined as a decrease of ≥50% in C-reactive protein (CRP) and/or fecal calprotectin (FC); remission as a normalization of these parameters.

Results

Eighteen out of the 51 (35.3%) UST-treated CD patients needed optimization of UST. The median time to optimization was 34.5 weeks (IQR 20.3-42.3). Response to dose optimization was assessed at a median of 15.5 weeks (IQR 6.8-19.3).



1. Re-induction

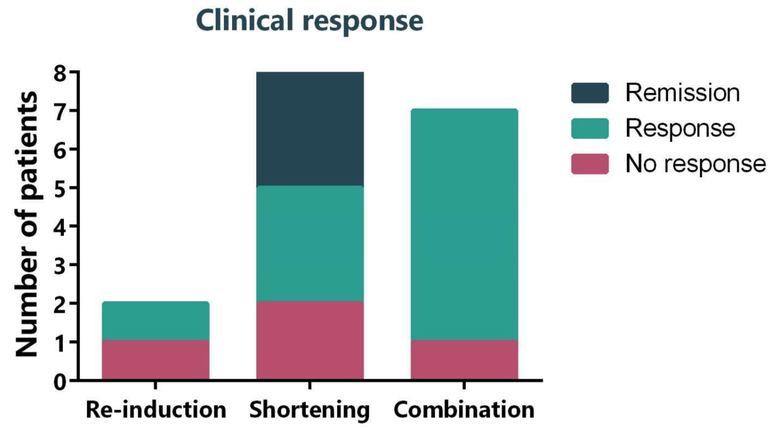
One of the 2 patients who underwent re-induction alone experienced a good clinical and endoscopic response; the other patient had no clinical, biological nor endoscopic response and UST was discontinued.

2. Shortening of interval

Nine patients underwent shortening of the dosage interval alone, which was successful in inducing a **clinical response** in 3/9 (33.3%) and a clinical remission in 4/9 (44.4%). Two patients (22.2%) had no clinical response. **Biological** remission was observed in 4/7 patients (57.1%) and 3/7 patients had no biological response (42.9%). **Endoscopic** evaluation in 4 patients showed a response in 2/4 and no response in the other 2. In 2/9 patients (22.2%) UST was stopped; one due to LOR and the other patient due to an adverse event (flare of underlying spondyloarthropathy).

3. Combination

A combined re-induction and shortening of the dosage interval was performed in 7 patients. Of these, 6 experienced a **clinical response** and 1 patient had no response. **Biological** remission was confirmed in 3/6 patients, whereas the other 3/6 had no biological response. **Endoscopic** response was observed in 1/3 patients. Despite optimization, UST was discontinued in one patient due to a persistent LOR.



AEs Other adverse events (AEs) were seen in 2 patients: 1 patient had arthralgia and 1 patient developed a rash, both AEs were mild and UST could be continued.

Conclusion

About a **third** of patients treated with maintenance UST underwent **optimization**. Of these 18 patients, **10** (55.6%) regained a **good clinical response** and **4** (22.2%) were in **clinical remission**. UST could be continued in the majority of patients.