Crohn's disease patients' and gastroenterologists' perspectives towards de-escalating inflammatory bowel disease therapy: a comparative European and American survey

Short title: Preferences for de-escalating IBD therapy

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Introduction

In Crohn's disease, combination therapy with anti-tumor necrosis factor (anti-TNF) agents and azathioprine/mercaptopurine has been shown to be superior to monotherapy with one of these treatments alone.[1] This combination has its best success rate when used early in the course of treatment.[2] However, due to the significant cost of these drugs and concerns over long-term side effects,[3, 4] many patients and providers often ask about stopping one or both of these medications.

There are limited data on the benefits and risks of de-escalating combination therapy to monotherapy for patients with Crohn's disease who are in remission.[5, 6, 7, 8] More prospective data are needed to support the strategy of de-escalation of combination therapy, and a trial called SPARE is currently underway internationally. As data emerge to guide this difficult clinical decision, patient and providers preferences need to be taken into account. The aim of this study was to understand gastroenterologists and patients' perspectives on stopping therapy for Crohn's disease when in remission, and to identify differences between European and United States (US) doctors and patients.

Methods

To understand patients' and providers' perspectives on de-escalating Crohn's disease therapy, a mixed-methods approach using qualitative focus groups (phase 1) and quantitative surveys (phase 2) was used. Patients were included from two different regions, France and the US and gastroenterologists were included from both Europe and the US. Focus groups and surveys were completed between February 2016 and July 2017.

Results

For the qualitative phase 1 of the study, 5 patients and 11 physicians were included to guide questionnaire development. In phase 2, 410 patients with Crohn's disease from the US (113) and France (297) completed the questionnaire. French patients were more likely than those in the US to consider stopping combination therapy if recommended by their doctor (66% vs 48%, $p<0.01$) (Figure 1a). Most patients in the US and France preferred to stop the immunomodulator (IM) (53% US, 47% France) as opposed to anti-TNF (26% US, 28% France). A majority of patients would not accept a risk of relapse higher than 25% to be able to de-escalate therapy. The proportion of time that patients were willing to accept having a flare, ranged from none to over 20% over a two-year timeframe. 309 gastroenterologists from the US (182) and Europe (127) completed the questionnaire. European gastroenterologists were significantly more likely to recommend stopping combination therapy for an average Crohn's disease patient in remission (44% Europe, 18% US) (Figure 1b). Gastroenterologists were more likely to stop the IM (75% Europe, 61% US, $p<0.05$) as opposed to biologic therapy (23% Europe, 29% US). In general, gastroenterologists would accept a higher risk of relapse than the patients.

Discussion

The main results of this study are that a high proportion of patients and gastroenterologists are willing to de-escalate therapy once in remission on combination therapy. European patients and gastroenterologists are significantly more likely than US patients and providers to want to de-escalate. Patients and gastroenterologists on both continents prefer stopping the immunomodulator as opposed to the biologic drug, driven by concerns over the risk of cancer with long-term exposure and overall reduction of side effects. There is a sizable minority of patients and providers who would not want to de-escalate therapy, with the most common reasons being concerns of flaring and not being

able to re-achieve remission, not wanting to “mess with a good thing”, and worry over having to go back on prednisone. Furthermore, there are a number of patients (and some providers) in the US and Europe who would never consider de-escalating therapy if there is any chance of their disease flaring again. It is relevant to note that the majority of the patients would accept their disease flaring up to 5% of the time to be able to de-escalate therapy. Patient characteristics were not associated with their responses. However, providers based in hospital settings were significantly more likely to de-escalate therapy than providers in other locations, and younger providers and those in practice for fewer years were more likely to stop immunomodulators as compared to their older counterparts.

In summary, patients and providers from both Europe and the US are willing to de-escalate therapy when in remission on a combination of a biologic agent and an immunomodulator. There are some differences between patients and gastroenterologists, and between European and US respondents, but overall the message is that there are varying perspectives that are likely based on individual preferences, experience with Crohn’s disease and with treatment, and cost that need to be accounted for when determining the best course of treatment.

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Figure Legend

Figure 1. (a) Patients' preferences for de-escalating therapy (**b)** Providers' preferences for de-escalating therapy

Figure 1a

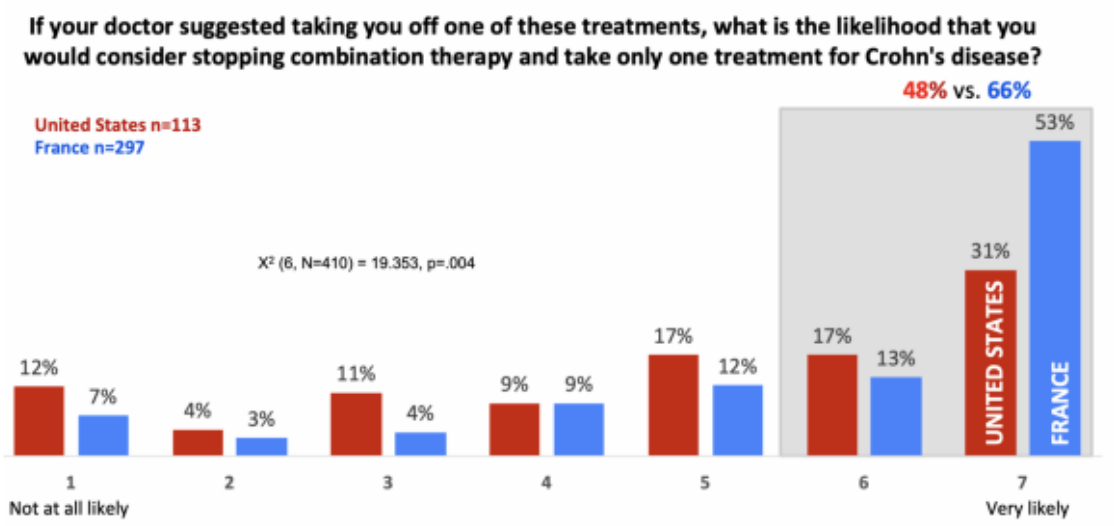

Figure 1b