Real life dose escalation of patients with ulcerative colitis and Crohn's disease undergoing biologic treatment in Portugal

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Cruz, J.P.[1]; Faria, M.[2]; Aleixo, A.[3]; Pereira, F.[3]

[1]Pharmacological Sciences Department, Centro Hospitalar Universitário Lisboa Norte, Portugal;

[2]Takeda Portugal, Lisbon, Portugal;

[3]IQVIA Solutions Portugal, Lisbon, Portugal.

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1 Background and Objectives

Background

- Inflammatory bowel disease (IBD), comprised by Crohn's disease (CD) and ulcerative colitis (UC), is a chronic, progressive, condition that causes inflammation in the gastrointestinal tract[1].
- Patients with moderate to severe IBD are treated with biologic therapies, which include anti-tumor necrosis factor therapies (Adalimumab, Golimumab, Infliximab), anti-integrin agents (Vedolizumab) and anti-interleukin 12/23 agents (Ustekinumab)[1,2].
- These treatments tend to lose their effectiveness over time, with some patients failing to remain in remission. In these cases, and to increase the treatment efficacy, patients usually undergo a dose escalation or an increase in the dosing frequency [2] .

Objectives

- The present work aims to assess the real-life dosage of patients with UC and CD under biologic treatment in Portugal.

2 Methods

- A set of 16 Portuguese public hospitals (~59% representativeness) provides clinical data to IQVIA on a monthly basis, reporting all the products consumed by patients within the hospital scope. The data provided is anonymized at the hospital and it is not possible to identify patients. The present work does not display any individual data, only aggregated results.
- For this retrospective study, patients with Adalimumab, Golimumab, Infliximab, Vedolizumab and/or Ustekinumab consumptions in gastroenterology cost centers were selected. Of these, those who started maintenance treatment from January 2020 onwards and who completed at least one year of maintenance were selected. Induction consumptions were identified and removed from the analysis. Patients taking Golimumab (n=9) were also removed from the analysis due to low sample size.
- In order to assess the real-life dosage of patients consuming the in-scope molecules, the following metrics were calculated:

Initial maintenance dosage

The initial maintenance dosage corresponds to the first dosage/posology taken by the patient, excluding any induction dosages. For each patient, the initial maintenance dosage was identified and compared with those defined in the summary of product characteristics (SmPC), allowing for the identification of the share of patients starting maintenance with dose escalation.

Annual maintenance dosage

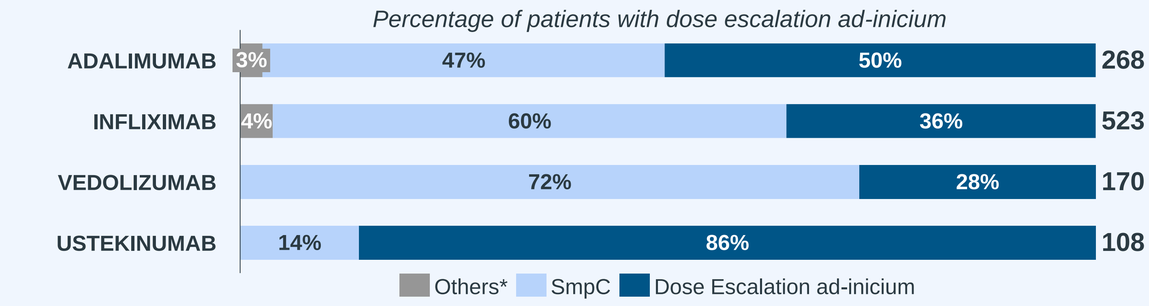
The annual maintenance dosage for each patient was obtained by summing all doses consumed over a twelve-month period (excluding induction phase). Then, the annual dosage was calculated according to the SmpC (based on the weekly and monthly intake frequency defined in the document, for example: Vedolizumab could be taken every 8 weeks or every 2 months). By comparing the real dosage and the SmpC defined dosages, it was possible to identify how many patients underwent dose escalation and the magnitude of that same escalation, in their first year of maintenance.

Patient Equivalence

Dose escalation prevalence and magnitude were used to quantify the equivalent patient treatment rate representing the number of patients per 100 that could have been treated with standard dosing, given the prevalence of dose escalation in the treated population

3 Results and Discussion

Initial Maintenance dosage

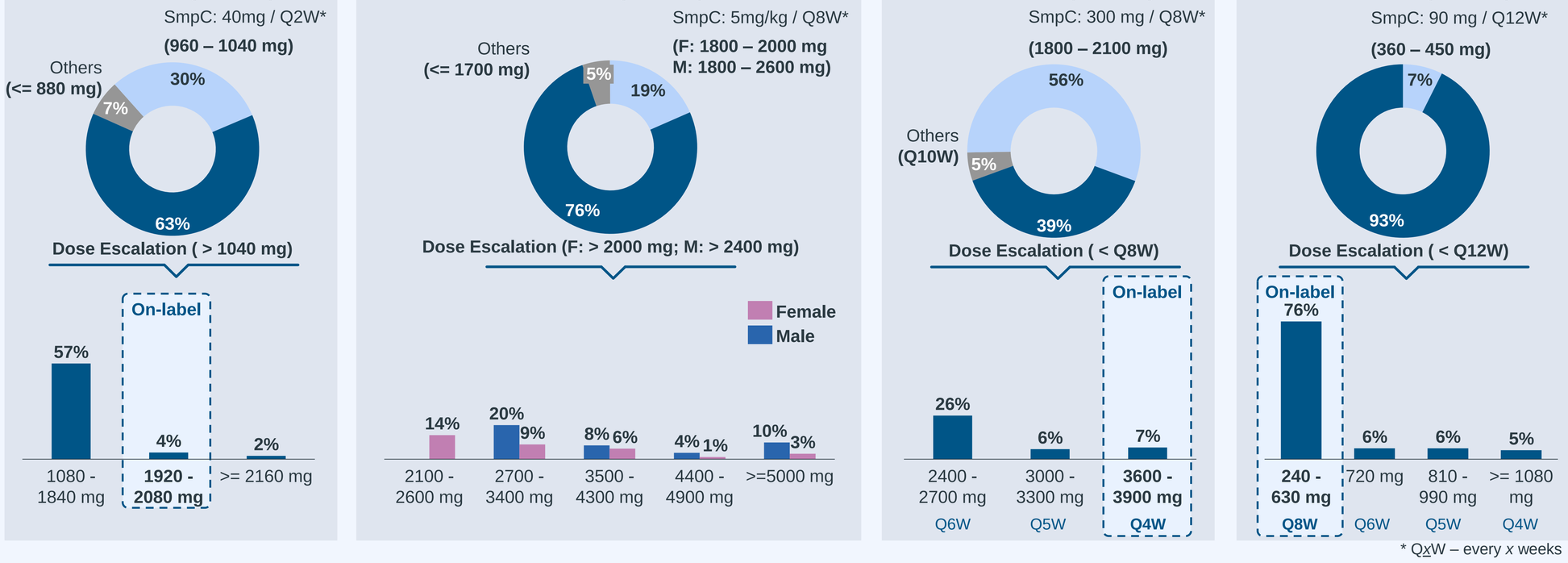


* Patients that consume a dosage bellow the one defined in the SmpC.

- Vedolizumab is the molecule with the highest percentage of patients (72%) starting maintenance treatment with the recommended SmpC dosage (300mg every 8 weeks).
- For Infliximab, the weight and gender of patients was considered for calculating dose possible dose escalation. From this analysis, it is observed that 60% of these patients start maintenance with the recommended SmPC dosage (5mg/kg every 8 weeks)
- Regarding Adalimumab, 50% of patients undergo dose escalation *ad-inicium,* meaning they start maintenance by taking more than 40 mg every 2 weeks
- The vast majority of patients taking Ustekinumab (86%), already start maintenance treatment with a dosage frequency above the one defined in the SmpC (90 mg every 12 weeks)

Annual Maintenance dosage

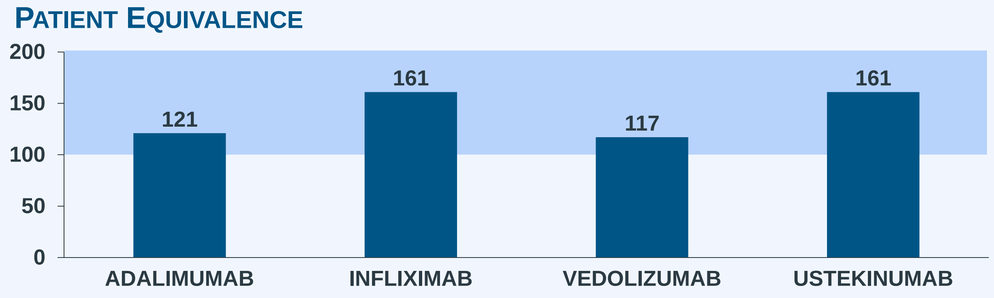
- In an annual perspective, most patients undergoing Adalimumab (63%), Infliximab (76%) or Ustekinumab (93%) will undergo a dose escalation.
- Among these molecules, Ustekinumab has the highest percentage of patients undergoing a dose escalation, having a proportion of 17% of patients taking dosages above the ones defined in the SmPC (90 mg every 8 weeks).
- More than half of patients on Adalimumab (57%) experience a dose escalation that is less than the dosage increase defined in the SmpC (40 mg every week or 80 mg every two weeks).



* Q*x*W – every *x* weeks

- Regarding Infliximab, an average weight of 60 kg was considered for women (300 mg every 8 weeks) and between 60 and 80 kg for male patients (300-400 mg every 8 weeks). This treatment shows the second highest percentage of patients undergoing a dose escalation of 76%, with a significant share more than doubling the dosage recommended in the SmPC.
- Contrarily to other molecules, most Vedolizumab patients (~56%) don't go trough an increase in the dosage frequency intake and continue to be administered 300 mg every 8 weeks, according to SmPC. From the patients that experience a dose escalation, none undergoes a dosage increase above the one recommend in the SmPC (300 mg every 4 weeks)

Patient Equivalence



- Estimating patient equivalence for a therapeutic agent helps payers gauge the potential cost impact at the population level, as it considers both the prevalence and extent of dose escalation.
- Ustekinumab and Infliximab have the highest patient equivalence. For both this molecules, the real-world dosing of 100 patients is equivalent to treating 161 if the recommended SmPC dosage was followed.
- For Adalimumab, the real-world dosing of 100 patients is equivalent to treating 121 patients with the recommended SmpC dosage.
- Vedolizumab has the smallest patient equivalence with the real-world dosing of 100 patients being equivalent to treating 117 patients with the dosage defined in the SmPC

4 Conclusion

- Patients diagnosed with IBD may require dosage escalation of their treatment to facilitate achieving and/or maintaining remission. However, this study demonstrated that there is a large percentage of patients in Portugal, who start maintenance treatment already with a dosage increase, this being especially noticeable with Ustekinumab, where the vast majority of patients has a dosage escalation *ad-inicium*.
- Regarding the annual maintenance dosage analysis (excluding the induction phase), it is possible to conclude that there is a large percentage of patients who undergo a dose escalation during the first year of maintenance. This phenomenon is visible in most molecules, with Vedolizumab being the exception, where less than half of the patients suffer a dosage increase.
- The utilization of patient equivalence methodology enabled the estimation of supplementary patients that can be treated using the standard therapy dose within a certain period, which is useful for budgetary planning. It is clear that, for Infliximab and Ustekinumab, the dose escalation for 100 patients is equivalent to treating 161 patients, in case the recommended SmPC dosage was followed. On the other hand, Adalimumab and Vedolizumab have the lowest patient equivalence with the real-world dosing of 100 patients being equivalent to treating 121 and 117 patients with the standard dosage, respectively.
- In summary, the dose escalations observed in the Portuguese clinical practice, may have clinical implications, resulting in unexpected drug costs to payers in Portugal.

Limitations

The data presented is provided in an aggregated form each month by the hospitals, without any weekly detail. Therefore, it is only possible to analyze monthly and annual dosages, which does not allow for the determination of the exact weekly intake frequency. Results are aggregated for both conditions (UC/CD).

The annual dosage analysis corresponds to the average annual consumption of the in-scope patients and does not consider the moment from which each patient undergoes a dose escalation. Additionally, since the dosage of Infliximab is determined based on the patient weight and this data is not provided by the hospitals, this calculation was made by considering the average weight of women and men.

Funding and Disclosures

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