

Real World Assessment of Biological Treatment of Inflammatory Bowel Disease at an Austrian Referral Centre: The ULTIMATE Study

Hans Peter Gröchenig^a, Evelyn Walter^b, Andreas Redl^c, Monika Bresztowanszky^a, Karin Steidl^a, Franz Siebert^a and Gottfried Novacek^d

^a Barmherzige Brüder Krankenhaus St. Veit/Glan, ^bIPF Institute for Pharmaeconomic Research, Vienna, ^c Datamedrix GmbH, ^d Medical University of Vienna

Background

Inflammatory bowel diseases (IBD) are characterized by a chronic or relapsing inflammation of affected gut segments leading to progressive gut damage and intestinal complications. Biologics are considered to be the most effective treatment options nowadays. However, primary nonresponse, loss of response and side effects may occur in a clinically relevant number of patients.

Objectives

The main objectives of this analysis were to describe treatment duration, dose escalations and additional dose requirement with biologics as well as hospitalisation rates during treatment periods.

Methods

This was a retrospective single centre cohort study at an Austrian referral IBD centre. All consecutive patients with Crohn’s disease (CD) (n=93) or ulcerative colitis (UC) (n=53) who initiated a biologic treatment with TNF-alpha-inhibitors and vedolizumab between 01/2006 – 10/2016 were included. Only patients with complete follow up were considered as treatment line. Medical characteristics including details of treatment with biologics were captured from chart review. The study outcomes were treatment duration, the need for dose escalation with biologics and hospitalisation rates. We performed a descriptive analysis.

Table 1: Patient characteristics			
	IBD	CD	UC
Patients; n	161	104	57
Female; n (%)	94 (58.4%)	64 (61.2%)	30 (52.6%)
Age (yrs); mean (SD)	44.7 (15.3)	43.4 (14.9)	46.7 (16.2)
Weight (kg); mean (SD)	69.1 (15.0)	67.8 (16.9)	71.2 (13.0)
Follow-up from the initiation of biologics (months); median (Q ₁ ; Q ₃)	35.2 (18.5;71.0)	41.8 (21.6;81.6)	26.5 (15.3;52.8)
Treatment lines; n	268	170	98

SD = Standard Deviation; Q₁; Q₃ = first and third quartile
The following inclusion and exclusion criteria must be fulfilled:

Inclusion Criteria:
1) Patients who received the first dose of any biologic therapy for the treatment of IBD (CD or UC) within the enrolment period that starts with 01/2006 – 10/2016.
Exclusion Criteria:
1) Biologic index date for initial therapy outside the enrolment period.
2) Lost to follow-up for reasons other than death.

Eligible patients must be willing to understand, accept and sign the Informed Consent Form (ICF) to participate in this project. If the patient refuses to participate for any reasons and does not sign the ICF, his data were excluded.
The project was approved by a national Independent Ethics Committee.

Results

The number of patients who received each treatment lines (N = 268) are presented in the table 2.

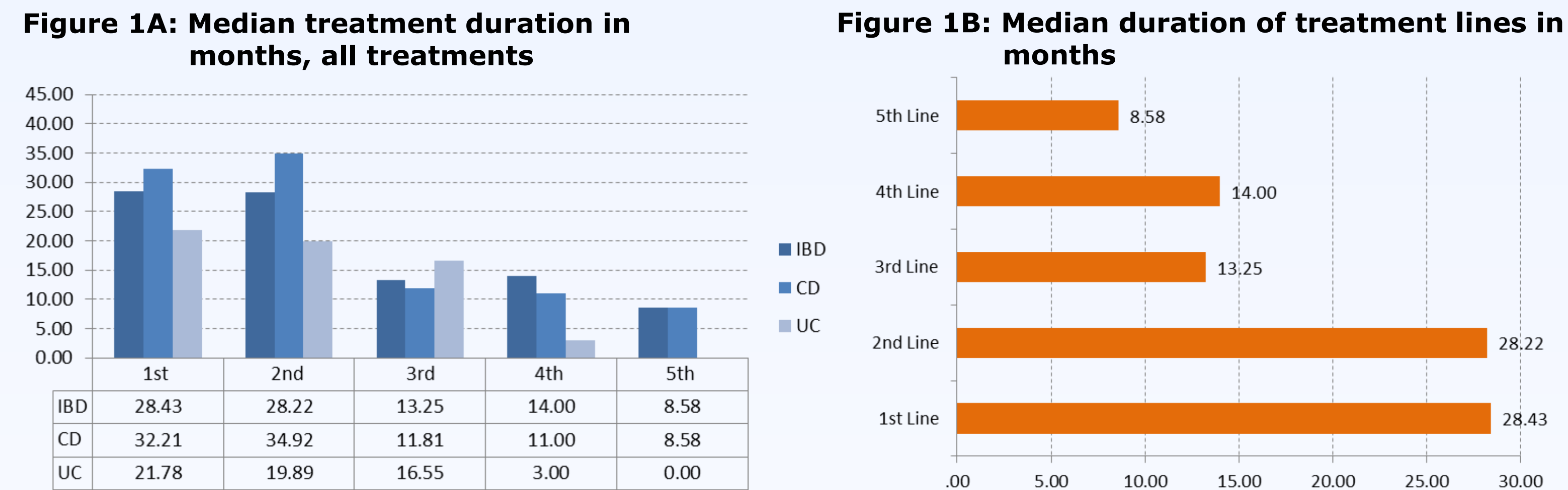
Table 2: Description of analysed treatment lines after conventional treatment of IBD patients (CD/UC)						
Treatment lines	Adalimumab	Infliximab	Vedolizumab	Golimumab	Other	Total
1 st line	73 (59/14)	61 (32/29)	6 (1/5)	6 (1/5)	0	146 (93/53)
2 nd line	26 (18/8)	20 (14/6)	26 (12/14)	3 (1/2)	3 (2/1)	78 (47/31)
3 rd line	1 (0/1)	6 (4/2)	16 (9/7)	2 (2/0)	2 (1/1)	27 (16/11)
4 th line	0	3 (3/0)	3 (3/0)	5 (3/2)	3 (2/1)	14 (11/3)
5 th line	0	0	0	1 (1/0)	2 (2/0)	3 (3/0)
Total	100 (77/23)	90 (53/37)	51 (25/26)	17 (8/9)	10 (7/3)	268 (170/98)

Other = Anti IL-12/IL-23

Importantly it has to be mentioned when interpreting results, that according to the Austrian reimbursement guidelines vedolizumab is reimbursed primary in the 2nd+ Lines.

Treatment duration

Over all treatment lines the median duration of line was 25.5 months. The median duration of a treatment line was longer in CD patients (29.3 months) than in patients with UC (20.0 months) (see Fig. 1A for details). Median duration of 1st, 2nd, and 3rd line biologic treatments in CD patients were 32.2, 34.9, and 11.8 months, respectively, compared to 21.8, 19.9, and 16.6 months in UC patients.



Considering the duration of the 2nd+ lines compared to TNF-alpha inhibitors, vedolizumab was below the median of the IBD therapy lines (p-value 0.0033). The median duration for TNF-alpha inhibitors was 32.8 months.

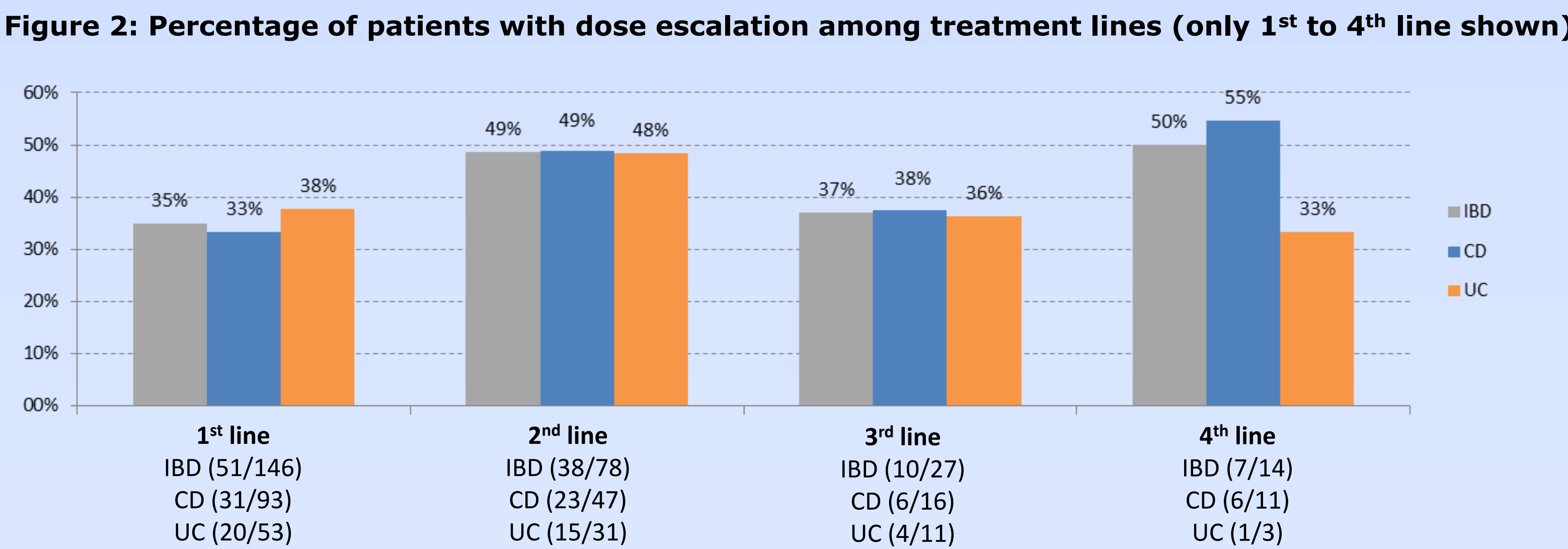
The median duration of 3rd and 4th line therapy with vedolizumab was numerical longer than the median duration of 3rd and 4th line therapy with TNF-alpha inhibitors (3rd line: 15.3 months vs. 12.6 months or 4th line: 19.5 months vs. 17.6 months).

Dose escalation

Dose escalation refers to maintenance therapy exclusively. The term dose escalation is defined as follows:

- dose increase
- shortening of the administration intervals
- both
- at least one dose escalation within a treatment line

Dose escalation was required in 39.6% of all therapy lines (n=106/N=268). This was required in 34.9% of all 1st line treatments (n=51/N=146) and increased in subsequent lines to 45.1% (n=55/N=122) (figure 2).



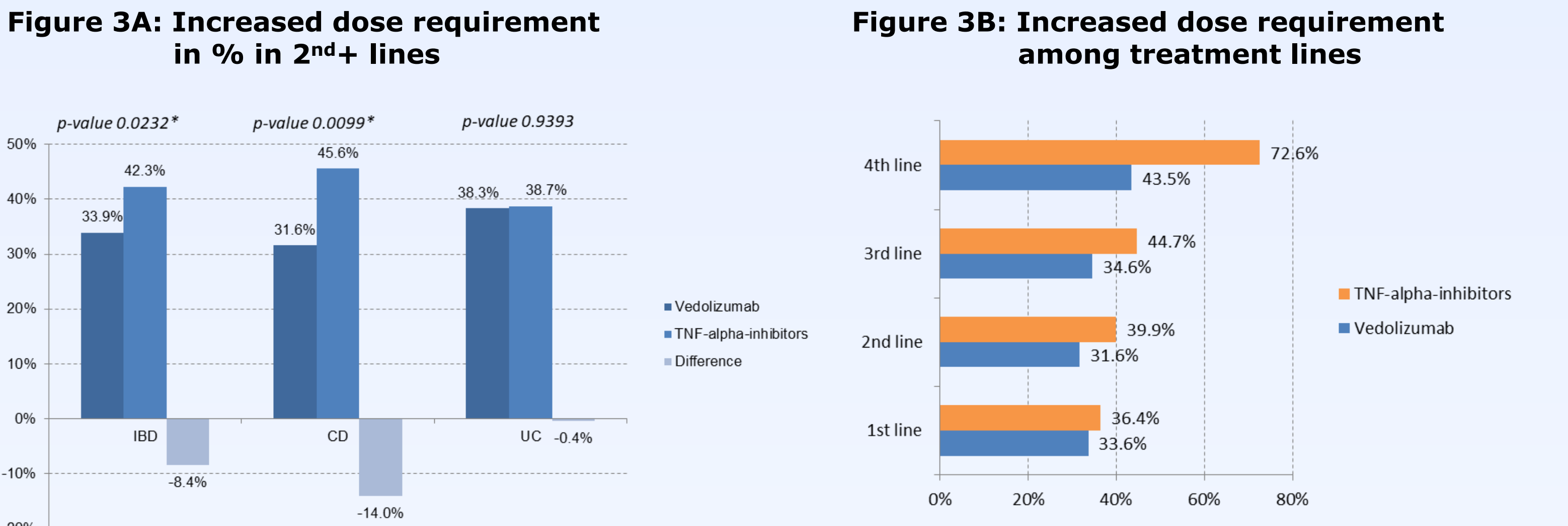
A consideration of the 2nd+ lines came to the following results: TNF-alpha inhibitor therapy (adalimumab, infliximab including biosimilars) was escalated in 48.2% (n=27/ N=56) of all cases. With vedolizumab there was a dose escalation in 57.8% of all cases (n=26/N=45) (p-value 0.0057). The observed time to first dose escalation was 52 weeks (SD 67.8) in average.

Increased dose requirement

The increased dose requirement resulted from the difference between the dosage stated in the product information (SPC dose) and the dose actually administered within a therapy line. Calculations thus compare the theoretical dosage (SPC dose) throughout the full time of a therapy line to the actually administered dose within a therapy line. For infliximab weight dependant dosage was considered and calculated.

In IBD patients the dose was increased by 37.1% compared to the standard dose in all treatment lines; of which 36.9% were in CD patients and 38.5% in UC patients.

In patients who received 2nd+ lines, the dose increase for TNF-alpha-inhibitors (adalimumab, infliximab including biosimilar) was higher (42.3%) compared to vedolizumab (33.9%) (p-value 0,0232); vedolizumab was primarily used as 2nd and 3rd line treatment. Detailed information are displayed in figure 3A and 3B.



Conclusion

The duration of 1st and 2nd biologic treatment lines were both nearly 3 years for CD and nearly 2 years for UC, respectively, and decreased with subsequent treatment lines. Overall, approximately 40% of all IBD patients needed dose escalation of their biologic treatment. Results are based on a single center experience that is not generalizable to overall IBD patients in EU.

Acknowledgement

This study was supported by Takeda Pharma Ges.m.b.H., Vienna, Austria