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DRUG DISCONTINUATION AND HEALTHCARE COST EVALUATION IN CROHN'S DISEASE PATIENTS UNDER BIOLOGIC THERAPY: AN ITALIAN RETROSPECTIVE ANALYSIS

CLICON S.R.L. HEALTH ECONOMICS & OUTCOMES RESEARCH

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BACKGROUND AND OBJECTIVES

Crohn's Disease (CD) is a highly debilitating chronic inflammatory condition affecting different gastrointestinal tracts [1]. The use of biologic drugs is indicated in patients with moderate-severe disease who have an inadequate response to conventional systemic therapy [2]. To date, evidence on the pharmacoutilization of biologics and resource consumption for the treatment of patients with CD in real-world clinical practice in Italy is limited [3].

This real-world analysis evaluated the persistence and healthcare direct costs in CD patients undergoing the biologic treatments currently available in Italy in a setting of real clinical practice.

METHODOLOGY

A retrospective analysis was conducted on administrative databases of geographically distributed Italian healthcare entities, covering about 10.4 millions health-assisted individuals (**Figure 1**).

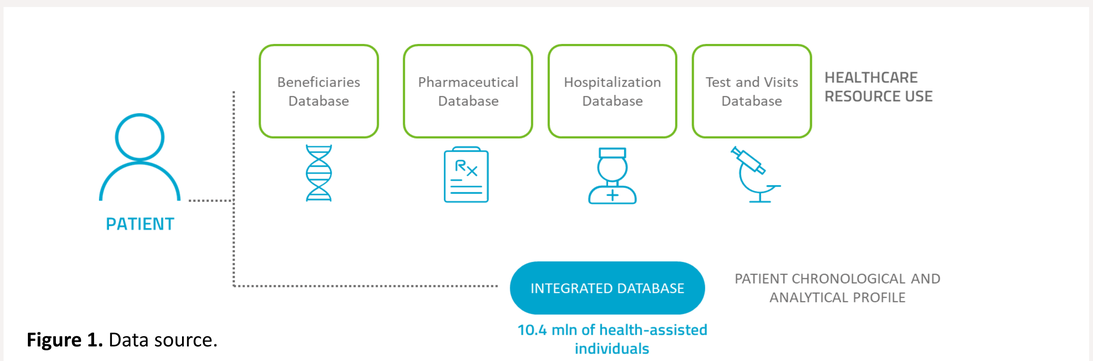

Figure 1. Data source.

STUDY POPULATION AND TREATMENTS

Adult CD-patients, **biologically-treated throughout 2015-2020** (inclusion period) were identified by at least one hospitalization (ICD-9-CM:555) or exemption code (009.555).

The following biologic drugs currently available in Italy [4] were evaluated: adalimumab (ATC code: L04AB04); infliximab (ATC code: L04AB02); vedolizumab (ATC code: L04AA33); ustekinumab (ATC code: L04AC05).

The index-data was the time of the first prescription of a biologic drug.

Patients were then attributed **to first- or second-line** based on absence/presence of biologic prescriptions 5-years prior the index date. Survival curves were built evaluating **drug-discontinuation**, meant as duration of therapy until discontinuation within the "grace-period" (twice the prescriptions interval, according to SmPC posology).

Healthcare mean direct costs/patient related to drugs (ex-factory prices), hospitalizations, specialistic services (visits/diagnostics tests) were assessed one-year before and after the index date. A multivariate model was performed for drug discontinuation by adjusting baseline variables.

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***DISCLOSURE**: Janssen-Cilag SpA purchased the study report that is the basis for this poster presentation. This poster was developed with Janssen-Cilag SpA and CliCon S.r.l. Società Benefit. The views expressed here are those of the authors and not necessarily those of the supporters. VP, MD, DS, MA, SA, AB, FB, ACavaliere, ACiaccia, MRC, RC, ACostantini, SDO, SG, RM, EM, CP, DR, FS, AV, LDE report no conflicts of interest in this work. The agreement signed by Clicon S.r.l. and Janssen-Cilag SpA does not create any entityship, joint venture or any similar relationship between parties. Clicon S.r.l. is an independent company. Neither CliCon S.r.l. nor any of their representatives are employees of Janssen-Cilag SpA for any purpose. OS, AS, AF are employees of Janssen-Cilag SpA.*

RESULTS

TREATMENT PATTERNS ACCORDING TO TREATMENT LINES DURING FOLLOW-UP

In total **1,398 CD patients were included**. Of them 89.8% (N=1,256) were in first-line treatment as follows: adalimumab (N=802), infliximab (N=361), vedolizumab (N=89), ustekinumab (N=52), during the follow-up. The remaining 9.7% (N=135) were in second-line treatment and the drug pattern was: adalimumab (N=144), infliximab (N=96), vedolizumab (N=86), ustekinumab (N=110), during the follow-up (**Figure 2**).

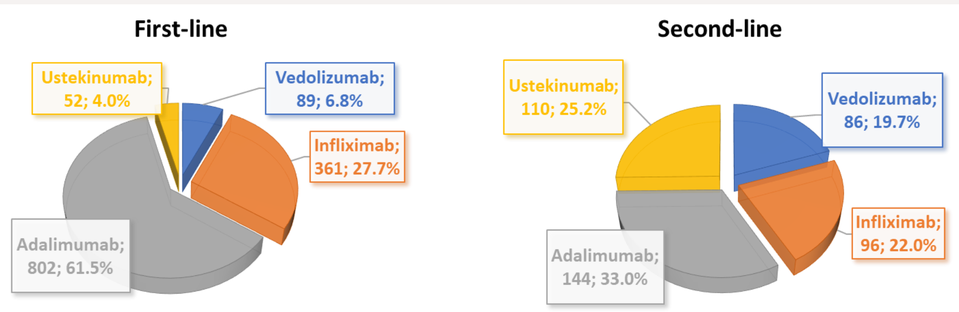

Figure 2. Biologic drug treatment patterns in first- and second-line treatment lines during follow-up.

PERSISTENCE ACCORDING TO BIOLOGIC DRUGS

Kaplan Meier curves revealed a higher persistence for ustekinumab compared to the other biologics both in first- and second-line (**Figure 3**).

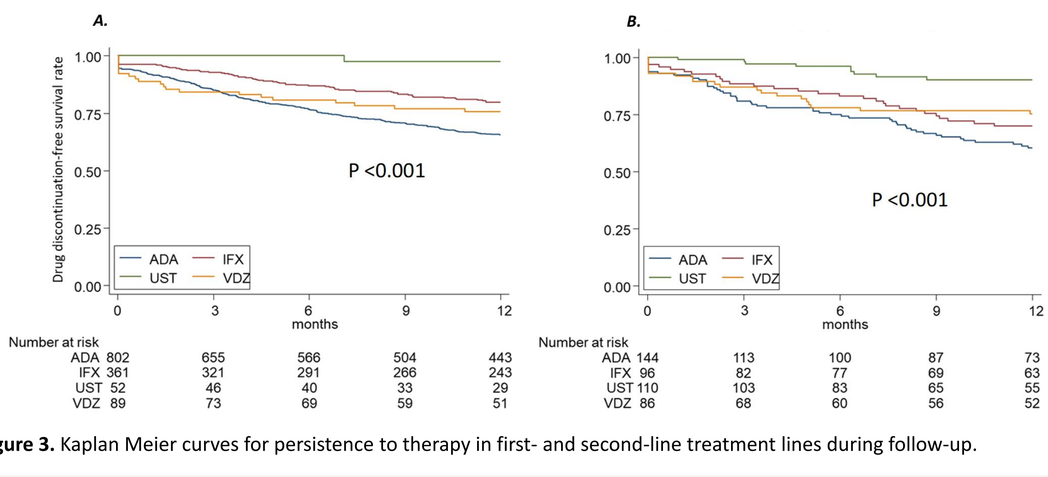

Figure 3. Kaplan Meier curves for persistence to therapy in first- and second-line treatment lines during follow-up.

Multivariate analysis, considering baseline variables and adalimumab as reference, showed that infliximab in first-line (HR: 0.537) and ustekinumab in first- (HR: 0.057) and second-line (HR: 0.213) resulted in a **significantly lower risk of drug-discontinuation**; vedolizumab showed no significant difference (**Table 1**).

Table 1. Multivariate model for persistence in first- and second-line treatment with biologics (discontinuation around grace period)

FIRST-LINE	HR	95% CI		p	SECOND-LINE	HR	95% CI		p
Adalimumab	**REF.**				**Adalimumab**	**REF.**			
Infliximab	0.537	0.412	0.701	**0.000**	Infliximab	0.702	0.444	1.109	0.129
Ustekinumab	0.057	0.008	0.404	**0.004**	Ustekinumab	0.213	0.105	0.432	**0.000**
Vedolizumab	0.740	0.471	1.161	0.190	Vedolizumab	0.687	0.408	1.154	0.156
Age	0.996	0.989	1.003	0.266	Age	0.980	0.966	0.994	**0.006**
Male	0.931	0.755	1.148	0.504	Male	0.919	0.624	1.352	0.667
CCI	1.036	0.883	1.214	0.667	CCI	1.211	0.857	1.711	0.277

MEAN HEALTHCARE COSTS PER PATIENTS IN FIRST- AND SECOND-LINE TREATMENT AT 1-YEAR FOLLOW-UP

After 1-year follow-up, in first-line the total average healthcare direct-costs/patient accounted for €13,636, €11,201, €17,104 and €18,339 in patients treated with adalimumab, infliximab, ustekinumab and vedolizumab, respectively; in second-line, 14,645€ with adalimumab, 12,199€ with infliximab, 17,270€ with ustekinumab, and 18,175€ with vedolizumab (**Table 2**).

Table 2. Healthcare direct costs for the management of CD patients during one year before (pre) and after (post) index date.

	ADALIMUMAB		INFLIXIMAB		USTEKINUMAB		VEDOLIZUMAB	
Patients in first-line	**pre**	**post**	**pre**	**post**	**pre**	**post**	**pre**	**post**
Total costs (€)	3,026	13,636	2,641	11,201	4,380	17,104	4,999	18,339
Patients in second-line	**pre**	**post**	**pre**	**post**	**pre**	**post**	**pre**	**post**
Total costs (€)	9,462	14,645	11,292	12,199	7,892	17,270	7,933	18,175

CONCLUSIONS

This **real-world analysis in CD biologic-treated patients** showed heterogeneity on persistence, being higher in ustekinumab-treated group.

The results should be interpreted in view of some study limitations, such as its observational design, the small sample size of certain subgroups, persistence rate evaluation based on the “grace period” approach since dosage schedule of some drugs could have contributed to the persistence rates observed.

Patients’ management was associated with quite comparable healthcare direct costs, mainly driven by drug-related costs.

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