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A PROPENSITY SCORE-WEIGHTED COMPARISON OF VEDOLIZUMAB AND ADALIMUMAB IN CROHN'S DISEASE: REAL-LIFE DATA FROM THE SICILIAN NETWORK FOR INFLAMMATORY BOWEL DISEASE (SN-IBD)

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BACKGROUND

- **The recent VARSITY study showed superiority of Vedolizumab (VDZ) over Adalimumab (ADA) in UC.**

- **There are no randomized controlled trials on direct comparisons between biologics in Crohn's disease.**

- **Relevant findings con be obtained with real-life observational studies, particularly when the comparison between different treatments is performed by propensity score analysis.**

AIMS

Web-based data from the cohort of the Sicilian Network for Inflammatory Bowel Disease (SN-IBD) were extracted to perform a multicentre, real-life comparison of the effectiveness of VDZ and ADA in Crohn's disease through a propensity score weighted study.

METHODS
Patients

- **The SN-IBD is a regional group composed of all 16 centers licensed to prescribe biologics in Sicily**

- **Since January 2013, these centers enter inside a web-based software detailed, real-life, prospective data on patients with IBD treated with biologics, with the aim of monitoring efficacy, safety, and costs of these therapeutics**

- **Data of all consecutive CD patients treated with VDZ or ADA from January 2016 to April 2019 were extracted from the cohort of the SN-IBD**

- **Subjects who received the biological treatment for extra-intestinal manifestations or complex perianal disease without active luminal disease, as well as those with less than 16 weeks of follow-up, were excluded from the analysis.**

METHODS
Measures of outcomes

- **The effectiveness was evaluated at 12, 52 weeks, and as treatment persistency at the end of follow up, and all adverse events were reported.**

- **Clinical endpoints:**
  - **Steroid-free clinical remission (Harvey-Bradshaw Index < 5 without steroid use)**
  - **Clinical response (reduction of the Harvey-Bradshaw Index ≥ 3 points with a concomitant decrease of steroid dosage compared with baseline)**
  - **Steroid-free clinical remission plus clinical response = clinical benefit**
  - **Treatment failure: discontinuation of VDZ or ADA due to adverse events or inefficacy**
  - **Rate of surgery at the end of follow-up**

- **Endoscopic endpoints (after at least 6 months of treatment):**
  - **Mucosal healing (SES-CD ≤ 2)**
  - **Endoscopic response (a reduction of SES-CD ≥ 50% compared with baseline)**

STATISTICS
Propensity score (IPTW)

- **A propensity score-weighted analysis was performed to reduce the effect of selection bias and simulate the effects of randomization.**

- **Propensity scores (the conditional probabilities of receiving VDZ or ADA given the observed covariates) were estimated using a non-parsimonious multiple logistic regression model based on all variables at baseline.**

- **Two distinct propensity score estimations were performed, one on the entire cohort for the assessment of the clinical outcomes at 12 weeks and at the end of follow-up, and another one for the assessment of the clinical outcomes at 52 weeks (for patients with at least 52 weeks of follow-up).**

- **Patient data were weighted with the Inverse Probability of Treatment Weighting (IPTW) method using stabilized weights.**

STATISTICS
Propensity score (IPTW)

- **IPTW-adjusted logistic regression analyses were performed to estimate the treatment effect at 12 and 52 weeks, while IPTW-adjusted Cox PH regression analyses were calculated for the estimation of the hazard ratio of the treatment effect on the discontinuation of the treatment and probability of surgery.**

- **A sensitivity analysis was made removing the subjects in the non-overlapping regions of the distribution of the propensity score, and performing IPTW-adjusted logistic regression and IPTW-adjusted Cox PH regression analyses.**

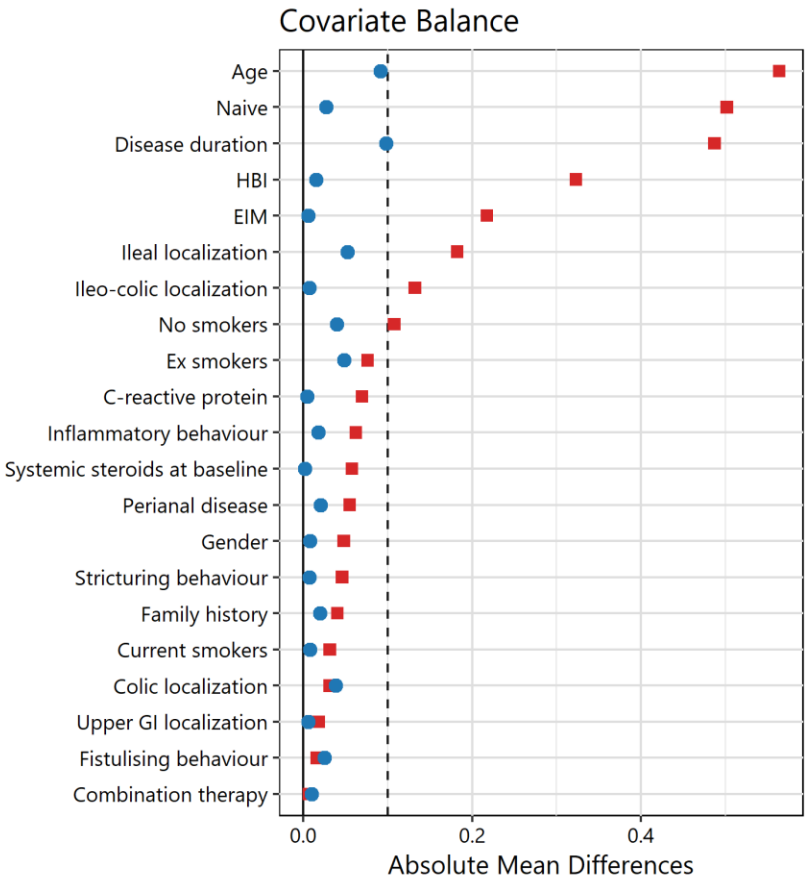
RESULTS
(N=585; median follow-up: 56 weeks)

Variable	ADA (n=308)	VDZ (n=277)	p
Age (years), median [I.Q.R.]	40.8 [28.5, 52.7]	52.0 [37.0, 64.0]	**<0.001**
Age at diagnosis (years), median [I.Q.R.]	31.0 [21.1, 43.0]	36.0 [23.0, 50.0]	**0.002**
Duration of disease (years), median [I.Q.R.]	6.0 [2.0, 12.0]	10.0 [6.0, 18.0]	**<0.001**
Extraintestinal manifestations, n (%)	62 (20.1%)	116 (41.9%)	**<0.001**
Previous resections, n (%)	117 (38.0%)	153 (55.2%)	**<0.001**
Disease Activity			
Harvey-Bradshaw Index, mean ± S.D.	5.6 ± 4.2	6.8 ± 3.6	**<0.001**
Simple endoscopic score for CD (SES-CD), median [I.Q.R.]	9.0 [7.0, 15.0]	9.0 [6.0, 15.0]	0.920
C-Reactive Protein above the U.L.N., n (%)	146 (47.6%)	112 (40.4%)	0.107
Previous lines of biologics, n (%)			
0 (naïve)	249 (80.8%)	85 (30.7%)	**<0.001**
1	56 (18.2%)	84 (30.3%)	
2	3 (1.0%)	108 (39.0%)	

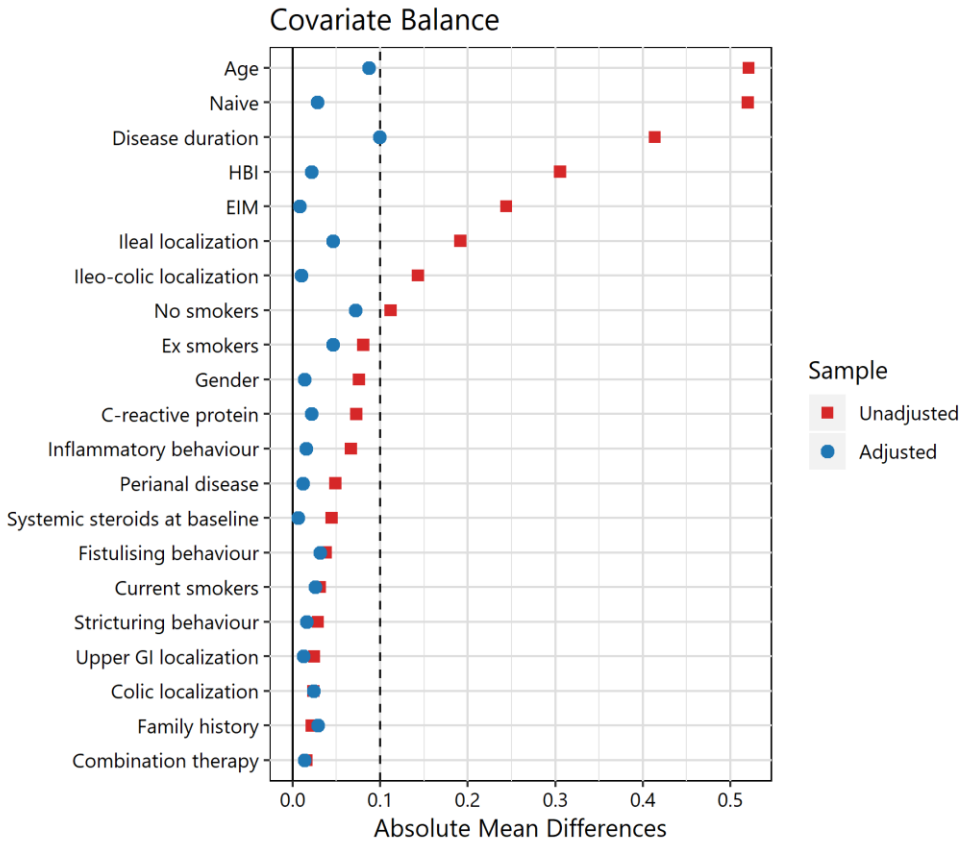
RESULTS

Plots of absolute standardized mean differences before and after propensity score weighting

Entire cohort



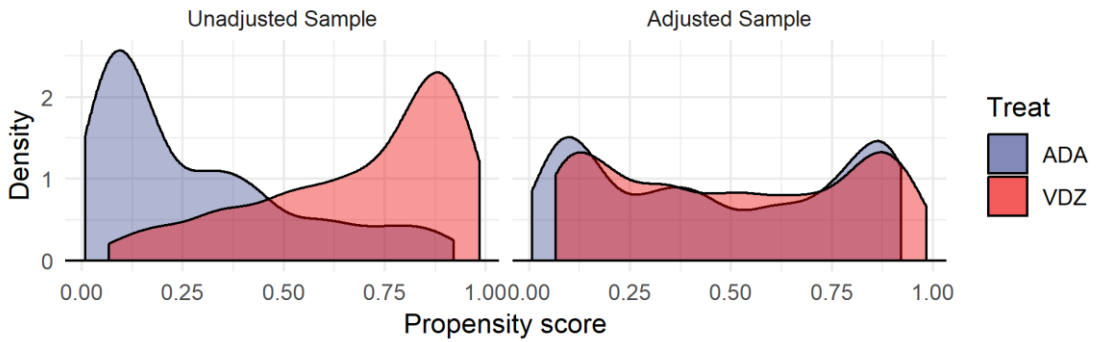
52 weeks of follow-up



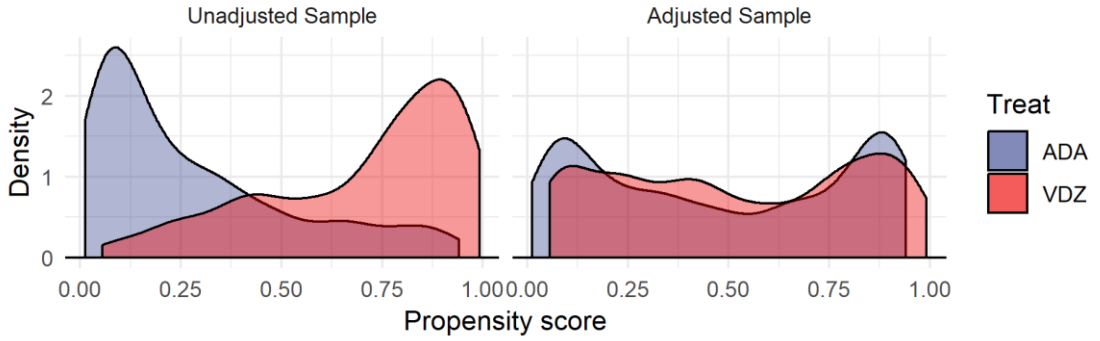
RESULTS

Overlap of the propensity score distributions between the two treatments

Entire cohort

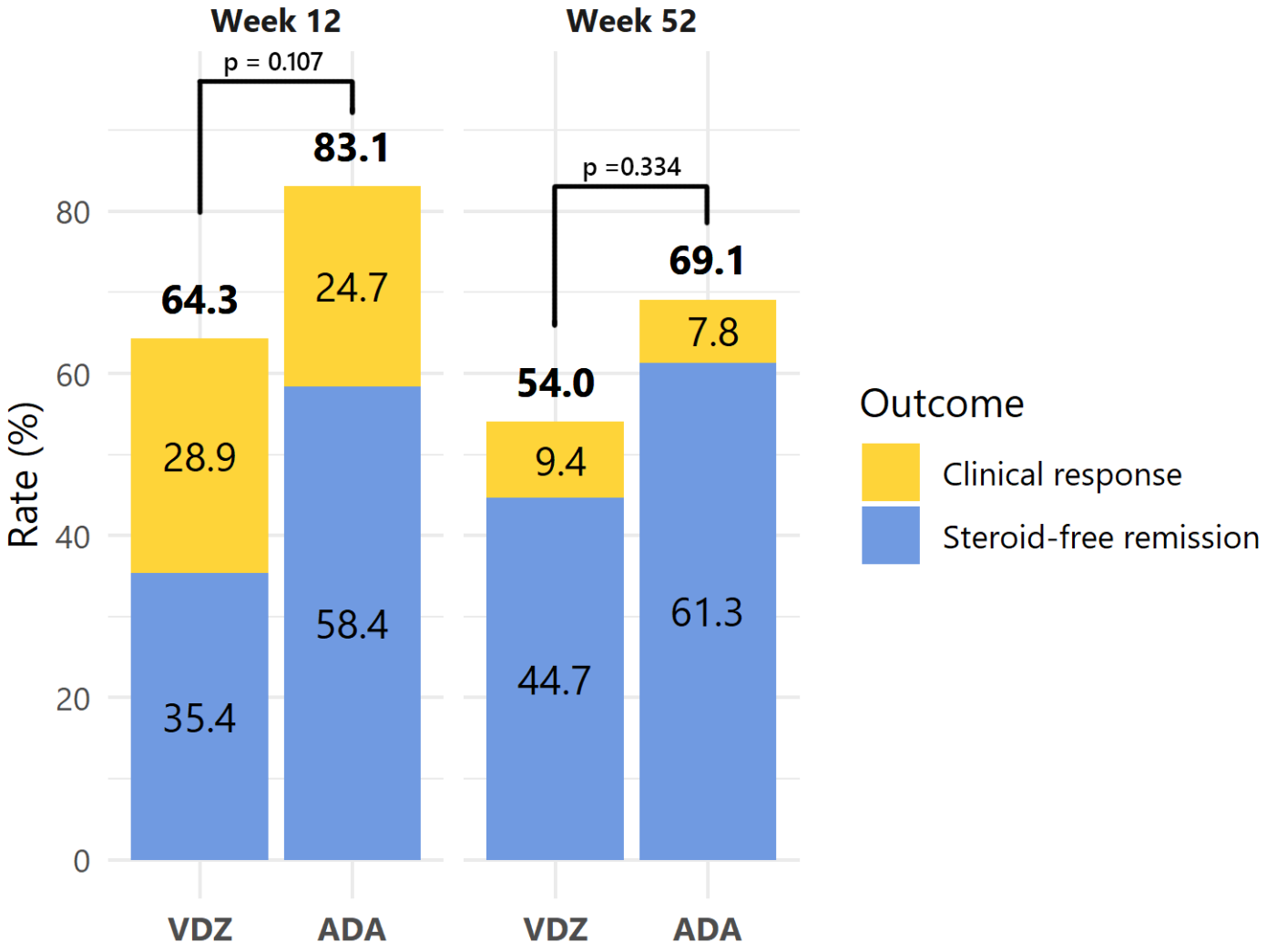


52 weeks of follow-up



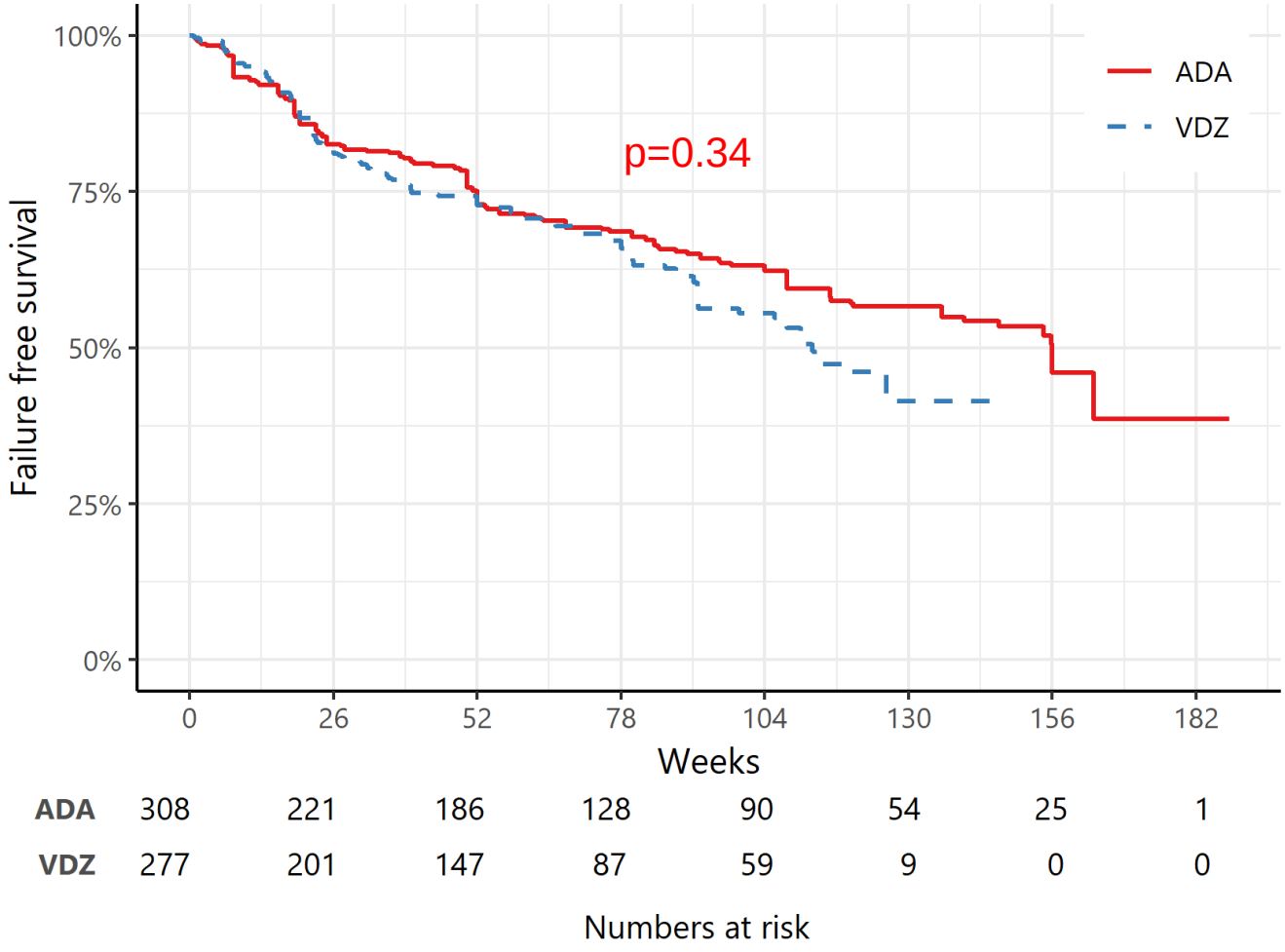
RESULTS

Clinical effectiveness at 12 and 52 weeks



RESULTS

Clinical effectiveness: treatment persistency



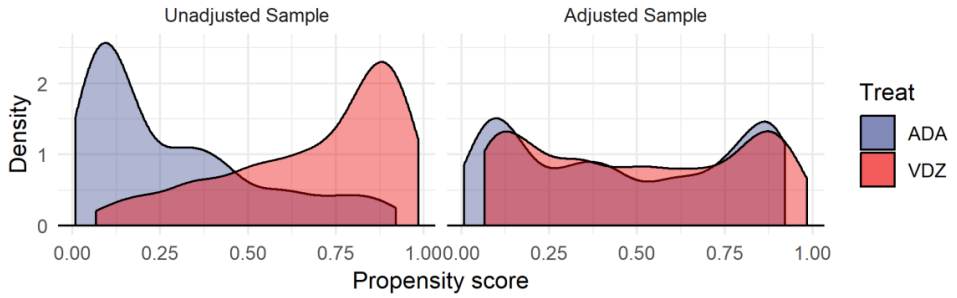
RESULTS

- At the end of follow-up, 28 patients (10.1%) treated with VDZ and 12 (3.9%) treated with ADA underwent surgery (HR for VDZ =2.21; p=0.136 in propensity score analysis)

- At the end of follow-up, 230 patients (39.3% of the entire cohort) underwent post-treatment colonoscopy (85 in the VDZ group and 145 in the ADA group):
  - Endoscopic response: 35.3% for VDZ and 25.5% for ADA, p=0.150
  - Mucosal healing: 31.8% for VDZ and 33.8% for ADA, p=0.850

- 58 adverse events were reported in patients treated with VDZ (IR=18.7 per 100 person-years) and 70 adverse events in patients treated with ADA (IR=16.7 per 100 person-years) The rates of adverse events were not significantly different between the two groups (IRR for VDZ=1.15 [95% CI 0.79-1.58], p=0.538).

- Sensitivity analysis: same results.



Conclusions

- **In the first real-life study comparing VDZ and ADA in CD patients via propensity score analysis, both drugs showed a comparable – and good – effectiveness after 12, 52 weeks, and as treatment persistence, with a similar safety profile.**

- **These results represent valid assistance for the physicians in the choice of the most appropriate treatments for CD.**

- **All real-life observational studies performed without propensity score analysis are inadequate to compare different treatments.**