

# Alcohol abuse and discretionary habits in psoriatic patients: impact on IL-17 and IL-23 inhibitors response

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## Summary

**Background:** Alcohol abuse is correlated with the onset and worsening of psoriasis, but its effects, as for smoking, on biological therapies are still poorly investigated.

**Materials and methods:** This study aimed to determine the prevalence of alcohol abuse and other discretionary habits (such as smoking and sedentary lifestyle) in patients with psoriasis treated with topicals, conventional systemic and biologic therapies. The second objective is to investigate the impact of discretionary habits, focusing on alcohol abuse, on the response to biological therapy. To identify alcohol dependence, the CAGE questionnaire was distributed among patients of our clinic.

**Results:** 305 patients were included with 18% at high risk of alcohol abuse. Clinically, guttate psoriasis and psoriatic arthritis were more common in patients at higher risk of alcohol abuse. Furthermore, patients with an alcohol problem who started biological therapy reported a higher PASI than those who drank less. None of the considered variables seemed to correlate with discontinuation of medication or with lower achievement of the analyzed outcomes (PASI100, PASI90, and PASI $\leq$ 3). There was a stronger association between alcohol dependence and patients receiving conventional therapy than with patients receiving biologics.

**Conclusions:** The efficacy of biologicals did not seem to be impacted by alcohol consumption, smoking, or sedentary lifestyle.

## KEYWORDS

alcohol, CAGE, drug survival, effectiveness, Psoriasis

## INTRODUCTION

Psoriasis is a chronic, recurrent, inflammatory skin disorder. The most common clinical manifestations are erythematous plaques and scaly plaques. The disease affects 0.5–11% of the adult population worldwide, with a prevalence of about 3% in Italy.<sup>1–4</sup> Mild forms of psoriasis can be managed with topical treatments including corticosteroids, vitamin D

analogues, steroid plus vitamin D analogue combinations, calcineurin inhibitors, and keratolytics. Phototherapy may be an option for moderate forms of psoriasis. Traditional systemic treatments such as methotrexate, cyclosporine A, and acitretin are still widely used as first-line treatments for moderate-to-severe forms of psoriasis.<sup>2–5</sup>

Biological therapies have demonstrated high efficacy and safety in the treatment of moderate-to-severe psoriasis in recent years.<sup>6</sup> Interleukin (IL)-17 and IL-23 inhibitors not only allow patients to achieve clinical scores such as Psoria-

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sis Area Severity Index (PASI)90 and PASI100, but also have an important impact on quality of life.<sup>1</sup> Lifestyle factors such as stress, smoking, alcohol abuse, and obesity are known to influence disease onset,<sup>3,4,7</sup> with the latter being related to sports activity and nutrition. However, their impact on psoriatic disease remains poorly understood.<sup>8,9</sup>

Iskandar et al. previously investigated the connection between alcohol abuse and psoriasis using the CAGE questionnaire, reporting that alcohol misuse correlates with the onset and worsening of disease, especially in patients not on treatment.<sup>8</sup> The aim of the present study is to describe alcohol addiction in the psoriatic population, and to elucidate the impact of discretionary habits (smoking habits and sedentary lifestyles) on biological treatment response.

## METHODS

### Population

Patients > 18 years of age with a diagnosis of psoriasis who presented to the clinic and completed the CAGE and discretionary habits questionnaires between October 1, 2002 and April 31, 2003 were included in the study, regardless of disease severity, type of ongoing treatment, or other demographic characteristics. Medical information was retrieved retrospectively from medical records, including pharmacological therapy, from the start of their therapy until the questionnaire visit.

### Endpoints

Primary endpoints:

- Describe alcohol addiction of psoriatic patients by a cross-sectional analysis of patients' responses to a specific questionnaire (CAGE),
- Describe discretionary habits in the same population with a general questionnaire on smoking habit and daily activity.

Secondary endpoints:

- Retrospectively describe the impact of discretionary habits on the response to biological treatment.

A cross-sectional analysis with the CAGE questionnaire was used to assess potential alcohol abuse or dependence in the psoriatic population that was followed at the Dermatologic Clinic of University of Turin. The CAGE questionnaire,<sup>10</sup> according to the American Addiction Center, is a 4-question screening tool that can be used by clinicians to help in the diagnosis of alcoholism. CAGE is an acronym for (Cutting Down; Annoyance by Criticism;

Guilty Feeling; Eye-openers). Each letter of the acronym corresponds to a specific question:

- Have you ever felt you should cut down on your drinking? (Cutting Down)
- Have people annoyed you by criticizing your drinking? (Annoyance by Criticism)
- Have you ever felt bad or guilty about your drinking? (Guilty Feeling)
- Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (Eye-opener)?

A positive CAGE ( $\geq 2$  affirmative answers) identifies patients with alcohol misuse. In addition to alcohol-related questions, the questionnaire also queried about lifestyle habits (smoking, body weight, and sedentary lifestyle). In order to assess the validity of the CAGE questionnaire, we calculated the number of alcohol units consumed per week and per month by each patient and assessed the results against the "binge drinker" category. According to the *National Institute on Alcohol Abuse and Alcoholism* (NIAAA), World Health Organization (WHO), Center for Disease Control (CDC), a "binge drinking episode" is defined as the consumption of five or more standard drinks for men and four or more standard drinks for women within a 2-hour period or on a single occasion.<sup>11</sup>

Information about lifestyle habits (minutes of walking per week, with less than 60 minutes considered as sedentary) and smoking habit (smokers, ex-smokers, non-smokers) was also recorded.

The information retrieved from the questionnaires was then compared to the severity of disease by PASI, sex, mean body mass index (BMI), clinical variant of psoriasis (psoriatic arthritis, guttate psoriasis, inverse psoriasis, vulgar psoriasis), and type of therapy (no therapy, topical therapy, traditional systemic therapy, and biological therapy). A retrospective analysis of patients on biological treatment was then performed to assess the impact of CAGE positivity on characteristics such as mean BMI, mean age of onset, naïve status, treatment response, and drug survival.

The treatment response was rated using drug survival (identifies the time until discontinuation) and mean PASI, PASI90, and PASI100 value at weeks 16, 28, and 52 from the start of treatment. The study complied with the *Ethical Standards of the 1975 Helsinki Declaration* and was approved by our local Ethics Committee under Protocol SS-Dermo20. All patients included in the study provided signed informed consent prior to their enrolment.

### Statistical Analysis

Continuous variables were described by mean  $\pm$  standard deviation (SD) or median and range, based on the distribution of each variable. Absolute and relative frequencies were reported for categorical variables. Percentages were

**TABLE 1** Percentage of affirmative responses per CAGE domain.

Domain	Results % (n°)
Cutting Down	21.97 (67)
Annoyance by Criticism	19.67 (60)
Guilty Feelings	18.36 (56)
Eye Openers	2.95 (9)

based on the number of non-missing values. Linear regression, using chi-squared test for categorical variables and t-student's test for continuous variables, followed by a mixed-effects logistic regression model, was used to investigate potential factors associated with CAGE positivity and the effect of discretionary habits (CAGE+, binge drinking, sedentary lifestyle), mean BMI, age of onset and bio-naïve status on achieving PASI100, PASI90 and PASI $\leq$ 3. To analyze drug survival, Kaplan-Meier analysis was employed. The event was defined as drug discontinuation for any reason while the time of observation was calculated as the date of the last follow-up – date of baseline. Cox (proportional hazards) regression was used to evaluate possible predictive factors associated with drug survival. Statistical analysis was conducted with STATA 15.1 SE (StataCorp., 2017). All tests were two-sided and statistical significance was set to  $\alpha = 0.05$ .

## RESULTS

A total of 305 patients (affected by psoriasis) were enrolled and were provided CAGE and discretionary habits questionnaires. Male patients were 64.9% (198), mean age 58 (SD 16), and mean BMI was 26 kg/m<sup>2</sup> (SD 5.3). Plaque psoriasis was diagnosed in 269 patients (87.9%), and 19 also presented aspects of guttate psoriasis; 55 patients presented only the guttate clinical variant (18%). Joint involvement was observed in 41 patients (13.4%). In all, 55 (18%) patients had a high risk of alcohol abuse or dependence according to CAGE criteria (at least 2 positive responses of the four questions).

Of the 305 patients, 111 (36.4%) responded positively to at least one question; 23 (7.5%) to at least three questions, and 1% all 4 questions of the CAGE questionnaire. In particular, 22% of patients responded yes to the "Cut Down" question, 19.67% to "Annoyed", 18.36% to "Guilty", and 2.95% to the "Eye opener" question, as shown in Table 1. Smoking habits were reported by 37.4% of patients (n = 114), past smoking habits by 34.4% (n = 105), and 28.2% of patients declared themselves as "never smoker". Sedentary lifestyle was reported by 49.7% of patients, i. e. walking less than 60 min per week.

We analyzed the number of alcohol units (AU) consumed per week and per month among CAGE positive and CAGE negative patients; first, binge drinkers had a higher probability of having CAGE positive results ( $p < 0.001$ ); also, binge drinkers had a greater alcohol intake compared to

non-binge drinkers ( $p = 0.001$ ), and those with a positive questionnaire had higher alcohol consumption both per week ( $p = 0.001$ ; AU mean = 6.58) and per month ( $p = 0.015$ ; AU = 4) (Table 2).

Several independent factors were directly associated with higher alcohol consumption (Table 3); these included high BMI (mean BMI in CAGE positive questionnaires of 28 kg/m<sup>2</sup>;  $p < 0.05$ ), male sex (23.23%), smoking (past or current smokers;  $p = 0.046$ ), or being a binge drinker (10.6%).

Regarding clinical diagnosis, patients affected by disease with clinical features different from vulgar psoriasis appeared to have a higher risk of alcohol misuse ( $p < 0.001$ ), even if they represented 11% of the sample. In particular, the guttate form of psoriasis was the most represented form in patients with CAGE positive questionnaires ( $p < 0.001$ ). In addition, patients presenting articular involvement were more prone to have alcohol misuse problems ( $p < 0.001$ ) (Table 4).

Mean PASI values analyzed at the time of questionnaire administration were higher in those with CAGE positive questionnaires compared to negative ones (4.93 vs. 2.12;  $p < 0.001$ ). We also evaluated possible differences in mean PASI if the questionnaire was administered at the start of systemic therapy (biological or traditional): in CAGE positive patients starting systemic therapy (n = 11) mean PASI was 12.18 vs. 6.77 in CAGE negative patients (n = 13) ( $p < 0.001$ ) (Table 4).

Regarding therapy, at the moment of questionnaire administration, 10% of CAGE positive patients were taking topical therapy, 35% conventional therapy, 13.62% biological agents, and 25% are using a combination of conventional and biological therapy. Biological therapy was associated with the least alcohol misuse ( $p < 0.001$ ). No significant differences were found between bio-experienced and bio-naïve patients when comparing CAGE results (15.9% vs. 16.1%); in bio-experienced group, no significant differences were detected between the multi-failure subgroup (defined as more than 4 biological failures),<sup>9</sup> and no multi-failure subgroup (18.75% vs. 18%) (Table 4).

Multivariate logistic regression of potential factors associated with a negative CAGE result was conducted (Table 3). Factors previously associated with a CAGE positive questionnaire, such as male sex (Odds Ratio [OR] 0.6; 95% confidence interval [CI] = 0.2–1.73;  $p = 0.341$ ), worse PASI (OR 0.88; 95% CI = 0.76–1.01;  $p = 0.074$ ) and being smokers (OR 1.04; 95% CI = 0.28–3.79;  $p = 0.955$ ), lost any significant correlation. However, being an ex-smoker was linked to a negative CAGE result (OR 3.3; 95% CI = 1.03–0.61;  $p = 0.045$ ). Guttate psoriasis and psoriatic arthritis (PsA) were strongly related to alcohol intake, both with an OR of 0.01 and a  $p < 0.001$  for negative CAGE. High BMI also showed a relation with alcohol abuse (OR 0.86; 95% CI 0.77–0.96;  $p = 0.007$ ), as well as binge drinking (OR 0.15; 95% CI 0.03–0.81;  $p = 0.027$ ). On the other hand, biologic therapy appeared to be significantly associated with the absence of alcohol addiction (OR 16.37; 95% CI 4.17–64.28;  $p < 0.001$ ).

**TABLE 2** Alcoholic units consumed by patients per week and per month, and CAGE positivity in binge drinkers and non-binge drinkers.

	AU per week			AU per month		
	Mean	SD	p value	Mean	SD	p value
CAGE +	6.58	2.96		4	0	
CAGE -	4.16	3.12	0.001	1.85	1.18	0.015
	Non-binge drinkers % (n)		Binge drinkers % (n)			
CAGE +	19.7 (40)		58.33 (14)			
CAGE -	80.3 (163)		41.67 (10)			

Abbr.: SD, standard deviation

**TABLE 3** Multivariate logistic regression model for CAGE negativity considering as independent factors: sex, guttate psoriasis, PsA, biological therapy, PASI, BMI, smoking habit (active or ex-smokers), binge drinking.

	p value	Odds ratio	95% CI
Sex	0.341	0.6	0.2–1.73
Guttate psoriasis	< 0.001	0.01	0–0.05
PsA	< 0.001	0.01	0–0.06
Biologic therapy	< 0.001	16.37	4.17–64.28
PASI	0.074	0.88	0.76–1.01
BMI	0.007	0.86	0.77–0.96
Smokers	0.955	1.04	0.28–3.79
Ex-smokers	0.045	3.3	1.03–10.61
Binge drinking	0.027	0.15	0.03–0.81

The secondary endpoint of the study evaluated the impact of discretionary habits and alcohol intake on biological treatment; 220 patients with at least 1 year of follow-up were included in the analysis. The aim was to identify possible connections between lifestyle and response to biological therapy through the evaluation of drug survival and PASI (PASI100, PASI90, PASI $\leq$ 3). The timepoints considered were 16, 28, and 52 weeks of therapy. First, no significant difference was detected for drug survival by CAGE ( $p = 0.295$ ) (Figure 1). Second, associations between drug survival and binge drinking, sedentary lifestyle and smoking were analyzed (Figure 1). None of the parameters considered were significantly associated with less or more risk of drug discontinuation, according to hazard cox-regression analysis, as summarized in Table 5.

CAGE positive patients showed lower achievement of PASI100 than CAGE negative patients at the same time points: at week 16, 39% vs. 43%, respectively; at week 52, this was achieved in 52% vs. 63% of patients, respectively (Table 6, Figure 2). For patients who achieved PASI90 or PASI $\leq$ 3, a similar trend was noted (Table 6, Figure 2).

None of the results correlating PASI values and possible alcohol misuse were significant in univariate analysis. In multivariate analysis, positive CAGE did not affect the achievement of PASI100, PASI90, or PASI $\leq$ 3 at week 16 ( $n = 220$ ), 28 ( $n = 184$ ), and 52 ( $n = 160$ ) after the start of biological therapy (Table 7). The decrease in patients at later time points made the multivariate model inaccurate, although no factor associated with achievement of PASI was found.

Other possible variables such as binge drinking, sedentary lifestyle, high BMI, age of psoriasis onset and bio-naïve status were evaluated in patients achieving PASI100, none of which reached statistical significance as shown in Table 7. A similar trend was observed for these variables for PASI90 (Table 7). An association between high BMI and greater disease severity in achievement of PASI $\leq$ 3 was found at week 28 ( $p = 0.016$ ), as shown in Table 7.

## DISCUSSION

Among patients with psoriasis in this study, 78.4% admitted to regular alcohol consumption, in contrast to 56% of the general Italian population.<sup>12</sup> A significant proportion of patients with psoriasis were CAGE positive (18%), indicating a probable alcohol problem: This value is slightly higher than that of the Italian population considered to be at “greater risk” in terms of health (15%) (Note: this percentage was not assessed by the CAGE questionnaire).<sup>12</sup> It can therefore be assumed that among patients with psoriasis there is a higher prevalence of alcohol abuse. On the other hand, no significant difference was reported between binge drinkers with psoriasis (7.9%) and the general Italian population (8%).<sup>12</sup> In the studies by MacAleer et al. and Kirby et al., between 13% and 30% of patients with psoriasis were considered to be alcoholics (percentage depending on the questionnaire used to evaluate alcohol dependence: Michigan alcohol screening test (MAST) or CAGE questionnaires).<sup>13–14</sup> In the study by Serwin et al., 20% of patients with psoriasis were excessive drinkers.<sup>15</sup> In the study by Gupta et al., 18.7% of psoriasis patients consumed more than 80 g alcohol per day.<sup>16</sup>

Among CAGE positive patients, the reported alcohol intake was 6.5 alcohol units per week, but this value may not be accurate, considering the strong tendency to admit to only a lower intake due to the fear of social shaming. The CAGE questionnaire has been validated for clinical practice to avoid such confounding factors (patients may underestimate their alcohol consumption and addiction when asked directly).

The differences between female and male sex are more evident in the sample of the psoriatic population than the healthy general population. One study found that 23.2% of men and 8.4% of women with psoriasis had risky alcohol

**TABLE 4** Association of CAGE results and independent variables.

Sex	CAGE +	CAGE -	p value
Man	23.23% (46)	76.77% (152)	
Woman	8.41% (9)	91.59% (98)	
<b>Smoke</b>			
Non-smoker	16.28% (14)	83.72% (72)	0.046
Past smoker	13.33% (14)	86.67% (91)	
Currently smoker	23.68% (27)	76.32% (87)	
<b>BMI</b>			
Mean BMI	28.28 kg/m <sup>2</sup>	26 kg/m <sup>2</sup>	0.005
<b>Clinical presentation</b>			
Atypical psoriasis	30.91% (15)	6.1% (15)	< 0.001
Classic psoriasis	69.9% (38)	93.9% (231)	
<b>Guttate psoriasis</b>			
Diagnosis YES	69% (9)	16% (46)	< 0.001
Diagnosis NO	31% (4)	84% (242)	
<b>Articular involvement</b>			
Absent	55% (30)	93% (230)	< 0.001
Present	45% (25)	7% (16)	
<b>PASI</b>			
PASI mean	4.93	2.12	0.001
PASI mean at biological prescription	12.18	6.77	0.039
<b>Therapy</b>			
No therapy	46.67%	53.33%	
Topical therapy	10%	90%	
Conventional therapy	35%	65%	
Biologic therapy	13.62%	86.38%	0.001 (less associated)
Conventional therapy+ biologic therapy	25%	75%	

**TABLE 5** Drug survival rates related to independent variables (CAGE positivity, binge drinking, sedentary lifestyle, smoking habits). Cox-regression analysis.

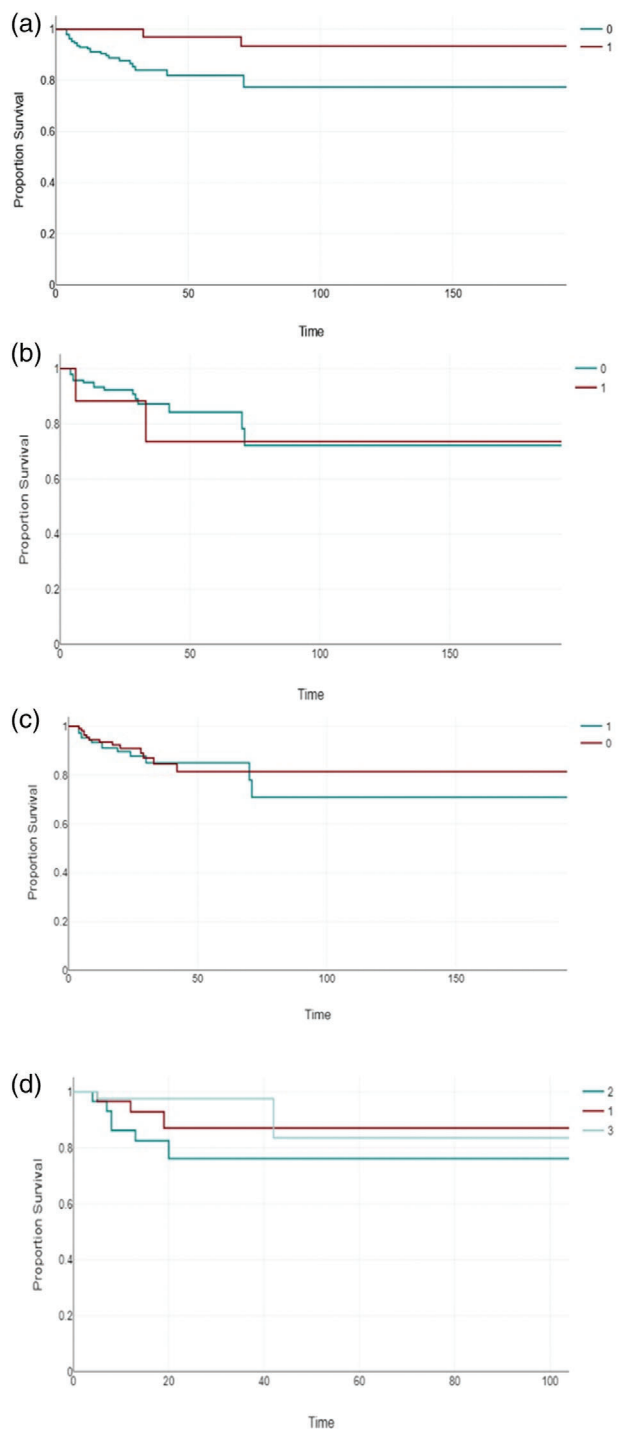
CAGE positivity	p value	Hazard ratio	95% CI
	0.183	0.35	0.08–1.64
<b>Binge drinking</b>			
	0.157	2.69	0.68–10.59
<b>Sedentary lifestyle</b>			
	0.632	1.26	0.49–3.24
<b>Compared to smokers</b>			
Ex-smokers	0.872	1.13	0.25–5.03
Non-smokers	0.427	0.44	0.06–3.35

consumption, compared to 19% and 12%, respectively, in healthy people.<sup>12</sup> However this result could be influenced by the poor representation of women in our study (31%). In addition, CAGE is known to be less sensitive at detecting abuse problems in the female population.<sup>17</sup>

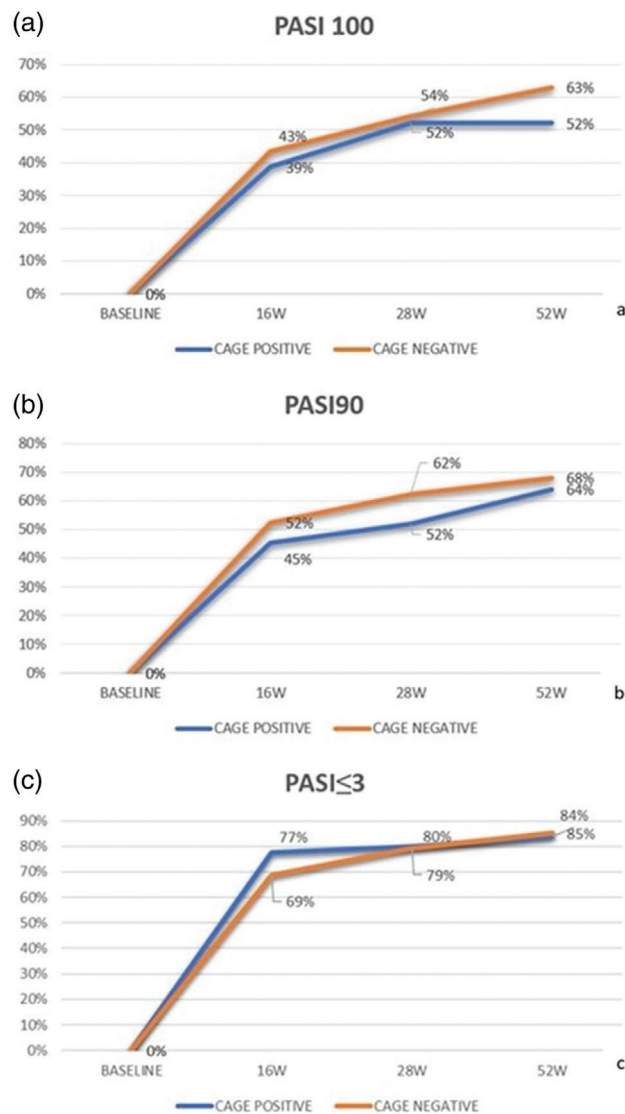
**TABLE 6** Achieved PASI100, 90, ≤3 in CAGE positive and negative patients at 16, 28 and 52 weeks. Univariate analysis.

	CAGE +	CAGE -	p value
<b>PASI100 achieved</b>			
Week 16	12 (39%)	82 (43%)	0.626
Week 28	13 (52%)	86 (54%)	0.846
Week 52	13 (52%)	85 (63%)	0.507
<b>PASI90 achieved</b>			
Week 16	14 (45%)	99 (52%)	0.456
Week 28	13 (52%)	99 (62%)	0.328
Week 52	16 (64%)	91 (68%)	0.702
<b>PASI≤3 achieved</b>			
Week 16	24 (69%)	130 (77%)	0,331
Week 28	20 (79%)	126 (80%)	0,931
Week 52	21 (85%)	114 (84%)	0.89

By multivariate analysis, CAGE positive questionnaires were mainly associated with patients having high BMI and



**FIGURE 1** (a) Drug survival by CAGE results expressed in weeks (time). In red = CAGE positive patients; in blue = CAGE negative patients. (b) Drug survival for binge-drinking patients expressed in weeks. In red = binge drinking patients; in blue = no binge drinking. (c) Drug survival rate for sedentary lifestyle habit expressed in weeks. In red = sedentary patients; in blue = no sedentary lifestyle. (d) Drug survival for smoking habit expressed in weeks. In light blue = active smokers; in red = non-smoker; in green = ex-smokers.



**FIGURE 2** (a) PASI100 reported at baseline, at 16, 28 and 52 weeks of biological therapy in CAGE positive and negative patients. (b) PASI90 reported at baseline, at 16, 28 and 52 weeks of biological therapy in CAGE positive and negative patients. (c) PASI ≤ 3 reported at baseline, at 16, 28 and 52 weeks of biological therapy in CAGE positive and negative patients.

for active smokers. From the literature, it is known that moderate alcohol intake has a significant effect on weight gain,<sup>18</sup> and it is also correlated with more severe psoriatic disease.<sup>19</sup> Smoking habit was associated with alcoholism and psoriasis by Higgins *et al.* in their study, where 47% of patients with CAGE positive results were also active smokers.<sup>20</sup> Herein, in multivariate analysis these factors lost significance, and there are probably other factors that need to be taken into account (e.g., sex, BMI, PASI, ongoing therapy) that are associated with an increased risk of alcohol abuse. Some of these behaviors have previously been reported and linked to underlying psychological conditions in psoriatic patients. In these patients, there is also a higher

**TABLE 7** Multivariate analysis of the influence of positive CAGE on the achievement of PASI100, PASI90 or PASI≤3 after the start of biological therapy.

<b>PASI100</b>	<b>Binge drinking</b>	<b>CAGE +</b>	<b>Sedentary lifestyle</b>	<b>BMI</b>	<b>Age at onset</b>	<b>Naïve</b>
<i>Week 16</i>						
p value	0.659	0.617	0.943	0.594	0.654	0.938
Odds Ratio	1.27	0.67	0.96	0.97	0.99	1.04
95% CI	0.44–3.71	0.14–3.23	0.35–2.65	0.88–1.08	0.96–1.02	0.37–2.94
<i>Week 28</i>						
p value	0.379	0.715	0.948	0.185	0.528	0.76
Odds Ratio	0.57	0.73	0.96	0.93	0.99	0.84
95% CI	0.17–1.97	0.14–3.94	0.32–2.88	0.83–1.04	0.96–1.02	0.27–2.61
<i>Week 52</i>						
p value	0.245	0.313	0.498	0.209	0.460	0.528
Odds Ratio	0.42	2.47	1.54	0.92	0.99	0.65
95% CI	0.1–1.81	0.43–14.33	0.44–5.35	0.81–1.05	0.95–1.02	0.17–2.5
<b>PASI90</b>	<b>Binge drinking</b>	<b>CAGE +</b>	<b>Sedentary lifestyle</b>	<b>BMI</b>	<b>Age at onset</b>	<b>Naïve</b>
<i>Week 16</i>						
p value	0.821	0.673	0.574	0.926	0.965	0.324
Odds Ratio	1.13	1.4	0.75	1.00	1.00	0.6
95% CI	0.4–3.19	0.29–6.79	0.28–2.04	0.91–1.11	0.97–1.03	0.22–1.66
<i>Week 28</i>						
p value	0.21	0.802	0.877	0.093	0.981	0.137
Odds Ratio	0.43	1.25	0.91	0.90	1.00	0.40
95% CI	0.11–1.62	0.22–6.92	0.29–2.91	0.8–1.02	0.96–1.04	0.12–1.34
<i>Week 52</i>						
p value	0.528	0.578	0.260	0.09	0.492	0.627
Odds Ratio	0.61	1.72	2.18	0.89	0.99	0.69
95% CI	0.13–2.84	0.25–11.68	0.56–8.44	0.77–1.02	0.95–1.03	0.16–3.03
<b>PASI≤3</b>	<b>Binge drinking</b>	<b>CAGE +</b>	<b>Sedentary lifestyle</b>	<b>BMI</b>	<b>Age at onset</b>	<b>Naïve</b>
<i>Week 16</i>						
p value	0.719	0.926	0.574	0.683	0.962	0.124
Odds Ratio	1.22	0.92	0.73	0.98	1.00	0.42
95% CI	0.1–3.69	0.15–5.57	0.25–2.15	0.88–1.09	0.97–1.03	0.14–1.27
<i>Week 28</i>						
p value	0.642	0.486	0.131	0.016	0.388	0.457
Odds Ratio	0.66	0.38	3.67	0.82	1.02	0.55
95% CI	0.12–3.77	0.03–5.64	0.68–19.8	0.69–0.96	0.97–1.08	0.11–2.67
<i>Week 52</i>						
p value	0.583	0.998	0.445	0.079	0.538	0.109
Odds Ratio	1.72	NA	0.48	1.22	0.98	5.09
95% CI	0.25–11.77	NA	0.07–3.14	0.98–1.51	0.92–1.04	0.69–37.3

incidence of anxiety disorders and depression, resulting in a decrease in quality of life.<sup>14</sup>

Statistical analyses suggest an association between major alcohol intake and clinical features of psoriasis different from the vulgar plaque type. This category of patients represented only 11% of the psoriatic population in our study, but among CAGE positive patients constituted 30.9%. The association with guttate psoriasis, identified

as highly significant, is of interest: 69.2% had risky alcohol consumption as confirmed by multivariate analysis. However, it should be considered that patients with the guttate variant in our population were more represented, at 4.3% of the sample, than the mean prevalence of this clinical variant, reported as 2% in the literature.<sup>6</sup>

The concomitant presence of PsA was significantly associated with high alcohol intake, as 65.2% of patients with

PsA reported a CAGE positive questionnaire. It has already been reported that there is an increased risk of developing PsA in patients with moderate alcohol consumption.<sup>21–24</sup>

Lifestyle and voluptuous habits are widely demonstrated consequences of psoriatic disease in the literature: alcohol consumption has a role both as a trigger and as a maintaining factor.<sup>20–22</sup> Notwithstanding, the effects of alcohol consumption on biological therapy are still not fully understood due to a scarcity of studies, and our aim was to investigate this aspect through PASI and drug survival. In order to correlate disease severity and CAGE questionnaires, we included PASI in our analyses. The first finding shows a higher mean PASI at the time of questionnaire administration, equal to 4.9, in CAGE positive patients compared to 2.1 of those with a negative questionnaire; this seems to confirm the hypothesis that the surface area involved is directly proportional to alcohol consumption.<sup>6</sup> However, this association lost significance in multivariate analysis.

To further investigate this possible relationship, the difference in PASI was examined in patients who were prescribed a biological drug at the time the questionnaire was administered. In this population there was a significantly different PASI: Mean PASI was 12.2 in patients with positive CAGE compared to 6.8 of those with a negative result.

In multivariate analysis, alcohol abuse was associated with fewer courses of biological treatment (only 13.62% with CAGE positive results were on biological therapy). This effect could depend on factors such as patient selection by the physician or greater awareness in patients about their health status.

Patients who at the moment of questionnaire completion were not on any treatment had a higher average level of alcohol consumption (46.7% of our CAGE positive population); from the literature, it is well-known that alcohol intake is the main reason for non-adherence to therapy.<sup>22</sup> In fact, we might infer that the psychological impact of the disease can lead patients who already consume alcohol to abuse it, in addition to non-compliance to therapy.

Moreover, it should be kept in mind that conventional drugs for psoriasis (methotrexate, acitretin, cyclosporine A) have hepatotoxic drug-drug interactions,<sup>7</sup> which should be a significant reason for not prescribing them to patients with alcohol issues. A higher percentage of CAGE positive patients, along with a poor response to treatment, was observed among those taking conventional therapy compared to those taking a biological drug, and is in line with the literature.<sup>8</sup> Analysis of the impact of alcohol consumption on drug survival in patients taking biological therapy showed no evidence of a significant association between alcohol intake, sedentary life, and smoking.

According to the results of the present study, patients with alcohol dependence could be switched to a biologic option in order to reduce the impact on liver function and increase efficacy of treatment.

## Conclusions

Alcohol misuse, which can relate to other lifestyle habits, such as smoking and obesity, was confirmed to be an influencing factor in the natural history of psoriasis. Clinically, the association with alcohol dependence and guttate psoriasis and PsA was highlighted. While no impact of alcohol abuse on drug survival and effectiveness of biologics was found, this class of drugs may be safer than traditional systemic therapy, although most patients with alcohol dependence are not receiving this treatment.

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## CONFLICT OF INTEREST STATEMENT

None.

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