



# Treat-to-Target Approach for the Management of Patients with Moderate-to-Severe Plaque Psoriasis: Consensus Recommendations

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## ABSTRACT

**Introduction:** Treat-to-target strategies are used in several chronic diseases to improve outcomes. Treatment goals have also been suggested for psoriasis, but there is currently no

consensus on targets, and guidance is needed to implement this strategy in clinical practice. The project ‘Treat to Target Italia’ was launched by a scientific board (SB) of 10 psoriasis experts to generate expert consensus recommendations.

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**Methods:** On the basis of the published literature, their clinical experience, and the results of a survey among Italian dermatologists, the SB identified four relevant topics: (1) clinical remission; (2) quality of life; (3) abrogation of systemic inflammation; (4) safety. They drafted 20 statements addressing these four topics and submitted them to a panel of 28 dermatologists, in a Delphi process, to achieve consensus (greater than 80% agreement).

**Results:** Consensus was reached on all statements. Treatment goals defining clinical remission should include a 90% improvement from baseline in the Psoriasis Area and Severity Index (PASI90 response) or an absolute PASI score of less than or equal to 3. Patient's quality of life

and satisfaction are important targets. If PASI targets are achieved, there should be no or very low impact of psoriasis on quality of life [Dermatology Life Quality Index (DLQI) score less than or equal to 3]. If PASI or DLQI goals are not achieved within 3–4 months, treatment should be changed. Abrogation of systemic inflammation may be crucial for preventing or delaying inflammatory comorbidities. Safety is an equally important target as efficacy.

**Conclusion:** These 20 consensus statements define the parameters of a treat-to-target strategy for psoriasis in Italy. It is hoped that use of these in the management of patients with psoriasis will improve treatment outcomes and patient health-related quality of life.

**Keywords:** Consensus; Plaque psoriasis; Quality of life; Systemic inflammation; Treat-to-target

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## Key Summary Points

### Why carry out this study?

Patients with moderate-to-severe psoriasis suffer from negative impacts on their health-related quality of life (HRQoL) and significant psychosocial disability.

Despite the availability of effective systemic therapy for these patients, many are undertreated, with a global study indicating that nearly 60% of patients fail to reach treatment goals.

A consensus-based treat-to-target approach in psoriasis may better guide clinicians, leading to improved treatment outcomes and patient HRQoL.

The ‘Treat to Target Italia’ project was undertaken by 10 psoriasis experts who developed 20 statements based on a literature review and results of a survey of Italian dermatologists; these statements were then reviewed by a panel of 28 dermatologists using the Delphi process to achieve consensus.

### What was learned from the study?

Consensus was reached on all statements, including those on treatment goals defining remission: a 90% improvement from baseline in the Psoriasis Area and Severity Index (PASI90 response) or an absolute PASI score of less than or equal to 3.

Dermatologists easily agreed on the treat-to-target strategy for patients with psoriasis that was patient-centred with emphasis on objective measures of disease severity and patient HRQoL, and on treatment safety.

## DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.13317611>.

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## INTRODUCTION

Psoriasis is a chronic, immune-mediated inflammatory disease of the skin frequently encountered in clinical practice, with plaque-type psoriasis being the most prevalent clinical form [1–3]. The type and severity of clinical manifestations are highly variable, but it is now widely recognised that the cutaneous manifestations represent one part of a complex disease phenotype [4, 5]. Furthermore, chronic plaque psoriasis is often associated with comorbidities that are typically characterised by systemic inflammation, such as psoriatic arthritis [6], atherosclerosis [7], metabolic syndrome [8] and obesity [8], which are known to increase the risk of myocardial infarction [9] and stroke [10].

Moderate-to-severe psoriasis causes significant psychosocial disability and negatively impacts patient health-related quality of life (HRQoL) [11, 12], increasing the risk of psychiatric comorbidities, such as depression and anxiety [13].

Patients with moderate-to-severe psoriasis are eligible for systemic therapies [14], including conventional systemic therapies and biologicals. The prescription of biological therapy is restricted to hospital-based dermatologists in Italy. Biological therapies selectively targeting mediators of psoriasis pathogenesis (including tumour necrosis factor  $\alpha$  [TNF $\alpha$ ], both interleukin [IL]-12 and IL-23, IL-17, and IL-23 alone) have proven to

be effective and well tolerated [15–24]. Clinical trials with these drugs have shown that a significant proportion of patients can achieve a 90% or 100% decrease of their baselines Psoriasis Area and Severity Index (PASI) scores (PASI90 or PASI100 response, respectively) [15–24]. These findings, along with a recognition of the need to manage the heterogeneous manifestations of psoriasis, have recently led to ambitious goals of treatment, such as the achievement of PASI90 or PASI100 responses, or an absolute physician's global assessment (PGA) score of 0–1 (clear/almost clear skin). These targets are now considered feasible for patients receiving treatment for moderate-to-severe plaque psoriasis in clinical practice [25–30]. In parallel, the possibility of implementing a treat-to-target approach to the management of psoriasis has raised considerable interest among dermatologists [25–27, 30–33].

Various treatment targets have also been suggested for the management of psoriasis [25, 27, 30–34]. For example, according to current Italian guidelines on the systemic treatment of moderate-to-severe plaque psoriasis, clear or almost clear skin is the ultimate goal of treatment and a PASI90 response is regarded as the most relevant treatment outcome [32]. Achieving an absolute PASI score of 1–2 may also be relevant according to these guidelines [26, 32].

Despite these efforts, a treat-to-target approach is being inconsistently applied in

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dermatological clinical practice. Data from several studies indicate that the treatment of psoriasis continues to be suboptimal, with substantial proportions of patients with moderate-to-severe psoriasis not receiving any therapy or receiving topical treatment only [35–37].

The treat-to-target approach to the management of psoriatic disease is still evolving, and requires clear guidance for physicians on the treatment goal, for both the cutaneous and other manifestations of psoriasis. The strategy also needs to be patient-centric, and not just the pursuit of clear skin at any cost. Patient's HRQoL needs to be considered, along with their comorbidities, the adverse effects of treatment and treatment preferences [38]. The project 'Treat to Target Italia' was launched by a group of psoriasis experts and was prompted by the need to develop recommendations for guiding dermatologists in the treatment-to-target of psoriasis in clinical practice in Italy. In particular, the project addressed the following four topics: (1) clinical remission of psoriasis; (2) patient HRQoL; (3) abrogation of systemic inflammation; and (4) safety of treatment. We present the results of the project and a set of 20 consensus statements addressing issues related to the four domains.

## METHODS

### Design

The 'Treat to Target Italia' project was launched in 2019 by a group of 10 Italian experts in psoriasis, who acted as the scientific board of the project. The aim of the project was to define the therapeutic objectives in the management of patients with psoriasis in clinical practice. More detailed objectives included identifying a therapeutic target and assessment of this target over time; establishing the time to the achievement of the target; identification of practice-oriented efficacy measures to improve disease staging and follow-up; understanding the correlation between disease state and HRQoL; defining personalised therapeutic targets; and describing the optimal timing of reassessments to ensure long-term maintenance

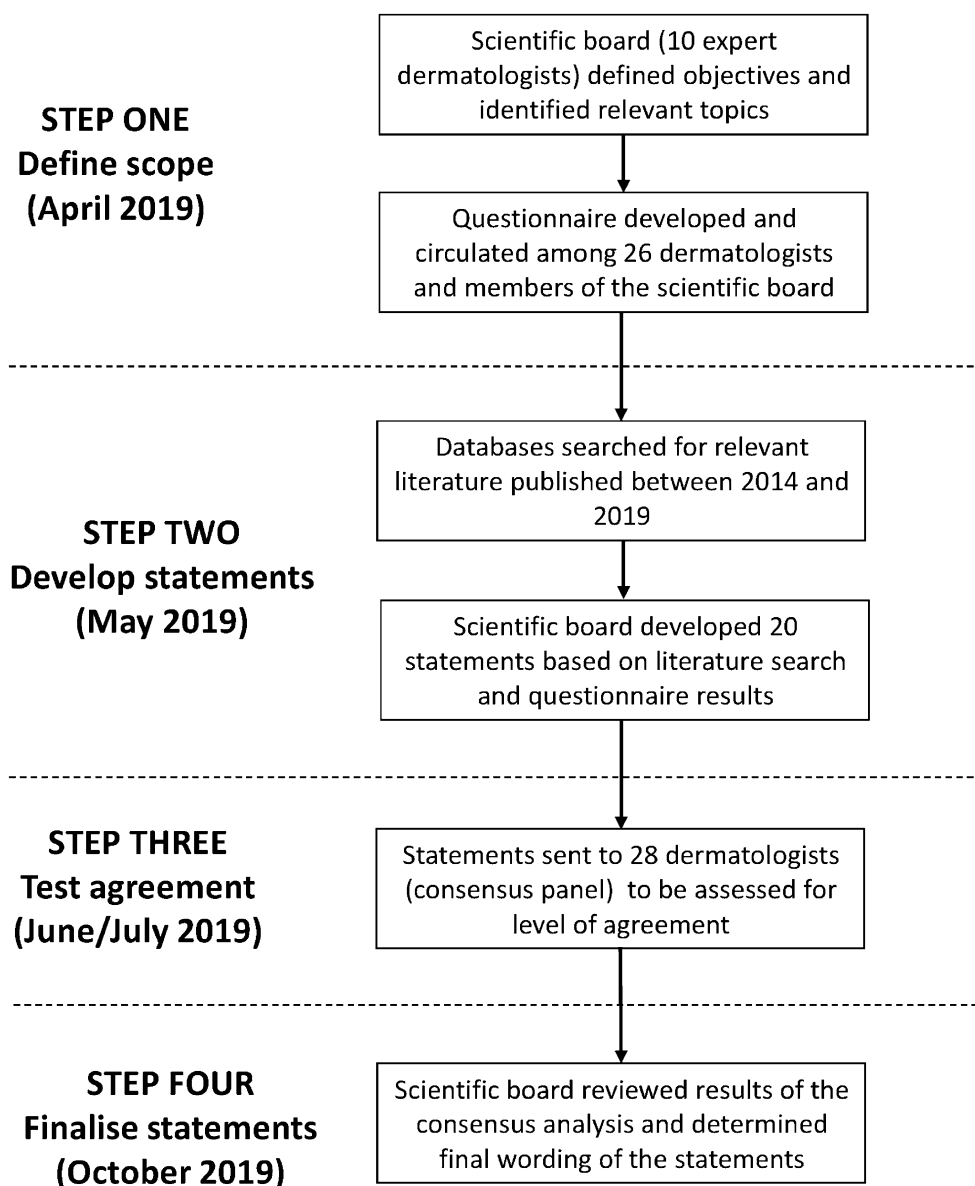
of the results achieved. The scientific board drafted a set of evidence- and consensus-based statements regarding therapeutic targets in psoriasis treatment and chose the Delphi method for consensus methodology [39, 40].

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

### Development of Consensus Statements

The consensus methodology is shown in Fig. 1. It consisted of a four-step process conducted between April 2019 and October 2019. The first step was to define the scope of the project. The scientific board met first in April 2019 in Rome to define the objectives of the 'Treat to Target Italia' project and identified topics relevant to the targeted treatment of psoriasis, based on published evidence and their expertise, namely (1) clinical remission of psoriasis; (2) patient HRQoL; (3) abrogation of systemic inflammation; and (4) safety of treatment. The scientific board also designed the strategy for searching the literature related to these topics (see below) and developed a survey to gauge the opinion of Italian dermatologists about the targets of psoriasis treatment. A 25-item questionnaire was developed and sent via e-mail to a panel of 26 dermatologists, as well as to each member of the scientific board (April–May 2019). The surveyed dermatologists were selected on the basis of their recognised expertise in the management of patients with moderate-to-severe psoriasis..

Step 2 of the consensus development process was to make statements based on the survey results and literature review. Literature was identified by searching the EBM Reviews, Cochrane Database of Systematic Reviews, Embase and MEDLINE databases for articles published in English between January 2014 and April 2019. The search involved various combinations of terms related to "inflammation", "clinical remission", "patient satisfaction/quality of life", "safety" and "psoriasis". A second meeting of the scientific board was held at the end of May 2019 in Milan to develop a set of statements covering the four topics, which had



**Fig. 1** Illustration of the consensus methodology consisting of a four-step process and including a Delphi exercise

been previously identified as relevant for the treat-to-target approach. To draft the statements, the scientific board relied on their expertise, the evidence from the published literature, and the results of the preliminary survey among Italian dermatologists. Each statement was extensively discussed during the meeting. A total of 20 statements (nine for the topic “Clinical remission”, three for “Patient quality of life”, five for “Abrogation of

inflammation”, three for “Safety”) were developed by the scientific board.

The third step in the process was to obtain feedback on these statements from a wider group of dermatologists testing the consensus (two additional experts were included in the panel to better represent the whole Italian territory). The 20 statements were circulated via an online survey to 28 dermatologists (consensus panel), most of whom had participated in the preliminary survey. These dermatologists were



asked to complete the survey in June/July 2019. The survey asked them to express their level of agreement/disagreement with each statement using a 5-point scale (1 = total disagreement, 2 = disagreement, 3 = agreement, 4 = strong agreement, 5 = total agreement). Consensus was defined by more than 80% agreement (scores of 3–5) or disagreement (scores of 1 or 2). The voting process was performed online and was anonymous.

In step 4, the scientific board analysed the results of the first round of voting. As consensus was reached on all statements, there was no need for a second round of voting. The results were discussed at a plenary meeting attended by the scientific board and the consensus panel of dermatologists in October 2019 in Rome. During this meeting, the statements underwent minor editing and were finalised to the present version.

## RESULTS AND DISCUSSION

Thirty-five of the 36 dermatologists (97%) invited to participate in the preliminary survey provided their opinion about various aspects and practicalities of the treat-to-target approach to psoriasis management by answering all questions in the 25-item questionnaire.

During the Delphi method, 28 dermatologists on the consensus panel expressed their agreement or disagreement on the 20 statements produced by the scientific board (100% response rate). Positive consensus was reached on all statements. The statements and results of the first and only round of voting are shown in Tables 1, 2, 3 and 4. The background of all the dermatologists included in the study was similar: they were university hospital doctors with a specific clinical expertise in managing patients with psoriasis with biological therapy.

In the following sections, the consensus statements from each topic will be discussed along with the most relevant results from the preliminary survey and the supporting scientific evidence when available.

### Clinical Remission of Psoriasis

There was full agreement among the members of the consensus panel regarding targets for clinical remission (Table 1). The choice of systemic therapy should consider several factors, including disease severity and localisation (i.e. sensitive areas), comorbidities (including psoriatic arthritis), impact on quality of life and patient preferences (statements 1.1 and 1.2). According to the consensus, treatment goals that define clinical remission of psoriasis include a PASI90 response or an absolute PASI score less than or equal to 3 (statements 1.3, 1.4 and 1.5). Such goals may, however, need to be reconsidered in patients with psoriasis affecting sensitive body areas, such as face, scalp, palms, soles, nails and genitalia (statement 1.6). Evidence shows that the involvement of these areas has a negative psychological impact [41], which translates into worse disease severity compared with disease severity assessed by objective measures (such as BSA or PASI) only [42, 43]. The treatment goal (PASI90 response or absolute PASI score less than or equal to 3) should be maintained over time, which implies a tight control of disease course (statement 1.8). If the treatment goal is not achieved within 3–4 months of treatment, therapy should be changed (statement 1.7). Finally, there was a strong consensus about the role of HRQoL when defining or adjusting treatment goals (statement 1.9).

The preliminary survey highlighted that around two-thirds of dermatologists considered a patient-centred approach as very important to the definition of treatment goals (63%) and their assessment (60%). PASI change from baseline and absolute PASI values were considered to be very effective measures of disease severity improvements by 39% and 48% of respondents, respectively.

PASI90 has been suggested by several authors as the new target of psoriasis treatment because, compared with other measures of psoriasis improvement, PASI90 appears to be associated with greater improvements in DLQI values and higher rates of absolute DLQI values of 0–1, corresponding to no impact of psoriasis on HRQoL [29, 44]. It also takes into account

**Table 1** Level of consensus on statements about clinical remission targets

| Statements   | Scores applied, <i>n</i> |   |   |    |    |       | Level of consensus, % |
|--|--------------------------|---|---|----|----|-------|-----------------------|
|  | 1                        | 2 | 3 | 4  | 5  | Total |                       |
| 1.1 An adaptable and personalised strategy aimed at achieving the therapeutic objectives (i.e. treat to target) can be useful in psoriasis clinical practice   | 0                        | 0 | 0 | 4  | 24 | 28    | 100                   |
| 1.2 Several factors should be considered when choosing a systemic treatment in patients with moderate-to-severe psoriasis. They include disease severity and localisation (i.e. sensitive areas), coexistence of psoriatic arthritis or other comorbidities, impact of the disease on the patient's quality of life, patient's preference and treatment risk–benefit ratio | 0                        | 0 | 0 | 4  | 24 | 28    | 100                   |
| 1.3 Dermatologists should use PASI or PGA or BSA to objectively assess psoriasis in daily practice   | 0                        | 1 | 6 | 6  | 15 | 28    | 96                    |
| 1.4 The PASI90 response best defines the therapeutic objective   | 0                        | 2 | 3 | 11 | 12 | 28    | 93                    |
| 1.5 The absolute PASI value that defines the optimal therapeutic objective should be less than or equal to 3   | 0                        | 3 | 5 | 6  | 14 | 28    | 89                    |
| 1.6 PASI90 or absolute PASI less than or equal to 3 could not be adequate treatment goals in the case of involvement of sensitive areas  | 0                        | 3 | 3 | 10 | 12 | 28    | 89                    |
| 1.7 If the target of PASI90 or absolute PASI score less than or equal to 3 is not reached after 3–4 months of therapy, a change in treatment should be considered  | 0                        | 5 | 5 | 12 | 6  | 28    | 82                    |
| 1.8 PASI90 or absolute PASI less than or equal to 3 should be maintained over time   | 0                        | 2 | 3 | 9  | 14 | 28    | 93                    |
| 1.9 The impact of psoriasis on patient's quality of life should be taken into consideration when considering treatment goals   | 0                        | 0 | 1 | 6  | 21 | 28    | 100                   |

*BSA* body surface area, *PASI* Psoriasis Area Severity Index, *PASI90* 90% decrease in PASI score, *PGA* physician's global assessment

baseline disease severity, which as noted above, was considered a very effective measure of treatment response by 39% of respondents. The clinical relevance and feasibility of PASI90 and PASI100 responses are also reflected in the increasing use of these measures as primary and secondary endpoints in clinical trials [15, 18, 19, 22, 24]. The first phase 3 trial to use PASI90 as a primary endpoint was the CLEAR trial, which compared secukinumab with ustekinumab in patients with moderate-to-severe psoriasis [23]. At week 16, PASI90 response rate was achieved in 79% of patients treated with secukinumab compared with 58% treated with ustekinumab ( $P < 0.0001$ ). PASI100

responses at 16 weeks were 44% and 28% in secukinumab and ustekinumab patients, respectively ( $P < 0.0001$ ). A systematic review and network meta-analysis of interleukin inhibitors in moderate-to-severe plaque psoriasis found that 12–16 weeks' treatment with IL-17, IL-12/23 and IL-23 inhibitors was associated with high efficiency in achieving PASI75, PASI100 and sPGA 0/1 or IGA 0/1 or PGA 0/1. The IL-23 inhibitor risankizumab was considered to have the greatest efficacy and lowest safety risk [45].

The Spanish Psoriasis Group recently redefined the targets of psoriasis treatment with biological therapy [25]. According to the



**Table 2** Level of consensus on statements about patient health-related quality of life targets

| Statements   | Scores applied, <i>n</i> |   |   |    |    |       | Level of consensus, % |
|--|--------------------------|---|---|----|----|-------|-----------------------|
|  | 1                        | 2 | 3 | 4  | 5  | Total |                       |
| 2.1 Quality of life is an important outcome from the patient and physician perspective and should be included in the therapeutic targets. Achievement of treatment goal implies no impact or minimal impact of the disease on quality of life, e.g. DLQI less than or equal to 3 | 0                        | 1 | 2 | 10 | 15 | 28    | 96                    |
| 2.2 Treat to target in psoriasis should include patient-centric targets, such as patient satisfaction  | 0                        | 0 | 2 | 15 | 11 | 28    | 100                   |
| 2.3 If the target of disease-related quality of life is not reached after 3–4 months of therapy, a change in treatment should be considered  | 1                        | 1 | 6 | 12 | 8  | 28    | 93                    |

*DLQI* Dermatology Life Quality Index

consensus achieved by that group, absolute PASI values are useful measures in clinical practice and correlate better with DLQI than relative PASI improvements. Absolute PASI values less than or equal to 3 define the achievement of treatment goals. A reduction in the dose of biological therapy is possible in patients with complete or near complete response (PGA 0/1; PASI90; absolute PASI from less than 2 to 3). Criteria for returning to full-dose biological therapy include absolute PASI values of at least 5 or loss of PASI75 response. The consensus statements issued by the Spanish group also provided detailed indications about the timing of response assessment, which varies according to the biological drug used: at week 12 for adalimumab, 14 for infliximab and 16 for ustekinumab and secukinumab (no consensus on etanercept or apremilast) [25].

An absolute PASI value less than or equal to 3 is also the criterion to continue current treatment recommended by the recent French expert-opinion guidelines on the use of systemic treatments for moderate-to-severe psoriasis [34]. According to these guidelines, absolute PASI values are easier to calculate than relative PASI values, are independent of baseline severity assessments and correlate more precisely with a clear/almost clear status (i.e. PGA score of 0–1). The relevance of absolute PASI scores has also been highlighted by a recent analysis of real-world data based on the British Association

of Dermatologists Biologics and Immunomodulators Register (BADBIR) [28]. This analysis found 90% concordance between an absolute PASI score of less than or equal to 2 and PASI90 response, and 88% concordance between absolute PASI less than or equal to 4 and PASI75 response. A 90% concordance was also reported for PGA clear/almost clear and PASI less than or equal to 2. The ‘Treat to Target Italia’ panel considered that an absolute PASI less than or equal to 2 and PGA of clear/almost clear was too restrictive, and that the PASI less than or equal to 3 goal recommended in the French and Spanish guidelines was more acceptable when applying the treat-to-target approach to psoriasis management in clinical practice. Indeed, the utility of absolute PASI scores has been illustrated in a recent post hoc analysis of pooled phase 3 study results. The authors found that compared with percentage PASI improvement, absolute PASI score was more reliable in determining disease activity in patients with moderate-to-severe plaque psoriasis [46].

### Patient Health-Related Quality of Life

As described above (relating to statement 1.9), patient HRQoL is an important target of treatment. If treatment targets are achieved, there should be no residual impact of psoriasis on HRQoL or the impact should be very low. A common measure of HRQoL in patients with

**Table 3** Level of consensus on statements related to abrogation of systemic inflammation

| Statements   | Scores applied, <i>n</i> |   |   |   |    |       | Level of consensus, % |
|--|--------------------------|---|---|---|----|-------|-----------------------|
|  | 1                        | 2 | 3 | 4 | 5  | Total |                       |
| 3.1 Psoriasis-related systemic inflammation can affect joints, liver, nervous system and cardiovascular system   | 0                        | 0 | 5 | 6 | 17 | 28    | 100                   |
| 3.2 Attention should be paid to early recognition of psoriatic arthritis   | 0                        | 0 | 0 | 6 | 22 | 28    | 100                   |
| 3.3 Moderate-to-severe psoriasis can be associated with various comorbidities that can benefit from, or be worsened by, anti-psoriatic therapy             | 0                        | 0 | 5 | 5 | 18 | 28    | 100                   |
| 3.4 Biological drugs showing a high selectivity in inhibiting inflammatory signals can improve comorbidities that share pathogenic pathways with psoriasis | 0                        | 2 | 3 | 8 | 15 | 28    | 93                    |
| 3.5 In obese patients, body weight reduction may positively impact on overall response to anti-psoriatic therapy   | 0                        | 0 | 2 | 8 | 18 | 28    | 100                   |

**Table 4** Level of consensus on statements related to treatment safety

| Statements  | Scores applied, <i>n</i> |   |   |    |    |       | Level of consensus, % |
|---|--------------------------|---|---|----|----|-------|-----------------------|
|   | 1                        | 2 | 3 | 4  | 5  | Total |                       |
| 4.1 Safety should be considered as important as efficacy  | 0                        | 0 | 3 | 3  | 22 | 28    | 100                   |
| 4.2 Targeted therapies show a very favourable safety profile                                      | 0                        | 0 | 2 | 13 | 13 | 28    | 100                   |
| 4.3 Safety should be assessed periodically, according to the patient's and drug's characteristics | 0                        | 0 | 2 | 7  | 19 | 28    | 100                   |

psoriasis is the DLQI, and a study investigated the relationship between such scores and patients' perception of the impairment of their skin-related quality of life. The following DLQI scores defined the degree of psoriasis interference: scores 0–1, no effect; 2–5, small effect; 6–10, moderate effect; 11–20, very large effect; 21–30, extremely large effect [47]. On the basis of these data, the consensus statement defines a DLQI goal of less than or equal to 3 (statement 2.1). Similar to the timing recommended for the assessment of treatment response and for treatment adjustments (statement 1.7), if the HRQoL target of DLQI less than or equal to 3 is not reached after 3–4 months of treatment, therapy should be changed (statement 2.3).

The preliminary questionnaire highlighted an elevated level of awareness among the

surveyed dermatologists about the importance of HRQoL in the treat-to-target management of psoriasis (85% considered HRQoL as a very important component of the treatment goals). According to the Delphi survey, 80% of dermatologists assess HRQoL of patients with psoriasis in their routine practice by calculating the DLQI score (74%), based on an overall assessment of patient satisfaction (89%).

The relevance of HRQoL in the treat-to-target management of psoriasis is supported by an increasing body of evidence suggesting that effective treatment correlates with improvement of DLQI scores [48–50]. A US survey involving dermatologists and patients investigated the relationship between psoriasis severity and quality of life (DLQI and EuroQoL 5-Dimension Health questionnaire) and work

productivity (Work Productivity and Activity Impairment questionnaire) [48]. More severe psoriasis correlated with increased symptoms (itching, pain and scaling), reduced quality of life, and impaired work productivity [48]. A real-world observational study in patients treated with adalimumab found that the improvements in patient HRQoL and psychological functioning reported at 16 weeks were paralleled by improvements in skin disease [49].

### Abrogation of Systemic Inflammation

Chronic systemic inflammation associated with psoriasis can affect a number of tissues and organs leading to the development or worsening of comorbidities, including psoriatic arthritis, cardiovascular disease and depression (statement 3.1) [51–53]. Early recognition of psoriatic arthritis is crucial (statement 3.2), particularly given the prevalence of this comorbidity in patients with psoriasis [6, 54]. Systemic therapies for psoriasis can improve or worsen comorbidities (statement 3.3). As biological drugs target inflammatory pathways that are also likely to be involved in the pathogenesis of comorbidities, their use may be beneficial for these comorbidities as well as psoriasis (statement 3.4). For example, there is emerging evidence that biological therapies have favourable effects on reversing the underlying pathogenic processes in cardiovascular disease such as endothelial dysfunction and atherosclerotic plaque progression [55, 56]. Also, early aggressive control of systemic inflammation may prevent or delay the damage associated with comorbidities, including psoriatic arthritis [52].

The preliminary survey showed that comorbidities associated with psoriasis, including psoriatic arthritis, metabolic syndrome, obesity, diabetes mellitus, cardiovascular disease, inflammatory bowel disease and depression, play a central role in therapeutic decisions.

### Safety

There was full agreement that safety of treatment is equally as important as efficacy when defining treatment targets (statement 4.1). The

safety of the selected therapy should be monitored according to medication and patient characteristics (statement 4.3). There was also full consensus about the more favourable safety profile of biologicals compared with traditional systemic treatments for psoriasis, especially for long-term therapy (statement 4.2).

The safety and tolerability of systemic therapy is a major issue in the management of moderate-to-severe psoriasis. Concern about the safety of systemic therapies is one of the main reasons why patients with moderate-to-severe psoriasis are often inadequately treated. However, a large body of evidence from clinical trials and post-marketing pharmacovigilance registries supports the safety of biologicals for the treatment of psoriasis [57–64]. Biologicals are better tolerated than conventional systemic therapies, particularly for long-term treatment. It should be noted that each class of biological therapy has a specific safety profile. Overall biologicals are associated with an increased risk of infection, including upper respiratory tract infections for TNF $\alpha$  inhibitors and candida infection for IL-17 inhibitors.

Drug retention rates are a useful measure of treatment effectiveness and safety [58]. Evidence shows that retention rates of traditional systemic treatments for psoriasis are shorter than retention rates of biologicals, mainly due to poor tolerability [58]. The most common reason for discontinuation of biologicals is loss of efficacy [58]. A real-world study using data from the BADBIR pharmacovigilance registry to evaluate the persistence of biologicals (adalimumab, etanercept, infliximab and ustekinumab) in biological-naïve patients with psoriasis found that treatment discontinuation was generally due to loss of response to treatment, rather than to safety issues [65]. Similar findings were provided by an analysis of data from the prospective, international Psoriasis Longitudinal Assessment and Registry (PSOLAR), in which the most common cause of treatment discontinuation was loss of efficacy [66].

## Limitations

We acknowledge the inherent bias in the non-random selection of 10 expert dermatologists, most of whom are from university hospitals. However, we believe this may be offset somewhat by the extensive range of clinical experience held by the scientific board, and their level of involvement in producing these high-quality guidelines, which might not have been possible if 10 dermatologists had been randomly selected. Another possible limitation is the lack of a patient perspective during consensus development; however, this was indirectly mitigated by an assessment of patient HRQoL data. Moreover, we acknowledge the limited number of dermatologists ( $N = 28$ ) answering Delphi as a limitation of the study. However, they were hospital-based specialists with a specific clinical expertise in managing patients with psoriasis with biological therapy.

## CONCLUSIONS

Defining treatment targets enables physicians and patients to closely follow treatment progress, to modify treatment when the goals are not met, and to optimise therapeutic interventions. Here, we provide 20 consensus statements to guide dermatologists in the adoption of the treat-to-target strategy for the management of psoriasis in clinical practice.

This is the first initiative to define the parameters of a treat-to-target strategy for psoriasis in Italy. It was somewhat surprising that complete consensus was reached on all statements after the first round of voting in the Delphi method. This may be explained by the fact that the dermatologists on the consensus panel had comparable expertise, were from specialised dermatology centres, and were fully acquainted with the latest treatment strategies for psoriasis. A consensus panel composed of general dermatologists with less expertise in managing psoriasis might have provided different results. On the other hand, it was encouraging to note that consensus exists on treatment goals among Italian psoriasis experts.

The treat-to-target strategy proposed here is strongly patient-centred with an emphasis on both objective measures of disease severity and patient HRQoL. Recommended targets are PASI90 response or alternatively absolute PASI less than or equal to 3, although these targets may be adjusted in patients with involvement of sensitive body areas. With regard to HRQoL, the proposed target is DLQI less than or equal to 3 (very low to no impact). If PASI and DLQI targets are not reached within 3–4 months, treatment should be modified. The present statements also stress the importance of early recognition of psoriatic arthritis and selecting agents that abrogate systemic inflammation. Abrogation of systemic inflammation is aimed at improving psoriasis and preventing or postponing the development of inflammatory comorbidities. Safety is a target that is as important as efficacy, and treatment with biologicals requires regular monitoring of adverse events.

As the treatment options for psoriasis continue to evolve, therapeutic targets will need to be updated. Currently, no general international consensus exists about treatment targets in psoriasis. This may be a consequence of the lack of clear correlations between suggested target scores and patient-reported outcomes. Further investigations on the impact of the treat-to-target strategy on patient HRQoL will contribute to refining the approach and identifying generally accepted targets.

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