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LETTER TO THE EDITOR

An international Delphi consensus to define a clinically appropriate definition of disease modification for plaque psoriasis

Dear Editor,

Plaque psoriasis (PP) affects an estimated 29.5 million adults globally and carries a significant disease burden through associated comorbidities.[1] Typically, treatment approaches follow the severity of the condition, with biologic agents usually reserved for use in patients with moderate-to-severe disease who have shown inadequate response to topical and phototherapy options.[2,3]

With the rise of targeted biologic therapies on the IL23p19 pathway that demonstrate high levels of efficacy (in some cases with patients achieving a PASI 90/100 response within 12–16 weeks of initiation),[4] questions have arisen as to whether PP can be controlled, modified or even brought into remission.[5]

However, PASI has limited utility within regular clinical settings and can demonstrate degrees of subjectivity and variability.[6,7]

The aim of this study was to develop a definition of disease modification (DM) that could be applied within a clinical setting.

A literature review was conducted in May 2021 to identify what trends exist that may define disease modification for PP. The search was conducted through the PubMed database. Fifty-nine studies were accepted, which were used to guide the expert-led discussion that followed.

The discussion took place in October 2021 with eight experts (Study authors 1–8) in psoriasis care from Europe and North America involved. Using a modified Delphi methodology guided by an independent facilitator (Triducive Partners Limited), the panel developed six themes and 35 statements (Table 1) for wider testing which were independently reviewed by each member before being used to build a 4-point *Likert* scale survey.

A total of 63 responses from across Europe and North America were analysed. From this, 22 statements attained very strong (≥90%) agreement, 10/35 strong (≥75%) agreement, and 3 statements fell below the established threshold (Figure 1).

The panellists discussed the results and developed the following definition for DM using the modified Delphi approach:

> A sustained improvement in the disease course of plaque psoriasis resulting from a change in pathophysiology that minimises the need for treatment.

To further define DM by how it could be measured, the panellists offer the following:

> In patients with moderate-to-severe plaque psoriasis, in the absence of precise biomarkers, disease modification may be evaluated by sustained BSA<1% / PGA 0/1 for >12 months following treatment cessation.

BSA and PGA were chosen as measurements as they have been shown to be more effective and easier to use in a clinical setting over PASI.[8,9] Twelve months was agreed as the timeframe as evidence shows a patient can relapse at any point within 1 year.[10]

The panellists believe that these outcome statements provide an appropriate definition for DM in PP as they clearly define the goal and end point that both the clinician and patient can understand. Furthermore, this definition considers how DM can be determined at the end of an episode of treatment, within a framework for longer-term goals, and how these could be conducted and measured in the clinical setting. The next step will be to determine the validity of this definition by applying and evaluating it within a real-world clinical environment.

FUNDING INFORMATION

The study was initiated and funded by Janssen Immunology. All authors (except for TS and NW) received honoraria from Janssen Immunology while undertaking this study. Janssen Immunology commissioned Triducive Partners Limited to facilitate the project and analyse the responses to the consensus statements in line with the Delphi methodology.

CONFLICT OF INTEREST STATEMENT

KE has received research grants, served as a scientific adviser, and/or speaker for Abbvie, Almirall, Boehringer Ingelheim, BMS, Galderma, Lilly, Leo, Janssen, Pfizer, Novartis, Sanofi and UCB. MS has received honoraria for participating in Advisory boards and given lectures for Leo

TABLE 1 Defined consensus statements developed for wider testing with psoriasis care HCPs, and corresponding levels of agreement attained from 63 responses.

No.	Statement	Agreement (%)
Topic A: Defining disease control, remission and modification		
1	Disease control is defined by control of all symptoms of plaque-type psoriasis with treatment, appreciating that cessation of treatment will result in plaque-type psoriasis symptoms reappearing	97
2	Disease remission is defined by control of all symptoms of plaque-type psoriasis that is maintained beyond 3 months after cessation of treatment	78
3	Disease modification is defined by a change to the better in the characteristics or course, topography, or progression of the disease that is maintained beyond 3 months after cessation of treatment	71
4	Disease modification is caused by a fundamental change in the underlying immunopathology that allows disease remission	89
5	Disease modification is reflected by quantitative differences of the inflammatory activity of the skin and/or improvement/prevention of comorbidities	95
6	Disease curation is the maximum result of disease modification	97
7	It is difficult to discriminate between disease control and disease modification of plaque-type psoriasis	79
Topic B: Defining disease modification: 1—absence of inflammatory activity		
8	Body surface area (BSA) of <1% is an indicator of minimal skin-related inflammatory activity	95
9	Permanent changes in the pathogenic molecular pathway are an indicator of disease modification, as evidenced by <1% BSA and PGA0/1	90
10	Sub-clinical disease activity is poorly measured in practice	95
11	Sub-clinical disease activity (e.g. elevated tissue resident memory T cells in resolved skin) indicates that disease modification has not been achieved	81
12	Elimination of sub-clinical disease activity indicates disease modification has been achieved	87
Topic C: Defining disease modification: 2—role of treatment		
13	Disease control is defined by achievement of a reduction in symptom frequency or severity to a minimal residual (PASI <3) during active treatment/intervention	94
14	Disease modification is defined by an ongoing reduction in symptom frequency or severity to a minimal residual during time periods following, but without, active treatment/intervention	94
15	Disease modification is defined by a reduction in symptom frequency or severity experienced with active treatment/intervention	48
16	Active treatment often achieves low disease activity today but is not indicative of disease modification	87
17	Drugs that require continuous use to achieve control of symptom severity or frequency do not achieve disease modification	78
18	In order to increase chances for disease modification, initiation of conventional systemic or biologic treatment should be as early as possible after diagnosis	95
19	Disease modification may be achievable with earlier initiation of therapy after diagnosis or clinical manifestations	95
Topic D: Defining disease modification: 3—role of time		
20	Disease modification is recognized if <1% BSA and PGA0/1 has been achieved for 1 year or more without active treatment/intervention	94
21	Disease modification is recognized if <1% BSA has been achieved for 1 year or more with active treatment/intervention	38
Topic E: Potential role of biomarkers		
22	Biomarkers to identify the course of disease may be helpful in the future	98
23	Identifying predictive markers for severe disease course would be helpful	100
24	Identifying predictive markers for mild disease course would be helpful	95
25	IL-19 is a potential biomarker to determine inflammatory severity of plaque-type psoriasis	78
26	Human ß-defensin 2 (HBD2) is a potential biomarker to determine inflammatory severity of plaque-type psoriasis	75
27	The role for and clinical utility of biomarkers in this area of medicine needs to be better understood	98
28	The future clinical use of non-invasive biomarkers should be investigated	100
29	The future clinical use of a combining clinical and laboratory biomarkers should be investigated	100
30	No good biomarkers have been identified for disease modification	87
Topic F: Future research		
31	The impact of over-treating plaque-type psoriasis patients should be better understood	97
32	The potential role for practical clinical tests (e.g. ratio of TRM/Treg) to support plaque-type psoriasis treatment selection should be further investigated	97
33	Identifying markers to confirm plaque-type psoriasis treatment cessation decision due to disease modification would be helpful	100
34	Future RCTs should include an arm that considers cessation of active plaque-type psoriasis treatment after 1 year	97
35	The future goal for new plaque-type psoriasis treatments should be disease modification	100

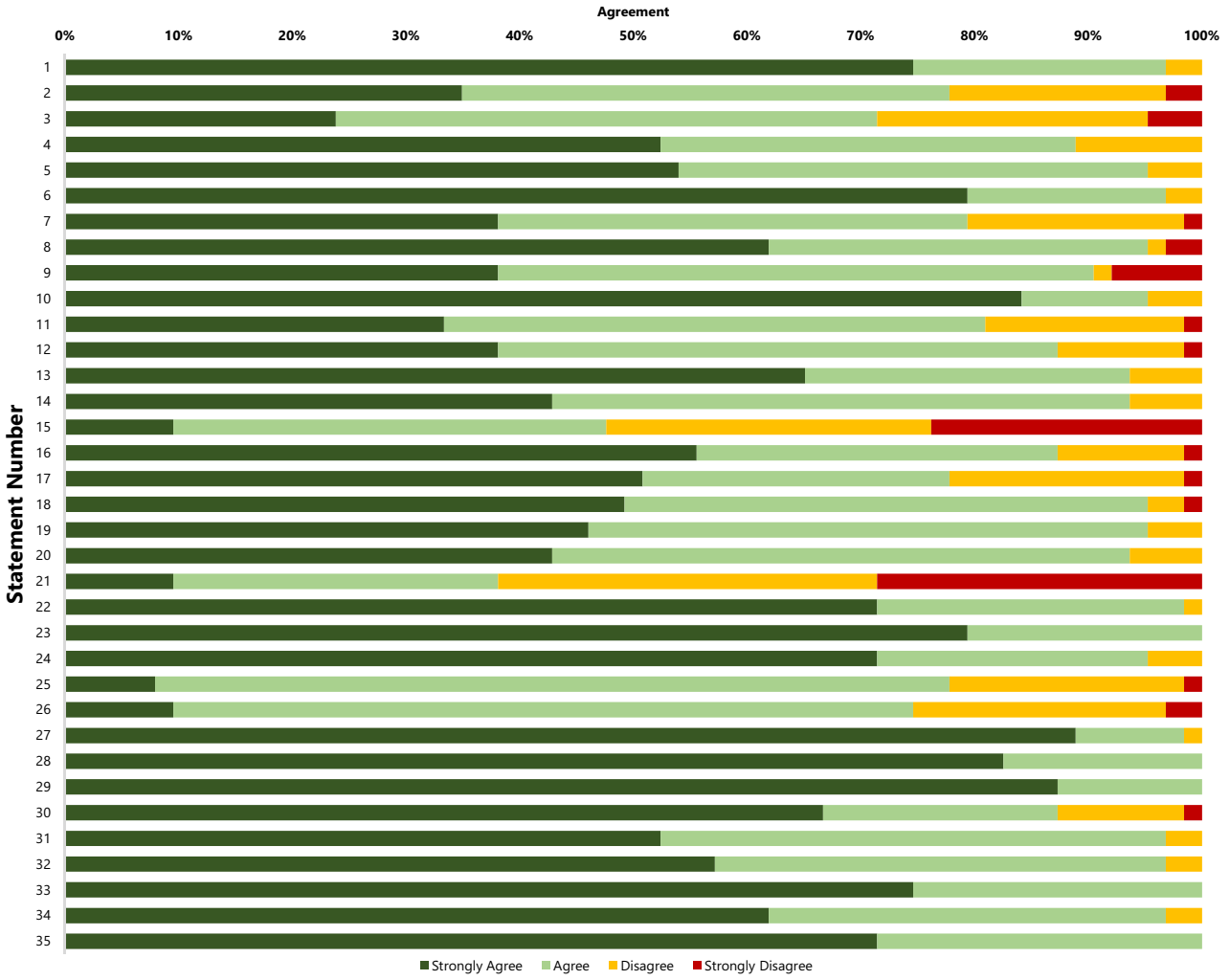

FIGURE 1 Consensus score distribution across the four-point Likert scale offered to respondents.

Pharma, Abbvie, Celgene, Eli Lilly, Novartis, Pfizer, UCB and Lipidor. KS has received consultancy/speaker's honoraria from and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Aristea Therapeutics, Boehringer Ingelheim, Celgene, Eli Lilly, Evelo, Galderma, Janssen-Cilag GmbH, LEO Pharma, Novartis, Pfizer, Sanofi Genzyme, TFS Trial Form Support GmbH and UCB. CC has received research grants, served as a scientific adviser, and/or clinical study investigator for AbbVie, Actelion, Almirall, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Eli Lilly, Galderma, Incyte, Janssen, LEO Pharma, MSD, Novartis, Pfizer, Samsung, Sanofi and UCB. AWA has served as a research investigator, scientific advisor and/or speaker to AbbVie, Almirall, Arcutis, ASLAN, Beiersdorf, BI, BMS, EPI, Incyte, Leo, UCB, Janssen, Lilly, Mindera, Nimbus, Novartis, Ortho Dermatologics, Sun, Dermavant, Dermira, Sanofi, Regeneron and Pfizer. LP has received consultancy/speaker's honoraria from and/or participated in clinical trials sponsored by Abbvie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen, Leo-Pharma, Lilly, Novartis, Pfizer, Sandoz, Sanofi and UCB. RG has received consultancy/speaker's honoraria from and/or participated in clinical trials for Bausch Health, AbbVie, Janssen, Eli Lilly, Kyowa Kirin, Mallincroft, Novartis, Sanofi and Sun Pharma. KJ has acted as a consultant for and/or received honoraria from AbbVie, Aclaris, Allergan, Almirall, Amgen, Arena, Aristea, Asana, Aurigene, Biogen Idec, Boehringer Ingelheim, Bristol-Myers Squibb, Escalier, Galapagos, Janssen, Lilly, MoonLake Immunotherapeutics, Nimbus, Novartis, Pfizer, Sanofi, Sienna Biopharmaceuticals, Sun Pharma, Target-Derm, UCB, Valeant and Ventyx. KJ has received grant support (to The Rockefeller University) from AbbVie, Akros, Allergan, Amgen, Avillion, Biogen, Botanix, Boehringer Ingelheim, Bristol-Myers Squibb, Exicure, Innovaderm, Incyte, Janssen, Kyowa Kirin, Lilly, Nimbus Lackshmi, Novan, Novartis, PAREXEL, Pfizer, Regeneron, UCB and Vitae Pharmaceuticals. TS is a full time employee of Triducive Partners Limited. NW is a full time employee of Triducive Partners Limited.

DATA AVAILABILITY STATEMENT

Research data are not shared. This is due to the anonymity and confidentiality of the Delphi methodology employed in this study.

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