Core outcomes in vitiligo trials: progress and challenges

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Vitiligo is the most common depigmentation disorder, affecting 0.5% of the population worldwide. It has a major negative impact on the quality of life of patients [1, 2]. Vitiligo that begins in childhood can be associated with significant psychological trauma that may have a long-lasting effect on personal self esteem [3]. However, vitiligo is still largely perceived as a cosmetic disorder and the only intervention licensed for vitiligo in the UK is cosmetic camouflage [4].

What outcomes are currently being measured in vitiligo trials?
A recent systematic review of outcomes in trials for vitiligo treatments found that 25 different outcomes had been measured in 54 eligible randomized controlled trials. These included repigmentation, time to reach repigmentation, pattern of repigmentation, cessation of spreading, quality of life and clinician global assessment, amongst others [5]. Although repigmentation was reported in 96% of trials, this was measured using 48 different scales. In particular, repigmentation was measured using a great variety of scales including grades, scores (0–4), categories (poor–excellent), quartiles and quintiles, percentages and mean difference in lesion size in millimeters [5]. Only 17 and 9% of trials assessed patients’ opinion of treatment and satisfaction with quality of life, respectively [5].

What recommendations have been made regarding outcome measures in vitiligo trials?
The Cochrane systematic review “Interventions for vitiligo” [4] and recent guidelines for designing and reporting clinical trials on vitiligo [6] have suggested that patient-centered outcomes should be incorporated into the design of future trials. A recent survey of most desirable outcomes for patients and clinicians in future vitiligo trials further highlighted the need for incorporating patient-reported outcomes, such as the cosmetic acceptability of the results [5]. This survey reported that “cosmetically acceptable” repigmentation (rather than “percentage of repigmentation”), quality of life, and long-term maintenance of repigmentation should be measured in future trials [5]. Recently, efforts have been made to create vitiligo-specific instruments such as the Vitiligo European Task Force scoring tool [7] and the vitiligo-specific health-related quality of life instrument [8], however these have not been used in vitiligo trials to date.

Why is it difficult to measure percentage of repigmentation in vitiligo trials?
Percentage of repigmentation is the most commonly assessed outcome in vitiligo trials; however, there is no evidence to justify this, especially from the patient’s perspective and considering the negative psychological impact of the disease on patients. What might be considered an improvement by clinicians in percentage terms may not be perceived

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as such by vitiligo patients. In addition, variability in the outcomes reported in randomized controlled trials for the treatment of vitiligo, means that combining trial results in meta-analyses is not usually possible, thus limiting the clinical conclusions that can be made [4].

Vitiligo results in patches of depigmented skin. Intuitively it would seem to be a simple matter to record treatment success or failure based on changes in the amount of repigmented skin observed. However, the following aspects make this assessment difficult:

- Vitiligo often affects multiple anatomical sites and lesions vary in size and shape, making physical measurement of lesions on all affected areas difficult and time consuming;
- When repigmentation of the vitiligo patches does occur, it can often be patchy with pigmented spots within the white areas (perifollicular), or of a different skin tone to a patient’s normal skin color. This can reduce the cosmetic acceptability of the treatment response and a simple assessment of percentage of repigmentation may fail to capture this aspect;
- Highly visible sites such as the hands and face are associated with higher psychological morbidity [9], again leading to a potential reduction in the acceptability of treatment response.

What changes in outcome measures for vitiligo are currently being proposed?

Whilst a standardized method of measuring percentage repigmentation will remain an important ‘objective’ assessment of improvement in disease following treatment, it is also important to consider how worthwhile the treatments are for individual patients. We recommend that measuring acceptability of treatment response from the patient’s perspective should be incorporated into future vitiligo trials as an important outcome. This could be done by simply asking patients whether or not they feel the treatment has been worthwhile, or whether they would wish to continue with treatment after the trial has ended. In addition, quality of life for people with vitiligo can be significantly impaired, and therefore measuring the impact of vitiligo treatments on quality of life is surely important [4,5,6]. In addition, further work is required to establish consensus as to how best to capture percentage repigmentation, so that all trials measure and report this outcome in a consistent manner [5].

In line with other areas of medicine, there is growing consensus that ‘core outcome sets’ should be developed for all disease areas in order to facilitate comparison of trial results and reduce research waste. This work is being led by the COMET initiative [10]. Currently, core outcome measures for vitiligo have not been established, although the international vitiligo research community is now starting to address this issue.

The Vitiligo European Task Force, a group of experts in vitiligo research, have started a collaboration with the Asian Society for Pigment Cell Research, the European Society for Pigment Cell Research, the Japanese Society for Pigment Cell Research and the Pan-American Society for Pigment Cell Research. This collaboration seeks to address these issues, and to develop a core outcome set for future vitiligo trials. Part of this process will be to achieve consensus amongst patients, clinicians and regulatory authorities regarding the most important outcomes (or domains) to be captured in future trials. Once this has been agreed, further work will take place to establish how best to measure these important outcomes in a consistent way.

Future perspective

We are hopeful that establishing core outcomes and unified scales in future vitiligo trials will allow vitiligo research to move forward for the benefit of patients and the clinical community.

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