criteria included <25% scalp area affected, pregnancy, significant cardiovascular disease or serious medical illness.

Diphencyprone powder (PPR Diagnostics, London, England) was dissolved in acetone at serial dilutions of 0.001%, 0.01%, 0.025%, 0.05%, 0.1%, 0.25%, 0.5%, 1.0%, 1.25%, 2.0%, 2.5%, 3%, 3.5%, 4.0% and 5% and stored at 4 °C in tightly sealed dark vials to prevent UV light degradation and evaporation.

At the first visit, each patient was sensitized with 2.5% DPC applied on a 5 cm diameter bald area of the scalp. After 1–2 weeks, according to the severity of the eczematous reaction one coat of 0.001% DPC was applied to the scalp using reinforced cotton-tipped applicator. This was repeated weekly while gradually increasing the DPC concentration according to each patient's response; the aim being to maintain erythema and itch for 48 h. The concentration was raised when the irritation induced became minimal. In most of our patients, the concentration was raised every 4–5 weeks. In patients with history of atopy, the initial concentration used was lowered to 0.0001% and each concentration was sometimes maintained for 7–8 weeks. Patients were instructed to avoid direct sun exposure and washing the scalp for 48 h after each application.

History before treatment included age at the start of DPC therapy, duration of disease, duration of the current episode of AA, presence of atopy and family history of AA. Data collected at the time of initial examination included the baseline extent of scalp AA (categorized as 25–49%, 50–74%, 75–99% or 100% hair loss); eyebrow and body hair loss and nail involvement.

An initial response was defined as appearance of any new terminal hair within treated sites. Excellent response was defined as >75% of the scalp covered with terminal hair. Relapse was defined as >25% hair loss. Maintenance topical immunotherapy, defined as ongoing therapy once every 1–4 weeks, was generally recommended for patients who achieved excellent response.

During treatment, data collected included the highest DPC concentration applied, duration of DPC treatment and its concentration at initial and excellent response if it was achieved, presence and type of side-effects, hair loss status at time of treatment discontinuation if >75% regrowth was not achieved and relapse during therapy.

Patients with excellent response were then divided into two groups; those choosing to continue on maintenance therapy and those preferring to stop therapy. Both groups were followed up to detect any relapse (>25% hair loss) of AA as well as development of side-effects.

Results

Patient data

In our 135 cases, 58% were males and 42% were females. Age at onset of disease ranged from 1 to 57 years (mean 15.53 ± 10.51 years), and age at onset of therapy with DPC ranged from 2.25 to 60 years (mean 22.05 ± 10.32 years). This study included 21 children (age ≤12 years), four were under the age of 5, three between 5 and 10, and 14 were over 10 years. An informed consent was taken from their parents before therapy. Disease duration ranged from 1.5 months to 30 years (mean 6.61 ± 6.03 years), and the duration of the last attack of AA ranged from 1.5 months to 22 years (mean 3 ± 3.15 years). In our patients, 9.6% were atopic, 3.7% had juvenile diabetes mellitus, 1.5% had thyroid disease, 12.6% had nail affection and 11.9% had a family member with AA. Patients were divided into five groups according to the area of scalp affected: Grade 1 AA: 25–49% scalp affection (18 patients); Grade 2 AA: 50–74% scalp affection (13 patients); Grade 3 AA: 75–99% scalp affection (38 patients); alopecia totalis: 32 patients and alopecia universalis: 34 patients. The duration of therapy ranged from 1 week to 36 months (mean 7.97 ± 6.22 m). The most common cause of discontinuation of therapy was lack of response and the inconvenience of attending the clinic for weekly therapy. In addition, therapy was stopped in four patients because of the development of tolerance and in three patients due to the development of vitiligo.

Response to therapy

Ninety-seven patients continued therapy for ≥3 months, 16 patients had just started therapy and did not complete 3 months, while 22 dropped out. Of those 97, 11 had Grade 1 AA, nine had Grade 2 AA, 28 had Grade 3 AA, 22 had AA totalis and 27 had AA universalis. The cumulative patient response rate to DPC immunotherapy overtime after an initial lag of 3 months is presented in Table 1. The median time needed to achieve excellent response was 12 months [95% confidence interval (CI) 11.2–12.8 months].

Of the 27 patients with AA universalis, three patients (11%) showed spontaneous regrowth of the eyebrows and eyelashes. No spontaneous improvement in nails occurred during DPC therapy.

Patient variables

Using the Cox regression model, the only patient variable that was associated with achievement of excellent response was the baseline extent of AA, while other patient variables including age at onset of disease, age at onset of therapy, disease duration, nail affection, presence of atopy, juvenile diabetes or thyroid disease and family history of AA did not affect the probability of regrowth (Table 2).

Table 1 Cumulative patient response rate to DPC immunotherapy overtime

Duration of DPC therapy (months)	Clinically significant hair regrowth, % (no. of patients)	Residual probability of hair regrowth, %
3	1 (1)	40
6	15.4 (15)	29.6
12	48.5 (47)	5.9
18	52.6 (51)	3
24	55.7 (55)	0.8

DPC, Diphencyprone.