Table II. Patients with grade 2 laboratory abnormalities or discontinuing methotrexate (any cause) during first 4 months of therapy by initial dose received

	Grade 2 abnormality*		Discontinued	
Category	**Yes**	**No**	**Yes**	**No**
Initial dose, mg				
5.0	2	57	2	57
7.5	2	72	4	70
10.0	0	33	3	30
12.5	0	3	0	3
15.0	0	2	0	2
Odds ratio†	0.73		1.11	
P value‡	.32		.48	

*Tests included were hemoglobin concentration, white blood cell count, absolute neutrophil count, platelet count, and alanine aminotransferase concentration.
†Odds ratio represents the odds of having a grade 2 abnormality or discontinuing methotrexate for each 1-mg increase in initial dose. Odds ratio was obtained from a logistic regression of having a grade 2 abnormality or discontinuing methotrexate on the initial dose of methotrexate.
‡*P* value for the odds ratio.

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Evaluating results of an interferon-γ release assay in patients with autoimmune disease who are taking hydroxychloroquine

To the Editor: New treatment options are emerging for patients with autoimmune diseases, and these treatments require careful evaluation before their initiation. Patients with autoimmune disease are already at an increased risk for reactivation of latent tuberculosis compared with the general population, and therefore great care must be exercised when starting immunosuppressive therapy.[1] Given these risks, standard of care requires screening for latent tuberculosis in this vulnerable population before initiating immunosuppressants. QuantiFERON-TB Gold (QFT-G) is a widely used interferon-γ release assay that is used to screen patients for tuberculosis. Briefly, patients' blood is incubated with *Mycobacterium tuberculosis* antigens; levels of interferon-γ released are then measured. Results, based on quantitative thresholds of interferon-γ detected, are reported as determinate—either clearly positive or clearly negative—or indeterminate.

Clinical studies on the efficacy of QFT-G demonstrate higher rates of indeterminate results among immunosuppressed populations compared with the general population.[1,2] This is clinically important, because indeterminate QFT-G results may preclude patients from starting certain therapies or enrolling in clinical trials. In addition, many patients with autoimmune disease are started on hydroxychloroquine before escalating therapy to immunosuppressive therapies, which require tuberculosis screening before their initiation.[3] Interestingly, hydroxychloroquine is proposed to reduce levels of interferon-γ and therefore may affect the results of a QFT-G test.[3,4] Taken together, this suggests that patients with autoimmune disease who are being treated with hydroxychloroquine may face barriers to accessing novel therapies when screened with QFT-G because of falsely indeterminate test results.

The medical records of 89 patients enrolled in prospective longitudinal databases for cutaneous lupus and dermatomyositis with QFT-G testing were reviewed. Patients were sorted into groups based on the presence or absence of

Table I. Patient characteristics

Demographics	Hydroxychloroquine, n = 45	Controls,* n = 44	*P* value
Age ± SD	44.7 ± 11.9	49.2 ± 16.6	>.05
Female, n (%)	38 (84)	37 (84)	
Race, n (%)			
African American	10 (22)	10 (23)	
White	32 (71)	31 (70)	
Asian	1 (2)	2 (5)	
Other	2 (4)	1 (2)	
Diagnosis, n (%)			
CLE/SLE	20 (44)	17 (23)	>.05
DM	25 (54)	27 (37)	>.05

CLE/SLE, Cutaneous lupus erythematosus/systemic lupus erythematosus; *DM*, dermatomyositis; *SD*, standard deviation.
*Patients in the control group were not taking hydroxychloroquine within the year before QuantiFERON-TB Gold testing.

Table II. Concomitant drugs

	Hydroxychloroquine, n = 45			Controls, n = 44			
Concomitant drugs	n (%)	Dose, mg	Duration, months	n (%)	Dose, mg	Duration, months	*P* value
Antimalarials							>.05
Chloroquine	0	0	0	5 (7)	250	7.2	
Quinacrine	15 (33)	100	12.73	9 (12)	100	6.4	
DMARDs							>.05
Mycophenolate mofetil	13 (28)	2057.7	7.3	7 (23)	1735.3	6.3	
Methotrexate	10 (22)	13.5	4	10 (23)	15	15	
Azathioprine	5 (11)	106.3	6.5	2 (5)	87.5	5	
Dapsone	1 (2)	100	8.5	2 (3)	75	8.5	
Prednisone	19 (41)	13.4	7.1	7 (16)	27.6	4.5	<.01

DMARD, Disease-modifying antirheumatic drug.
Patients in the control group were not taking hydroxychloroquine within the year before QuantiFERON-TB Gold testing. Drugs were used by the patient from the date of QuantiFERON-TB Gold testing up to 1 year before testing. Dose and duration represent an average during the 1-year time period.

hydroxychloroquine use within 1 year of QFT-G testing. We also evaluated the concomitant use of additional antimalarials, prednisone, and disease-modifying antirheumatic drugs (DMARDs).

In the study population of 89 patients, 45 were in the hydroxychloroquine group, while 44 did not use hydroxychloroquine in the year before testing. The basic demographic characteristics of both groups are presented in Table I. In total, there were 22 (25%) indeterminate, 54 (61%) negative, and 2 (2%) positive QFT-G results. The hydroxychloroquine group had significantly more indeterminate QFT-G results (38%) compared with the nonhydroxychloroquine group (6.6%; $P < .01$). There was no significant difference in concomitant use DMARDs ($P > .05$) between groups (Table II). The hydroxychloroquine group had significantly more patients who were taking prednisone compared with the nonhydroxychloroquine group ($P < .01$). However, a subanalysis revealed that there was no significant difference in the rate of indeterminate results between patients who were taking prednisone (38%) and patients who were not taking prednisone (20%; $P > .05$).

These results reveal that patients who were taking hydroxychloroquine at the time of QFT-G testing are significantly more likely to have an indeterminate result compared with those who were not taking the medication, and this finding was not explained by the concomitant use of prednisone or DMARDs. Indeterminate QFT-G results may delay the initiation of immunosuppressive therapy and exclude patients from clinical trials for novel drugs. These findings suggest a need for further study to evaluate the most appropriate tuberculosis testing in patient populations that are being treated with hydroxychloroquine. Some centers have recently switched from the QuantiFERON-TB Gold assay to a newer generation assay called the QuantiFERON-TB Gold Plus. Our research group is currently comparing QuantiFERON-TB Gold Plus against T-SPOT.*TB*, an alternative tuberculosis screening test.

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Tofacitinib therapy for children with severe alopecia areata

To the Editor: Alopecia areata (AA) is a common autoimmune disorder that might progress to alopecia totalis (AT) and alopecia universalis (AU), which significantly affect patients' psychologic well-being and quality of life. The disease can start at any age, but severe forms often start during childhood. Several studies and case reports have shown promising results of using Janus kinase (JAK) inhibitors for the treatment of AA.[1] Previous case series have reported the use of systemic tofacitinib in adolescent patients aged 12 to 19 years and the use of topical tofacitinib and ruxolitinib in pediatric patients aged 3 to 17 years.[2-4] A recent case series showed favorable response to systemic tofacitinib among 4 patients with AA aged 8 to 10 years.[5] In this report, we have presented 3 children aged 5 years or younger with AT and AU treated with systemic tofacitinib.

We reviewed the records of patients with AA, AT, or AU who were treated with tofacitinib in the Taipei Veterans General Hospital between January 2016 and January 2018. The inclusion criteria were patient age less than 12 years, a clinical diagnosis of AA with at least 50% scalp hair loss, AT, AU, stable or worsening disease for at least 6 months, and treatment with tofacitinib for at least 4 months. Disease severity was assessed by dermatologists using the validated Severity of Alopecia Tool (SALT) score. Safety was evaluated by physical examinations; review of systems; and laboratory monitoring, including complete blood count with differential, complete metabolic panel, and fasting lipid panel before treatment, after 4 weeks of treatment and then every 3 months. This study was approved by the institutional review board of Taipei Veterans General Hospital (2018-01-018AC).

The baseline characteristics and treatment response are shown in Table I. We identified 3 pediatric patients who failed previous treatment before tofacitinib therapy. All patients were treated with tofacitinib, 2.5 mg once daily, in the beginning. Patient 3 experienced unsatisfactory hair regrowth (<20% improvement) after 6 months of treatment; thereafter, the patient's dose was adjusted to 2.5 mg once daily for 4 doses and 5 mg once daily for the other 3 doses each week. One patient achieved greater than 90% hair regrowth after 12 months of treatment (Patient 2, Fig 1), and the other 2 patients showed greater than 50% improvement by 6 months and 21 months, respectively. Patient 3 had complete regrowth of the eyebrows and eyelashes and partial regrowth of the scalp hair. Although response was not complete, we decided to continue treatment at the same dose, as there are no safety data for higher-dose tofacitinib in such young children and the parents did not wish to consider other treatments such as systemic corticosteroids because of the potential side effects. The side effects were mild and limited to diarrhea (patients 1 and 3) and upper respiratory tract infection (patient 2). These symptoms resolved completely despite ongoing therapy.