Effectiveness of Less Commonly Used Systemic Monotherapies and Common Combination Therapies for Moderate to Severe Psoriasis in the Real World Setting: Results from the Dermatology Clinical Effectiveness Research Network (DCERN)

Junko Takeshita, MD, PhD,[1,2] Shuwei Wang, BS,[1] Kristina Callis Duffin, MD,[3] Gerald G. Krueger, MD,[3] Andrea B. Troxel, ScD,[2] Abby S. Van Voorhees, MD,[1] Joel M. Gelfand, MD, MSCE[1,2]

[1]Department of Dermatology, [2]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, PA, USA

[3]Department of Dermatology, University of Utah, Salt Lake City, UT, USA

Introduction

- Despite an increasing number of therapies available for treatment of moderate to severe psoriasis, data on the effectiveness of such therapies in the real world clinical setting remain scant.
- We recently reported the effectiveness of commonly used systemic therapies (methotrexate, adalimumab, etanercept, ustekinumab) and phototherapy to be lower in the clinical setting compared to what is reported in randomized controlled trials (RCTs).
- In this study, we evaluate the effectiveness of the less commonly used systemic monotherapies and common combination therapies for moderate to severe psoriasis in the clinical setting.

Methods

- *Study Design:* Cross-sectional.
- *Study Population:* Consecutively enrolled patients with moderate to severe plaque psoriasis who presented for routine follow-up at any one of 8 dermatology practices (2 academic practices - University of Pennsylvania and University of Utah; 6 private practices in Georgia, Pennsylvania, New York, and Colorado) within the Dermatology Clinical Effectiveness Research Network (DCERN).
- *Primary Outcome:* Physician Global Assessment (PGA) 6 point scale dichotomized as clear or almost clear disease (0-1) vs. mild to severe disease (2-5).
- *Covariates Assessed:* Medical history, current and past psoriasis treatments, sociodemographic factors, psoriasis characteristics, height, weight, alcohol history, and tobacco history.
- *Statistical Analysis*:
  - Univariate analyses: Kruskal-Wallis test for grouped ordinal data; unpaired 2-tailed t tests and Mann-Whitney tests for pairwise comparisons of continuous data; χ^2 or Fisher exact test for dichotomous data.
  - Multivariable analyses: Modified Poisson regression with robust error variance was used to calculate the relative response rate (i.e., relative risk (RR)) using methotrexate (mtx) as the reference group.

Results

Table 1. Baseline Patient and Psoriasis Characteristics

Characteristic[a] (n=203)	N (%)
Age, year	
Mean (SD)	50.4 (14.7)
Median (IQR)	51 (40-62)
Female Sex	100 (49.3)
White Race	187 (92.1)
BMI, median (IQR)	30.2 (25.8-35.7)
Number of comorbidities, median (IQR)[b]	3 (1-5)
Duration of psoriasis, median (IQR)	21 (10-31)
Psoriatic arthritis	79 (38.9)
Number of previous biologic, oral, systemic, or phototherapy treatments, median (IQR)	2 (1-3)
Previous psoriasis treatment[c]	
Biologic	100 (49.3)
Oral systemic	117 (57.6)
Phototherapy	89 (43.8)
None	37 (18.2)

Abbreviations: SD, standard deviation; IQR, interquartile range.
[a]Patients with plaque psoriasis receiving acitretin, cyclosporine, infliximab, adalimumab+mtx, etanercept+mtx, or infliximab+mtx.
[b]Including cardiovascular, lung, infection, gastrointestinal, renal, endocrine, musculoskeletal, psychiatric, neurologic, malignant or autoimmune diseases.
[c]Percentages do not total 100 because some patients may have used more than one previous treatment.

Table 2. Treatment Characteristics

Current Psoriasis Treatment	N (%)	Treatment dose and frequency	Duration w/o interruption, median (IQR), month (P=0.003)[d]	Prescription topical use in past week, median (IQR), day (P<0.001)[d]	Mtx dose, median (IQR), mg/week (P<0.001)[d]
Mtx	168 (45.3)	<7.5 mg/wk: 1.8% 7.5-27.5 mg/wk: 92.2% ≥30mg/wk: 6.0%	10 (4-24)	2 (0-7)	15 (15-20)
Acitretin	37 (10.0)	<10mg/d: 5.4% 10-25mg/d: 86.5% 30-50mg/d: 8.1%	15 (4-33)[e]	5 (3-7)	NA
Cyclosporine	19 (5.1)	<2.5mg/kg/d: 47.4% 2.5-5mg/kg/d: 36.8% >5mg/kg/d: 15.8%	4 (1-12)	0 (0-7)	NA
Infliximab	42 (11.3)	5mg/kg/8wk: 29.3% >5mg/kg/8wk: 70.7%	24 (7-60)	0 (0-4)	NA
Adalimumab + Mtx	49 (13.2)	40mg/wk: 18.4% 40mg/2wk: 79.6% 40mg/>2wk: 2.0%	8 (4-16)	1 (0-6)	10 (7.5-15)
Etanercept + Mtx	22 (5.9)	25mg/wk: 4.6% 50mg/wk: 72.7% >50mg/wk: 22.7%	11.5 (3-24)	4 (2-7)	11.3 (7.5-17.5)
Infliximab + Mtx	34 (9.2)	5mg/kg/8wk: 20.6% >5mg/kg/8wk: 79.4%	11 (3-24)	0 (0-4)	15 (10-22.5)

[d]Kruskal-Wallis test; [e]Missing data n=1.

Table 3. Physician and Patient Reported Outcomes, Crude Response Rate and Relative Rates of PGA Clearance

Current Treatment	PGA Median (IQR) (P=0.001)[f]	DLQI Median (IQR) (P=0.08)[f]	Crude Response Rate PGA ≤ 1 % (95% CI) (P<0.001)[g]	Adjusted RR (95% CI)[h]	Response Rate Difference (95% CI)[i]	NNT[j]
Mtx (n=169)	1.7 (1.3-2)	3 (1-5)	22.3 (16.2-29.3)	1 [Reference]		
Acitretin (n=37)	1.3 (1-1.7)	2.0 (1-6)	35.1 (20.2-52.5)	2.01 (1.18-3.41)	0.22 (0.04-0.54)	4.4
Cyclosporine (n=19)	1.3 (0.7-2)	5 (2-15)	36.8 (16.3-61.6)	1.44 (0.75-2.74)	0.10 (-0.05-0.39)	NA
Infliximab (n=42)	1.3 (1-2)	1 (0-4)	46.3 (30.7-62.6)	1.93 (1.26-2.98)	0.21 (0.06-0.44)	4.8
Adalimumab + Mtx (n=49)	1.0 (0.3-2)	1 (0-5)	59.2 (44.2-73.0)	3.04 (2.12-4.36)	0.45 (0.25-0.75)	2.2
Etanercept + Mtx (n=22)	1.2 (1-2)	4 (1-7)	50.0 (28.2-71.8)	2.22 (1.25-3.94)	0.27 (0.05-0.66)	3.7
Infliximab + Mtx (n=34)	1.3 (0-2)	1 (0-6)	44.1 (27.2-62.1)	1.72 (1.10-2.70)	0.16 (0.02-0.38)	6.2

Abbreviations: DLQI, Dermatology Life Quality Index.
[f]Kruskal-Wallis test; [g]χ^2 test; [h]Adjusted for age, sex, marital status, practice setting of dermatologist, body mass index, psoriasis response to natural light, topical medication frequency; [i]Difference between adjusted and baseline response rate; [j]Number of patients needed to treat with particular treatment to gain one additional patient with PGA clearance relative to response achieved with mtx.

Conclusions

- Less than 50% of patients on each examined therapy were clear/almost clear of psoriasis except for those on adalimumab + mtx.
- Effectiveness of the examined therapies was less than their reported efficacies in RCTs
  - Infliximab: 46.3% vs 74% in the European Infliximab for Psoriasis (Remicade) Efficacy and Safety Study I (Lancet. 2005;366(9494):1367-1374).
  - Etanercept + mtx: 50.0% vs 71.8% in an RCT of etanercept + mtx (The British Journal of Dermatology. 2012;167(3):649-657).
- Patients on infliximab monotherapy exhibited longest median duration of uninterrupted therapy, and a high proportion received escalated doses.
- Absolute differences among therapy response rates were small, and no corresponding difference in patient-reported outcomes were observed.
- Limitations: cross-sectional design, selection and channeling biases, phenomenon of clinical drift (which may overestimate effectiveness).

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