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Apremilast for the treatment of active psoriatic arthritis: a single centre real-life experience

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Key message: Real life experience of apremilast in PsA suggests enhanced efficacy in early disease.

Sir, Apremilast (Otezla; Celgene, Summit, NHJ, USA) is a small-molecule phosphodiesterase-4 inhibitor which offers a novel oral therapeutic option for patients with psoriasis (Pso) and psoriatic arthritis (PsA). Recent randomized controlled trials (RCTs) show that Apremilast is effective in both Pso and PsA (1-6) however there are still a paucity of real-life data in unselected patients.

We performed, at our tertiary centre, a retrospective analysis of the effectiveness and tolerability of Apremilast at a standard dose of 30 mg BID in subjects with PsA treated in a dedicated out-patient clinic following a Zero cost scheme prior to NICE approval in the UK.

All subjects fulfilled Classification Criteria for PsA (CASPAR) (7) and had active disease according to the treating clinician. In addition, all subjects had previously been exposed to adequate trials of DMARDs. Ethical approval was not required as this report was an audit of standard practice and service evaluation.

As part of our local clinic algorithms, subjects were assessed at baseline and every 6 (±3) months. Clinical assessments at each visit included tender (0-78) and swollen (0-76) joint count and C-reactive protein (CRP) levels. When patient and physician global assessment on a 5-point Likert scale were available on clinical notes review, PsA response criteria (PsARC) were also calculated (8).

Subjects were classified as responders and non-responders based on the overall physician judgement of clinical status (yes/no), specifically: the absence of peripheral arthritis, enthesitis and dactylitis on clinical examination; or improvement of clinical signs at physical examination and concurrent patient's reported improvement of symptoms as per

PsARC. Response was defined based on the last available follow-up assessment as compared with the baseline evaluation.

Binomial variables were expressed as number and percentages, continuous variables as median (range) or mean±SD as appropriate. Comparison between baseline and follow-up measurements was performed using Wilcoxon matched-pairs signed rank test. Significant differences between responders and non-responders were defined as those at a level of $p<0.05$, by unpaired t-test or Fisher's/chi-square test. Statistical analysis was carried out using GraphPad Prism software V.7.0.

A total of 71 patients (n=33 [46.5%] male) with a mean follow-up of 172.6±105.5 days were identified and included in this report. Clinical characteristics are summarized in Table 1. Of the 71 patients started on Apremilast, 51 had at least a 6 (±3) months follow-up assessment. Based on overall clinician judgement, 31 out of 51 (60.8%) patients were classified as responders and 20 (39.2%) as non-responders. In patients in which joint count was recorded at the baseline and at the follow-up assessment (n=22), there was a statistically significant improvement of tender ($p=0.004$) and swollen ($p=0.003$) joint count. In patients with abnormal CRP levels at baseline, measurements slightly decreased at follow-up ($p=0.04$). Of note, responders had a shorter disease duration compared to non-responders (5.23±4.46 vs 9.15±6.8 years, $p=0.016$), and had a lower exposure to previous biological DMARDS (bDMARDS) ($p=0.0055$) and conventional or synthetic DMARDS (cDMARDS), although this latter difference did not reach statistical significance ($p>0.05$). No other significant differences were found between the two groups.

A total of 28 (39.4%) subjects required drug discontinuation after a mean period of 129.7 (±77.7) days due to either lack of efficacy and/or to side effects. Overall, 27 (38%) patients

developed one or more side effects (Table 1). The most common side effects were gastro-intestinal (GI) symptoms (19/71) including: nausea (9/71), vomiting (3/71), diarrhea (13/71) and abdominal pain with loss of appetite (1/71). Two patients experienced depression (2.8%), of which one had associated suicidal ideation and concomitant headache and GI symptoms which required drug withdrawal within the eighth week.

To our knowledge, this is the first real-life report of the use of Apremilast in unselected PsA patients. Previously published RCTs showed that Apremilast is effective in patients with PsA and Pso with an acceptable safety profile. In patients with PsA treated with apremilast 30 BID, ACR20 response ranged between 32.1% and 41% at week 16, in three different phase III RCTs (4-6). Despite using different response criteria, our data from an unselected tertiary centre population confirm these results. A main limitation of our report are the low numbers treated and the amount of missing data which reflects a real population observation, and is in part due to the use of paper based assessments in our hospital.

An important observation however and despite the low numbers, is that clinical response appeared to be enhanced in the subset of patients with shorter disease duration suggesting that apremilast may be better placed earlier on in the treatment algorithm for PsA although this observation would need to be confirmed with larger numbers.

In conclusion, our data provide real life evidence of the short-term efficacy of apremilast in the treatment of active PsA and suggest that this may be enhanced in the earlier disease stages. Apremilast represents a valuable, additional, oral, synthetic molecule for the treatment of PsA. Larger observational cohort studies with health economic evaluation will help confirm the placing of apremilast in the treatment algorithm for PsA.

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Table 1. Baseline clinical characteristics of 71 PsA patients treated with Apremilast

Male, n (%)	33 (46.5)
Age, years, mean (SD)	51, 13.2
DD PsA, years, mean (SD)	7.7, 6.4
Peripheral involvement (all poly-articular), n (%)	71 (100)
Axial involvement, n (%)	22 (31)
Psoriasis, n (%)	59 (83.1)
Nail involvement, n (%)	20 (44.4)
Entheseal/Dactylitis involvement, n (%)	38 (60.3)
CRP baseline, mg/L, median (range)	7.1 (5-115)
Tender Joints count, median (range)	7 (0-40)
Swollen Joints count, median (range)	3 (0-16)
Patient's disease activity, 1-5, median (range)	4 (1-5)
Physician's disease activity, 1-5, median (range)	3 (1-5)
Current cDMARDS	n (%)
MTX	18 (25)
SZ	1 (1.4)
HCQ	2 (2.8)
Leflunomide	1 (1.4)
Combination (MTX + SZ, MTX +HCQ)	2 (2.8)
Current bDMARDS	n (%)
Certolizumab	2 (2.8)
Golimumab	2 (2.8)
Ustekinumab	2 (2.8)
Adalimumab	1 (1.4)
Etanercept	1 (1.4)
Secukinumab	1 (1.4)
Tocilizumab	1 (1.4)
Previous cDMARDS, n (%)	67 (94.4)

Previous bDMARDS, n (%)	40 (56.3)
Contraindication to bDMARDS, n (%)	10 (14.1)
Apremilast discontinuation, n (%)	28 (39.4)
Ineffective	11 (15.5)
Side effects:	27 (38)
GI symptoms	19
General malaise	2
Headache	8
Depression, suicidal ideation	2, 1
Time to discontinuation, days	
mean (SD)	129.7 (77.7)
median (range)	132 (21-313)
Time of follow-up, days	
mean (SD)	172.6 (105.5)
median (range)	153 (21-519)

Percentage in parenthesis is calculated based on the number of patients with the specific feature among the total patients with the available data on clinical notes review. bDMARDS: biologic disease modifying antirheumatic drugs; cDMARDS: conventional disease modifying antirheumatic drugs; DD: disease duration; GI: gastrointestinal; SZ: Sulfasalazine.