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CLINICAL REPORT

Efficacy and Safety of Systemic Treatments for Psoriasis in Elderly Patients

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Management of psoriasis in elderly patients can be challenging, because of the impairment of immune system efficiency and the presence of comorbidities that contraindicate systemic therapies. We studied the safety and efficacy of systemic traditional and biological treatments in 187 consecutive psoriatic patients aged >65 years. At week 12 of therapy, Psoriasis Area and Severity Index 75 was achieved by 49%, 27%, 46% and 31% of patients who received methotrexate, acitretin, cyclosporine or PUVA, and 64%, 65%, 93%, 57% and 100% of patients who received etanercept, adalimumab, infliximab, efalizumab and ustekinumab. The rate of adverse events was 0.12, 0.32, 1.4 and 0.5 per patient-year in the methotrexate, acitretin, cyclosporine and PUVA groups and 0.11, 0.35, 0.19, 0.3 and 0.26 in the etanercept, adalimumab, infliximab, efalizumab and ustekinumab groups. Traditional drugs were less effective than biologics in our elderly population. Etanercept was associated with a lower rate of adverse events compared with other treatments. ***Key words: psoriasis; elderly; methotrexate; cyclosporine; acitretin; biologics; TNF alpha-inhibitors.***

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Psoriasis is a common inflammatory disease that affects 2% to 3% of the population (1). Due to its chronic nature and to the ageing of the general population, psoriasis increasingly affects the geriatric population. People aged 65 years or over will account for a predicted 19% of the US population by 2030 (12.4% in 2000) (2) and 29.5 % in Europe by 2060 (17.4 % in 2010) (3).

Many elderly psoriatic patients are not adequately treated and suffer both physical and psychological effects of psoriasis. One of the most common concerns when treating an older patient with psoriasis is the progressive impairment of the immune system with age (4). Moreover, geriatric patients often suffer from diseases that may contraindicate systemic therapies for psoriasis, and most of them take several drugs, which could potentially interact with systemic anti-psoriasis therapies.

Limited data are available in the literature regarding systemic treatment of psoriasis in the elderly population. We have therefore studied 187 consecutive patients (109 males) >65 years of age affected by chronic plaque psoriasis who were treated with at least one systemic traditional or biological drug.

PATIENTS AND METHODS

All patients who received a new treatment with systemic traditional drugs or biologics for chronic plaque psoriasis in various Italian Dermatology Departments were enrolled in a prospective patient registry, in which daily practice efficacy and pharmacovigilance data on these therapies were collected. This Italian registry was part of the regional health authorities that appointed reference centres for the systemic treatment of psoriasis, linking drug prescription data to information on effectiveness and safety. Patients were required to give written informed consent prior to participation in the programme, which consisted of a baseline assessment, on the occasion of the prescription of a new systemic anti-psoriasis treatment, and scheduled follow-up visits in which information regarding treatment outcome, laboratory parameters, adverse events, and any medical event was recorded.

Data were retrospectively extracted for all patients enrolled in the registry between September 2005 and September 2010 who were >65 years at the start of the treatment.

Clinical assessments were performed at screening and every 8 weeks thereafter. Baseline assessments included routine haematochemical tests, viral hepatitis markers, tuberculin skin test, chest radiography and other examinations aimed at excluding contraindications to the use of systemic anti-psoriasis drugs. Routine laboratory tests (including full blood count, renal and liver function tests) were regularly repeated during the observation period at the discretion of the dermatologist, also in accordance to the type of treatment prescribed and to the patient's characteristics. Efficacy was evaluated with the Psoriasis Area and Severity Index (PASI) (5). The primary end-point was the proportion of patients who had at least 75% improvement in the PASI score from baseline to week 12 (PASI 75).

The adverse event rate throughout the observation period was a secondary end-point. Reported adverse events and abnormal haematologic and laboratory values were analysed and categorised in predefined categories. The adverse event rate was expressed per patient-year of exposure to each single drug.

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Statistical analysis

Demographic data and patient characteristics were recorded and expressed as *n* (%) and means ± SD. For efficacy analyses at week 12, patients with missing post-baseline data or who interrupted the treatment due to side-effects or any reason were imputed as non-responders. Results were expressed as mean ± SD. Means were compared by the Student's *t*-test. Ordinal data were analysed using the Pearson's χ^2 test and, in situations with low cell count, the Fisher's exact test. Two-sided *p*-values < 0.05 were considered to indicate statistical significance.

RESULTS

Patient characteristics

Baseline demographic, disease characteristics and comorbidities of the 187 patients (109 males) are listed in Table I.

The mean age was 71 years (range 65–89). The mean duration of psoriasis was 22 ± 15.8 years. Mean baseline PASI score in the total patient population was 14.2. Approximately 1/4 of the patients had a history of psoriatic arthritis and more than 90% had one or more comorbidities. The most common comorbidities (treated with at least one drug) were: cardiovascular diseases ($n = 115$), metabolic syndrome ($n = 55$), hepatic steatosis ($n = 34$), renal insufficiency ($n = 24$), chronic obstructive pulmonary disease ($n = 23$), thyroid diseases ($n = 19$), latent tuberculosis ($n = 18$), previous cancer ($n = 12$), and hepatitis C virus (HCV) infection ($n = 11$).

Table I. *Demographic and clinical data of 187 psoriatic patients >65 years old and treated with systemic traditional or biologic drugs*

Variable	
Age, years, mean ± standard deviation (SD)	71.3 ± 5
Male/female, *n* (%)	109/78 (58.3/41.7)
Psoriasis duration, years, mean ± SD	22.1 ± 15.8
Psoriasis Area and Severity Index, mean ± SD	14.2 ± 6.1
Psoriatic arthritis, *n* (%)	49 (26.2)
Other comorbidities, *n* (%):	169 (90.4)[a]
Cardiovascular disease	115 (61.5)
Metabolic syndrome	55 (29.4)
Hepatic steatosis	34 (18.2)
Renal insufficiency	24 (12.8)
Chronic obstructive pulmonary disease	23 (12.3)
Latent tuberculosis	18 (9.6)
Hypothyroidism	18 (9.6)
History of neoplasm	12 (6.4)
Hepatitis C virus infection	11 (5.9)
Gastric disease	9 (4.8)
Hepatitis B virus infection	7 (3.7)
Neurologic diseases	5 (2.7)
Prostatic hypertrophy	5 (2.7)
Hyperthyroidism	1 (0.5)

[a]Most patients suffered from more than one comorbidity.

Treatments

Ninety-three patients had been treated with only one anti-psoriasis systemic drug, 60 with 2, 20 with 3 and 14 with 4 drugs. All anti-psoriasis treatments were taken in different periods (i.e., not concomitantly). In particular, 74 patients were treated with methotrexate (MTX), 62 with acitretin, 36 with cyclosporine, and 14 with PUVA (Table II). The baseline PASI score in the cyclosporine group was significantly higher than the PASI score in the other group ($p < 0.01$). The mean treatment duration was 50.2 weeks for MTX, 39.9 weeks for acitretin, 19.8 weeks for cyclosporine and 33.6 weeks for PUVA. The mean duration of cyclosporine treatment was significantly lower compared with MTX and acitretin ($p < 0.001$).

Eighty-three patients were treated with etanercept, 18 with adalimumab, 16 with infliximab, 14 with efalizumab and 4 with ustekinumab (Table III). Fourteen patients had 2 different biologics. The mean ± SD treatment duration was 103.9 ± 88.9 weeks for etanercept, 71.5 ± 49.2 weeks for adalimumab, 121.5 ± 84.1 weeks for infliximab, 50.4 ± 42.8 weeks for efalizumab and 55.6 ± 31.5 weeks for ustekinumab. Patients treated with efalizumab had a significantly lower treatment duration compared with those treated with etanercept or infliximab ($p < 0.05$).

Efficacy

At week 12, 49%, 27%, 46% and 31% of patients who received MTX, acitretin, cyclosporine and PUVA, respectively, reached PASI 75.

The mean effective therapeutic dose of MTX was significantly lower for patients >70 years than patients <70 years, even though the baseline PASI scores were comparable (10.1 mg/week vs 13.4 mg/week, $p < 0.05$; mean baseline PASI 12.3 ± 6 vs 11.8 ± 6.4, p = ns; mean PASI after 12 weeks 4.6 ± 4.5 vs 4.5 ± 7, p = ns).

At week 12, 64%, 65%, 93%, 57% and 100% of patients who received etanercept, adalimumab, infliximab, efalizumab and ustekinumab, respectively, achieved PASI 75. The proportion of patients achieving PASI 75 with acitretin was significantly lower than that of

Table II. *Characteristics of systemic traditional treatments*

	Methotrexate ($n = 74$)	Acitretin ($n = 62$)	Cyclosporine ($n = 36$)	PUVA ($n = 14$)
Baseline Psoriasis Area and Severity Index, mean ± SD	12.7 ± 5.8	14.8 ± 6.9	17 ± 5.9	14.9 ± 5.6
Range	4–32	2–32	6–32	10–30
Duration of treatment, weeks, mean ± SD	50.2 ± 46.6	39.9 ± 33	19.8 ± 22.8	33.6 ± 24
Range	4–156	4–280	2–104	3–108
Follow-up, patient-years	76	47.3	14.4	7.7
Mean dose	11.7 mg/week	0.38 mg/kg	3.5 mg/kg	

Table III. *Characteristics of biologic treatments*

	Etanercept ($n=83$)	Adalimumab ($n=18$)	Infliximab ($n=16$)	Efalizumab[a] ($n=14$)	Ustekinumab ($n=4$)
Baseline Psoriasis Area and Severity Index, mean ± SD	14.9 ± 6.4	14.3 ± 4.1	14.8 ± 5.7	16.2 ± 4.5	17.2 ± 1.9
Range	3–35	9–20	4–20	10–25	15–19
Duration of treatment, weeks, mean ± SD	103.9 ± 88.9	71.53 ± 49.2	121.5 ± 84.1	50.4 ± 42.8	55.6 ± 31.5
Range	8–416	12–178	22–300	3–120	24–87
Follow-up, patient-years	147.6	25.2	37.2	12.9	3.7

[a]Not marketed any longer.

patients treated with MTX, etanercept, adalimumab, infliximab or efalizumab ($p=0.01$, $p<0.0001$, $p<0.01$, $p<0.0001$, $p<0.05$, respectively). The PASI 75 response achieved by patients treated with infliximab was significantly higher than that reached by patients on MTX, cyclosporine and PUVA ($p<0.01$, $p<0.01$ and $p<0.001$, respectively).

Safety

The mean treatment duration was extremely variable and showed substantial differences between treatments which must be taken into account when evaluating safety data. Table SI[1] summarises the adverse events observed in each treatment groups.

The total rate of adverse events was 0.12, 0.32, 1.4 and 0.5/patient-year in the MTX, acitretin, cyclosporine and PUVA groups, respectively. The rate was significantly higher for patients treated with cyclosporine compared with MTX ($p<0.0001$). Among patients treated with biologics, the total rate of adverse events was 0.11, 0.35, 0.19, 0.3 and 0.26 per patient-year in the etanercept, adalimumab, infliximab, efalizumab and ustekinumab groups, respectively. Patients treated with adalimumab had a significantly higher rate of adverse events compared with patients treated with etanercept ($p=0.05$). Other differences in the incidence of overall adverse events between different treatment groups did not reach statistical significance.

Rates of infections per patient-year were 0.01 for MTX and 0 for acitretin, cyclosporine and PUVA. Among biological drugs, the rates of infections per patient-year were 0.05 for etanercept, 0.12 for adalimumab, 0.05 for infliximab and 0 for efalizumab and ustekinumab. The difference between the infection rates with MTX (0.01/patient-year) and adalimumab (0.12/patient-year) tended to be significant ($p=0.057$).

With regard to serious adverse events, one patient treated with etanercept and one patient treated with infliximab required hospitalisation for pneumonia. Two patients had myocardial infarction (one treated with MTX, the other with infliximab). Other causes of hospitalisation were: herpes zoster, atrial fibrillation, myasthenia gravis and pericarditis in the etanercept group (1 patient for each adverse event), thromboembolism in the infliximab group, breast carcinoma in the efalizumab group and ovarian carcinoma in the MTX group (1 patient each). Two patients (14.3%) treated with PUVA developed multiple skin squamous cell carcinomas, one after 118 sessions and the other after 50 sessions. Both patients had skin type II and had never been treated with immunosuppressive drugs.

DISCUSSION

The management of psoriasis in older patients is challenging. These patients often suffer from multiple comorbidities, such as cardiovascular disease, diabetes mellitus, hypertension, dyslipidaemia, liver disease, osteoporosis or renal insufficiency. Some of these conditions contraindicate the use of certain antipsoriatic drugs. Moreover, the multidrug regimens commonly seen in the geriatric population expose the patient to the risk of potentially health-threatening drug interactions. Another relevant concern is linked to the many alterations in both innate and acquired immunity that tend to occur in older patients, leading to a condition usually defined as "immunosenescence" (4). Immunosenescence may play a role in the greater risk of neoplasms and infectious diseases in elderly people, and may impair the response to vaccination and protection against infection and related diseases (6). In addition, there are scarcity of data in the literature regarding treatment of psoriasis in the elderly population. Therefore, physicians tend not to use systemic drugs in older patients affected by psoriasis and to prescribe topical therapies alone, which can be inadequate and insufficient in some cases (7, 8).

We investigated the safety and efficacy of traditional systemic drugs and biologics in 187 elderly psoriatic patients. More than 90% of the patients suffered from at least one comorbidity. Cardiovascular conditions, including coronary artery disease, heart failure and hypertension, were the most common comorbidities. Twenty-nine per cent of patients had metabolic syndrome and 18% hepatic steatosis. Yet, the use of systemic treatments was, in general, well tolerated by our elderly patients. The total rate of adverse events was

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lower during etanercept therapy (0.11/patient-year) compared with other biologics (0.19, 0.26, 0.3 and 0.35 per patient-year during infliximab, ustekinumab, efalizumab and adalimumab therapy, respectively) and with traditional systemic drugs (0.12, 0.32, 0.5 and 1.4 per patient-year during treatment with MTX, acitretin, PUVA and cyclosporine). The difference reached statistical significance only when comparing etanercept-treated patients with adalimumab and cyclosporine-treated patients ($p < 0.0001$). In our population cyclosporine was associated with the highest risk of adverse events (1.4/patient-year), mainly hypertension (0.76/patient-year) and renal insufficiency (0.35/patient-year). To our knowledge, no studies have systematically evaluated the safety profile of cyclosporine in the elderly. Given the baseline age-related renal impairment, the high prevalence of cardiovascular comorbidities and the high risk of drug interactions, this treatment should be used with extreme caution in elderly patients.

One of the most common concerns when treating an elderly patient with psoriasis is the use of immunosuppressive agents in an already immunosuppressed individual, which can predispose to both a higher risk of infections and the development of more severe infections. In the studied population, infections appeared to be the most frequent adverse event associated with anti-psoriatic treatments. Overall, infectious events were reported in 13 patients, and caused hospitalisation of 3 patients, 2 for pneumonia and one for herpes zoster. Rates of infections/patient-year tended to be higher for adalimumab compared with other drugs (0.12 vs 0.05 for etanercept and for infliximab, 0.01 for MTX and 0 for acitretin, cyclosporine, PUVA, efalizumab and ustekinumab; $p \leq 0.05$); however, the small number of patients did not allow complete statistical evaluation, and therefore definite conclusions cannot be drawn.

Interestingly, post-hoc analyses of clinical trials of etanercept vs placebo for rheumatoid arthritis have compared rates of infection in patients under or over 65 years of age, showing that the incidence of serious adverse events, infectious, and malignancies was not different in these 2 groups (9, 10). A more recent study compared the risk of serious infections in 11,798 anti-TNF-treated patients with rheumatoid arthritis and 3,598 patients treated with disease modifying antirheumatic drugs (DMARD) (11). This study showed that increasing age is a risk factor for severe infections in both the cohort treated with anti-TNF and the cohort treated with nonbiologic-DMARDs. Furthermore, after adjustment for the presence of comorbidities, smoking, steroid use and disease severity, anti-TNF therapy did not increase this risk any further in elderly patients than in younger patients (11).

Overall, traditional drugs appeared to be less effective than biologics in our elderly psoriatic population. At 12 weeks, the most effective traditional drug was MTX (PASI 75 achieved by 49% of patients), followed by cyclosporine (46%), PUVA (31%) and acitretin (27%). The response to PUVA was lower compared with the response generally obtained in younger patients, likely because of poor compliance and the common use of phototoxic drugs in the elderly, which may exaggerate PUVA-induced erythema. We found a significant correlation between the minimum therapeutic dose of MTX and patient age. Mean weekly doses needed to obtain a PASI 75 response were lower for patients older than 70 years compared with younger patients (10.1 vs 13.4 mg/week, $p < 0.05$). This is in agreement with a previous study on 23 patients older than 50 years treated with MTX, showing an inverse correlation between the minimum therapeutic doses and patient age. Six of 10 patients > 70 years old were treated with less than the generally recommended dose of MTX for younger patients (12). It is likely that the increase in drug accumulation that occurs with older age and with age-related impairment of kidney function may account for the lower mean doses of MTX needed to achieve clinical response in the elderly. MTX clearance has been found to decrease with decreasing creatinine clearance (13). Therefore, as serum creatinine measurement may overestimate renal function in the elderly, more accurate methods (i.e., creatinine clearance) have been suggested for the adjustment of dosage regimen. Moreover, an interesting aspect in the pharmacological profile of MTX is the presence of limited drug interactions, with very few having clinical significance (14). A recent systematic review has also downgraded the relevance of interaction between MTX and nonsteroidal anti-inflammatory drugs in patients with inflammatory arthritis (15). In particular, the concurrent administration appeared to be safe when appropriate monitoring is performed, with the exception of anti-inflammatory doses of aspirin.

All biologics showed a PASI 75 response close to or higher than 60% after 12 weeks of therapy (100%, 93%, 65%, 64% and 57% for ustekinumab, infliximab, adalimumab, etanercept and efalizumab-treated patients, respectively). It should be pointed out however, that the number of patients who received ustekinumab was extremely low.

There are only two published studies evaluating the efficacy of biologics in older patients with psoriasis (16, 17). In a post-hoc analysis of 2 phase III trials of etanercept, 77 patients > 65 years old were evaluated (16). The PASI 75 response after 12 weeks was 58.3%, similar to what we found in our study. In a post-hoc subgroup analysis of the phase III REVEAL trial, Menter et al. (17) found that 61% of 54 elderly patients with psoriasis (age ≥ 65 years) treated with adalimumab achieved PASI 75 at week 16 compared with 70% of 455 patients aged 40 to 64 years and 74% of 305 patients < 40 years (17). The efficacy rate was similar to what we reported in our patient study (65%). There is no published information

available regarding the efficacy and safety of infliximab or ustekinumab in elderly patients with psoriasis.

It should be underlined that our study has several limitations mainly related to the observational and retrospective nature, as well as to the small sample size and the heterogeneous duration of treatment. Prospective studies investigating the efficacy and safety profiles of systemic treatments in adequate samples of elderly psoriatic patients and for long periods of observation are needed to draw definite conclusions.

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REFERENCES

1. Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. Lancet 2007 21; 370: 263–271.
2. Population structure and ageing-Statistics Explained (2012/8/5) http: //epp.eurostat.ec.europa.eu/statistics_explained/index.php/Population_structure_and_ageing.
3. http: //www.aoa.gov/aoaroot/aging_statistics/index.aspx.
4. Agarwal S, Busse PJ. Innate and adaptive immunosenescence. Ann Allergy Asthma Immunol 2010; 104: 183–190.
5. Fredriksson T, Pettersson U. Severe psoriasis – oral therapy with a new retinoid. Dermatologica 1978; 157: 238–244.
6. McElhaney JE, Effros RB. Immunosenescence: what does it mean to health outcomes in older adults? Curr Opin Immunol 2009; 21: 418–424.
7. Wong JW, Koo JY. The safety of systemic treatments that can be used for geriatric psoriasis patients: a review. Dermatol Res Pract 2012; 2012: 367475.
8. Grozdev IS, Van Voorhees AS, Gottlieb AB, Hsu S, Lebwohl MG, Bebo BF Jr, et al; National Psoriasis Foundation. Psoriasis in the elderly: from the Medical Board of the National Psoriasis Foundation. J Am Acad Dermatol 2011; 65: 537–545.
9. Fleischmann R, Baumgartner SW, Weisman MH, Liu T, White B, Peloso P. Long term safety of etanercept in elderly subjects with rheumatic diseases. Ann Rheum Dis 2006; 65: 379–384.
10. Bathon JM, Fleischmann RM, Van der Heijde D, Tesser JR, Peloso PM, Chon Y, et al. Safety and efficacy of etanercept treatment in elderly subjects with rheumatoid arthritis. J Rheumatol 2006; 33: 234–243.
11. Galloway JB, Hyrich KL, Mercer LK, Dixon WG, Fu B, Ustianowski AP, et al. Anti-TNF therapy is associated with an increased risk of serious infections in patients with rheumatoid arthritis especially in the first 6 months of treatment: updated results from the British Society for Rheumatology Biologics Register with special emphasis on risks in the elderly. Rheumatology 2011; 50: 124–131.
12. Fairris GM, Dewhurst AG, White JE, Campbell MJ. Methotrexate dosage in patients aged over 50 with psoriasis. BMJ 1989; 298: 801–802.
13. Bressolle F, Bologna C, Kinowski JM, Arcos B, Sany J, Combe B. Total and free methotrexate pharmacokinetics in elderly patients with rheumatoid arthritis. A comparison with young patients. J Rheumatol 1997; 24: 1903–1909.
14. Bourré-Tessier J, Haraoui B. Methotrexate drug interactions in the treatment of rheumatoid arthritis: a systematic review. J Rheumatol 2010; 37: 1416–1421.
15. Colebatch AN, Marks JL, Edwards CJ. Safety of non-steroidal anti-inflammatory drugs, including aspirin and paracetamol (acetaminophen) in people receiving methotrexate for inflammatory arthritis (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, other spondyloarthritis). Cochrane Database Syst Rev 2011: CD008872.
16. Militello G, Xia A, Stevens SR, Van Voorhees AS. Etanercept for the treatment of psoriasis in the elderly. J Am Acad Dermatol 2006; 55: 517–519.
17. Menter A, Gordon KB, Leonardi CL, Gu Y, Goldblum OM. Efficacy and safety of adalimumab across subgroups of patients with moderate to severe psoriasis. J Am Acad Dermatol 2010; 63: 448–456.