The use of pegylated interferon a-2a in a cohort of Greek patients with Mycosis Fungoides

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INTRODUCTION

IFN a with its cytotoxic and immunological effects on tumorous T cells has been introduced in the treatment of cutaneous T-cell lymphoma since the 1980s.

The average response rates varie from 45-80% as monotherapy and are improved with combination schemes mostly with photochemotherapy (PUVA). IFN a is included as a treatment option in the past and the current CTCL guidelines. The published experience from the majority of trials is mostly based on the use of the recombinant IFN a-2a (Roferon A, Hoffmann-La Roche,Basel, Switzerland) or IFN a-2b (Intron A, Schering-Plough, Kenilworth, NJ, USA). However, these recombinant interferon regiments are no longer commercially available in Europe and therefore, its pegylated analogue (pegylated IFN a-2a, Pegasys; Hoffmann-La Roche) has been currently used to treat CTCLs.

Objective: The purpose of the current study was to evaluate the efficacy and safety profile of pegylated IFN a-2a in the treatment of mycosis fungoides (MF).

METHODS

Data were collected from three referral Cutaneous Lymphoma Units in Greece, covering a 2-year period.

The **primary endpoint** was to determine the effectiveness of peg IFN as measured by the overall response rate (RR) in this cohort.

Secondary endpoints were difference in RRs with respect to gender, disease stage, presence of folliculotropism and treatment features, time to best response, duration of response, drug survival, reasons for drug discontinuation and safety profile.

Statistical analysis of the data was performed using the Statistical Package for Social Sciences (SPSS), version 15.0.

Data included demographics, MF histologic subtype, TNMB stage at MF diagnosis, TNMB stage at peg IFN initiation, disease duration, type of regimen (monotherapy vs. combination therapy), dosage, therapeutic response, duration of therapy and adverse events (AEs).

Treatment response was clinically categorized as complete disappearance of clinical evidence of disease (complete response; CR), >50% clearance of skin lesions (partial response; PR), <50% clearance of skin lesions (stable disease; SD) and progression with >25% increase in disease activity while on therapy (progressive disease; PD) according to clinical evaluation.

Drug survival was defined as the interval from first to last dose of medication. Safety was evaluated by physical examination, incidence of AEs and clinically significant changes in laboratory values.

All continuous variables were expressed as the mean ± standard deviation, median and range. Shapiro–Wilk test was used to test the normality of continuous variables. Chi-square or Fisher's exact tests were used for categorical variables. All tests were two sided and the significance level was chosen to be a = 0.05.

RESULTS

Overall, 31 patients were included. Baseline patients' characteristics are summarized in Table 1. Most patients (n = 12; 38.7%) had IB-stage disease at peg IFN initiation. In all, 11 (35.5%) patients received Peg IFN monotherapy, while 20 (64.5%) subjects on peg IFN concomitantly received bexarotene, acitretin, methotrexate or topical chemotherapy. PegIFN was administered in the majority of patients as third line of therapy (21/31).

A 54.8% (17/31) overall response rate was noted: 9.7% (3/31) and 45.2% (14/31) for CR and PR, respectively (Table 2). In our cohort, no differences in RRs with respect to gender (p = 0.427), disease stage (p = 0.179) or presence of folliculotropism (p = 0.532) was observed. Peg IFN was not more effective as monotherapy than as a subsequent agent with respect to overall response (p = 0.680). Mean time to best response was 7.29±4.99 months. Only two patients experienced disease progression with the median duration of response to be 10 months. Treatment dose was reduced in 8 (25.8%) cases due to drug intolerance.

Adverse effects were recorded in 21 (67.7%) cases with leukopenia (n = 16; 76.1%), fatigue (n = 9; 42.8%) and anemia (n = 4; 19.0 %) being the most recorded. Among the 13 patients who changed from interferon a2a to peg IFN, four presented with less tolerance (fatigue and leucopenia) after the introduction of the new regimen.

Table 1: Baseline patients' characteristics

Patients' characteristics	N = 31
Gender	
Male	19
Female	12
Median age (years)	62,6
Stage at peg-IFN initiation	
IA	5
IB	12
IIA	1
IIB	7
III	3
IV	3
MF type	
Classic MF	26
Folliculotropic MF	5
Type of treatment	
Monotherapy	11
Combination therapy:	20
Topical chemotherapy	8
Retinoids + topical chemotherapy	1
Retinoids	7
Methotrexate	4
Peg-Intron initial dose	
135μg	9
180μg	22
Lines of treatment	
First line	2
Second line	8
Third line	21

Table 2. Best treatment response per stage

TNMB Stage	Best Treatment Response						ORR (%)
	CR	PD	PR	SD	S	Total	
IA	0	0	3	1	1	5	60.0
IB	2	1	7	2	0	12	75.0
IIA	0	0	0	1	0	1	0.0
IIB	1	0	2	4	0	7	42.8
IIIA	0	0	0	1	0	1	0.0
IIIB	0	1	0	1	0	2	0.0
IVA	0	0	2	1	0	3	66.6
IVB	0	0	0	0	0	0	n/a
Total	3	2	14	11	1	31	54.8

DISCUSSION

Higher toxicity of Peg IFN has been already described in a German cohort study of 17 consecutive CTCL patients, which was managed by a dose reduction of approximately 33%. In an open-label, multicenter, dose-escalation study which evaluated the safety, tolerability, and efficacy of subcutaneous PEG-IFN a-2a in patients with cutaneous T-cell lymphoma, it was found that was generally well tolerated, with a moderate number of reductions or withholding of doses because of adverse events. The only dose-limiting toxicity was a grade 3 elevation of liver enzymes in the 270-mg dose group.

Overall, peg IFN may be considered an effective additional regimen in the treatment of MF, with a rather good tolerance and safety profile. The optimal dosing needs to be evaluated in larger cohorts.

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