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# Treatment of Thrombocytosis in Chronic Myeloproliferative Disorders with Interferon Alfa-2b

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**Thirty-six patients with chronic myeloproliferative disorders (CMPD) with thrombocytosis (essential thrombocythaemia 19 patients, chronic megakaryocytic granulocytic myelosis five, polycythaemia vera six, chronic myelogenous leukaemia six) were treated with interferon alfa-2b to reduce the platelet count. The pre-treatment platelet count was in the range 450-700 x 10⁹/L in eight patients, 700-1000 x 10⁹/L in eight and above 1000 x 10⁹/L in 20. In the induction phase of treatment 22 patients were treated with interferon alfa-2b 3 million units (MU) daily subcutaneously for 2 months or until the platelet count returned to normal, if earlier. Fourteen patients received 5 MU interferon alfa-2b daily in the same way. In the maintenance phase the doses were reduced to 3 MU and 5 MU thrice weekly, respectively. Complete response (CR), defined as a reduction of platelet count to below 450 x 10⁹/L, was achieved in 78% of patients (within 2 months of induction in 64%). The platelet depleting effect was dose dependent: CR in 2 months in 52% on 3 MU interferon alfa-2b versus 75% on 5 MU. Reduction of interferon dose was followed by an increase in platelet count in 39% of patients. The white cell count fell by 50% in Philadelphia-negative CMPD. Side effects were common, though generally mild, but led to withdrawal of treatment in six patients. Three patients suffered cerebrovascular events during treatment and one shortly thereafter.**
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## INTRODUCTION

THROMBOCYTOSIS is a common finding in patients with chronic myeloproliferative disorders (CMPD). By definition the platelet concentration is raised above 600 x 10⁹/L in all cases of essential thrombocythaemia (ET), but in most patients it exceeds 1000 x 10⁹/L [1]. Thrombocytosis is invariably found in chronic megakaryocytic granulocytic myelosis (CMGM, the cellular phase of agnogenic myeloid metaplasia). Elevated platelet counts are also found in 52% of patients with polycythaemia vera (PV), 39% of patients with chronic myelogenous leukaemia (CML) and 20% of patients with more advanced CMGM [2]. Thrombocytosis may be asymptomatic, especially in younger patients, but if there is any evidence of impaired microcirculation, thrombosis or bleeding episodes, treatment is urgent.

Treatment will depend on symptoms, but for most patients the first line of therapy will be platelet depletion; in a few others observation only or inhibition of platelet aggregation will be appropriate. Inhibition of platelet aggregation is a simple procedure, but it increases the risk of haemorrhagic complications, sometimes dramatically. Of the platelet reducing strategies, radiophosphorus and cytostatic drugs such as busulphan or melphalan are highly effective and have no immediate adverse reactions. They are, however, known to be leukaemogenic [3]. It is also uncertain whether hydroxyurea is free of mutagenic effects [4]. Because of these disadvantages, alpha interferon has been tested in ET and CMPD with thrombocytosis.

The precise mechanisms of interferon action on bone marrow are poorly understood. Alpha interferon induces qualitative or quantitative changes in megakaryocytopoiesis and proliferation of megakaryocytic precursors [5,6]. An inhibitory effect on megakaryocytopoiesis and shortening of the megakaryocytic lifespan are assumed [7]. A shortening of the platelet half life has also been observed [8], suggesting a primary effect of interferon on the reticulo-endothelial system [9].

Preliminary reports have demonstrated the value of alpha interferon in the control of excessive platelet production [8,10-12]. The purpose of the clinical study described here was to demonstrate the effects of low- to intermediate-dose interferon alfa-2b in CMPD with thrombocytosis.

## PATIENTS AND METHODS

Thirty-six patients (18 men, 18 women), median age 60 years (range 26-73 years), with CMPD and thrombocytosis were selected for treatment with interferon alfa-2b. According to the classification of CMPD used [13], patients were allocated to four groups: ET (19 patients), CMGM (five), PV (six) and CML (six). Duration of disease before the start of interferon treatment was 1-144 months (median ET 2 months, CMGM 8 months, PV 36 months, CML 1 month). Four patients had been pre-treated with busulphan or radiophosphorus. Details of the four groups are shown in Table 1. Disease-related symptoms before onset of treatment were found as follows:

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*Table 1. Details of patients at entry to study*

| Type of CMPD | Patients *n* | M:F | Age (yr; median and range) | Duration of disease before treatment (month; median and range) | Previous therapy |
|---|---|---|---|---|---|
| ET | 19 | 9:10 | 58 (26-73) | 2 (1-24) | Busulphan (1) Radiophos (1) |
| CMGM | 5 | 2:3 | 62 (26-64) | 8 (6-60) | 0 |
| PV | 6 | 3:3 | 63 (34-69) | 36 (1-144) | Busulphan (1) Radiophos (1) |
| CML | 6 | 4:2 | 51 (38-66) | 1 (1-4) | 0 |

CMGM: chronic megakaryocytic granulocytic myelosis; ET: essential thrombocythaemia; PV: polycythaemia vera; CML: chronic myelogenous leukaemia.; CMPD: chronic myeloproliferative disorders

subjective neurological symptoms (15 patients), peripheral microcirculatory manifestations (eight), previous arterial or venous thrombosis (five), left upper abdominal discomfort due to splenomegaly (four), and bleeding episodes (two). Twelve patients had no symptoms. Platelet counts ranged between 536 and 1972 x 10⁹/L. Elevated platelet counts were graded as: mild, 450-700 x 10⁹/L; moderate, 700-1000 x 10⁹/L; and excessive, > 1000 x 10⁹/L. According to this classification, most patients with CML were in the mild range and most of those with ET in the excessive range, whereas patients with CMGM or PV were more evenly distributed (Table 2).

Informed consent was obtained from all patients before entry to study.

*Table 2. Initial platelet count according to type of CMPD*

| Platelets x 10⁹/L | Total | Patients *n* ET | CMGM | PV | CML |
|---|---|---|---|---|---|
| 450-700 | 8 | 1 | 1 | 2 | 4 |
| 700-1000 | 8 | 2 | 2 | 2 | 2 |
| > 1000 | 20 | 16 | 1 | 2 | |

Abbreviations: see Table 1.

*Treatment*

Recombinant human interferon alfa-2b (Schering-Plough) was obtained as a lyophilized powder in 1 ml vials containing 3 or 5 MU of interferon.

Twenty-two patients were treated with a daily subcutaneous dose of 3 MU interferon alfa-2b for 2 months (9 weeks) or until the platelet count had returned to normal (if earlier). Maintenance treatment was continued at a reduced dose of 3 MU interferon alfa-2b three times a week (t.i.w.) for a year. Fourteen patients were started on 5 MU interferon alfa-2b daily and reduced to 5 MU t.i.w. in the same manner.

*Evaluation*

Physical examination and routine haematological and serum tests were done before the start of treatment, weekly for the first 3 weeks of treatment, every other week until week 9 and monthly thereafter. Bone marrow specimens were obtained from the posterior iliac crest by the method of Jamshidi and Swaim [14] before the start of treatment. Specimens were embedded in methyl-methacrylate and processed by semi-thin sectioning without decalcification. Karyogenetic analysis was done routinely in all patients with CML and a few of the others.

*Criteria for response*

A primary complete response (CR) was defined as a platelet count below 450 x 10⁹/L in the induction phase and a secondary CR as a platelet count below 450 x 10⁹/L in two consecutive examinations in the maintenance phase. A primary partial response (PR) was defined as a reduction in platelet count to below 50% of the initial value but above 450 x 10⁹/L. Secondary PR was a similar reduction measured on two consecutive occasions in the maintenance phase, whether the primary response had been a CR or failure. Primary failure was defined as failure of the platelet count to fall in the induction phase, either to below 450 x 10⁹/L or (if the level achieved was above 450 x 10⁹/L) to less than 50% of initial value. Secondary failure was defined as failure of the platelet count to fall in the maintenance phase to below 450 x 10⁹/L or (if the level achieved was above 450 x 10⁹/L) to less than 50% of initial value in patients who had shown a primary CR or PR.

## RESULTS

Thirty-four patients were treated with alpha interferon for at least 3 months. Two patients had cerebral events during the induction period. For all patients the median reduction in platelet count during the first 2 months was over 50% (Table 3). The platelet count returned to normal (< 450 x 10⁹/L) during the induction period in 10/18 patients with ET

*Table 3. Reduction of platelet count after interferon alfa-2b*

| Type of CMPD | Platelet count (x 10⁹/L; median and range) Before treatment | After 2 months on interferon | % initial count |
|---|---|---|---|
| ET | 1212 (676-1972) | 449 (299-668) | 39 (22-60) |
| CMGM | 905 (697-1100) | 412 (247-555) | 40 (33-61) |
| PV | 906 (558-1319) | 422 (314-665) | 49 (44-64) |
| CML | 556 (536-780) | 121 (60-208) | 22 (11-30) |

Abbreviations: CMPD: chronic myeloproliferative disorders; and see Table 1.

(one not evaluable), 3/5 CMGM, 4/6 PV and 6/6 CML (total 23/36 = 64%). Normal platelet counts were obtained within 2 weeks of starting treatment in nine patients, in 3-4 weeks in 11 patients, and in the second month in three (Table 4).

The impact of initial platelet count on response rates and reduction in platelet count is shown in Table 5. Platelet counts returned to normal within 2 months in all patients with mild thrombocytosis, in two of six with moderate thrombocytosis

*Table 4. Time for platelet count to return to normal*

| Type of CMPD | Patients in CR | Platelet count returned to normal (no. of patients) | | | | |
|---|---|---|---|---|---|---|
| | | 1-2 weeks | 3-4 weeks | 2 months | 3 months | 15 months |
| ET | 13/19 | 1 | 7 | 2 | 2 | 1 |
| CMGM | 5/5 | 1 | 2 | | 2 | |
| PV | 4/6 | 1 | 2 | 1 | | |
| CML | 6/6 | 6 | | | | |
| Total | 28/36 | 9 | 11 | 3 | 4 | 1 |
| % | 78 | | 64 (57*) | | | |

Abbreviations: see Tables 1 and 3.
*Excluding CML.

and in 11 of 19 with very high platelet counts. Figures for CML are omitted since all patients with CML returned to normal within 14 days, as shown in Table 4 and discussed later.

*Table 5. Relation between initial platelet count and nadir after 2 months on interferon (CML excluded)*

| Initial platelets (x 10⁹/L) | Patients *n* | Median platelet nadir at 2 months (x 10⁹/L) | With CR *n* | | Median absolute reduction in platelets (x 10⁹/L) |
|---|---|---|---|---|---|
| 450-700 | 4 | 337 | 4 | (100%) | 435 |
| 700-1000 | 6 | 519 | 2 | (33%) | 482 |
| 1000 | 19 | 449 | 11 | (58%) | 832 |

CR: complete response.

The effect of interferon dosage during the induction period is shown in Table 6. CR was seen in 11 (52%) of 21 patients treated with 3 MU interferon alfa-2b daily and in 12 (86%) of 14 patients given 5 MU (6/8 [75%], excluding CML patients).

*Table 6. Effect of interferon dosage on complete response (CR) at 2 months*

| Type of CMPD | 3 MU | | 5 MU | |
|---|---|---|---|---|
| | Patients *n* | With CR *n* | Patients *n* | With CR *n* |
| ET | 12 | 6 | 6 | 4 |
| CMGM | 4 | 2 | 1 | 1 |
| PV | 5 | 3 | 1 | 1 |
| CML | | | 6 | 6 |
| Total | 21 | 11 | 14 | 12 |
| % CR | | 52 | | 86 (75*) |

Abbreviations: see Tables 1 and 3.
*Excluding CML.

*Effects of interferon dosage reduction*

The dose of alpha interferon was reduced in 18 patients achieving a decrease in platelet count to below 450 x 10⁹/L: from 3 MU daily to 3 MU t.i.w. in 14 patients and from 5 MU daily to 5 MU t.i.w. in four. The platelet count rose above 450 x 10⁹/L in seven patients (39%): six of 14 in the 3 MU group, and one of four in the 5 MU group. The platelet count rose to 51-76% of the initial level, with an absolute increase of 93-340 x 10⁹/L (median 187 x 10⁹/L). One CML patient showed a transient rise in platelet levels of 950 x 10⁹/L, in association with acceleration of CML.

In the induction phase 64% of patients showed a CR, 19% a PR and 14% a failure. In the following month of treatment there was an increase of failures resulting from the reduction of dosage. Four of the primary non-responders showed a response in the third month of treatment and one patient responded later. During the whole period of observation there were some secondary failures after primary CR and vice versa. At the end of observation (either cessation of therapy or last consultation) 30 patients (excluding those with CML) remained in the study. Fifteen (50%) of these showed a CR, four (13%) a PR and 10 (33%) a failure. One patient was not evaluable.

*Red cell count and leucocytes*

Patients in all four groups of CMPD with thrombocytosis showed a slight median fall in erythrocyte count in the induction period. This was followed by a slight median rise in the following months in patients with CMGM, PV and CML (Table 7). Although three out of six patients with PV were regularly phlebotomized before interferon alfa-2b therapy, this procedure was not necessary during treatment. During the induction period the granulocyte count fell in CML patients to a median of 28% of initial values and in all other patients with CMPD and thrombocytosis to a median of 50%. CML patients were subsequently treated according to white cell count. In all other patients the leucocyte count remained steady during maintenance treatment.

*Table 7. Red cell count during induction and maintenance interferon treatment*

| Type of CMPD | Change in red cell count (x 10⁹/L; median and range)* | |
|---|---|---|
| | Induction | Maintenance |
| ET | -200 (-800 to +300) | -200 (-600 to +1000) |
| CMGM | -100 (-300 to +100) | -50 (-1000 to +800) |
| PV | 0 (-500 to +300) | +150 (-600 to +1400) |
| CML | -200 (-400 to - 100) | +100 (-100 to +500) |

*Compared with pretreatment count.
Abbreviations: see Tables 1 and 3.

*Duration of treatment*

Thirty-six patients were treated for a total of 347 months, the median treatment times being 5+ months for ET, 15+ for CMGM, 9+ for PV and 12+ for CML. Out of the whole group of 19 ET patients, nine were treated for 2 to 4+ months and ten were treated for 5 to 20 months.

*Side effects*

During the first days of treatment almost all patients noticed one or more of the following symptoms: moderate to severe fever, headache, myalgia or bone pain, malaise and fatigue. From the second visit (day 14) the frequency of drug-related symptoms decreased, but only seven patients were free of any adverse effects. Side effects were mild or moderate in most patients but were intolerable in six (Table 8).

*Table 8. Late side effects of interferon treatment*

| Symptom | % |
|---|---|
| Arthralgia, myalgia, bone pain | 54 |
| Fever | 40 |
| Fatigue, lethargy | 31 |
| Anorexia, weight loss | 20 |
| Headache | 20 |
| Vertigo | 17 |
| Nausea | 14 |
| Paraesthesiae | 14 |
| Hair loss | 14 |
| Tinnitus | 12 |
| Stomatitis, gingivitis | 9 |
| Diarrhoea | 6 |
| Depression | 6 |
| Pruritus | 3 |
| No symptoms | 20 |
| Unacceptable symptoms | 17 |

*Causes of cessation of interferon therapy*

Treatment was withdrawn in four patients because of unacceptable side effects (one depression, two bone pain/myalgia, one lethargy, malaise and weight loss). All four patients were in CR and had been treated for 9-20 months.

Treatment failures led to withdrawal of interferon in six ET patients (after 3 to 9 months), the platelet counts ranging from 545 to 967 x $10^9$/L. In two CMGM patients (after 9 and 10 months) platelet counts were 632 and 695 x $10^9$/L, respectively, and in two PV patients (after 5 and 9 months) 520 and 635 x $10^9$/L. One PV patient in PR after 6 months (platelets 666 x $10^9$/L) was also withdrawn from interferon therapy. In addition, two of these patients also had unacceptable bone pain and lethargy, respectively.

Other causes of cessation of treatment were:

1) Progressive stroke (one ET patient, after 4 weeks of treatment, whose platelet count was within normal limits; the patient died);
2) Transient ischaemic attack (one ET patient after 6 weeks of treatment, whose platelet count was 530 x $10^9$/L);
3) Cerebral multi-infarction (one CMGM patient, after 10 months of treatment; the patient was a secondary failure, with a platelet count of 695 x $10^9$/L; the patient also had insulin-dependent diabetes mellitus, diabetic microangiopathy, type IV hyperlipidaemia, arterial hypertension and hypertensive heart disease; the patient died);
4) Blast crisis (one CMGM patient who was a secondary failure);
5) Pregnancy (one CMGM patient);
6) Subnormal platelet count (one CMGM patient);
7) Blast crisis (one CML patient);
8) Allogeneic bone marrow transplantation (two CML patients).

*Disease-related symptoms and interferon therapy*

Three cerebral events were observed. Neurological symptoms and peripheral microcirculatory complaints decreased with reduction in platelet count and were specified in only four of 10 failures. Peripheral arterial or venous thrombosis did not occur during treatment time.

*Post-interferon treatment procedures*

Interferon was withdrawn in six patients with ET, two with CMGM and two with PV because of treatment failure. Four were changed to busulphan and four to radiophosphorus. In two of these patients interferon alfa-2b was tried again after 9 and 12 months. Both patients are still on interferon and in PR. One PV patient in PR was changed to busulphan; cerebral infarction occurred 4 weeks later and the patient died. One patient with CMGM and one with CML went into blast crisis and were treated accordingly. Two patients with CML have had successful allogeneic bone marrow transplants. In seven patients with CR, treatment was stopped after 9 to 20 months (median 15 months). Thereafter two patients remained stable and four showed a rise in platelet count. One of the latter was switched to busulphan and three patients refused further therapy.

## DISCUSSION

Several studies on CMPD with thrombocytosis treated with alpha interferon have included patients with CML as well as those with Philadelphia chromosome ($Ph^1$) negative CMPD [8,15,16]. This present study, however, shows clear differences between CML and $Ph^1$-negative CMPD in the therapeutic effect of interferon on thrombocytosis. In all CML patients the platelet count came into the normal range in the first 14 days of treatment, but in most patients with other CMPD the platelet count returned to normal values in the second 14 days. CML patients also tended to have the least raised platelet count initially: levels of 450-700 x $10^9$/L were found in four of six CML patients, compared with one of 19 ET, one of five CMGM and two of six PV patients. In all patients with minimally raised platelet levels, the platelet count returned to normal within 2 months, compared with 50% of those with moderately raised and 58% of those with very high levels. Since the fall in leucocyte count was also more pronounced in CML patients than in those with other CMPD (72% versus 50%), we assume that the more rapid reduction in platelet count was attributable to the CML itself rather than to the lower initial platelet count. Lazzarino *et al.* [17], however, demonstrated a statistically significant difference in mean pretreatment platelet levels between CMPD patients achieving complete haematological response and non-responders. The difference might, however, reflect the low initial interferon dosage used. Induction dosage seems to influence the time taken for the platelet count to return to normal. With 1 MU interferon alfa-2b daily, the median time to response was 12 weeks [17], whereas, in our study, all but one patient responded within 3 months (median 3-4 weeks) on a dosage of 3 to 5 MU

interferon alfa-2b daily. Other studies using initial doses of up to 10 MU alpha interferon daily [16,18,19] show similar or even better results. In our study the CR rate in the first 2 months of treatment was higher with 5 MU interferon alfa-2b daily than with 3 MU (75% versus 52%). These results suggest that the induction period should be 3 months rather than 2 months.

Although there was a 16% increase in failures during maintenance treatment, we found that 3 to 5 MU interferon alfa-2b t.i.w. was, in most cases, an adequate dose to control platelet count within normal limits. Other reports with similar doses for maintenance therapy confirm this strategy [10,20,21]. Violations of protocol (i.e., departures from the prescribed dose) occurred rarely, for short periods only and almost always because of side effects (and in two cases because of long-lasting primary failure).

Although side effects were only mild in most cases, the older patients, especially, experienced neurological symptoms, such as fatigue or lethargy, headache, vertigo, paraesthesiae, tinnitus and depression. The rate of withdrawal because of side effects (17%) is comparable to the rates observed by other authors [15-17].

The red cell count was not greatly influenced by interferon treatment in our patients. However, three PV patients had regular phlebotomies before treatment, while none of these patients needed phlebotomy during interferon treatment. Similar findings with comparable interferon dosages are reported elsewhere [22].

Cerebral events occurred during interferon therapy in three patients and shortly after cessation of treatment in one. In two of these patients platelet counts were raised at the time of the cerebral attack; in the other two they were within the normal range. In all other patients thrombocytosis-related symptoms disappeared when the platelet count fell. Further studies are required to determine how far the platelet count needs to be adjusted in order to prevent vascular complications - whether it should be reduced to within strictly normal limits or to a level easily achieved without risk of interferon intolerance. The effects of alpha interferon on the rate of red cell production in PV and the formation of collagen fibres in the cellular phase of AMM should be investigated in future studies, although in accelerated AMM at best a marginal effect could be shown, as reported elsewhere [23].


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## GROUP DISCUSSION

**Question from the floor:** Dr Yataganas, did you exclude Ph¹-negative CML patients from your study?

**Yataganas (Greece):** Patients with essential thrombocythemia (ET) did not have the Ph¹ chromosome, so we did not check them for bcr-abl. The CML patients in this study were bcr-abl positive.

**Question from the floor:** Among 32 patients with ET that we have treated with interferon alfa-2b, there were seven patients who were resistant to conventional chemotherapy, such as hydroxyurea. These patients all achieved a complete response on interferon. After 1 year of treatment, they were again given chemotherapy and we found that they had a restored responsiveness to chemotherapy. This is an important point because it suggests there is no cross-resistance between interferon and chemotherapy in resistant patients. A second point is that, although interferon is effective for induction of remission in ET patients, this is a very chronic disease. Is it really possible to give high doses (5 MU/m²) of interferon daily for the whole life of these patients? Would it be better to use chemotherapy to achieve a major debulking of the disease, as in this setting interferon may work at very low doses, making it more comfortable for patients on long-term treatment.

**Yataganas (Greece):** The need for long-term therapy is, of course, a problem. If you achieve cytogenetic remission in CML, you may induce a long-lasting remission — we don't know yet. This would be a goal of long-term maintenance therapy but we don't know how long therapy should go on to achieve this, and most of the patients complain after 1 year of therapy.

**Giralt (Spain):** In my opinion, interferon has a definitive place in ET as in other chronic myeloproliferative diseases; nevertheless, the situation is very different for ET, which is a very chronic and benign disease compared to the other myeloproliferative syndromes, which have lower expected survival times. For old patients, it may be better to begin with chemotherapy and then give interferon, because side effects are not uncommon. We must treat with interferon young patients with symptoms and very important thrombocytosis — perhaps more than a million platelets. I am sure that interferon employed in rather a low dose and probably with a different schedule than I have shown previously will be very useful in ET.

**Seewann (Austria):** In our experience, the average dosage of interferon necessary to keep platelets below 450 x 10⁹/L is 3-5 MU three times weekly. There are very few patients who need only twice weekly interferon at 3 or 5 MU, and most of the patients get side effects after 9-15 months on this treatment regimen, especially patients in the older age group. With regard to early debulking with an agent such as hydroxyurea, I don't think that this influences the maintenance treatment, because patients respond very quickly to interferon, achieving complete remission in 2 or 3 months. So interferon also induces debulking of disease, but I think the crucial point is the long-term treatment.

**Yataganas (Greece):** We have had young patients with platelet counts of around 6-700,000 platelets with symptoms. On the other hand, we were amazed to see how extensive a reticulin content there can be at diagnosis in some patients whose platelet count is not as high as one million. So I would say that the indication for treatment should be based on several facts: what agents are available, which are less toxic, presence of symptoms and myelofibrosis, and age.

**Question from the floor:** I think one should distinguish between other myeloproliferative disorders and ET, which is most often a disease of the young and of long duration. Patients with ET should be treated only if there are symptoms or a very high platelet count. In view of the long duration of the disease and the benign course, one should begin with some non-leukaemogenic therapy, such as (supposedly) hydroxyurea, and give interferon only if there are side effects or resistance to hydroxyurea. The situation is different with chronic myelogenous leukaemia (CML),and here I would use interferon in the case of high platelet counts. For polycythaemia vera, I would use interferon even with platelet counts that are not so high because there are at least two factors of vascular risk. I would like to ask Professor Seewann to comment on the cerebrovascular events in his study - were they young people or old and what was the basic diagnosis?

**Seewann (Austria):** The patients who had cerebrovascular events were in an age group between 60 and 75 years; one patient had PV and two patients had ET. The patient with PV was, at the time of the cerebrovascular event, in a normal haematocrit range. The platelet count was clearly elevated in two patients and was normal in one ET patient, who had a cerebrovascular event in the first phase of treatment in the 6th week after onset of treatment.

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# Alpha Interferon Therapy in the Treatment of Idiopathic Thrombocytopenic Purpura

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**Treatment of patients with idiopathic thrombocytopenic purpura (ITP) varies according to the severity of the condition, the patient's age and the phase of the disease. The mainstay of treatment is corticosteroid therapy, with splenectomy for non-responding patients. For the 5%-10% of patients with refractory disease and bleeding problems, intravenous immunoglobulins are often used. Danazol achieves a response in about 30%-40% of refractory patients. At our centre, we have now treated 13 patients with interferon alfa-2b, all of whom had severe steroid-unresponsive ITP of various durations. All patients received 12 injections of 3 million units (MU) interferon subcutaneously three times a week. The platelet count rose significantly in 10 patients after interferon therapy and in one patient during therapy. Three patients had a complete response and eight a partial response. One complete responder relapsed at 5 months but again responded to retreatment with interferon. Responses were similar in splenectomized and non-splenectomized patients, and platelet-associated immunoglobulin levels remained essentially unchanged. Based on a compilation of data from this and other studies, the positive response rate (platelets at least 30-200 x 10⁹/L for at least 6 weeks) is 69% (22/32 patients). The future role and dosage of interferon in ITP remains to be determined and particularly in direct comparison with intravenous IgG therapy.**

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## INTRODUCTION

THE CLINICAL manifestations of idiopathic thrombocytopenic purpura (ITP) are related to the haemostatic defect caused by a low platelet count. Haemorrhages, which vary in intensity, are often cutaneous [1]. The incidence of ITP ranges from 6 to 11 cases per 100,000 persons. Women between the ages of 20 and 40 years are affected more commonly than men by a ratio of 3:1 [2]. An increasing incidence of ITP has been observed recently in patients who are positive for human immunodeficiency virus (HIV), including

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