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Trenimon Treatment in Chronic Hemoblastoses

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During the last five years we have observed almost 800 cases of hemoblastosis (Tab. 1) and since February 1962 we could treat with Trenimon almost 200 patients with chronic hemoblastosis (Quattrin *et al.*, 1962, 1965, 1966; Dini and Quattrin, 1965).

As far as we know the entity of our case material is surpassed only by the one of Linke (1960, 1964) who firstly very largely used this drug.

Trenimon (Linke, 1964; Quattrin *et al.*, 1962; Quattrin, 1966), ethyleneiminobenzoquinone, is a compound derived of " E 39 " (Domagk) synthesized by Bayer (Leverkusen), and contains in its molecule two active principles, namely the benzoquinone ring and the three ethylene-imino groups. Its activity is very powerful

Tab. 1. 758 personal cases of hemoblastosis (1960-66)

	Acute forms	Chronic forms
Leukemias	315	152
Other forms	39	252
Total	354	404

since it is effective in vitro five times more than Trisethylenmelammine. The propedeutic data concerning our cases are summarized in Tab. 2. From this table it results that we treated with Trenimon, alone or alternatively with other chemotherapeutics, almost a half of the cases of chronic hemoblastosis, that we observed. With few exceptions each of these patients underwent several cycles of the drug and was controlled for a long period, namely two-four years.

Tab. 3 shows the results we have obtained in the single forms of chronic hemoblastosis. The analysis of this table shows that in some forms, and precisely in chronic myeloid leukemia, in Vaquez's disease, in hemorrhagic thrombocytemia, the therapeutical effect of Trenimon is constant and almost always very satisfactory. The rapidity of the remission is variable from one another subject, but it depends rather scarcely on the dose. This behaviour is analogous to the Busulphan one.

Tab. 2. 185 cases of chronic hemoblastosis treated with Trenimon

Disease	Observed cases	Treated cases
Chronic lymphatic leukemia	64	42
Chronic myeloid leukemia	90	30
Subacute leukemias	3	3
Chronic reticuloses	5	3
Hodgkin's disease	101	54
Lympho - Ret. - Sarcoma	50	28
Plasmocytoma	48	7
Waldenstrom's disease	10	3
Essential cryoglobulinemia	13	3
Vaquez's disease	14	9
Haemorrhagic thrombocythemia	6	3
Total	404	185

Tab. 3. Results of treatment with Trenimon

Disease	Treated cases	Not valuab. cases	Posit. cases	%
Chr. lymph. leuk.	42	7	33	94
Chr. myeloid leuk.	30	5	25	100
Subacute leuk.	3	—	2	—
Hodgkin's disease	54	8	32	69
Lymph. - Ret. - Sarc.	28	5	15	65
Plasmocytoma	7	2	4	—
Other Paraproteinemias	6	1	5	—
Vaquez's disease	9	—	9	100
Hemorrh. thrombocythemia	3	—	3	—

In particular we have to emphasize the efficacy of this drug in the chronic myeloid leukemia even in those cases already treated with Busulphan for a long time. All the 20 of our patients belonging to this group resulted to be quite sensible to this drug too.

This is important because it makes us hope for a longer survival of these leukemic patients through the cyclic therapy alternatively with Busulphan and Trenimon.

Excellent results are obtained with Trenimon-therapy on the Vaquez's disease and on the hemorrhagic thrombocythemia. In these two forms of hemoblastosis, which some authors considered asre lated, Trenimon operates at low doses and distanced cycles. In Figs. 1-4 are shown some of the most significant observations we have been treating even for 4-5 years.

Quite efficacious results the drug against the erythroblastic proliferation of mediterranean anemias too (Fig. 5).

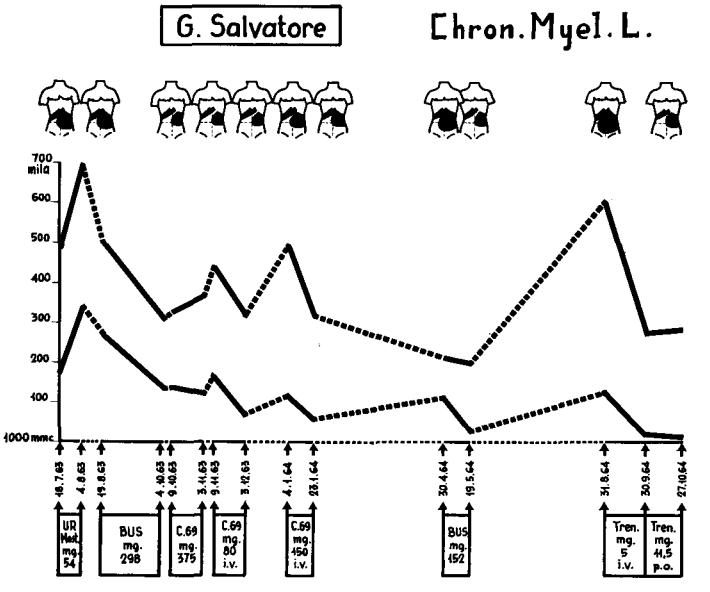

Fig. 1

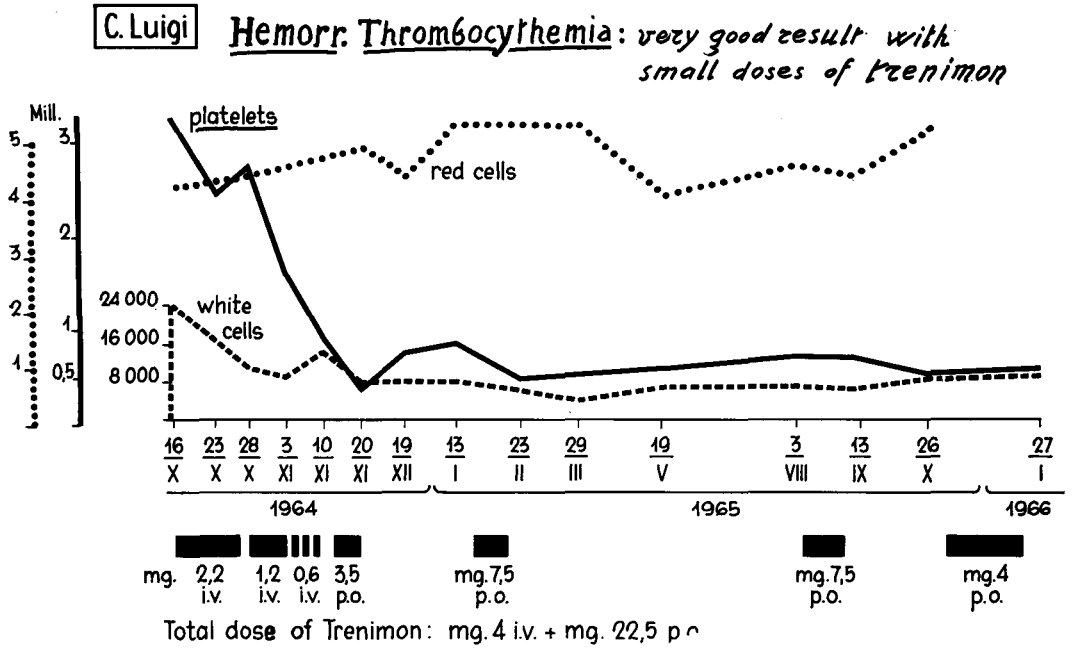

Fig. 2

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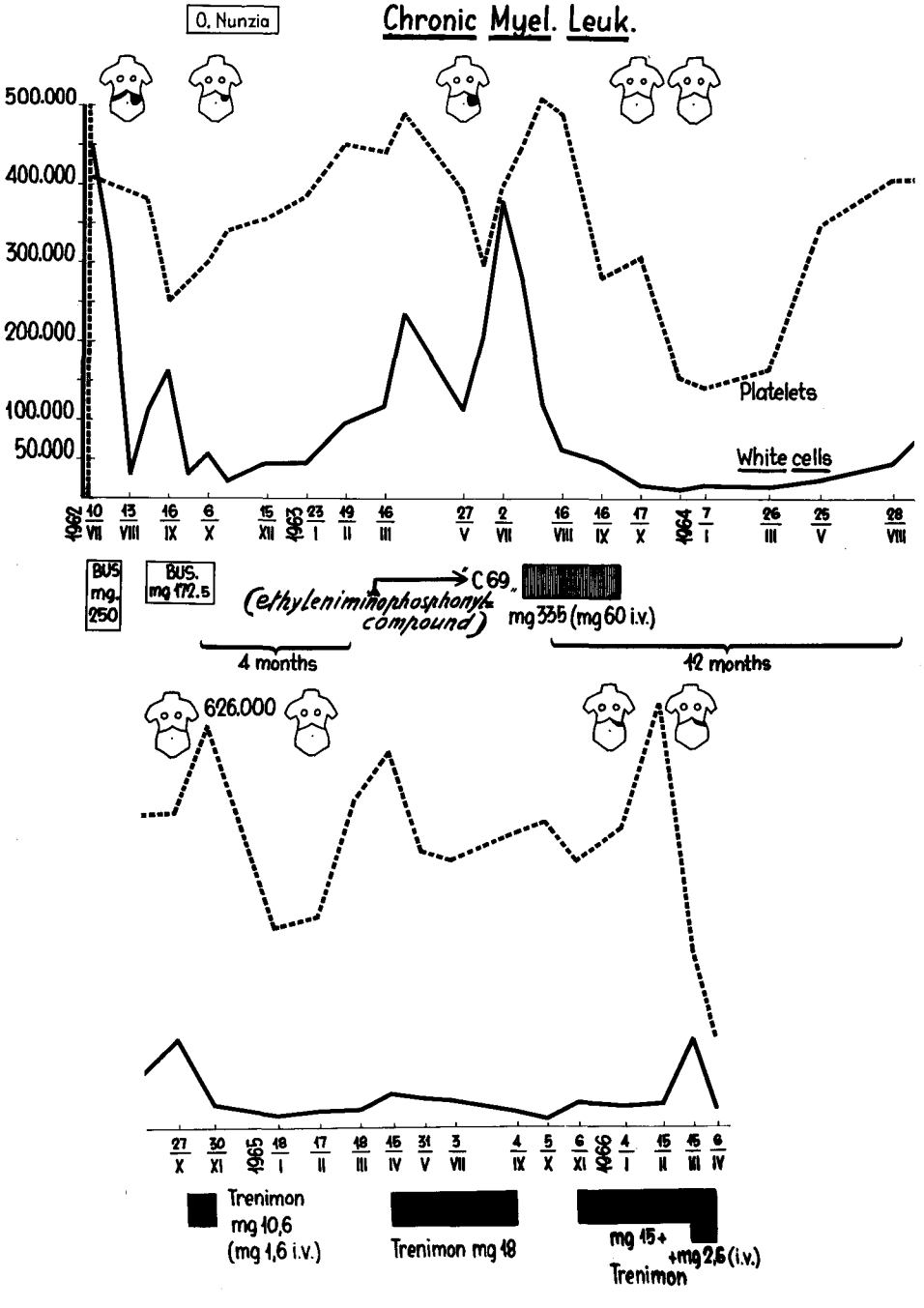

Fig. 3

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Effects of a little cycle of Trenimon in Vaquez's Disease.

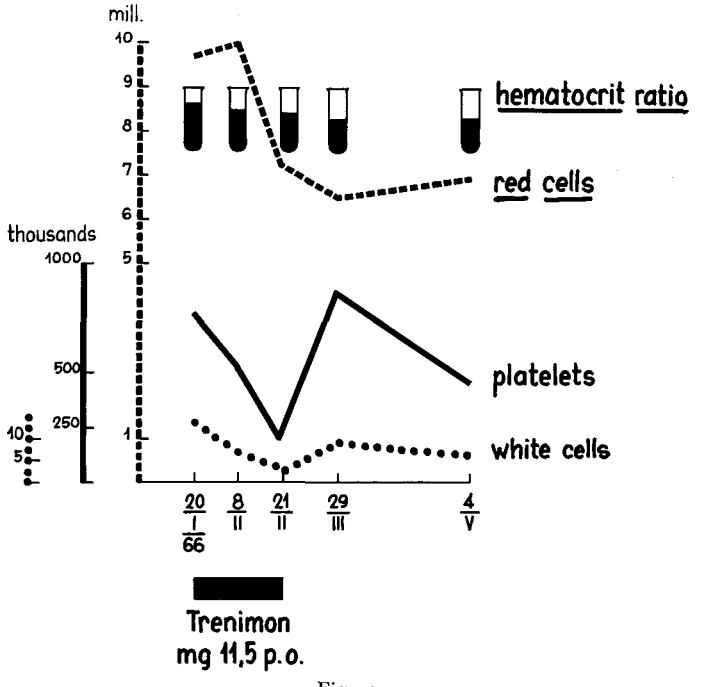

Fig. 4

P.F.
Cooley's-like Anemia with marked erythroblastosis.

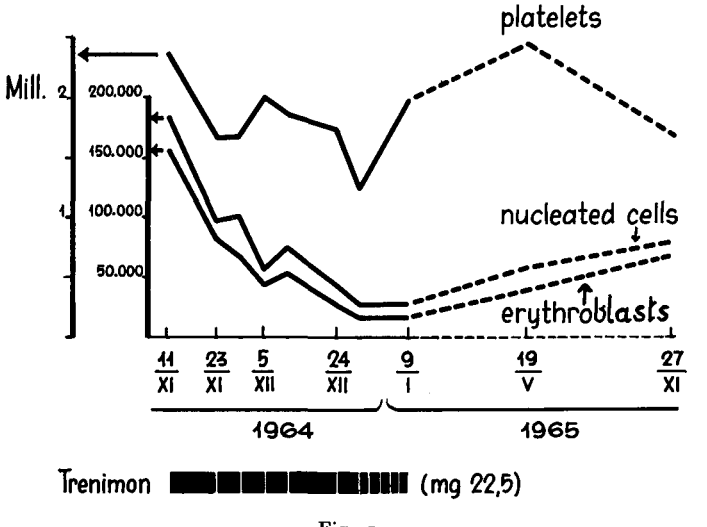

Fig. 5

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In the lymphatic chronic leukemia Trenimon operates at middle low doses and very distanced cycles or with a little maintenance therapy (a pill every 3-5 days at alternate months). It is interesting to notice that the drug operates more on the physical symptomatology than on the peripheric lymphatic proliferation and besides it depresses conspicuously the granulocytopoiesis too.

In seriously thrombocytopenic patients it is advisable to do a cortison treatment before the Trenimon one.

During the last two years we applied without discrimination Trenimon-treatment to all our patients affected by Hodgkin's disease. In this way we could estimate the effect of the drug also in this hemoblastosis. Our conclusions in this respect can be stated as following: Trenimon has a long efficacy on about one third of lymphogranulomatous patients, independently on stadium and type of the form. Such a treatment is not prejudicial to other successive therapies. Of course in those cases where

Tab. 4. Total results of treatment with Trenimon on 185 cases of chronic hemoblastosis

Good result	95	82%
Fairly good result	37	
Negative result	28	
Not valuable result	25	

the disease is localized, Roentgentherapy remains the elective treatment (Symposium sur le Radiothérapie de la maladie de Hodgkin, 1966).

The Lymphoreticulosarcomas are less influenced by Trenimon mainly because the effect is, as a rule, just moderate even in positive cases.

Difficult is the evaluation of the drug in the plasmocytoma, where it can be useful, while very good results we obtained in other paraproteinemias and particularly in Waldenstrom's disease.

Tab. 4 summarizes our therapeutical experience from which it appears that Trenimon operates in 82% of all the chronic forms of hemoblastosis.

Toxicity

Trenimon is very well tolerated either orally or intravenous. Never in these past 4 years of use, we encountered worrying side effects. Like all antiblastic substances, Trenimon depresses the leucopoiesis and, less, the thrombocytopoiesis. Such an effect is however light and usually disappears rapidly when the administration is interrupted.

Summary

1. Trenimon has three remarkable pharmacological characteristics, namely: very low toxicity, easy way of employing, big therapeutic action.

2. It results particularly useful in lymphatic and myeloid chronic leukemias, Vaquez's disease, hemorrhagic thrombocythemia, Waldenstrom's disease. It has to be noticed that Trenimon action is valuable in chronic myeloid leukemia even when it has been already treated with Busulphan for a long time.

3. Good results are obtained also in several cases of Hodgkin's disease, while the drug is less efficacious in Lympho-reticulosarcoma. Uncertain still being its action in plasmocytoma.

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RIASSUNTO

I. Il Trenimon ha tre notevoli caratteristiche farmacologiche: tossicità molto bassa, facilità di impiego, elevata azione terapeutica.

II. Esso risulta particolarmente utile nelle leucemie linfatica e mieloide cronica, nel Mb di Vaquez, nella trombocitemia emorragica e nel Mb. di Waldenstrom. Va notato che l'azione del Trenimon è efficace nella leucemia mieloide cronica anche quando sia stato già effettuato un lungo trattamento con Busulfan.

III. Buoni risultati vengono anche ottenuti in numerosi casi di Mb. di Hodgkin, mentre il medicamento è meno efficace nel linforeticolosarcoma, e la sua azione nel plasmocitoma è ancora incerta.

RÉSUMÉ

I. Le Trenimon possède trois remarquables caractéristiques pharmacologiques: toxicité très baisse, facilité d'emploi, action thérapeutique élevée.

II. Il résulte spécialement utile dans le traitement des leucémies lymphatiques et myéloïdes chroniques, maladie de Vaquez, trombocytémie hémorragique, maladie de Waldenstrom. Il est à remarquer que le Trenimon est efficace dans la leucémie myéloïde chronique même après un long traitement avec Busulfan.

III. De bons résultats sont aussi obtenus en plusieurs cas de maladie de Hodgkin, tandis que le médicament paraît moins efficace dans le lymphoréticulosarcome et son action est incertaine dans le plasmocytome.

ZUSAMMENFASSUNG

I. Das Trenimon zeichnet sich vor allem durch eine ganz geringe Toxizität, leichte Anwendung und hohe therapeutische Wirkung aus.

II. Es erwies sich besonders wirksam bei chron. Myelose und Lymphadenose, bei Polyzythämie (Vaquez), bei hämorrhagischer Thrombozythämie und bei der Waldenströmschen Krankheit. Bei der chron. Myelose ist das Trenimon auch dann noch wirksam, wenn sie schon lange mit Busulfan behandelt wurde.

III. Gute Erfolge erzielte man auch bei zahlreichen Fällen von Lymphogranulomatose (Hodgkin); hingegen ist die Wirkung des Medikaments weniger gut beim Lymphoretikulosarkom. Beim Plasmozythom ist seine Wirkung noch ungewiss.

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