easily available[3], most of the attention was centered on IFN's anti-proliferative properties. I recall that, during our first visit to Kari Cantell's laboratory in Finland, in April, 1981, he told us how he had been asked more than once for alpha leukocyte interferon to treat cancer patients, and complained that some of the requests, made via telephone from the United States, did not bear in mind the different time zones, waking him up in the dead of night. It is in these circumstances that Cuba began working with interferons. The original decision to produce interferon in our country was aimed at having another weapon against cancer[4]. However, the 1981 hemorrhagic Dengue and hemorrhagic Conjunctivitis epidemics centered our attention on its anti-viral possibilities and, in fact, this became the most extended use of the drug in Cuba during the decade. Interferons alpha have been used to treat patients with the most common viral diseases due to RNA virus (Dengue, Enterovirus, Coxsackie, respiratory infections), as well as to DNA virus (Hepatitis B, Herpes simplex, Herpes zoster, Papilloma) and retrovirus (Human Immunodeficiency Virus-HIV).

It is interesting to note the variety of viral diseases which have been treated with interferons. This should not come as a surprise when we consider that their anti-viral effect is due to actions on cells, not on the virus[5]. This low specificity with respect to viruses is thus a therapeutical advantage.

The use of interferon in Dengue[6] is an example of its application against a disease from tropical, developing countries, where a small amount of the product could avoid very serious complications. Its application took place during an epidemic and it fulfilled a social purpose since it allowed a camp for "Pioneer Children" to remain open[4], but it had no other scientific basis than interferons' general anti-viral effect. The inhibiting effect of alpha and gamma interferon on Dengue 2 virus *in vitro* was shown later on[7].

Virus Hepatitis B is probably the disease for which more interferon alpha has been used in Cuba. In sub-acute hepatic necrosis (fulminant hepatitis) it may be stated that interferon alpha decisively contributes to patient survival[8,9]. It has also been demonstrated that it improves the prognosis of chronic patients. Several recommendations on the use of interferon alpha in fulminant, acute and chronic Hepatitis B have been made, so that it is used uniformly throughout the country[10].

Diseases due to Humam Papilloma Virus (HPV): papillomatosis, condyloma, warts, are health problems in which the use of IFN alpha has brought unquestionable benefits. It has totally changed the patients' evolution in Laryngeal Papillomatosis, offering a possible cure. The organization of the health-care system in Cuba has permitted the development of a National Program[11], guaranteeing treatment of all existing and new cases since 1983. Although it is not very frequent (6-10 new cases per year), the degree of disability caused by this disease (speaking and breathing difficulties, repeated surgery, including tracheotomies) especially in children, makes us proud of this achievement. HPV infections are important since condyloma is among the most common venereal diseases[12], and are linked to cancer development, particularly cervical cancer[13]. In Cuba, the Papilloma Virus infection- alpha IFN system has been approached from the basic point of view, demonstrating inhibition of the expression

of viral genes in cultured cells. This aspect is discussed in greater detail in another lecture of this series.

Treatment of HIV-infected individuals in Cuba is one of the most prolonged uses of interferon, worldwide. This trial began in May, 1986, with leukocyte IFN alpha, and with recombinant IFN alpha-2b in October, 1987. Both preparations produced a significant delay in the appearance of AIDS symptoms and signs in asymptomatic individuals or with the AIDS-related complex, as well as less opportunistic infections and non-infectious complications[14].

Since other anti-viral drugs such as Acyclovir, trifluorothymidine, etc., presently being used in the world, are expensive and imported, it may be said that at present, alpha interferons (leukocyte or recombinant alpha-2b) constitute the first anti-viral weapon available for Cuban practitioners.

THE USE OF INTERFERON IN NEOPLASIAS

Cuba has also done intensive clinical research aimed at defining the role of interferons in the treatment of malignant neoplasias. The country's findings do not greatly differ from those of world literature. The use of interferons in these diseases can be done in two ways:

a) as cytostatic agents, for which high concentrations of the product are required and since this may produce side effects, they cannot be used for long periods;

b) as growth and cellular differentiation regulators or as immunomodulators, requiring lower concentrations and longer periods ("go low and slow").

In Cuba, the second "philosophy" on the use of interferons predominates. With the exception of work on advanced melanoma[15,17], there are no documented studies using high systemic doses of interferon. By regional or intratumoral use, however, this cytostatic effect may be achieved in the tumor area without producing systemic side effects. This has been so in work with conjunctiva melanoma[17], sarcoma of the mastoid[18] and tumors of the Central Nervous System[19,20].

Satisfactory results have been obtained in cases of Chronic Myeloid Leukemia[21] and non-Hodgking Lymphoma of medium and low- degree of malignancy[22] with relatively low doses of the product (less than 10 million IU daily) as a remission maintainance therapy.

Unquestionably, in our country and throughout the world, interferons play a role in the fight against cancer. Their use, however, still poses many questions to researchers and these will be answered only carrying out well-controlled studies, supported by appropriate laboratory research.

Work on non-operable lung cancer is an example of what can be done. A very encouraging result obtained in a pilot study with leukocyte interferon alpha plus radiotherapy[23] led to other therapeutical surveys with more or less relative success. The stringently controlled, over 3-year long multi-center randomized study did not produce significant differences between the "with" and "without" IFN groups[24, 25]. However, it did inspire new proposals based on other studies in which better results were obtained with other schemes[26] aimed at improving the outcome. At any rate, we will continue the struggle, creating new variants and continuing to search for laboratory factors or parameters which condition or allow a prediction of the response.

Another example of rational studies are those on cervix cancer. As was mentioned before, this neoplasia is closely related to HPV infection. After proving the inhibition of the expression of viral genes in

transformed cell lines as well as their phenotypic reversion[27,28] *in vitro*, a clinical trial is now in process, seeking the same result *in vivo*.

At present, the tendency is to use interferons as adjuvants of other anti-neoplasia treatments, such as surgery, chemotherapy or other biotherapeutical procedures. The combination of alpha and gamma interferons is of particular interest due to their synergism of action[29]. Our country has the capacity to work in this field since it has both molecules and can apply practically all of the existing therapeutical procedures. Nowadays our clinical researchers face the challenge of developing their creative sense in order not to miss this opportunity.

THE USE OF INTERFERON IN OTHER DISEASES

Although interferons (especially alpha's) are mainly prescribed for viral diseases and neoplasia, its immunomodulating action and the unknown origin of some illnesses where viruses or, at least, the immune system are involved, have prompted its use in other pathological conditions.

This has also been the case in Cuba and research protocols involving several diseases of this kind have been developed. The most interesting of them -- due to results obtained and their originality -- are those on Schizophrenia. Initially based on the hypothesis of the viral origin of the disease[30], several pilot studies were done that showed a significant clinical improvement[31-33] with the intrathecal use of recombinant interferon alpha-2b. A double-blind study was made later on in which recombinant interferon alpha-2b was slightly more effective than the usual neuroleptic treatment[34]. These results are a milestone in handling this disease, for which there are no effective measures available. Though the intrathecal route did not produce specific complications, it is not the most convenient so intramuscular administration is now being studied.

SECONDARY ADVERSE EFFECTS

The main side effects reported from the use of Cuban-produced interferon alpha have been: fever (72%), chills (68%), general malaise (75%), myalgias (40%), anorexia (9%) with weight loss (2%), slight leukopenia (32%), and thrombocytopenia (4%). There have been rare cases of increased serum levels of liver damage marker enzymes (less than 1%). Slight, occasional allergic reactions (skin rash, pruritus) have been seldom noted and in one case of non-Hodgkin's lymphoma, there was a nephrotic syndrome episode that reverted after suspending the IFN treatment. In children receiving interferon alpha for more than 2 months because of hepatitis B, laryngeal papillomatosis or malignant neoplasias, no adverse effects were found on either their growth or psychosomatic development.

Intrathecal injection produces a lymphocyte reaction in the spinal fluid which may be accompained by a slight meningeal reaction.

The secondary effects of the two preparations (leukocyte and recombinant) have been similar when analyzed in detail.

Anti-alpha-2 interferon neutralizing antibodies have been detected in 9% of patients treated with Cuban recombinant interferon alpha-2b. This has been related to non-response to recombinant interferon alpha-2b therapy in 6 patients with chronic Hepatitis B. No anti-alpha interferon neutralizing antibodies have been detected in patients treated with leukocyte interferon.

ALPHA LEUKOCYTE VS RECOMBINANT INTERFERON

The availability of two interferon alpha preparations raises some questions:

a) Why continue to produce alpha leukocyte interferon if recombinant-alpha IFN is cheaper and available in larger amounts?

b) Are there therapeutical differences between them?

c) Are there specific indications for either one?

The two preparations do not have the same molecular composition. The IFN alpha obtained by Sendai virus induction of leukocytes is a mixture of several IFN alpha sub-types while recombinant alpha- 2b is totally homogeneous from that point of view. There are glycosylated molecules in the natural preparation, alpha-2 itself among them, which cannot exist in the IFN of bacterial origin.

There are no proven qualitative therapeutical differences between the two preparations. That is, recombinant IFN has been useful in the same pathological conditions as natural leukocyte IFN. In order to detect quantitative differences, controlled comparative studies must be carried out. This kind of trial has not yet been made in Cuba or abroad, although it would be worthwhile. It is expected that if one of the preparations is advantageous, it should be leukocyte interferon, due to the possibility of synergic effects among the different sub-types.

On the other hand, it has been reported that patients who become resistant to recombinant IFN alpha-2 treatment due to the presence of neutralizing antibodies still respond to therapy with leukocyte IFN alpha. This is a precise indication for the latter.

GAMMA INTERFERON

Several studies have been made in Cuba with this molecule. Those related to malignant neoplasias have already been mentioned and, apparently, a combination of alpha and gamma interferons has greater possibilities[35].

However, this molecule has great prospects as an immunomodulator and it has been used successfully in rheumatoid arthritis[36,37] and several intracellular parasitic diseases such as Leprosy and Leishmaniasis, where immunological deficiencies related to the production or action of gamma Interferon have been found.[38,39] Gamma IFN has been used in Cuba, for the treatment of Lepromatous leprosy with initially successful results[40], and studies on Leishmaniasis are underway in cooperation with foreign centers, since this disease does not exist in Cuba. An interesting prospective use of interferon gamma is as an adjuvant for new vaccines developed at our research centers.

CONCLUSION

The total number of patients involved in the studies listed on Table 1 is approximately 1500. Large numbers of patients have received interferon in Cuba in unreported studies that have not been yet concluded, or in applications not included in research protocols. The end of this 10-year period should represent a new starting point for IFN research work.

This work should continue on a rational basis, and be aimed at solving some of the existing problems regarding the clinical use of interferons. To those already mentioned in this article I may add the development of new pharmaceutical forms (i.e., sustained release) and administration methods (why not orally?).

Even if the question included in the title of this article had not been answered by the results of clinical studies, work with interferon has unquestionably served the country as a take-off point for its biotechnological industry and for the development of therapy with biological response modifiers. And it can continue to set trends.

ONE YEAR LATER

In reviewing this lecture for publication, I would like, without altering its original content, to add the most relevant developments of the last twelve months. This has been a busy year in this field, in preparation for the Biotecnología/ Habana'92 Congress. Several significant papers were presented there. Their short reports appear in this same volume.

The use of interferon alpha for the treatment of chronic hepatitis C began simultaneously with the domestic development of a diagnostic system[91]. The results hav been very satisfactory[92] in an initial series of 17 cases. This application has been experimented elsewhere[93]. A controlled, nation-wide extension of this trial is in preparation and it should have started by the time this article comes out. The National Program for the use of IFN alpha in Laryngeal Papillomatosis reached 125 cases. Relapses have been completely eliminated in 70% of them[94]. The initial trial on the topical use of IFN alpha on cervical condilloma finished with good results as well[95].

The use of combined IFN's alpha and gamma in advanced ovarian carcinoma continued in chemotherapy-resistant patients[96] and as adjuvant maintainance therapy[97] for response stabilization. The double-blind trial on the intramuscular administration of interferon alpha in paranoid Schizophrenia was concluded. A decrease in the frequency and duration of crisis, symptom improvement and reduction in the amount of neuroleptic drugs necessary for the patient's control were found[98].

Work with interferon gamma has continued. The trial on Lepromatous Leprosy reached 10 treated cases, and the initial results were confirmed[99]. The trial on Juvenile Rheumatoid Arthritis has continued and comprises 6 cases. Four of them have finished 6 months of treatment and are still under control[100].

SUMMARY OF THE USE (DOCUMENTED) OF INTERFERON IN HUMAN BEINGS IN CUBA (The number of cases in each study refers to patients who received interferon; controls are not included)

Study	Institution	Therapeutical modality	Number of cases	Type of study	Results	Ref.
VIRAL DISEASES						
Dengue (Type 2 virus) (children)	National Pediatrics Group	Intramuscular leu IFN alpha	165	controlled	When used early it prevented more serious complications (shock and death) as compared to the control group.	6
Dengue (Type 2 virus) (adults)	CIMEQ	Intramuscular leu IFN alpha	9	double blind	Improved recovery of laboratory parameters when compared with the control group.	6
Hemorrhagic Conjunctivitis (Enterovirus 70)	National Ophthalmology Group	topical eye-drops leu IFN alpha	100	double blind	More rapid disappearance of symptoms with IFN eye-drops.	41
Hemorrhagic Conjunctivitis (Coxsackie A23)	National Ophthalmology Group	topical eye-drops rec IFN alpha-2b prophylactic use	15	double blind	Significant difference in preventing the disease in comparison to group receiving placebo	42
Severe Acute Hepatitis B or non-A, non B with unfavourable evolution	Gastroenterology Institute	Intramuscular leu IFN alpha	5	pilot	Outstanding improvement with IFN treatment. Histological and biochemical healing criteria by 6 months.	9
Acute Hepatitis B (multi-center study)	Gastroenterology Institute (coordinator)	Intramuscular intraperitoneal leu IFN alpha	173	controlled	A larger proportion of cases normalized hepatic and viral markers at 6 months.	43
Acute Hepatitis B	"Luis Díaz Soto" Hospital	Intramuscular intraperitoneal leu IFN alpha	17	double blind	No significant difference with control group in terms of persistence of HBsAg at 12 months.	8
Acute Hepatitis B	"Luis Díaz Soto" Hospital	Intramuscular rec IFN alpha-2b	20	double blind	No significant difference with control group in terms of HBsAg persistence at 12 months.	8
Acute Hepatitis B (30 weeks pregnant women)	Marianao Ginecological-Obstetrics Hospital	Intramuscular leu IFN alpha	4	application	Favorable response; fetuses born normal and without hepatitis.	44
Chronic active Hepatitis B (children)	Gastroenterology Institute	Intramuscular leu IFN alpha	25	application	HBeAg seroconversion in 25%. HBsAg seroconversion in 20% and decreases in 28% at the end of treatment. Histological improvement in 52% at 6 months.	45
Chronic active Hepatitis B	Gastroenterology Institute	Intramuscular leu IFN alpha	26	controlled	47% HBeAg seroconversion at the end of treatment. 14% HBsAg negativization. 77% histological improvement.	46

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Study	Institution	Therapeutical modality	Number of cases	Type of study	Results	Ref.
Non-A, non B chronic active Hepatitis (delta)	Gastroenterology Institute	Intramuscular leu IFN alpha	4	pilot	HBsAg negativization in all 4 cases. Histological improvement in 2 cases and 2 evolved to chronic persistent hepatitis.	46
Hepatitis B (asymptomatic carriers)	ICBP "Victoria de Girón"	Intraperitoneal leu IFN alpha	15	pilot	Dose dependant decrease in viral markers.	47
Chronic active Hepatitis B	Gastroenterology Institute	Intramuscular leu IFN alpha	11	controlled	ALAT normalization in 10 cases and decrease in one. GGT normalization in 7 cases. Decreases in biliary acids. Histological improvement in 75% of cases as compared to only 30% in the control group.	48
Non A, non B chronic active Hepatitis	Gastroenterology Institute	Intramuscular leu IFN alpha	1	pilot	ALAT decreases. Disappearance of chronic active hepatitis lesions in the biopsy.	48
Chronic active Hepatitis B	Gastroenterology Institute	Intramuscular, intraperitoneal leu IFN alpha	30	controlled	ALAT decreases in 50%. HBsAg decreases in all cases (negativization in 3). HBeAg seroconversion in 50%. Histological improvement in 17 cases.	49
Chronic active Hepatitis B (long term follow-up)	Gastroenterology Institute	Intramuscular leu IFN alpha	10	application	Histological improvement in 8 cases after 6 months of treatment. One year later cases continued to improve without treatment except for one which evolved to a cirrhosis	50
Chronic active Hepatitis B	Gastroenterology Institute	Intramuscular leu IFN alpha	21	application	Normalization of circulating immunocomplexes values in 3 cases and of ALAT in 8. HBsAg decreases in 81%; significant IgA, IgM and C3 increase.	51
Viral Hepatitis with sub-acute liver necrosis	"L. Díaz Soto" Hospital	Intramuscular, intraperitoneal leu IFN alpha	7	application	Survival of all patients. Clinical humoral and histological healing without evolution to chronicity	8
Chronic Hepatitis B in children with Acute Lymphoblastic Leukemia	Pediatrics Hospital of Santa Clara	Intramuscular leu IFN alpha	20	pilot	After 7 months of treatment: normalization of liver function tests and ALAT; decreases in HBsAg. Results were less significant in the 4 cases who continued receiving cytostatic drugs.	52, 53

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Study	Institution	Therapeutical modality	Number of cases	Type of study	Results	Ref.
Chronic Hepatitis B	Gastroenterology Institute	rec IFN alpha-2b with or without previous immunosuppresion	50	controlled	Better results in the previously immunosuppressed group concerning negativization of viral markers and liver biopsy.	54
Hepatitis B assymptomatic carriers (children)	Gastroenterology Institute	Intramuscular rec IFN alpha-2b	20	application	No benefit was obtained with respect to liver damage	55
Chronic active Hepatitis B (children)	Gastroenterology Institute	Intramuscular rec IFN alpha-2b	22	application	Beneficial effect as to normalization of viral, humoral and histological markers.	56
Chronic active Hepatitis B	Gastroenterology Institute	Intramuscular rec IFN alpha-2b and immunossuppression	31	controlled	24 with a satisfactory evolution; 2 non-satisfactory; 5 non-evaluable. Biopsy and antigen in tissue were studied	57
Laryngeal Papillomatosis (adults)	"C. García" Hospital	Intramuscular leu IFN alpha for one year, after surgical removal	11	pilot	Marked improvement in 9 cases, with less frequency of surgical interventions. No improvement in 2 cases which had a longer period of evolution before treatment	58
Laryngeal Papillomatosis (children)	"Marfán" Pediatrics Hospital	Intramuscular leu IFN alpha for one year, after surgical removal	5	pilot	Significant improvement in all cases including one who had a permanent tracheotomy. Only one suffered a slight relapse	58
Laryngeal Papillomatosis. National Program (adults)	National Otorhinolaryngology Group	Intramuscular leu IFN alpha for one year, after surgical removal	27	application	16 cases concluded treatment without further relapses; 5 under treatment without relapses; 6 IFN-resistant.	11
Laryngeal Papillomatosis. National Program (children)	National Otorhinolaryngology Group	Intramuscular leu IFN alpha for one year after surgical removal	68	application	38 cases concluded treatment and have had no relapses; 25 under treatment without relapses; 5 IFN-resistant; 4 cases with permanent tracheotomy were decanulated.	11
Condyllomata Accuminata	"Hnos. Ameijeiras" Hospital	Intramuscular leu IFN alpha and topical cream	20	controlled	Decrease in size and number of lesions in 95% of the cases.	59
Condyllomata Accuminata	"Hnos. Ameijeiras" Hospital	Intramuscular rec IFN alpha-2b and topical cream	15	double blind	Favorable clinical response with negativization of HPV probes hybridization signal in comparison to control with placebo.	60
Cervical Condyllomata	"10 de Octubre" Gineco-Obstetrics Hospital	rec IFN alpha-2b topical gel	10	double blind	Favorable clinical response in all cases treated with IFN alpha when compared with placebo control group.	61

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Study	Institution	Therapeutical modality	Number of cases	Type of study	Results	Ref.
Plantar warts	"Hnos. Ameijeiras" Hospital	Intramuscular leu IFN alpha and topical cream	20	controlled	Decrease in size and number of lesions and disappearance of pain in all cases.	62
Plantar warts	"Hnos. Ameijeiras" Hospital	Intramuscular leu IFN alpha, several schedules: one with superficial radiotherapy	50	controlled	Dissapearance of pain in all cases and of lesions in 25. Decreased lesions in 23 cases. Faster response when IFN was combined with radiotherapy.	63
Herpes zoster	"Hnos. Ameijeiras" Hospital	Intramuscular leu IFN alpha and topical cream	10	controlled	Total disappearance of pain and lesions in less time than in the control group	64
Herpes zoster	"Hnos. Ameijeiras" Hospital	Intramuscular leu IFN alpha; several schedules	100	controlled	Good response to treatment in all cases but healing was faster in the group that received the highest dose	65
Herpes zoster	Cienfuegos Provincial Hospital	Intramuscular leu IFN alpha and topical cream	42	controlled	Disappearance of pain and clinical cure were faster in cases treated with IFN than in controls	66
Hemorrhagic Varicella	Cienfuegos Provincial Hospital	Intramuscular leu IFN alpha	4	controlled	Three cases had a satisfactory evolution and one died. Three cases not treated with IFN died.	67
Herpes simplex (genital)	"Ramón González Coro" Hospital	Intramuscular leu IFN alpha and topical cream	20	controlled	Faster healing of lesions and fewer relapses with IFN than in the control group treated with other anti-viral agents.	68, 69
Human Immunodeficiency Virus carriers	Stgo. Vegas Sanatorium	Intramuscular leu IFN alpha	52	controlled	Delayed appearance of AIDS symptoms. Negativization of HBsAg positive cases.	14
HIV Carriers	Stgo. Vegas Sanatorium	Intramuscular rec alpha IFN	74	controlled	Delayed appearance of AIDS symptoms. Negativization of HBsAg positive cases.	14
Viral upper respiratory tract infections	CIMEQ	Topical nose drops leu IFN alpha;	36	double blind	Fewer episodes of infections with intranasal IFN	70
Bronchiolitis (children)	Cienfuegos Pediatrics Hospital	Intramuscular leu IFN alpha	34	controlled	Faster radiological improvement and fewer related infections than in the control group	71

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Study	Institution	Therapeutical modality	Number of cases	Type of study	Results	Ref.
Cervix carcinoma stage III and IV	INOR	Intramuscular leu IFN alpha combined with radiotherapy	14	controlled	71% response combined with radiotherapy	76
Lung cancer	"C. García" Hospital	Intramuscular leu IFN alpha combined with radiotherapy	10	pilot	Radiological improvement in all cases. Longer survival than the group of historical paired controls	23
Lung cancer (multicenter PAHO study)	Multicenter	Intramuscular leu IFN alpha combined with radiotherapy	26	controlled	Objective response in 40%; progression in one. No significant difference with control radiotherapy alone. Correlation between survival and NK stimulation activiy and IFN production capacity	24, 25
Lung cancer	Villa Clara Provincial Hospital	Intramuscular rec IFN alpha-2b combined with radiotherapy	7	pilot	1 CR; 5 PR; 1 MR. Mean survival was 15.2 months	26
Lung Cancer	Cienfuegos Provincial Hospital	Intramuscular leu IFN alpha combined with radio-therapy and cisplatinum	7	pilot	5 CR; 1 PR; 1 MR	77
Esophagus cancer	"C. García" Hospital	Intramuscular leu IFN alpha combined with radiotherapy	10	pilot	Clinical and radiological improvement after IFN and radiotherapy	78
Cancer of the anus	"C. García" Hospital	Intramuscular leu IFN alpha combined with radiotherapy	10	pilot	Clinical response and improvement in all cases that could undergo surgery	79
Cancer of the rectum	"C. García" Hospital	Intramuscular leu IFN alpha combined with radiotherapy	17	pilot	Clinical response and improvement in all cases that could undergo surgery	79
Breast cancer	"C. García" Hospital	Intramuscular leu IFN alpha	5	pilot	Favorable evolution in patients who refused chemotherapy	80
Undifferentiated sarcoma on the mastoid (girl)	CIMEQ	Intratumoral and intramuscular leu IFN alpha	1	case report	Complete remission for 5 years after intratumoral use	18

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Study	Institution	Therapeutical modality	Number of cases	Type of study	Results	Ref.
Multiple fibromatosis (boy)	"W. Soler" Hospital	Intramuscular leu IFN alpha	1	Case report	Complete remission of 120 fibro-mixomas	81
Heart fibroma (boy)	"W. Soler" Hospital	Intramuscular rec IFN alpha-2b	1	Case report	Complete remission of post-surgery recurrent tumor	82
Kaposi's sarcoma	Stgo. Vegas Sanatorium	Intramuscular; intrale-sional rec IFN alpha-2b	2	report	Complete remission in both cases; one for 3 years and the other for 1 year	83
Pancreas cancer	"10 de Octubre" Clinical-Surgical Hospital	Intramuscular rec IFN alpha-2b with palliative surgery; one case with IFN gamma	4	report	Three cases died at 13 days 6 months and 7 months after surgery respectively. One case lived 24 months receiving a combination of recombinant alpha and gamma IFNs	84
Ovarian cancer	INOR	rec IFN alpha-2b and rec IFN gamma and chemotherapy	5	report	Re-sensitization to chemotherapy in previously resistant patients. 1 RC; 2 RP; 1 EE and 1 progression	35
OTHER DISEASES						
Alzheimer's disease	Cienfuegos Provincial Hospital	Intramuscular intrathecal leu IFN alpha	1	report of one case	The clinical condition did not change; lymphocytary reaction in the CSF	85
Amyotrophic lateral sclerosis	Cienfuegos Provincial Hospital	Intramuscular intrathecal leu IFN alpha	4	pilot	Significant neurological improvement in 2 cases; 2 worsened; mild secondary reactions; lymphocytary reaction in the CRF	86
Multiple sclerosis	Neurology Institute	Intrathecal leu IFN alpha	15	pilot	Significant neurological improvement in 3 cases; 5 stabilized progression in 7	87
Schizophrenia	Havana Psychiatric Hospital	Intramuscular and intrathecal rec. IFN alpha-2b	16	pilot	Significant improvement in 9 cases; 5 did not change and one worsened. Improvement was more evident in women	31
Schizophrenia	Cienfuegos Provincial Hospital	Intrathecal rec IFN alpha-2b	2	pilot	Improvement of the disease's productive symptoms	32
Schizophrenia	Cienfuegos Provincial Hospital	Intrathecal rec IFN alpha-2b	9	pilot	Improvement in the 8 cases with the paranoid type. No improvement in one case of pseudo-neurosis; symptoms and social evolution were measured	33
Schizophrenia	Cienfuegos Provincial Hospital	Intrathecal rec IFN alpha-2b	9	double blind	More evident improvement in cases that received IFN when compared with a group with neuroleptics	34

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Study	Institution	Therapeutical modality	Number of cases	Type of study	Results	Ref.
Idiopathic Thrombocytopenic Purpura	Hematology and Immunology Institute	Intramuscular rec IFN alpha 2b	9	pilot	Favorable response in 4 cases; treatment had to be suspended in 3 due to secondary reactions and 2 received a second cycle	88
Lepromatous Leprosy	"Hnos. Ameijeiras" Hospital	Intramuscular rec IFN alpha-2b combined with chemotherapy	17	double blind	Increase in blastic transformation test in patients treated with IFN when compared with control group. There were no clinical differences.	89
Lepromatous Leprosy	"Hnos. Ameijeiras" Hospital	rec gamma IFN combined with chemotherapy	1	preliminary report	Response better than that of one case treated with placebo. Disappearance of bacilli	40
Rheumatoid Arthritis	Rheumatology Institute	Intramuscular rec IFN gamma	30	controlled	There was no favorable response in 10 cases resistant to treatment with gold salts. There was objective and subjective significant clinical improvement in 20 new cases.	36
Juvenile Rheumatoid Arthritis (children)	"Pedro Borrás" Pediatrics Hospital	Intramuscular rec IFN gamma	2	pilot	Favorable clinical response in two cases. Need for steroids was reduced	37
Psoriasis	"Hnos. Ameijeiras" Hospital	Intramuscular rec IFN alpha-2b	15	double blind	Clinical improvement in 62% with IFN vs 36/ with placebo. Histological improvement in 37% with IFN vs 9% with placebo. These differences were not significant	90
ONE YEAR LATER						
Chronic hepatitis C	"Luis Diaz Soto" Hosp.	rec IFN alpha-2b; intramuscular	17	controlled	Normalization of ALAT and histological improvement in 14 cases (83%) after 9 months treatment. The rest improved.	92
Laryngeal Papillomatosis.(National program in adults and children)	National ORL Group	leu IFN alpha (or rec alpha-2b); intramuscular	125	application	No relapses in 70% of the cases. Tracheotomy is not more necessary. 10% resistant cases.	94
Cervical condilloma	"10 de Octubre" Gineco-Obstetric Hosp.	rec IFN alpha-2b in topic gel	10	double blind	All cases responded compared with a control group without response.	95
Advanced ovarian cancer stage III or IV	INOR	rec IFN alpha-2b and gamma intraperitoneal combined with poly-chemotherapy	20	pilot	10 CR; 6 PR; 1 SD; 2 P	96

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Study	**Institution**	**Therapeutical modality**	**Number of cases**	**Type of study**	**Results**	**Ref.**
Advanced ovarian cancer stage IV, previously resistant to chemotherapy	INOR	rec IFN alpha-2b and gamma intraperitoneal. Afterwards chemotherapy	10	pilot	2 CR; 1 PR; 1 disappearance of liver metastasis; reduction of ascitis.	97
Schizophrenia	Cienfuegos Provincial Hosp.	rec IFN alpha-2b intramuscular	10	double blind	More improvement in IFN treated cases as compared to a group with neuroleptics only. Reduction in crisis frequency duration and in the amount of neuroleptic drug necessary for their control	98
Lepromatous Leprosy	"Hnos. Ameijeiras" Hospital	rec IFN gamma combined with chemotherapy	4	double blind; preliminar report	Better clinical and histological response than in cases treated with chemotherapy and placebo. Bacilli cleared. There was no modification of lymphocyte function marker tests	99
Juvenile Rheumatoid Arthritis (children)	"Pedro Borrás" Pediatric Hospital	rec IFN gamma intramuscular	4	pilot	Favourable clinical response in the 4 cases. Steroids could be suspended or dose-reduced.	100

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