



SUMMARY

This study concerns the evolution of 11 patients with hepatitis C under treatment with Interferon alpha 4C, Interferon Gamma 4C, Interferon gamma 30 C for a period of 6 months. The evaluation is based on the clinical evolution as well on lab tests. It was taken into consideration the presence of the markers for hepatitis C, AB anti HCV (EIA) qualitative and HCV - RNA quantitative (real-time CPR), at the beginning and end of treatment. The dynamic evolution of biochemical tests reflecting the liver functional state. The biochemical tests considered: GOT, GPT, gamma GT, total and fractional bilirubin and proteins. In 9 cases a significant reduction of the quantitative presence of marker (HCV - RNA quantitative - real time CRP) (eg: at 2,650,000 / ml to 95,000 / ml) was obtained. In the majority of the cases, one month after the beginning of the treatment an improvement has been registered in the biochemical indices that reflect the liver function.

According to the principles of PRM, the association of the therapy with Interferon alpha 4C, Interferon gamma 4C with homotoxicologic detoxifying treatment for the change of the treatment with Interferon gamma 30CH has led to normalization of biochemical tests in 8 cases in the following 2 months.

We consider very interesting the liver reactivity at the beginning of the treatment expressed by biochemical tests which seem to indicate an initial aggravation. That may suggest the immediate effect of the treatment with Interferon gamma 4C, on one hand, on the other hand, the PRM concept to integrate this treatment with a general psycho-neuro-immuno-endocrine rebalancing therapy.

- It is presented a detailed analysis of the evolution of two cases where the results show the evident efficiency of the treatment after 3 and 6 months.

The final proposal is to initiate a web forum for patients treated with Interferon gamma 4C, 30C where they can share the results, their experience encouraging others to choose this efficient, non aggressive treatment.

KEY WORDS

HEPATITIS C, INTERFERON ALPHA 4C, INTERFERON GAMMA 4C, INTERFERON GAMMA 30 C, HEPATIC FUNCTION, PRM

INTERFERON ALPHA 4C AND INTERFERON GAMMA 4C: THEIR THERAPEUTIC SYNERGY IN LIVER PATHOLOGIES ACCORDING TO PHYSIOLOGICAL REGULATING MEDICINE

"A different point of view is simply a view from a place where you were not."

- In spite of tremendous progress in virology and molecular biology, at the beginning of the millennium, liver pathology still remains the 6th leading cause of mortality.

There are an increasing number of new drugs for potential use in liver diseases and though they will undoubtedly improve results, there are still significant limitations in the treatment of liver pathologies. It is necessary to find new solutions to improve the treatment methods for hepatic diseases.

Currently, there are no effective therapies available for patients with chronic hepatitis C who have failed to respond to optimal interferon alpha-based treatments.

Chronic hepatitis C is the major cause of chronic liver diseases, cirrhosis, and liver cancer in most of the Western world. It affects approximately 4.2 million Americans, and more than 200 million people worldwide are infected with HCV. In Romania, the prevalence

of anti-HCV (around 5%) prior to the introduction of routine screening was 10 times higher than in Western European countries.

The hepatitis C virus (HCV) is a serious health concern and an important cause of chronic liver disease, leading to cirrhosis and hepatocellular carcinoma in humans. Of particular concern is that the virus establishes a chronic infection in 85% of cases (FIG. 1) and that there are no specific and broadly effective anti-HCV compounds to date. Belonging to the *Flaviviridae* family, HCV is a single-stranded RNA virus of positive polarity (FIG. 2) encoding a single polypeptide chain that is cleaved co- and post-translationally into both structural (core, E1, E2, p7) and non-structural (NS2, NS3, NS4A, NS4B, NS5A, NS5B) proteins (reviewed in Reed and Rice, 2000).

The hepatitis C virus NS2/3 protein is a highly hydrophobic protease responsible for the cleavage of the viral polypeptide between non-structural pro-

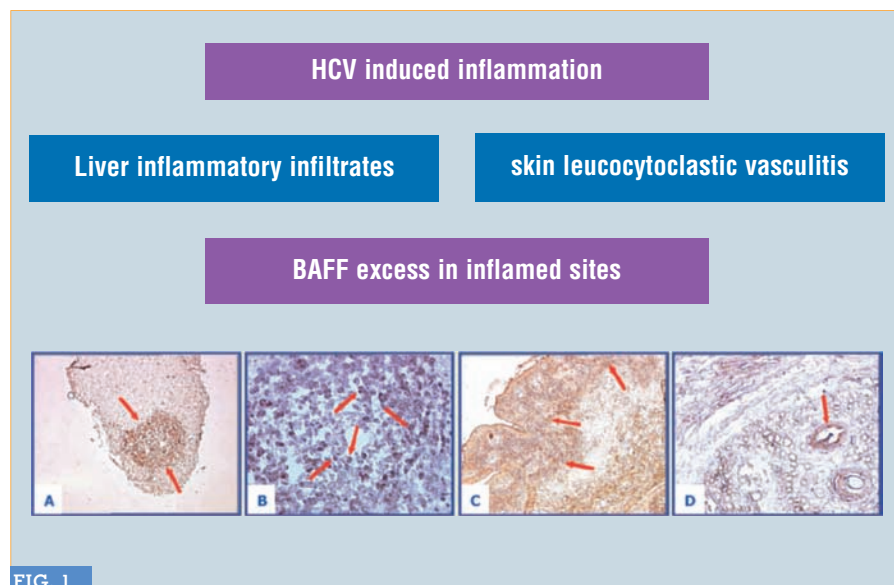


FIG. 1

HCV-induced inflammation mechanism.

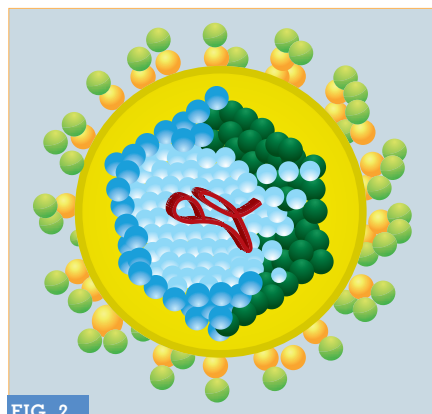


FIG. 2

Hepatitis C Virus.

teins NS2 and NS3. However, many aspects of the NS2/3 protease's role in the viral life cycle and mechanism of action remain unknown. Based on the recently elucidated crystal structure of NS2, NS2/3 has been proposed to function as a **cysteine protease** despite its lack of sequence homology to proteases of known function. In addition, although shown to be required for HCV genome replication and persistent infection in chimpanzee, the role of NS2/3 cleavage in the viral life cycle has not yet been fully investigated. However, several recent studies are beginning to clarify possible roles of the cleaved NS2 protein in modulation of host cell gene expression and apoptosis.

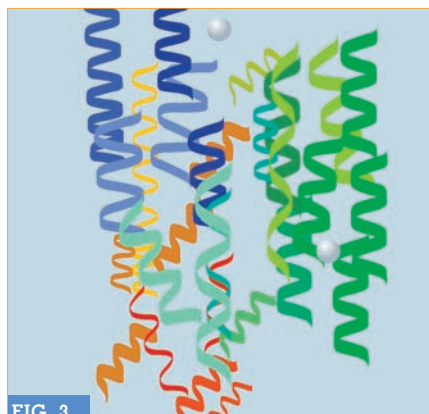


FIG. 3

Interferon alpha.

The role played by hepatitis C virus (HCV)-specific immune responses in the outcome of HCV infection is incompletely understood. Because HCV is believed to be noncytopathic, **the immune response has been thought to play a key role in the hepatic damage and ensuing fibrosis that occurs during chronic infection.** However, accumulating data from multiple laboratories have indicated that there is an association between enhanced HCV-specific T cell immunity and both recovery from acute infection and antiviral therapy-induced viral clearance. These data suggest that vigorous and broad-based HCV-specific T cell immunity is beneficial to the host and favors viral clearance.

ALLOPATHIC TREATMENT

The Interferons are a group of protein immunoregulators synthesized by T lymphocytes, macrophages, fibroblasts and other types of cells, after stimulation with viruses, antigens, mitoses, DNA, etc.

Interferon increases the ability of macrophages to destroy tumor cells, viruses and bacteria.

They are classified as **alpha**, **beta** and **gamma**, with the latter also being referred to as immune-Interferon.

What studies point out about the allopathic treatment.

Interferon alpha (FIG. 3) was approved as a therapy for hepatitis C in 1991. However, the overall rate of sustained virologic response, defined as the absence of HCV RNA in serum at least 6 months after the discontinuation of therapy, is low (generally <20%) with Interferon alpha monotherapy.

The subsequent addition of the oral antiviral agent *Ribavirin* to Interferon led to a marked improvement in rates of sustained virologic response (40 to 45%). *Ribavirin* alone lowered serum enzyme levels but had little effect on HCV RNA levels.

- The most recent important advance in the treatment of hepatitis C was the development of a long-acting Interferon, *pegylated Interferon* (pegInterferon), produced by the covalent attachment of polyethylene glycol to the Interferon molecule. With its increased half-life, pegInterferon can be given as a weekly dose. In two large trials, the rates of sustained virologic response to a 48-week course of pegInterferon and *Ribavirin* were 54 and 56%, as compared with 44 and 47% with standard Interferon and *Ribavirin* and only 29% with pegInterferon alone. Response rates were higher among patients with genotype 2 or 3 than among those with genotype 1. A subsequent trial of different regimens of pegInterferon alpha-2a and *Ribavirin* showed that patients

with genotype 2 or 3 could be treated with a lower dose of *Ribavirin* (800 mg rather than 1000 to 1200 mg daily) and that the rates of sustained virologic response after 24 weeks of therapy (81 and 84%) were similar to the rates after 48 weeks of therapy (79 and 80%).

Therapy is recommended for adults with chronic hepatitis C who have detectable HCV RNA in serum, elevations in aminotransferase levels, histological evidence of progressive liver disease, and no other serious coexisting conditions or contraindications. Specific qualitative assays for HCV RNA are available that have a lower limit of sensitivity of 10 to 50 IU (approximately 40 to 100 genome equivalents) per milliliter. In addition, HCV RNA can be quantified; most patients with chronic infection have HCV RNA levels between 0.2 and 5 million IU (approximately 1 to 20 million genome equivalents) per milliliter.

- An elevated serum alanine aminotransferase level is one of the criteria for instituting therapy because most persons with normal alanine aminotransferase levels have mild, nonprogressive disease. However, the degree of elevation does not always reflect the severity of disease and is not predictive of a patient's response to therapy.

Thus, normal aminotransferase levels should not exclude patients from therapy. *In vitro* studies demonstrate that exposure of primary neuron cultures of mice to Interferon alpha has the effect of loss of dendritic arborisations which becomes more obvious as the dose of Interferon is increased, resulting in permanent neuronal damage.

Conclusions about the antiviral activity of allopathic Interferon alpha and gamma.

The antiviral effects of Interferon gamma have been assessed in several small studies in chronic viral hepatitis, but mostly in chronic hepatitis B. In a study of hepatitis B, Interferon gamma had similar effects to Interferon alpha

PROTOCOL

Interferon gamma 4C:
20 drops x 3/day, for 3 months

Interferon gamma 30C:
20 drops x 3/day, for 3 months

CODICE: 2013 G: 2 A M: 289 Nome:									
Medico:									
Riferimento 2013					del: 30/06/08			-03/04/67	
Analisi	Risultato	Unità	Valori di Riferimento	Uomini					
Esame del: 30/06/08									
Chimica Clinica									
GLICEMIA BASALE	77 mg/dl	da	60	a	110				
Color.									
GOT	36 U/l	da	0	a	40				
Cinetico-spettof.									
GPT	48 U/l	da	0	a	30				
Cinetico-spettof.									
GAMMA GT	157 U/l	da	15	a	60				
Cinetico Spettrof.									
BILIRUBINA TOTALE E FRAZIONATA									
Colorimetrico									
SODIO	141 mEq/l	da	135	a	150				
Spettrofotometrico									
POTASSIO	4.1 mEq/l	da	3.6	a	5				
spettrofotometrico									
BILIRUBINA TOTALE	0.88 mg/dl	da	0.2	a	1.1				
BILIRUBINA DIRETTA	0.12 mg/dl	da	0.1	a	0.4				
BILIRUBINA INDIRETTA	0.76 mg/dl	da	0.15	a	0.8				
Ematologia									
ES. EMOCROMOCITOMETRICO									
Ematologia									
Markers Epatite C									
HCV- RNA QUANTITATIVO*	95.000.000 copie/ml	-	Limite inferiore di sensibilità:						
Real Time PCR	23.700.000 UI/ml		500 UI/ml						
Questo laboratorio partecipa al sistema V.E.Q. (valutazione esterna di qualità) Le analisi con asterisco sono eseguite in service presso il Centro BIANALISI S.r.l. via Russolillo, 63 00138 Roma									
ActaLab -2000- Licenza N. AL60300410135 Stampato il: 10/07/08									
Beginning of the treatment with INTERFERON γ ch4, for 2 month than INTERFERON γ 30ch, 15 drops x 3 times daily, long term									

Case No. 1

Lab tests (before the treatment).

on serum levels of HBV DNA polymerase, but therapy for up to 6 months was poorly tolerated and did not lead

to sustained remissions in disease. Furthermore, when administered together, there was no evidence of synergy

CODICE: 390 **G:** 4 **A** **M:** 77 **Nome:** _____
Medico: _____

Riferimento 390 **del:** 09/02/09 **-03/04/67**

Analisi **Risultato** **Unità** **Valori di Riferimento** **Uomini**

Esame del: 09/02/09

Chimica Clinica

GLICEMIA BASALE	94 mg/dl	da	60	a	110
Color.					
SODIO	133 mEq/l	da	135	a	150
Spettrofotometrico					
POTASSIO	4.6 mEq/l	da	3.6	a	5
Spettrofotometrico					
SIDEREMIA	88 mcg/dl	da	70	a	160
Colorimetrico-ferene					
FERRITINA	113.6 ng/ml	da	22	a	322
ELFA					
COLESTEROLO TOTALE	132 mg/dl				123 - 180
Colorimetrico					123 - 200
GOT	35 U/l	da	0	a	40
Cinetico-spettrof.					
GPT	49 U/l	da	0	a	30
Cinetico-spettrof.					
FOSFATASI ALCALINA	139 IU/l				Neonati 150 - 600
Cinetico Tamp. DEA					Da 1 a 11 anni 250 - 950
					Da 12 a 13 anni 200 - 875
					Da 14 a 15 anni 170 - 970
					Da 16 a 18 anni 75 - 720
					> di 18 anni 90 - 280
GAMMA GT	165 U/l	da	15	a	60
Cinetico Spettrof.					
BILIRUBINA TOTALE E FRAZIONATA					
Colorimetrico					
BILIRUBINA TOTALE	0.70 mg/dl	da	0.2	a	1.1
BILIRUBINA DIRETTA	0.14 mg/dl	da	0.1	a	0.4
BILIRUBINA INDIRETTA	0.56 mg/dl	da	0.15	a	0.8

Elettroforesi

PROTIDOGRAMMA **Vedi allegato**
 Elettoretico

Ematologia

ES. EMOCROMOCITOMETRICO **Vedi allegato**
 Contaglobuli CELL DINE 3000

Questo laboratorio partecipa al sistema V.E.Q. (valutazione esterna di qualità). Le analisi con asterisco sono eseguite in service presso il Centro BIANALISI S.r.l. via Russolillo, 63 00138 Roma

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CODICE: 390 **G:** 4 **A** **M:** 77 **Nome:** _____
Medico: _____

Riferimento 390 **del:** 09/02/09 **-03/04/67**

Analisi **Risultato** **Unità** **Valori di Riferimento** **Uomini**

Markers Epatite C

AB ANTI HCV*	Presenti	Assenti
EIA		
HCV- RNA QUANTITATIVO*	2.650.000 copie/ml -	Limite inferiore di sensibilità:
Real Time PCR	662.000 UI/ml	500 UI/ml
HCV RNA QUALITATIVO *	Positivo	Negativo
PCR		

Questo laboratorio partecipa al sistema V.E.Q. (valutazione esterna di qualità). Le analisi con asterisco sono eseguite in service presso il Centro BIANALISI S.r.l. via Russolillo, 63 00138 Roma

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between Interferon alpha and gamma. Several studies from other groups confirmed the lack of potent effects of Interferon gamma in chronic hepatitis B. Therapy with Interferon alpha led to decrease in serum aminotransferase levels, whereas Interferon gamma had little effect. HCV RNA testing was not done, and only a single dose and regimen was evaluated. A second study from Japan used Interferon alpha for 24 weeks followed by Interferon gamma for 2 weeks, making it difficult to interpret whether interferon gamma had any antiviral activity above and beyond that of Interferon alpha.

Both Interferon alpha and gamma have antiviral activity against HCV and together show evidence of synergy. The current clinical studies demonstrated no evidence of antiviral activity of Interferon gamma against HCV, but was not designed to assess possible synergy of the two cytokines. Interferon gamma has also been shown to have antifibrotic effects, but such activity was not the aim of the clinical studies, and preliminary data from a phase II of Interferon gamma have failed to show a significant effect in reversing fibrosis in cirrhotic patients with chronic hepatitis C.

These findings indicate that even if higher doses were effective, they probably would not be tolerated clinically.

In conclusion, **there is not any significant antiviral effect of Interferon gamma against HCV replication in patients with chronic hepatitis C who have previously failed to achieve a sustained response to Interferon alpha therapy**, despite showing biological effects as demonstrated by decreases in neutrophil and red blood cell counts. While the combination of Interferon gamma and alpha may reveal synergistic antiviral effects between these two cytokines, the current results suggest that Interferon gamma by itself is unlikely to have significant antiviral effects against the hepatitis C virus in humans.

Allopathic Interferon treatment is not for everyone.

Interferon therapy is not for everyone. The presence of other medical conditions may affect the use of Interferon alpha.

Bleeding problems, convulsions, history of mental problems (depression), diabetes, heart disease, kidney disease, lack of blood supply to any part of the body, lung disease, thyroid disease, autoimmune disease (problems with overactive Immune System).

Lab tests should be done at least once a month to monitor any abnormalities within the white blood cells, the platelets, and the red blood cells.

Also, Interferon should not be used by pregnant women because it is not known whether Interferon alpha will be harmful to an unborn baby.

In addition, it is not known whether Interferon passes into breast milk. This medication should not be used during breast-feeding.

Absolute contraindications.

- Pregnancy
- Breast-feeding
- Allergy to either drug.

Relative contraindication

Decompensated liver disease, ascites, bleeding esophageal varices, hepatic encephalopathy, major neuropsychiatric disease, coronary or cerebrovascular disease, renal failure, history of solid organ transplantation, alcohol abuse, anaemia, thrombocytopaenia, or leucopaenia, renal dysfunction.

Adverse effects.

Side effects of classical treatment affect virtually all patients who receive it.

The most common adverse effects are muscle aches and fatigue, but more difficult to manage are the psychological side effects such as depression, anxiety, irritability, and sleep.

Haemolysis and anaemia are the major

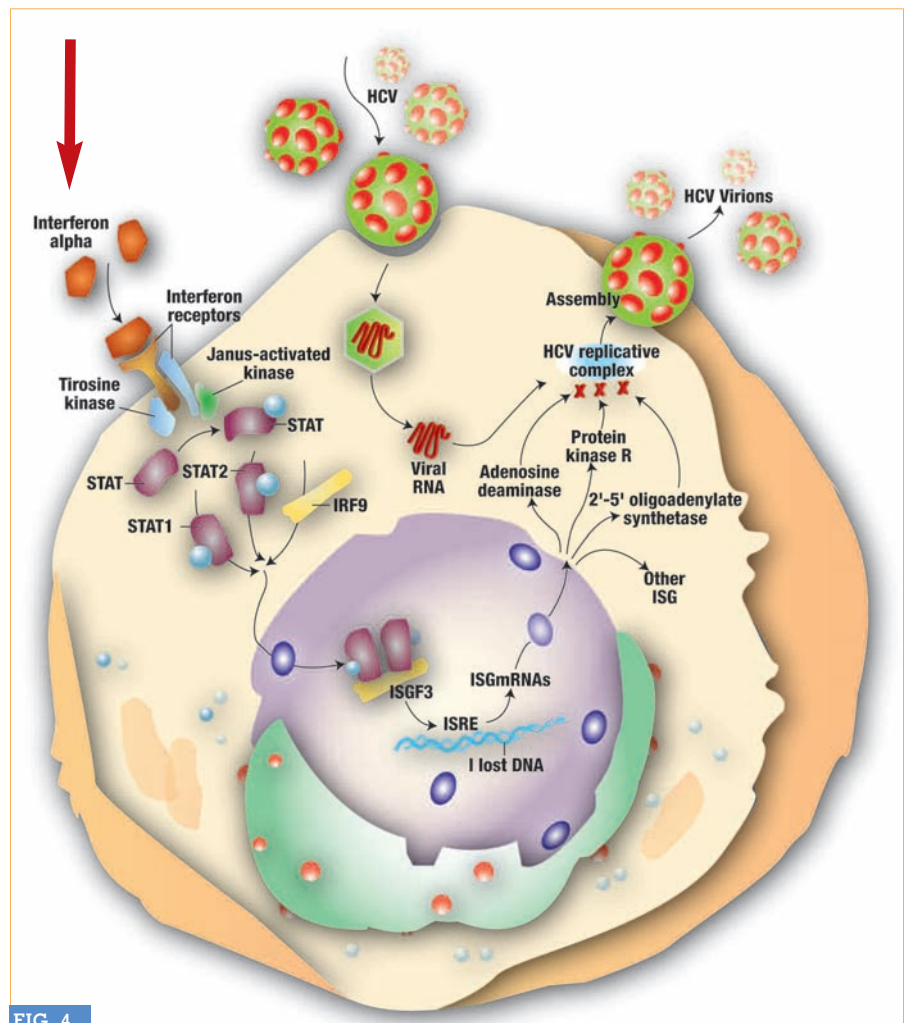


FIG. 4

The possible mechanism of Interferon alpha.

The NEW ENGLAND JOURNAL of MEDICINE (med 355; 23, December 7, 2006). Massachusetts Medical Society.

reasons for dose reduction. The stress of the sudden onset of anaemia can induce myocardial infarction in persons with pre-existing coronary disease or stroke in those with cerebrovascular disease. *Ribavirin* is also teratogenic and strict adherence to an effective means of birth control is mandatory for both women and men who receive this drug.

Serious side effects of combination therapy occur in 1 to 2% of patients and permanent injury and death can occur.

► *The New England Journal of Medicine 2006. Massachusetts Medical Society* "The cost of a 48-week course of peginterferon and *Ribavirin* ranges from \$30,000 to \$40,000, depending on local charges and the dose and brand of

drugs used. The expenses for monitoring and physician visits also need to be considered in weighing the costs of therapy."

WHY INTERFERON LOW DOSE ?

Physiological Regulating Medicine in accordance with informational medicine, uses **homeopathic cytokines** as initiating the Neuro-Immuno-Endocrine Reprogramming.

■ Low dose action mechanism (homeopathic cytokines activate some units of cellular or plasmatic receptors in the same dilution as these substances work physiologically 10^{-6} – 10^{-9}), through an UP-REGULATION mechanism.

- Affinity and redundancy [biological effect with minimal ligand concentration – only a small fraction (10%) of the receptors need to be occupied to get a large (50%) response].
- PRM proposes a general action that is non-toxic and multi-level without any contraindications or side effects, enabling the Immune System to express its whole potential.
- It doesn't substitute the Immune System, doesn't force or block it, just informs in a soft way.
- It's compatible and synergic with any other treatment, being situated borderline between conventional and non conventional medicine.
- Produced by bio-technology, recombinant DNA.
- Assumptions of Arndt – Schultz's Law.
- Efficiency.
- Could be used in all cases when allopathic interferon is not indicated.
- Very low costs.

A possible mechanism of action of low dose Interferon alpha.

As we see, the initiation of the chain of reactions is determined **qualitatively not quantitatively**. The mechanism of action of the homeopathic cytokines (Interferons) consists of the sensitization or activation of some of the units of cellular or plasmatic receptors. *Low doses* of 10^{-6} – 10^{-9} work the same as these substances work physiologically.

According to Physiological Regulating Medicine, the response of a cell to a messenger depends on the number of receptors occupied. Only a small fraction (10%) of the receptors need to be occupied to get a large (50%) response.

According to *the New England Journal of Medicine* 355123 (2006, Massachusetts

PROTOCOL

Interferon gamma 4C
20 drops x 3/day, for 3 months

Guna®-Matrix
20 drops x 3/day

Guna®- Liver
5 pellets x 3/day

Eubioflor 1
20 drops x 3/day

I.B.I. "Dr. Matei Bals", Bucuresti **GENETICA MOLECULARA**

Buletin de analize medicale

Data setului de analize 21.06.2007 11:56

Recoltat la data de: Validat la data de: 29.06.2007 09:3

Set lucrat de: Cod set AD3477

Nume: Varsta: 48 Medic:

Prenume: Cod prezentare: 701354

C.N.P.: 1590108400087 Nr. FO: 74627 / 07 Departament SECTIA ZI ADULTI

Urgenta NU

Teste Cantitative

Test	Rezultat	Val. norm./unit. mas.
HCV-RNA Cobas TaqMan	2070000	<2.80E+01 - >1.4E+09 / U/mL

Lucrat de: genetica user

La inceperea trat. cu Interferon Gamma 20 cdt.

Tiparit de: Olimpia Sandru Data tiparii 17.07.2007 14:30

pag. 1 / 1

Case No. 2

Lab test (before the treatment).

Medical Society) a mechanism of action of Interferon alpha could be the following:

Interferon alpha (FIG. 4) engages receptors on the hepatocyte cell-surface membrane, causing them to dimerize and to activate Janus-activated and tyrosine kinases that phosphorylate the cytoplasmic signal transducers and activators of transcription (STAT) proteins. STAT1 and STAT2 dimerize and bind Interferon regulatory factor 9 (IRF9), creating a large complex (Interferon-stimulated gene factor 3, or ISGF3) that is translocated into the nucleus, where it binds to Interferon-stimulated response elements (ISREs) on DNA. This engagement causes the

transcription of multiple (>100) Interferon-stimulated gene (ISG) mRNAs, which exit the nucleus and encode proteins that alter cell metabolism and interfere with virus replication, protein synthesis, and assembly. Major ISGs thought to be important in inhibiting HCV replication include 2',5' oligoadenylate synthetase, which activates antiviral RNases; RNA-specific adenosine deaminase, which edits viral RNA; and protein kinase R, which inactivates protein translation from viral mRNA. The HCV replicative complex is associated with the cytoplasmic membranes of hepatocytes and comprises RNA replicative

intermediates, viral mRNA, structural and nonstructural viral proteins, and assembling virions.

A possible mechanism of action of Interferon alpha *low dose*.

This study was designed to assess the antiviral activity of Interferon alpha and gamma in homeopathic doses (4C, 30C) in patients having anti-HCV in serum, and having HCV RNA in levels above 10,000 IU/ml.

The dynamic of clinical evolution and lab tests of the patients following the association of this treatment with detoxification and drainage using the PNEI concept.

PATIENTS AND METHODS

Selection of patients:

Eleven patients were enrolled including 7 women and 4 men with ages between 32 and 62 years old, with **chronic HCV infection** with a detectable serum HCV RNA level.

- 2 patients also had HIV infections
- 1 hepatocellular carcinoma
- 2 were non-responders to a previous therapy with Interferon alpha and Ribavirin.

PROTOCOL OF THERAPY

■ **Interferon alpha 4C** for 3 months alternated with **Interferon gamma 4C** for 3 months (20 drops x 3/day).

■ 6 patients were given drainage and detoxification treatment:

- **Guna®-Matrix + Eubioflor®**, 20 dps x 3/day + **Guna®-Liver** 5 pellets x 3/day.

■ For the patient with hepatocellular carcinoma: **Guna®-Rerio** (20 drops x 3/day).

Analiza	Um	Rezultat	Valori biologice de referinta		Incadrare
			Minim	Maxim	
Glicemie	mg/dl	119.00	70	115	(-----)*
TGO	U/L	32.00	0	37	(----*)
TGP	U/L	63.00	0	40	(-----)*
Trigliceride serice	mg/dl	151.00	0	200	(---*)
Acid uric seric	mg/dl	6.46	3.4	7	(----*)

Responsabil de analiza

Teste coagulare					
Fibrinogen seric	mg/dl	320	200	400	(---*)

Responsabil de analiza

Serologie					
Ac HCV		PREZENT			
Proteina C reactiva		ABSENTA < 6 mg/l			

Responsabil de analiza

Informatii despre serviciile oferite la: www.drnicolesumaria.webcad.ro, sugestii si reclamatii la: drnicolesumaria@yahoo.com
 Analizele s-au efectuat conform procedurilor specifice: PS-01B, PS-02, PS-03B, PS-03F, PS-03D, PS-03E, PS-16, PS-12, PS-14, PS-15C, PS-15D.

Medic:

Interlink Suport Informatic asigurat de SC Medical Robotics SRL, tel. 0766 369 831. Toate drepturile rezervate

Case No. 2

Lab test (before the treatment).

La 3 luni de la inceperea trat. cu Interferon Gamma 30CH.

INSTITUTUL NATIONAL DE BOLI INFECTIOASE "DR. MATEI BALȘ"
str. Dr. Grozovici nr. 1
sector 2, București

Clinica _____

BULETIN DE ANALIZĂ
25. 03.2008
REZULTAT

NUME ȘI PRENUME _____ SEXUL M/F _____

Examenul cerut HCV-RNA

Rezultatul analizei _____

HCV-RNA REAL TIME PCR
M2000 RT (ABBOTT)

1.112.935 ui/ml.

Lucrat de: _____

Tipărit la SC GRAFOPRESS Tel./fax: 0242-314647

Case No. 2

Lab test (after 3 months of treatment).

CLINICAL STUDY DESIGN

Patients underwent an initial evaluation that included a medical history and physical examination, a battery of blood tests, and a quantitative determination of serum HCV RNA and CRP in real time.

Patients were stratified according to previous response or combined pathology (responders or relapses to Interferon alpha, other associated diseases), protocol was modified according to pathology.

The primary endpoint of this study was a decrease of HCV RNA levels by one log or more during treatment as detected by quantitative CRP as well the improvement of the functional state of liver (normalizing of biochemical lab tests).

RESULTS

■ In **9 cases** a significant reduction of the quantitative presence of marker (HCV – RNA quantitative – real time CRP) was obtained.

■ In the **majority of cases**, one month (or two) after the beginning of the treatment there was a visible increase in biochemical indices that reflected liver function aggravation.

■ After **6 months** of treatment in 8 cases, the lab tests were improved.

Lab tests of two clinical case are presented ([Case No1](#), [Case No2](#)).

CONCLUSIONS

- Even in *low doses*, the homeopathic cytokines (Interferon alpha and gamma) have demonstrated effectiveness in the complementary treatment of hepatitis C, decreasing HCV RNA levels.

In addition, the initial aggravation of biological tests demonstrates the action of the treatment.

INSTITUTUL NATIONAL DE BOLI INFECTIOASE
"DR. MATEI BALS"
Str. Dr. Grozovici nr.1
Sector 2, Bucuresti

Nr. 12637
Data recoltari La 6 luni de la inceperea trat. cu Interferon Gamma 30 CH

BULETIN DE ANALIZA

SR
AGC
ISO 9001

Clinica: LAB. GENETICA

Nume si prenume: _____

Examenul cerut: HCV - RNA
HCV - RNA REAL TIME PCR Maxiscript (ABBOTT)

Rezultatul analizei:

12.637 ui/ml

Lucrat de: _____

Medic sef de laborator,

Case No. 2

Lab test (after 6 months of treatment).

Association of detoxification and drainage rebalancing the liver functions, significantly improving the laboratory tests (gamma GPT). ■

References


1. Bianchi I. - Homeopathic Materia Medica of Cytokines. Nuova Ipsa, Palermo, **2007**.
2. Bogdan C. - The function of type I interferons in antimicrobial immunity. *Curr Opin Immunol*, **2000**; 12: 419-424.
3. Callin G.A., Dumitru C.D., Smmizu M. et Al. - Frequent deletions and down-regulation of micro-RNA genes miR15 and miR16 at 13q14 In chronic lymphocytic leukemia. *Proc Natl Acad Sci USA*, **2002**; 99: 15524-15529.
4. Callin G.A., Ferracin M., Cimmino A. et Al. - A MicroRNA signature associated with prognosis and progression In chronic lymphocytic leukemia. *N Engl J Med*, **2005**; 353(17): 1793-1801.
5. Chelbi-Alix M.K., Wietzerbin J. - Interferon, a growing cytokine family: 50 years of interferon research. *Biochimie*, **2007**; 89: 713-718.
6. Chen X.M., Splinter P.L., O'Hara S.P. et Al. - A cellular micro-RNA, let-7i, regulates Toll-like receptor 4 expression and contributes to cholangiocyte Immune responses against *Cryptosporidium parvum* Infection. *J Biol Chem*, **2007**; 282(39): 28929-28938.
7. Cimmino A., Callin G.A., Fabbri M. et Al. - miR-15 and miR-16 induce apoptosis by targeting BCL2. *Proc Natl Acad Sci USA*, **2005**; 102(39): 13944-13949.

8. Johnnidis J.B., Harris M.H., Wheeler R.T. et Al. - Regulation of progenitor cell proliferation and granulocyte function by microRNA-223. *Nature*, **2008**; 451(7182): 1125-9.
9. Kasashima K., Nakamura Y., Kozu T. - Altered expression profiles of microRNAs during TPA-Induced differentiation of HL-60 cells. *Biochem Biophys Res Commun.*, **2004**; 322: 403-410.
10. Kriitzfeldt J., Rajewsky N., Braich R. et Al. - Silencing of microRNAs in vivo with 'antagomirs'. *Nature*, **2005**; 438(7068): 685-68.
11. Li Q.J., Chau J., Ebert P.J. et Al. - miR-181a is an intrinsic modulator of T cell sensitivity and selection. *Cell*, **2007**; 129: 147-161.
12. Malzac J.L.R. - *Materia Medica Omeopatica di Immunologia Clinica*. Nuova Ipsa, Palermo; **2007**.
13. Michael M.Z., O' Connor S.M., van Hoist Pellekaan N.G. et Al. - Reduced accumulation of specific microRNAs In colorectal neoplasia. *Mol Cancer Res.*, **2003**; 1: 882-891.
14. Milani L., Amadori M., Begni B. - Anti-inflammatory activity of low dose IFN-alpha – in vitro study on porcine leukocytes. *PRM*, **2007**; 29-35.
15. Naguibneva I., Ameyar-Zazoua M., Polesskaya A. et Al. - The microRNA miR-181 targets the homeobox protein Hox-A11 during mammalian myoblast differentiation. *Nat Cell Biol.*, **2006**; 8: 278-284.
16. Neilson J.R., Zheng G.X., Burge C.B. et Al. - Dynamic regulation of miRNA expression in ordered stages of cellular development. *Genes Dev.*, **2007**; 21: 578-589.
17. Ramkissoon S.H., Mainwarling L.A., Ogasawara Y. et Al. - Hematopoietic-specific microRNA expression In human cells. *Leuk Res.*, **2006**; 30(5): 643-647.
18. Soza A., Heller T., Ghany M., Lutchman G. et Al. - Pilot study of interferon gamma for chronic hepatitis C. *Journal of Hepatology* 43, **2005**; 67-71.
19. Xiao C., Calado D.P., Gauer G. et Al. - MiR-150 controls B cell differentiation by targeting the transcription factor c-Myb. *Cell*, **2007**; 131(1): 146-159.
20. Zhou B., Wang S., Mayr C. et Al. - miR-150, a microRNA expressed in mature B and T cells, blocks early B cell development when expressed prematurely. *Proc Natl Acad Sci USA*, **2007**; 104(17): 7080-7085.


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PHYSIOLOGICAL REGULATING MEDICINE



Homeopathic medicine





USES

For the temporary relief of symptoms due to: **Post surgery recovery, Tonsillitis, Childhood illnesses, Tender lymph nodes.**

DIRECTION

Adults and Children 6 years and over: 10 drops 3 times a day in a little water.
Children 6 years and under: ½ adult dosage.
 Take 15 minutes before meals.

MOST COMMON COMBINATIONS

Patients with good liver function	Guna-Lympho + Guna-Matrix + Guna-Liver
Patients with good bowel function	Guna-Lympho + Guna-Matrix + Guna-Bowel
Patients with good kidney function	Guna-Lympho + Guna-Matrix + Guna-Kidney
Venous insufficiency with lymphatic stasis	Guna-Lympho + Guna-Vein
Trauma with serious extravasations; hyarthrosis	Guna-Lympho + Guna-Trauma
Lymphadenopathies	Guna-Lympho + Guna-Tonsil

INGREDIENTS

Active ingredients:
 Apis mellifica 8X HPUS, Calendula officinalis 1X HPUS, Capillary tissue 6X, DLmalic acid 6X, Equisetum hyemale 3X HPUS, Fumaricum acidum 6X HPUS, Graphites 6X, 12X, 30X, 200X HPUS, Hydrastis canadensis 1X HPUS, Hydrocotyle asiatica 1X HPUS, Juglans regia 3X HPUS, Levothyroxin 6X, 12X, Lymphatic vessel 6X, Magnesia phosphorica 6X, 12X, 30X, 200X HPUS, Myosotis 3X HPUS, Natrum oxalacetikum 6X HPUS, Nat pyr 6X HPUS, Phytolacca decandra 3X HPUS, Sarsaparilla 3X HPUS, Taraxacum officinale 1X HPUS, Trichinoyl 6X, Vein 6X.

Inactive ingredient: Ethyl alcohol 30%

PACKAGE SIZE

30 ml / 1.0 fl. oz. bottle