

Medical Writers' Circle

a series of articles

written by medical
professionals about
the management
and treatment of
Hepatitis C

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Why Interferon Induction Therapy has been a Failure

Giving initially high doses of interferon for the first few weeks of treatment is called induction therapy. It is hoped that by slamming the virus, mutations will be prevented, and resistance to interferon can be prevented. The theory behind induction interferon is sound on the surface. It lowers the viral level quickly,

but nearly every clinical trial has failed to show better results with induction therapy. I recommend against induction therapy.

Some patients are very sensitive to even low doses of interferon, and the high doses used with induction therapy are often intolerable. Thus, curable patients sometimes quit because they are miserable. Non-

responders, by definition, do not respond even to these high doses.

I have treated 1,200 HCV-infected patients, and each patient responds differently to antiviral therapy. The concentration of the virus, HCV-RNA, falls exponentially. This is the same way that radioactive materials decay. It is the exact opposite of compound interest.

Table 1.

RELATIONSHIP BETWEEN % HCV-RNA FALL AFTER 30 DAYS OF TREATMENT TO THE VIRAL ELIMINATION HALF-LIFE

Pretreatment HCV-RNA	HCV-RNA after 30 days	Viral elimination half-life (days)	% Fall at 30 days
1000000	50	2.1	99.995
1000000	100	2.258	99.99
1000000	1000	3.01	99.9
1000000	1500	3.198	99.85
1000000	10000	4.515	99
1000000	20000	5.316	98
1000000	30000	5.93	97
1000000	40000	6.46	96
1000000	50000	6.941	95
1000000	60000	7.391	94
1000000	70000	7.82	93
1000000	80000	8.233	92
1000000	90000	8.636	91
1000000	100000	9.031	90
1000000	200000	12.92	80
1000000	250000	15	75

In my opinion, induction therapy is wrong because it is backwards. You should use lower interferon doses at the start of treatment and higher doses at the end of treatment. ■
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To understand it, you have to think in terms of half-lives. If the viral level is 500,000 IU/ml before treatment and falls to 250,000 after a week, the half-life is 7 days. A week later it should be 125,000, and so forth. It usually takes about 33 half-lives for successful treatment. Table 1 converts the percent fall in HCV-RNA in 30 days into half-life.

When you take very high doses of interferon with induction therapy at the beginning of treatment, you will have a short viral elimination half-life. This causes severe side effects because you are killing billions of viral particles. When the induction period is over, the interferon dose is reduced. The viral elimination half-life prolongs. If it takes 33 half-lives to get to a zero level of the virus, what good is it to shorten the half-life for only the first few weeks?

It makes more sense to start off with a low dose of the interferon, so that the side effects are less. The viral level is checked before treatment and after 30 days.

You calculate the percent fall with the formula:

Initial HCV-RNA minus the HCV-RNA after 30 days of treatment = viral fall in 30 days.

Divide the viral fall in 30 days by the initial HCV-RNA level and multiply by 100 = the percent fall at 30 days.

For example, if the HCV-RNA concentration is 500,000 IU/ml before treatment and falls to 50,000 IU/ml after 30 days of treatment, the viral fall is 450,000. Divide 450,000 by 500,000 = 0.90. 0.90 multiplied by 100 is a 90% fall.

You can get a good idea about your chance of success after 30 days of treatment. If your viral levels are falling less than 90% per month, you will need a higher interferon dose. I check the viral level again at 3 months and then about every 2 months. This tells if the treatment is still working.

Once the viral level is undetectable, you cannot measure it. This means that you cannot be sure that it is still falling 90% or more per

month. I like to raise the interferon dose for the last few months of treatment as insurance. This is well tolerated by patients, because they have few side effects from higher doses, when they have already killed 99.99% of the virus in them. Remember, to be cured, you have to kill every single viral particle by the end of the treatment. If you leave any behind when you stop, you will relapse.

In my opinion, induction therapy is wrong because it is backwards. You should use lower interferon doses at the start of treatment and higher doses at the end of treatment. It will require a large randomized clinical trial to prove this, and hopefully I will get funding next year to conduct the trial.



Medical Writers' Circle

is a program of the Hepatitis C Support Project.

The Mission of the Hepatitis C Support Project is to offer support to those who are affected by the hepatitis C Virus (HCV) and HIV/HCV coinfection.

Support is provided broadly, through information and education, as well as access to support groups. The (Project) seeks to serve the HCV community as well as the general public.

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