increment every 2 to 4 weeks. With this approach, we have had very few patients fail drug initiation." Thus, Frohman teaches to err on the side of an extended titration schedule.

[00021] It is therefore desirable to provide a method for further reducing flu-like symptoms associated with intramuscular interferon administration, which will promote compliance and continuation of interferon therapy for MS.

SUMMARY OF THE DISCLOSURE~~INVENTION~~

[00022] The inventors have surprisingly found that by decreasing the time period of the dose titration schedule for the intramuscular administration of interferon ("fast titration"), the appearance of flu-like symptoms is significantly reduced as compared to a longer dose titration schedule ("slow titration").

[00023] As such, the present disclosure~~invention~~ provides a method for treating multiple sclerosis, which includes intramuscularly administering an interferon to a patient once per week, and specifically includes an initial titration period wherein the interferon is administered in an escalating dose regimen (a "titration period"). In particular, the titration period includes a one-quarter dose in week one, a one-half dose in week two, a three-quarter dose in week 3, and a full therapeutically effective dose in week 4 and thereafter.

[00024] The present disclosure~~invention~~ also provides a method for reducing flu-like symptoms associated with the administration of an interferon to a patient with multiple sclerosis, including (a) intramuscularly administering the interferon to the patient according to an escalating dosing regimen in weeks 1 to 3; and (b) intramuscularly administering a full therapeutically effective dose of interferon in week 4.

[00025] The disclosure~~invention~~ also relates to a titration package for enabling compliance with these methods, wherein the dosage of interferon changes over a period of time. The titration package includes interferon delivery devices containing an interferon, and instructions for the patient to administer the interferon in an escalating dose regimen during a titration period.

[00025a] In one aspect, there is provided the use of an interferon-β-1a in the manufacture of a medicament for reducing the severity of flu-like symptoms associated with treating a patient having multiple sclerosis with intramuscularly administered interferon-β-1a over an eight week period,

wherein the medicament is to be administered intramuscularly once a week to a patient having multiple sclerosis according to a first schedule comprising:

intramuscular administration of 7.5 μg of interferon-β-1a to the patient in week one;

intramuscular administration of 15 μg of interferon-β-1a to the patient in week two;

intramuscular administration of 22.5 μg of interferon-β-1a to the patient in week three; and

intramuscular administration of 30 μg of interferon-β-1a to the patient in week four and each week thereafter,

wherein the severity of the flu-like symptoms is reduced at 4-6 hours and at 12-15 hours after each intramuscular administration of interferon-β-1a throughout the eight week period

(i) when compared to the severity of the flu-like symptoms at 4-6 hours and at 12-15 hours after each intramuscular administration of the medicament in a second schedule comprising once a week intramuscular administration of 30 μg of interferon-β-1a to a patient having multiple sclerosis for eight weeks; and

(ii) when compared to the severity of the flu-like symptoms at 4-6 hours and at 12-15 hours after each intramuscular administration of the medicament in a once a week intramuscular administration of the medicament to a patient having multiple sclerosis according to a third schedule comprising:

intramuscular administration of 7.5 μg of interferon-β-1a to the patient in weeks one and two;

intramuscular administration of 15 μg of interferon-β-1a to the patient in weeks three and four;

intramuscular administration of 22.5 μg of interferon-β-1a to the patient in weeks five and six; and

intramuscular administration of 30 μg of interferon-β-1a to the patient in week seven and each week thereafter.

[00025b] In another aspect, there is provided a titration package for reducing the severity of flu-like symptoms associated with treating a patient having multiple sclerosis with intramuscularly administered interferon-β-1a over an eight week period,

wherein the titration package comprises interferon-β-1a and delivery devices for once a week intramuscular administration to a patient having multiple sclerosis according to a first schedule comprising:

a first delivery device for intramuscular administration of 7.5 μg of interferon-β-1a to the patient in week one;

a second delivery device for intramuscular administration of 15 μg of interferon-β-1a to the patient in week two; and

a third delivery device for intramuscular administration of 22.5 μg of interferon-β-1a to the patient in week three;

wherein the severity of the flu-like symptoms is reduced at 4-6 hours and at 12-15 hours after each intramuscular administration of interferon-β-1a throughout an eight week period which includes once a week intramuscular administration of 30 μg of interferon-β-1a to the patient in week four through eight,

(i) when compared to the severity of the flu-like symptoms at 4-6 hours and at 12-15 hours after each intramuscular administration of interferon-β-1a in a second schedule comprising once a week intramuscular administration of 30 μg of interferon-β-1a to a patient having multiple sclerosis for eight weeks; and

(ii) when compared to the severity of the flu-like symptoms at 4-6 hours and at 12-15 hours after each intramuscular administration of interferon-β-1a in a once a week intramuscular administration of the medicament to a patient having multiple sclerosis according to a third schedule comprising:

intramuscular administration of 7.5 μg of interferon-β-1a to the patient in weeks one and two;

intramuscular administration of 15 μg of interferon-β-1a to the patient in weeks three and four;

intramuscular administration of 22.5 μg of interferon-β-1a to the patient in weeks five and six; and

intramuscular administration of 30 μg of interferon-β-1a to the patient in week seven and eight.

[00026] The foregoing and other objects, features and advantages of the disclosure~~invention~~ will be apparent from the following more particular description of preferred embodiments of the invention.

BRIEF DESCRIPTION OF THE FIGURES

[00027] The accompanying Figures, which are incorporated herein and form part of the specification, illustrate embodiments of the present invention and, together with the description, further serve to explain the principles of the invention.

[00028] Figure 1 is a flow chart showing the design of a "fast vs. slow" titration trial. Note that in the Example below, additional subjects were investigated.