

CLAIMS

1. A method for treating an inflammatory or autoimmune disease or disorder in a patient in need thereof, comprising administering to said patient a therapeutically effective amount of a S1P receptor modulator or agonist, in such a way that the adverse events possibly associated with administering said S1P receptor modulator or agonist are controlled, limited, reduced or abolished, wherein said method comprises the steps of
i) monitoring the patient during a specific period of time after the first administration of said S1P receptor modulator or agonist,
wherein said patient monitoring comprises one or more steps of
 - a) monitoring infections or infestations, e.g. viral infections, throughout administering said S1P receptor modulator or agonist,
 - b) performing an ophthalmologic examination,
ii) optionally interrupting the administration of said S1P receptor modulator or agonist and/or modifying the treatment regimen thereof.
2. A method of controlling, reducing, or abolishing the possible adverse events associated with treating a patient suffering from an inflammatory or autoimmune disease or disorder with a S1P receptor modulator or agonist, comprising administering to said patient a therapeutically effective amount of said S1P receptor modulator or agonist, wherein said method comprises one or more steps of
 - a) monitoring infections or infestations, e.g. viral infections, and
 - b) performing an ophthalmologic examination,
ii) optionally interrupting the administration of said S1P receptor modulator or agonist and/or modifying the treatment regimen thereof.
3. Method according to claim 1 or 2 wherein the patient monitoring further comprises a step of
 - c) monitoring the heart rate of the patient at least during the first hours after the first administration of said S1P receptor modulator or agonist, e.g. the 1 to 10 hours after the first administration of said S1P receptor modulator or agonist.
4. Method according to any preceding claim further comprises a step of

d) observing the patient for the 1 to 10 hours after the first administration of said S1P receptor modulator or agonist to monitor the heart rate of the patient, e.g. during the first 6 hours.

5. Method according to any preceding claim wherein the ophthalmologic examination is performed at least 3 to 4 months after starting administration.

6. Method according to any preceding claim wherein the patient monitoring further comprises one or more of steps of performing liver function tests, performing dermatological examinations, performing pulmonary functions tests.

7. A method for treating an inflammatory or autoimmune disease or disorder in a patient in need thereof, comprising administering to said patient a therapeutically effective amount of S1P receptor modulator or agonist in such a way that the adverse events possibly associated with said S1P receptor modulator or agonist are controlled, limited, reduced or abolished, wherein said method comprises i) checking specific parameters of the patient before initiating and/or during administration of said S1P receptor modulator or agonist, wherein said parameters comprise one or more of

- a) signs of infections or infestations, e.g. viral infections,
- b) visual acuity
- c) liver enzymes
- d) blood pressure

and ii) as necessary, interrupting the administration of said S1P receptor modulator or agonist and/or modifying the treatment regimen thereof.

8. Method of claim 7 wherein signs of infections or infestations are monitored throughout administering said S1P receptor modulator or agonist.

9. Method of claim 7 or 8 wherein visual acuity is monitored at initiating administration of said S1P receptor modulator or agonist or within the months preceding the first administration of said S1P receptor modulator or agonist, e.g. within the 6 months preceding the first administration of said S1P receptor modulator or agonist.

10. Method of claim 7 to 9 wherein visual acuity is monitored within the next months following the first administration of said S1P receptor modulator or agonist, e.g. within the 1 to 12 months following the first administration of said S1P receptor modulator or agonist.

11. Method of claim 7 to 10 wherein liver enzymes are monitored at initiating administration of said S1P receptor modulator or agonist, and optionally throughout administering said S1P receptor modulator or agonist .
12. Method of claim 7 to 11 further comprising checking the heart rate of the patient at initiating administration of said S1P receptor modulator or agonist and optionally within the 1 to 10 hours following the first administration of said S1P receptor modulator or agonist.
13. Method of claim 7 to 12 further comprising checking the respiratory function of the patient at initiating administration of said S1P receptor modulator or agonist and/or throughout administering said S1P receptor modulator or agonist .
14. Method of claim 7 to 13 further comprising checking the presence of dermatological disorders or skin cancer.
15. Method according to any preceding claim wherein modifying the treatment regimen thereof consists of increasing or decreasing the daily dosage and/or increasing the period of time between two consecutive administrations.
16. Method according to any preceding claim wherein the step ii) comprises administering a second drug which mitigates said possible adverse events, for example administering a second drug which is an anti-infection drug.
17. Method according to any preceding claim wherein step ii) is performed in case the monitoring reveals infections or an eyes disease.
18. Method according to any preceding claim wherein specific parameters of the patient are checked before initiating said S1P receptor modulator or agonist, said parameters being selected from blood analysis (e.g. complete blood count), liver enzymes, ophthalmologic examination, electrocardiogram (ECG), pulmonary functions tests, dermatological examination, and liver function tests.
19. A method according to any preceding claim wherein step i) comprises one or more steps of determining whether the patient is under beta blockers, shows resting bradycardia, high grade AV block or sick-sinus symptom.

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20. A method according to any preceding claim wherein the S1P receptor modulator or agonist is fingolimod (FTY720), a phosphate derivative thereof or a pharmaceutically acceptable salt thereof.

21. A method according to claim 20 wherein the S1P receptor modulator or agonist is administered at a daily dosage not exceeding about 0.5mg to the patient, e.g. of about 0.5mg.

22. A method according to claim 20 wherein the S1P receptor modulator or agonist is administered at a daily dosage exceeding 0.5mg to the patient, e.g. of 1.25mg.

23. A method of controlling, reducing, limiting or abolishing the possible adverse events associated with a treatment of a patient suffering from an inflammatory or autoimmune disease or disorder, wherein said treatment comprises administering a daily dosage of a drug selected from fingolimod (FTY720), a phosphate derivative thereof or a pharmaceutically acceptable salt thereof, not exceeding about 0.5mg to the patient, such a method comprising monitoring the patient during a specific period of time after the first administration of said drug, and if necessary either interrupting the administration of said drug, either modifying the treatment regimen thereof and/or administering a second drug which mitigates said possible adverse events, wherein said monitoring comprises one or more steps of

a) monitoring infections or infestations, e.g. viral infections, throughout drug administration, and

b) performing an ophthalmologic examination after starting administration.

24. Method according to any one of claims 20 to 23 wherein modifying the treatment regimen consists of administering a daily dosage of fingolimod, a phosphate derivative thereof or a pharmaceutically acceptable salt thereof, that is lower than 0.5 mg and then increasing the dosage up to a daily dosage of about 0.5mg, or increasing the period of time between two consecutive administrations thereof.

25. Method according to any one of claims 20 to 23 wherein fingolimod, a phosphate derivative thereof or a pharmaceutically acceptable salt thereof is co-administered with a second drug which mitigates said possible adverse events, for example with a second

drug which is selected from the group consisting of anti-cancer agents, anti-infection agents and anti-hypertensive drugs.

26. A method for treating multiple sclerosis comprising

(a) administering a varied dose of a drug selected from the group consisting of fingolimod (FTY720), a phosphate derivative thereof or a pharmaceutically acceptable salt thereof in a patient in need thereof,

(b) monitoring adverse events occurring in said patient,

(c) monitoring reduction or abolition of symptoms associated with multiple sclerosis, and

(d) determining optimal dose for said patient ,

wherein the daily dose of the drug does not exceed 0.5mg.

27. A method for treating multiple sclerosis comprising

(a) administering a varied dose of a drug selected from the group consisting of fingolimod (FTY720), a phosphate derivative thereof or a pharmaceutically acceptable salt thereof in a patient in need thereof,

(b) monitoring adverse events occurring in said patient,

(c) monitoring reduction or abolition of symptoms associated with multiple sclerosis, and

(d) determining optimal dose for said patient ,

wherein the daily dosage of the drug exceeds 0.5mg, e.g. is about 1.25mg.

28. A method for determining a personalized therapeutic treatment regimen of a drug selected from the group consisting of fingolimod (FTY720), a phosphate derivative thereof or a pharmaceutically acceptable salt thereof , in a patient suffering from an inflammatory or autoimmune disease, wherein said method comprises

(a) administering a varied dose of said drug to the patient,

(b) monitoring adverse events occurring in said patient,

(c) monitoring reduction or abolition of symptoms associated with multiple sclerosis, and

(d) determining optimal dose for said patient,

wherein said regimen is adapted for treating said disease or disorder and controlling, reducing, or abolishing the possible adverse events associated with administering said S1P receptor modulator or agonist.

29. A method of any one of claim 26 to 28, wherein step (b) comprises one or more steps of

- i) monitoring infections or infestations, e.g. viral infections,
- ii) performing an ophthalmologic examination, e.g. 3 to 4 months after starting drug administration.

30. Method according to any one of claims 20 to 29 wherein the adverse events are selected from bradycardia, atrioventricular conduction abnormalities, macular edema, skin cancer, altered liver functions, infections and hypertension.

31. A method for treating an inflammatory or autoimmune disease in a patient in need thereof and further suffering from bradyarrhythmia or at risk thereof, said method comprising administering a therapeutically effective amount of a S1P receptor modulator or agonist, and comprising the steps of

- i) monitoring the patient during a specific period of time after the first administration of said S1P receptor modulator or agonist, and
- ii) optionally interrupting the administration of said S1P receptor modulator or agonist and/or modifying the treatment regimen thereof,

wherein said patient monitoring comprises the steps of

- a) monitoring infections or infestations, e.g. viral infections, throughout administering said S1P receptor modulator or agonist,
- b) performing an ophthalmologic examination,
- c) monitoring the heart rate of the patient at least during the first hours after the first administration of said S1P receptor modulator or agonist, e.g. the 1 to 10 hours after the first administration of said S1P receptor modulator or agonist, and optionally
- d) observing the patient for the 1 to 10 hours after the first administration of said S1P receptor modulator or agonist to monitor the heart rate of the patient, e.g. during the first 6 hours.

32. Method of according to any preceding claim wherein the patient is vaccinated before initiating administration of said S1P receptor modulator or agonist, e.g. vaccinated against viral infection.

33. A combination containing a first drug which is selected from the group consisting of fingolimod (FTY720), a phosphate derivative thereof and a pharmaceutically acceptable salt thereof, and a second drug which is selected from the group consisting of drugs which

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treat or prevent macular edema, anti-cancer agent, anti infection agents and anti-hypertensive drugs, whereby the daily dosage of the first drug is not exceeding about 0.5 mg.

34. A kit containing daily units of medication of a first drug which is selected from the group consisting of fingolimod (FTY720), a phosphate derivative thereof or a pharmaceutically acceptable salt thereof, and a second drug which is selected from the group consisting of anti-cancer agent, anti-infection agents and anti-hypertensive drugs, whereby the daily dosage of the first drug is above 0.5 mg.

35. A method, combination, or kit according to any preceding claim wherein the treatment is for a chronic long term disease, e.g. for multiple sclerosis.

36. S1P receptor modulator or agonist, e.g. FTY720, a phosphate derivative thereof or a pharmaceutically acceptable salt thereof, for use in a method for treating an inflammatory or autoimmune disease according to any one of claims 1 to 32.

37. FTY720, a phosphate derivative thereof or a pharmaceutically acceptable salt thereof, for use in a method for treating an inflammatory or autoimmune disease according to any one of claims 1 to 32, wherein said disease is multiple sclerosis, e.g. RRMS.

CLAIMS

1. An invention not claimed in any divisional application.