ClinicalTrials.gov includes disclosure of a research study to assess the safety, pharmacokinetics and pharmacodynamics of 25HC3S in patients with AH, with dose escalation including three doses: 30 mg, 90 mg, and 150 mg. See ClinicalTrials.gov Identifier: NCT03432260.

There is an urgent need for improved methods to treat AH.

SUMMARY

The present disclosure provides a variety of methods of treating alcoholic hepatitis (AH). The methods involve administering an effective amount of 5-cholesten-3,25-diol, 3-sulfate (25HC3S) or salt thereof. In certain instances, the methods involve administering an effective amount of 5-cholesten-3,25-diol, 3β-sulfate or salt thereof.

The results of the present disclosure are surprising for several reasons. For instance, in some examples, the low dose of the present disclosure is surprising. Further, in some examples, the low dose frequency is surprising. Still further, in some examples, the low number of doses to attain efficacy in the treatment of AH is surprising. The results of the present disclosure are also surprising to the extent that the low dose amount, low dose frequency, and low total number of doses can provide results that are similar to or better than corticosteroids which require larger dose amounts, more frequent dosing, and/or a higher total number of doses. Still further, the present disclosure is also capable of achieving efficacious results in AH patients characterized by particular diagnostic criteria, such as Model for End-stage Liver Disease (MELD) score and/or other criteria discussed elsewhere herein.

In one aspect of the present disclosure, there is provided a use of 5-cholesten-3,25-diol, 3-sulfate (25HC3S) or salt thereof, in the manufacture of a medicament for treating alcoholic hepatitis in a human subject in need thereof, wherein the 25HC3S or salt thereof is to be administered to the human subject in a total amount of 10 mg to 400 mg in a period of one month, wherein:

the total amount is to be administered in one or more separate doses comprising at least a first dose;

the period of one month is measured from the beginning of administration of the first dose; and

each of the one or more separate doses comprises from 10 mg to 120 mg of the 25HC3S or salt thereof.

Further embodiments of the disclosure:

CLAIMS

1. Use of 5-cholesten-3,25-diol, 3-sulfate (25HC3S) or salt thereof, in the manufacture of a medicament for treating alcoholic hepatitis in a human subject in need thereof, wherein the 25HC3S or salt thereof is to be administered to the human subject in a total amount of 10 mg to 400 mg in a period of one month, wherein:

the total amount is to be administered in one or more separate doses comprising at least a first dose;

the period of one month is measured from the beginning of administration of the first dose; and

each of the one or more separate doses comprises from 10 mg to 120 mg of the 25HC3S or salt thereof .

2. The use of claim 1, wherein the total amount is not more than 200 mg.

3. The use of claim 1 or 2, wherein the total amount is to be administered in one dose or in two separate doses, preferably as a single dose.

4. The use of any one of claims 1 to 3, wherein the total amount is to be administered in two or more separate doses that are administered at a dose frequency ranging from daily to once every week.

5. The use of claim 1 or 2, wherein:

- the total amount is to be administered in one dose or in two separate doses; and
- the two separate doses are to be administered at a dose frequency ranging from once every two days to once every four days.

6. The use of claim 1, wherein:

the total amount is to be administered in one dose or in two separate doses;

the one dose comprises from 20 mg to 40 mg of the 25HC3S or salt thereof;

each of the two separate doses comprises from 20 mg to 40 mg of the 25HC3S or salt thereof; and

the two separate doses are to be administered at a dose frequency ranging from once every two days to once every four days.

7. The use of claim 1 or 2, wherein:

the total amount is to be administered in one dose or in two separate doses;

the one dose comprises from 80 mg to 100 mg of the 25HC3S or salt thereof;

each of the two separate doses comprises from 80 mg to 100 mg of the 25HC3S or salt thereof; and

the two separate doses are to be administered at a dose frequency ranging from once every two days to once every four days.

8. The use of any one of claims 1 to 7, wherein the 25HC3S or salt thereof is to be parenterally, intravenously, intramuscularly, or subcutaneously administered.

9. The use of any one of claims 1 to 8, wherein the 25HC3S or salt thereof is to be administered by injection.

10. The use of any one of claims 1 to 9, wherein the 25HC3S or salt thereof is to be administered in a formulation comprising the 25HC3S or salt thereof and a pharmaceutically acceptable carrier.

11. The use of any one of claims 1 to 10, wherein the human subject has a Model for End-stage Liver Disease (MELD) score of at least 11.

12. The use of any one of claims 1 to 11, wherein the human subject has a Maddrey's discriminant function (MDF) of at least 32.

13. The use of any one of claims 1 to 12, wherein the 25HC3S or salt thereof comprises a salt of 25HC3S.

14. The use of claim 13, wherein the salt of 25HC3S is the sodium salt.