CLAIMS

1. Use of a CXCL8 inhibitor in the manufacture of a medicament for the treatment of patients with COVID-19 pneumonia, wherein said CXCL8 inhibitor is either an allosteric inhibitor or an orthosteric antagonist of CXCR1 receptor or of both CXCR1 and CXCR2 receptors.

2. The use according to claim 1, wherein said inhibitor is for use in improving respiratory function in said patients, wherein said respiratory function is measured as partial arterial oxygen pressure (PaO2) to fraction of inspiration O2 (FiO2) ratio.

3. The use according to claim 1 or claim 2, wherein said patients have values of partial arterial oxygen pressure (PaO2) to fraction of inspiration O2 (FiO2) ratio before the treatment of the invention below 400 mmHg, more preferably between 100 and 300mmHg (wherein 1mmHg = 0.133kPa) and/or a respiratory rate of or above 30 breaths/min without oxygen supplementation.

4. The use according to any one of claims 1 to 3, wherein said improving respiratory function comprises increasing partial arterial oxygen pressure (PaO2) to fraction of inspiration O2 (FiO2) ratio of at least 20%, 50%, 80%, 100%, 120% 150%, 200% or 250% in comparison with the ratio before treatment.

5. The use according to any one of claims 1 to 4, wherein said patients have lymphocytopenia.

6. The use according to claim 4, wherein said patients are adult patients (age of 14 years and above) and have blood concentration of lymphocytes below 1000, below 900, below 850, below 800 or below 750 cells/microliter or said patients are children (age below 14 years) and have blood concentration of lymphocytes below 3000, below 2800, below 2500, below 2300 or below 2000 cells/microliter.

7. The use according to any one of claims 1 to 6, wherein said CXCL8 inhibitor is to be administered in combination with treatment with at least one drug selected from:

i) antiviral drugs, preferably remdesivir;
ii) antipyretic; analgesic and antiinflammatory drugs, preferably non-steroidal anti-inflammatory drugs, corticosteroids, cytokine, chemokine and interleukin inhibitors, more

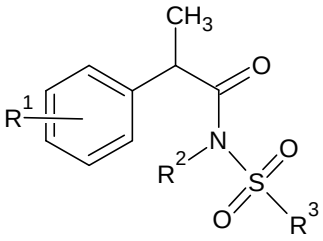
preferably selected from dexhamethasone, paracetamol, anakinra, celecoxib, prednisone, prednisolone, methylprednisolone, piryrone, and tramadol;

iii) antibiotics, preferably selected from piperacillin in association with tazobactam, azithromycin and ceftriazone; and

iv) anti-coagulants and antithrombotic drugs, preferably selected from enoxaparin and acetylsalicylic acid.

8. The use as claimed in any one of claims 1 to 7, wherein said CXCL8 inhibitor inhibits the activity of CXCL8 mediated by CXCR1 receptor or mediated by both CXCR1 and CXCR2 receptors.

9. The use as claimed in any one of claims 1 to 8, wherein said CXCL8 inhibitor is a compound of formula (I):



(I)

wherein

R^1 is selected from a linear or branched C_1-C_6 alkyl, benzoyl, phenoxy, and trifluoromethanesulfonyloxy;

R^2 is selected from hydrogen atom and linear or branched C_1-C_3 alkyl; and

R^3 is a linear or branched C_1-C_6 alkyl or trifluoromethyl,

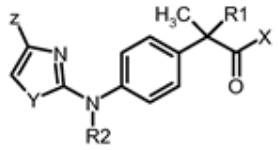
or a pharmaceutically acceptable salt thereof.

10. The use as claimed in any one of claims 1 to 9, wherein said CXCL-8 inhibitor is selected from:

- 2-(4-isobutylphenyl)propionyl methansulfonamide, preferably R-(-)-2-(4-isobutylphenyl)propionyl methansulfonamide and pharmaceutically acceptable salts thereof, preferably the lysine salt thereof, and
- 2-(4-trifluoromethanesulfonyloxy)phenyl-N-methanesulfonyl propionamide, preferably R(-)-2-(4-trifluoromethanesulfonyloxy)phenyl-N-methanesulfonyl propionamide and pharmaceutically acceptable salts thereof, in particular the sodium salt thereof.

11. The use as claimed in any one of claims 1 to 10, wherein said CXCL8 inhibitor is R-(-)-2-(4-isobutylphenyl)propionyl methansulfonamide, wherein said inhibitor is to be administered to said patient intravenously at a dose between 2 and 3 mg/kg body weight/hour, preferably of 2.772 mg/kg body weight/hour, for 5 days.

12. The use as claimed in any one of claims 1 to 8, wherein said CXCL8 inhibitor is a compound of formula (II):

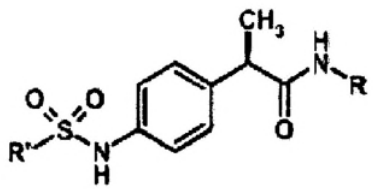


(II)

and pharmaceutically acceptable salts thereof, wherein:
R1 is hydrogen;
X is OH;
R2 is hydrogen or linear C_1-C_4 alkyl,
Y is a heteroatom selected from S, O and N,
Z is selected from linear or branched C_1-C_4 alkyl, linear or branched C_1-C_4 alkoxy, halo C_1-C_3 alkyl and halo C_1-C_3 alkoxy.

13. The use as claimed in any one of claims 1 to 8 and 12, wherein said CXCL8 inhibitor is 2-(4-{[4-(trifluoromethyl)-1,3-thiazol-2-yl]amino}phenyl)propanoic acid, preferably (2S)-2-(4-{[4-(trifluoromethyl)-1,3-thiazol-2-yl] amino} phenyl) propanoic acid or the sodium salt thereof.

14. The use as claimed in any one of claims 1 to 8, wherein said CXCL8 inhibitor is a compound of formula (III):



(III)

and pharmaceutically acceptable salts thereof, wherein:
R is selected from

H, OH, C_1-C_5-alkyl, C_3-C_6-cycloalkyl, C_2-C_5-alkenyl, C_1-C_5-alkoxy and phenyl,
a heteroaryl group selected from unsubstituted pyrrole, thiophene, furane, indole, imidazole, thiazole, oxazole, pyridine and pyrimidine,
a residue of formula CH2CH2O(CH2CH2)nR'', wherein R'' is H or C_1-C_5 alkyl and n is an integer from 0 to 2;
R' is selected from

- linear or branched C_1-C_5-alkyl, C_3-C_6-cycloalkyl, C_2-C_5-alkenyl and trifluoromethyl;
- phenyl unsubstituted or substituted with a group selected from halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, trifluoromethyl;
- unsubstituted benzyl;
- an heteroaryl group selected from unsubstituted pyridine, pyrimidine, pyrrole, thiophene, furane, indole, thiazole and oxazole.

15. The use as claimed in claim 14, wherein said CXCL8 inhibitor is 2-{4[(isopropylsulfonyl)amino]phenyl} propanamide, preferably (2R)-2-{4[(isopropylsulfonyl)amino]phenyl} propanamide, and pharmaceutically acceptable salts thereof, preferably the sodium salt thereof

16. Use of a pharmaceutical composition comprising (i) a CXCL8 inhibitor, a salt thereof with a pharmaceutically acceptable organic or inorganic acid or base, or an ester prodrug thereof, as defined in any one of claims 1 to 15, and (ii) at least one inert pharmaceutically acceptable excipient, in the manufacture of a medicament for the treatment of patients with COVID-19 pneumonia.