Claims

1. Use of an interleukin-2/interleukin-15 receptor βγ (IL-2/IL-15Rβγ) agonist in the manufacture of a medicament for treating or managing cancer or infectious diseases, wherein the IL-2/IL-15Rβγ agonist is to be administered to a human patient using a cyclical administration regimen, wherein the cyclical administration regimen comprises:

   (a) a first period of x days during which the IL-2/IL-15Rβγ agonist is to be administered at a daily dose on y consecutive days at the beginning of the first period followed by x-y days without administration of the IL-2/IL-15Rβγ agonist,
   wherein x is 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21 days, preferably, 7 or 14 days, and
   y is 2, 3 or 4 days, preferably 2 or 3 days;

   (b) repeating the first period at least once; and

   (c) a second period of z days without administration of the IL-2/IL-15Rβγ agonist, wherein z is 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 28, 35, 42, 49, 56, 63 or 70 days, preferably 7, 14, 21 or 56 days, more preferably 7 or 21 days,

   wherein the IL-2/IL-15Rβγ agonist is an interleukin 15 (IL-15)/interleukin-15 receptor alpha (IL-15Rα) complex comprising the human IL-15Rα sushi domain or a derivative thereof and human IL-15 or a derivative thereof.

2. Use of the IL-2/IL-15Rβγ agonist of claim 1, wherein the IL-2/IL-15Rβγ agonist is to be administered to a human patient using a cyclical administration regimen, wherein the cyclical administration regimen comprises:

   (a) a first period of x days during which the IL-2/IL-15Rβγ agonist is to be administered at a daily dose on y consecutive days at the beginning of the first period followed by x-y days without administration of the IL-2/IL-15Rβγ agonist,
   wherein x is 5, 6, 7, 8 or 9 days, preferably, 6, 7 or 8 days, more preferably 7 days, and
   y is 2, 3 or 4 days, preferably 2 or 3 days, more preferably 2 days;

   (b) repeating the first period at least once; and

(c) a second period of z days without administration of the IL-2/IL-15Rβγ agonist, wherein z is 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 days, preferably 7 or 14 days, more preferably 7 days.

3. Use of the IL-2/IL-15Rβγ agonist of claims 1 or 2, wherein x is 7 days, y is 2, 3 or 4 days and z is 7 days, preferably wherein y is 2 days and z is 7 days.

4. Use of the IL-2/IL-15Rβγ agonist of claims 1 to 3, wherein the daily dose is 0.1 µg/kg to 50 µg/kg, preferably 0.25 µg/kg to 25µg/kg, more preferably 3 µg/kg to 20 µg/kg, even more preferably 6 to 12 µg/kg.

5. Use of the IL-2/IL-15Rβγ agonist of claim 4, wherein the daily dose selected within the dose range of 0.1 to 50 µg/kg is not increased during the administration regimen, preferably wherein the dose is maintained during the administration regimen.

6. Use of the IL-2/IL-15Rβγ agonist of claims 1 to 3, wherein the daily dose is a fixed dose independent of body weight of 7 µg to 3500 µg, preferably 17.5 µg to 1750 µg, more preferably 42 µg to 700 µg and especially 140 µg to 700 µg.

7. Use of the IL-2/IL-15Rβγ agonist of claims 1 to 4 or 6, wherein the daily dose is increased during the administration regimen, preferably wherein the daily dose is increased after each period of x days, more preferably wherein the daily dose is increased by 20% to 100%, especially by 30% to 50% after each period of x days.

8. Use of the IL-2/IL-15Rβγ agonist of claim 7, wherein the daily dose is increased once after the first period of x days.

9. Use of the IL-2/IL-15Rβγ agonist of claim 8, wherein the daily dose is increased by 20% to 100%, preferably by 30% to 50% after the first period of x days.

10. Use of the IL-2/IL-15Rβγ agonist of any of claims 1 to 9, wherein the daily dose is to be administered in a single injection.

11. Use of the IL-2/IL-15Rβγ agonist of any of claims 1 to 9, wherein the daily dose is split into 2 or 3 individual doses that are to be administered within one day, wherein the time interval between administration of the individual doses is at least about 4 h and preferably not more than 14 h, more preferably wherein the daily dose is split into 3 individual doses

that are to be administered within one day, wherein the time interval between administration of the individual doses is 5 to 7 h, especially about 6 h, or wherein the daily dose is split into 2 individual doses that are to be administered within one day, wherein the time interval between administration of the individual doses is 6 h to 10 h, especially about 8 h.

12. Use of the IL-2/IL-15Rβγ agonist according to any of claims 1 to 11, wherein the IL-2/IL-15Rβγ agonist is to be administered subcutaneously (s.c.) or intraperitoneally (i.p.), preferably s.c..

13. Use of the IL-2/IL-15Rβγ agonist according to any of claims 1 to 12, wherein administration of the IL-2/IL-15Rβγ agonist in step (a) results in
(1) an increase of the % of Ki-67$^+$ NK of total NK cells in comparison to no administration of the IL-2/IL-15Rβγ agonist, and wherein administration of the IL-2/IL-15Rβγ agonist in step (b) results in a Ki-67$^+$ NK cell level that is at least 70% of the of the Ki-67$^+$ NK cells of step (a), or
(2) maintenance of NK cell numbers or preferably an increase of NK cell numbers to at least 110% as compared to no administration of IL-2/IL-15Rβγ agonist after at least one repetition of the first period, preferably after at least two repetitions of the first period, and/or
(3) NK cell numbers of at least 1.1 x 10^3 NK cells/µl after at least one repetition of the first period, preferably after at least two repetitions of the first period.

14. Use of the IL-2/IL-15Rβγ agonist according to any of claims 1 to 13, wherein the cyclic administration is repeated over at least 3 cycles, preferably 5 cycles, more preferably at least 10 cycles and even more preferably until disease progression.

15. Use of the IL-2/IL-15Rβγ agonist according to any of claims 1 to 14, wherein the IL-2/IL-15Rβγ agonist has an *in vivo* half-life of 30 min to 24 h, preferably 1 h to 12 h, more preferably of 2 h to 6 h.

16. Use of the IL-2/IL-15Rβγ agonist according to any of claims 1 to 15, wherein the IL-2/IL-15Rβγ agonist is a fusion protein comprising the human IL-15Rα sushi domain or derivative thereof, a flexible linker and the human IL-15 or derivative thereof, preferably wherein the human IL-15Rα sushi domain comprises the sequence of SEQ ID NO: 6, and

wherein the human IL-15 comprises the sequence of SEQ ID NO: 4,
more preferably wherein the IL-15/IL-15Rα complex is SEQ ID NO: 9.

17. Use of the IL-2/IL-15Rβγ agonist according to any of claims 1 to 16, wherein a further therapeutic agent is to be administered in combination with the IL-2/IL-15Rβγ agonist, preferably wherein the further therapeutic agent and the IL-2/IL-15Rβγ agonist are to be administered on the same days and/or on different days.

18. Use of the IL-2/IL-15Rβγ agonist according to claim 17, wherein the further therapeutic agent is selected from a checkpoint inhibitor,
preferably an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-PD-L2 antibody, an anti-LAG-3 antibody, an anti-TIM-3 antibody, an anti-CTLA4 antibody or an anti-TIGIT antibody, more preferably an anti-PD-L1 antibody or an anti-PD-1 antibody, or a therapeutic antibody,
preferably an anti-CD38 antibody, an anti-CD19 antibody, an anti-CD20 antibody, an anti-CD30 antibody, an anti-CD33 antibody, an anti-CD52 antibody, an anti-CD79B antibody, an anti-EGFR antibody, an anti-HER2 antibody, an anti-VEGFR2 antibody, an anti-GD2 antibody, an anti-Nectin 4 antibody and an anti-Trop-2 antibody, more preferably an anti-CD38 antibody,
especially wherein in weeks with anti-CD38 antibody administration, the anti-CD38 antibody is to be administered on the 1st day or the 3rd day of the week.

19. Use of the IL-2/IL-15Rβγ agonist according to claim 18, wherein the checkpoint inhibitor or therapeutic antibody is to be administered at the beginning of the first period (a) of each cycle.

20. Use of the IL-2/IL-15Rβγ agonist according to claim 18 or claim 19, wherein the x days and z days are adapted that
an integral multiple of x days + z days equal the days of one treatment cycle of the checkpoint inhibitor or the therapeutic antibody, or
if the treatment cycle of the checkpoint inhibitor or the therapeutic antibody changes over time, equal to each individual treatment cycle of the checkpoint inhibitor or the therapeutic antibody.