CLAIMS:

1. At least one peptide, suitable for eliciting an immune response, wherein the or each peptide corresponds to a fragment of the RAS protein but has one to three point mutations thereof, for use in the treatment of cancer by simultaneous or sequential administration with an anti-metabolite chemotherapeutic agent.

2. The at least one peptide for use according to claim 1, wherein the or each peptide comprises a region of at least 8 amino acids which includes position 12 or 13 of the RAS protein, wherein said region has at least 6 amino acid residues, other than at position 12 or 13 respectively, which are identical to the corresponding region of the RAS protein, and wherein the or each peptide has a point mutation at the amino acid residue corresponding to said position 12 or 13 respectively.

3. The at least one peptide for use according to claim 1 or 2, wherein one of said point mutations is selected from a G13A, G13C, G13D, G13R, G13S, G13V, G12A, G12C, G12D, G12R, G12S or a G12V mutation.

4. The at least one peptide for use according to any preceding claim, wherein the at least one peptide comprises two or more peptides, each peptide having a different point mutation.

5. The at least one peptide for use according to any preceding claim, wherein the at least one peptide comprises:

a peptide having a G13D mutation
a peptide having a G12A mutation
a peptide having a G12C mutation
a peptide having a G12D mutation
a peptide having a G12R mutation
a peptide having a G12S mutation, and
a peptide having a G12V mutation,

preferably wherein the at least one peptide comprises a peptide consisting of the sequence represented by SEQ ID NO: 13, a peptide consisting of the sequence represented by SEQ ID NO: 14, a peptide consisting of the sequence represented by SEQ ID NO: 15, a peptide consisting of the sequence represented by SEQ ID NO: 16,

a peptide consisting of the sequence represented by SEQ ID NO: 17, a peptide consisting of the sequence represented by SEQ ID NO: 18 and a peptide consisting of the sequence represented by SEQ ID NO: 19.

6. The at least one peptide for use according to any one of claims 1-4, wherein the at least one peptide comprises:

a peptide having a G13D mutation
a peptide having a G13C mutation
a peptide having a G12A mutation
a peptide having a G12C mutation
a peptide having a G12D mutation
a peptide having a G12R mutation
a peptide having a G12S mutation, and
a peptide having a G12V mutation,

preferably wherein the at least one peptide comprises a peptide consisting of the sequence represented by SEQ ID NO: 13, a peptide consisting of the sequence represented by SEQ ID NO: 14, a peptide consisting of the sequence represented by SEQ ID NO: 15, a peptide consisting of the sequence represented by SEQ ID NO: 16, a peptide consisting of the sequence represented by SEQ ID NO: 17, a peptide consisting of the sequence represented by SEQ ID NO: 18, a peptide consisting of the sequence represented by SEQ ID NO: 19 and a peptide consisting of the sequence represented by SEQ ID NO: 20.

7. The at least one peptide for use according to any preceding claim, wherein the anti-metabolite chemotherapeutic agent is a pyrimidine analogue, or a pharmaceutically acceptable salt thereof, preferably wherein the pyrimidine analogue is gemcitabine or a pharmaceutically acceptable salt thereof.

8. The at least one peptide for use according to any preceding claim, wherein the cancer comprises cells which express a mutated RAS protein, preferably wherein the cancer is pancreatic cancer, more preferably resected pancreatic cancer.

9. The at least one peptide for use according to any preceding claim, wherein the anti-metabolite chemotherapeutic agent is first administered at least three weeks after the first dose of the at least one peptide.

10. The at least one peptide for use according to claim 8, wherein the cancer is resected pancreatic cancer and the anti-metabolite chemotherapeutic agent is first administered 12 weeks or fewer after surgical resection of the pancreatic cancer.

11. The at least one peptide for use according to any preceding claim, wherein the anti-metabolite chemotherapeutic agent is administered within 24 hours of the at least one peptide.

12. The at least one peptide for use according to claim 11, wherein the anti-metabolite chemotherapeutic agent is administered after the at least one peptide has been administered.

13. The at least one peptide for use according to any preceding claim, wherein the at least one peptide is administered at a dosage of 0.01-10mg, preferably 0.1-2mg, and more preferably 0.7mg per dose.

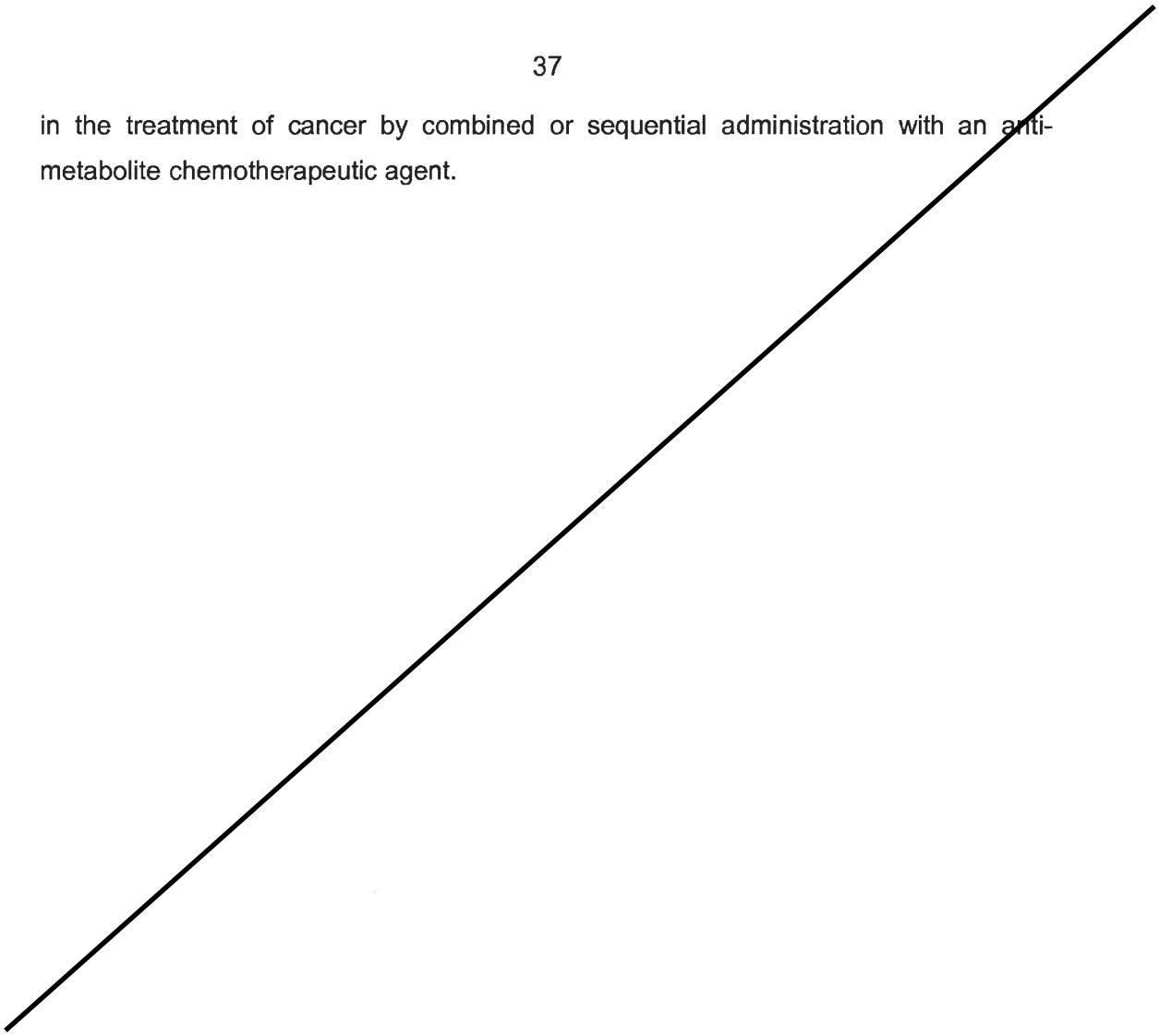
14. The at least one peptide for use according to any preceding claim, wherein the anti-metabolite chemotherapeutic agent is administered at a dosage of 100-10,000 mg/m^2, preferably 500-2000 mg/m^2, and more preferably 1000mg/m^2.

15. The at least one peptide for use according to any preceding claim, wherein the at least one peptide and the anti-metabolite chemotherapeutic agent are administered simultaneously or sequentially at at least two instances, and more preferably at at least three instances, wherein each instance of administration is separated by at least one week, and more preferably by at least 2 weeks.

16. At least one T-cell specific for the at least one peptide according to any of the preceding claims, or a T-cell preparation comprising T-cells specific for the at least one peptide as defined in any of the preceding claims when presented on an MHC molecule, for use in the treatment of cancer by simultaneous or sequential administration with an anti-metabolite chemotherapeutic agent.

17. A pharmaceutical composition comprising at least one peptide as defined in any of claims 1-15, or at least one T-cell or a T-cell preparation as defined in claim 16, for use

in the treatment of cancer by combined or sequential administration with an anti-metabolite chemotherapeutic agent.



CLAIMS:

1. Use of at least one peptide, suitable for eliciting an immune response, for the manufacture of a medicament for the treatment of cancer by simultaneous or sequential administration with an anti-metabolite chemotherapeutic agent, wherein the or each peptide corresponds to a fragment of a wild-type RAS protein but has one amino acid substitution thereof, and wherein the or each peptide comprises a region of at least 8 amino acids which includes position 12 or 13 of the RAS protein, and wherein the amino acid substitution of the or each peptide is at said position 12 or 13, respectively, and is selected from a G13A, G13C, G13D, G13R, G13S, G13V, G12A, G12C, G12D, G12R, G12S or a G12V substitution.

2. Use of the at least one peptide according to claim 1, wherein the at least one peptide comprises two or more peptides, each peptide having a different amino acid substitution.

3. Use of the at least one peptide according to any preceding claim, wherein the at least one peptide comprises:

a peptide having a G13D substitution
a peptide having a G12A substitution
a peptide having a G12C substitution
a peptide having a G12D substitution
a peptide having a G12R substitution
a peptide having a G12S substitution, and
a peptide having a G12V substitution.

4. Use of the at least one peptide according to claim 1 or 2, wherein the at least one peptide comprises:

a peptide having a G13D substitution
a peptide having a G13C substitution
a peptide having a G12A substitution
a peptide having a G12C substitution
a peptide having a G12D substitution
a peptide having a G12R substitution
a peptide having a G12S substitution, and
a peptide having a G12V substitution.

5. Use of the at least one peptide according to any preceding claim, wherein the anti-metabolite chemotherapeutic agent is a pyrimidine analogue or a pharmaceutically acceptable salt thereof.

6. Use of the at least one peptide according to any preceding claim, wherein the at least one peptide comprises a peptide consisting of the sequence represented by SEQ ID NO: 13, a peptide consisting of the sequence represented by SEQ ID NO: 14, a peptide consisting of the sequence represented by SEQ ID NO: 15, a peptide consisting of the sequence represented by SEQ ID NO: 16, a peptide consisting of the sequence represented by SEQ ID NO: 17, a peptide consisting of the sequence represented by SEQ ID NO: 18, a peptide consisting of the sequence represented by SEQ ID NO: 19 and a peptide consisting of the sequence represented by SEQ ID NO: 20.

7. Use of the at least one peptide according to any preceding claim, wherein the cancer comprises cells which express a mutated RAS protein.

8. Use of the at least one peptide according to any preceding claim, wherein the anti-metabolite chemotherapeutic agent is first to be administered at least three weeks after the first dose of the at least one peptide.

9. Use of the at least one peptide according to claim 7, wherein the cancer is resected pancreatic cancer and the anti-metabolite chemotherapeutic agent is first to be administered 12 weeks or fewer after surgical resection of the pancreatic cancer.

10. Use of the at least one peptide according to any preceding claim, wherein the anti-metabolite chemotherapeutic agent is to be administered within 24 hours of the at least one peptide.

11. Use of the at least one peptide according to claim 10, wherein the anti-metabolite chemotherapeutic agent is to be administered after the at least one peptide has been administered.

12. Use of the at least one peptide according to any preceding claim, wherein the at least one peptide is to be administered at a dosage of 0.01-10mg.

13. Use of the at least one peptide according to any preceding claim, wherein the anti-metabolite chemotherapeutic agent is to be administered at a dosage of 100-10,000 mg/m^2.

14. Use of the at least one peptide according to any preceding claim, wherein the at least one peptide and the anti-metabolite chemotherapeutic agent are to be administered simultaneously or sequentially at at least two instances, wherein each instance of administration is separated by at least one week.

15. Use of at least one T-cell specific for the at least one peptide according to any of the preceding claims, or a T-cell preparation comprising T-cells specific for the at least one peptide as defined in any of the preceding claims when presented on an MHC molecule, for the manufacture of a medicament for the treatment of cancer by simultaneous or sequential administration with an anti-metabolite chemotherapeutic agent.

16. A pharmaceutical composition comprising at least one peptide as defined in any of claims 1-14, or at least one T-cell or a T-cell preparation as defined in claim 15, for the manufacture of a medicament for the treatment of cancer by combined or sequential administration with an anti-metabolite chemotherapeutic agent.