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(54) Title: USE OF 7-T-BUTOXYIMINOMETHYLCAMPTOTHECIN FOR TREATING UTERINE NEOPLASMS

(57) Abstract: The use of 7-t-butoxyiminomethylcamptothecin is described in the preparation of a medicament useful for the treat-
ment of uterine neoplasms, particularly cancer of the endometrium and of the neck of the womb.

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Use of 7-t-butoxyiminomethylcamptothecin for the preparation of a medicament for the treatment of uterine neoplasms

The present invention relates to the use of 7-terbutoxyiminomethylcamptothecin for the preparation of a medicament with anticancer activity, particularly against advanced uterine tumours.

Background to the invention

Anticancer chemotherapy agents are the drugs with the most restrictive therapeutic window. In fact, since their cytotoxic activity is non-selective, they can indiscriminately damage all the cells of the body with which they come into contact.

Over the past twenty years uterine cancers, the term including both cervical and endometrial carcinoma, have become the most frequent pelvic cancers in women. Surgery is the treatment of choice in most patients. The use of chemotherapy is generally confined to the treatment of metastatic or advanced disease. The chemotherapeutic agents commonly prescribed for the treatment of uterine cancers are characterised by a fairly low positive response level, ranging typically from 20% to 35%. There is therefore still a perceived need to identify an anticancer drug capable of yielding a higher positive response rate and at the same time presenting fewer side effects or at least to a more tolerable extent. 7-terbutoxyiminomethylcamptothecin (CPT184 or ST 1481 or gimatecan) is an orally active camptothecin derivative and is described in European Patent EP 1 044 977, where its activity on the non-small-cell lung cancer cell line is specified, and uterine cancers are not mentioned.

Summary of the invention

It has now been found that gimatecan is also active in advanced uterine tumours, particularly of the endometrium and neck of the womb.

Therefore, in one aspect the present invention provides the use of 7-t-butoxyiminomethylcamptothecin, hereinafter also referred to as gimatecan, for the preparation of a medicament for the treatment of advanced uterine cancers, particularly of the endometrium and neck of the womb.

In another aspect the present invention provides a method for treating a patient suffering from an advanced uterine neoplasm comprising administering to said patient an effective amount of 7-t-butoxyiminomethylcamptothecin.

The medicament which is the subject of the present invention will take the form of a pharmaceutical composition, such as is described, for example, in the above-mentioned European Patent. Preferably, the pharmaceutical form will be suitable for oral administration. In a preferred form, the active ingredient will be incorporated in liposomal formulations, such as are described, for example, in international patent application PCT/IT00/00137, or in some other form that allows its administration via the parenteral route.

The following example further illustrates the invention.

Example 1

Gimatecan is a new anticancer compound that has shown a high therapeutic index in preclinical trials *in vivo*. Moreover, gimatecan is characterised by an anticancer activity that is maintained with different administration regimens, both intermittent and prolonged.

In the light of this preclinical evidence, a European phase I trial was conducted in which gimatecan was administered as a single therapeutic agent with different administration regimens. The patients studied were affected by advanced cancers for which curative or standard therapy was no longer indicated. Although the aim of the study was to assess the tolerability of the treatment with gimatecan, in the course of this clinical trial gimatecan produced a number of lasting objective

clinical responses. Particularly worthy of mention are the responses of a number of patients with uterine cancers, both of the cervix and the endometrium, including forms which had received substantial previous treatments and presented metastatic disease. These clinical responses were defined as partial responses, that is to say they presented a more than 30% reduction of the tumour lesion or lesions, as assessed by means of diagnostic imaging techniques such as computed tomography.

These responses were subjected to two independent assessments by experts not taking part in the clinical trial, who confirmed the observations.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. Use of 7-t-butoxyiminomethylcamptothecin in the preparation of a medicament for the treatment of advanced uterine neoplasms.
2. Use according to claim 1, in which said neoplasm is cancer of the endometrium.
3. Use according to claim 1, in which said neoplasm is cancer of the neck of the womb.
4. Use according to any one of claims 1 to 3, in which said medicament is suitable for oral administration.
5. Use according to any one of claims 1 to 4, in which said medicament is a liposomal formulation.
6. Use according to any one of claims 1 to 5, in which said medicament is suitable for parenteral administration.
7. A method for treating a patient suffering from advanced uterine neoplasm comprising administering to said patient an effective amount of 7-t-butoxyiminomethylcamptothecin.
8. A method according to claim 7, in which said neoplasm is cancer of the endometrium.
9. A method according to claim 7, in which said neoplasm is cancer of the neck of the womb.

12. A method according to claim 7, in which said 7-t-butoxyiminomethylcamptothecin is administered parenterally.

13. A use or method according to any one of claims 1 to 12 substantially as hereinbefore described.