~~New antibody drug conjugates (ADCs) and the use thereof~~

FGFR ANTIBODY DRUG CONJUGATES (ADCS) AND THE USE THEREOF

The present application relates to new binder-drug conjugates (ADCs) of N,N-dialkylauristatins that are directed against the target fibroblast growth factor receptor 2 (FGFR2), to active metabolites of these ADCs, to processes for preparing these ADCs, to the use of these ADCs for treating and/or preventing illnesses, and also to the use of these ADCs for producing medicaments for treating and/or preventing illnesses, more particularly hyperproliferative and/or angiogenic diseases such as, for example, cancer diseases. Such treatments may be practised as a monotherapy or else in combination with other medicaments or further therapeutic measures.

Cancer diseases are the consequence of uncontrolled cell growth in a wide variety of tissues. In many cases the new cells penetrate existing tissue (invasive growth), or they metastase into remote organs. Cancer diseases occur in a wide variety of organs, and the illnesses often progress in a tissue-specific manner. The designation “cancer disease” as a generic term therefore describes a large group of defined diseases of different organs, tissues and cell types.

Early-stage tumours may be able to be removed by surgical and radiotherapeutic measures. Metastasized tumours can generally only be given palliative therapy by means of chemotherapeutic agents. The objective in that case is to achieve the optimum combination of improving quality of life and prolonging remaining lifetime.

The majority of the chemotherapeutic agents which are presently administered parenterally are often not target-directed at the tumour tissue or the tumour cells, but instead, as a result of their systemic administration, are distributed non-specifically within the body, hence including at locations at which exposure to the drug is undesirable, such as in healthy cells, tissues and organs, for example. This may lead to unwanted side-effects and even to serious effects of general toxicity, which then often greatly limit the therapeutically useful dose range of the drug, or necessitate complete cessation of medication.

The improved and selective availability of these chemotherapeutic agents in the tumour cell or the immediately surrounding tissue, and the associated boost in effect, on the one hand, and minimization of toxic side-effects, on the other hand, have therefore been a focal point for a number of years in the development of new chemotherapeutic agents. Many attempts have been made to date to develop efficient methods of introducing the drug into the target cell. Optimizing the association between drug and intracellular target and minimizing the intercellular distribution of drug, to adjacent cells, for example, nevertheless continue to constitute a difficult problem.

Monoclonal antibodies, for example, are suitable for the target-directed addressing of tumour tissue and tumour cells. The significance of such antibodies for the clinical treatment of cancer