ANTIBODY DRUG CONJUGATES (ADCS) AND ANTIBODY PRODRUG CONJUGATES (APDCS) WITH ENZYMATICALLY CLEAVABLE GROUPS

Introduction and state of the art

The invention relates to novel binder-prodrug conjugates (ADCs) in which binders are conjugated with inactive precursor compounds of kinesin spindle protein inhibitors, and to binder-drug conjugates ADCs, to active metabolites of these binder-prodrug conjugates and binder-drug conjugates, to processes for preparing these APDCs and ADCs, to the use of these conjugates for the treatment and/or prophylaxis of diseases and to the use of these conjugates for preparing medicaments for treatment and/or prevention of diseases, in particular hyperproliferative and/or angiogenic disorders such as, for example, cancer diseases. Such treatments can be effected as monotherapy or else in combination with other medicaments or further therapeutic measures. According to the invention, the binder is preferably an antibody.

Cancers are the consequence of uncontrolled cell growth of the most diverse tissues. In many cases the new cells penetrate into existing tissue (invasive growth), or they metastasize into remote organs. Cancers occur in a wide variety of different organs and often have tissue-specific courses. The term "cancer" as a generic term therefore describes a large group of defined diseases of different organs, tissue and cell types.

Some tumours at early stages can be removed by surgical and radiotherapy measures. Metastased tumours as a rule can only be treated palliatively by chemotherapeutics. The aim here is to achieve the optimum combination of an improvement in the quality of life and prolonging of life.

Conjugates of binder proteins with one or more drug molecules are known, in particular in the form of antibody drug conjugates (ADCs) in which an internalizing antibody directed against a tumour-associated antigen is covalently attached via a linker to a cytotoxic agent. Following introduction of the ADCs into the tumour cell and subsequent dissociation of the conjugate, either the cytotoxic agent itself or a cytotoxic metabolite formed therefrom is released within the tumour cell and can unfold its action therein directly and selectively. In this manner, in contrast to conventional chemotherapy, damage to normal tissue is contained in significantly narrower limits [see, for example, J. M. Lambert, *Curr. Opin. Pharmacol.* 5, 543-549 (2005); A. M. Wu and P. D. Senter, *Nat. Biotechnol.* 23, 1137-1146 (2005); P. D. Senter, *Curr. Opin. 13*, 235-244 (2009); L. Ducry and B. Stump, *Bioconjugate Chem.* Thus, WO2012/171020 describes ADCs in which a plurality of