Likewise, modulating the neonatal Fc receptor (FcRn) binding of IgG antibodies in order to modulate pharmacokinetics has also gained increased notoriety.

Specifically in view of above, the comprehensive adaptation of antibodies to the respective areas of application is and remains a challenge. Therefore, a need still exists in the field for improved bispecific antibodies, especially for use in more effective targeted delivery methods, specifically pre-targeting, for therapeutic and diagnostic agents.

SUMMARY OF THE INVENTION

It is the objective of the present invention to provide improved bispecific antibodies for pre-targeting of tumors for subsequent specific delivery of therapeutic or diagnostic agents.

The objective is solved by the subject matter of the present invention.

The inventive antibodies bind selectively to tumor antigens and HSG hapten moieties. Said antibodies have significant affinity for the tumor antigen and sufficient residence time at the desired tumor location. Non-tumor-antigen bound antibodies are cleared from the circulation and exposure of normal tissues by subsequent administered therapeutic or diagnostic agents is minimized.

In one aspect, provided herein is a bispecific anti-tumor antigen/anti-HSG antibody, comprising at least one binding site specifically recognizing a tumor antigen and a binding site specifically recognizing HSG, comprising a light chain variable (VL) domain comprising a sequence selected from the group consisting of SEQ ID NOs 17 and 19, with glutamine at position 100 (Q100), glutamic acid at position 105 (E105) and isoleucine at position 106 (I106) according to Kabat numbering, and a heavy chain variable (VH) domain comprising a sequence selected from the group consisting of SEQ ID NOs 4, 6, 8, and 10 with arginine at position 19 (R19) according to Kabat numbering.

In another aspect, provided herein is use of the antibody as described herein in the manufacture of a medicament for the treatment or detection of malignancies, wherein said antibody is to be administered to a subject in a first step and a HSG moiety is to be administered in a second step, wherein said HSG moiety binds to the antibody.

In another aspect, provided herein is a pharmaceutical composition comprising the antibody as described herein together with a pharmaceutical excipient, specifically the pharmaceutical composition is formulated to be administered intravenously.

In another aspect, provided herein is use of the pharmaceutical composition as described here in the manufacture of a medicament for the treatment of a patient suffering from cancer, specifically the treatment of solid tumors, more specifically the treatment of colorectal cancer, ovarian cancer, breast cancer, prostate cancer, pancreas cancer, and lung cancer.

In yet another aspect, provided herein is the antibody or the pharmaceutical composition as described herein for use in therapy.

Herein provided are bispecific anti-tumor antigen/anti-HSG antibodies, comprising a binding site specifically recognizing a tumor antigen and a binding site specifically recognizing HSG, comprising

- a light chain variable (VL) domain comprising a sequence selected from the group consisting of SEQ ID NOs: 17, 19, 89, 90, and 91, or
- a light chain variable (VL) domain comprising a sequence selected from the group consisting of SEQ ID NOs: 17, 19, 89, 90, and 91 with one or two further amino acid substitutions and with glutamine at position 100 (Q100), glutamic acid at position 105 (E105), and isoleucine at position 106 (I106) according to Kabat numbering, and
- a heavy chain variable (VH) domain comprising a sequence selected from the group consisting of SEQ ID NOs: 4, 6, 8, and 10, or
- a heavy chain variable (VH) domain comprising a sequence selected from the group consisting of SEQ ID NOs: 4, 6, 8, and 10 with one or two further amino acid substitutions and with arginine at position 19 (R19) according to Kabat numbering.

The bispecific anti-tumor antigen/anti-HSG antibody of the invention has very low immunogenicity, specifically due to the modified anti-HSG VL and VH domains. The