Table 1: Properties of type I and type II anti-CD20 antibodies

type I anti-CD20 antibodies	**type II anti-CD20 antibodies**
type I CD20 epitope	type II CD20 epitope
Localize CD20 to lipid rafts	Do not localize CD20 to lipid rafts
Increased CDC (if IgG1 isotype)	Decreased CDC (if IgG1 isotype)
ADCC activity (if IgG1 isotype)	ADCC activity (if IgG1 isotype)
Full binding capacity	Reduced binding capacity
Homotypic aggregation	Stronger homotypic aggregation
Apoptosis induction upon cross-linking	Strong cell death induction without cross-linking

Bendamustine

Bendamustine (trade names Ribomustin and Treanda; also known as SDX-105) is a nitrogen mustard used in the treatment of chronic lymphocytic leukemia (CLL) (Kath, R., et al., J. Cancer Res. Clin. Oncol. 127 (2001) 48-54) and non-Hodgkin's lymphoma (NHL). It belongs to the family of drugs called alkylating agents. It is also being studied for the treatment of sarcoma (Bagchi, S., Lancet Oncol. 8 (2007) 674).

Bendamustine has been used as a therapeutic agent with different other agents, including rituximab (Cheson, B.D., et al., J Clin Oncol. 27(9) 2009 1492-501; Knauf, W., Expert Rev Anticancer Ther. (2) 9 (2009) 165-74; Plosker, G.L., et al., Drugs. 68(18) (2008) 2645-60).

Summary of the Invention

Surprisingly we have now found out that the combination of bendamustine with an afucosylated anti-CD20 antibody showed synergistic (e.g. even more than additive) antiproliferative effects compared to the combination with non-afucosylated CD20 antibody rituximab.

In a first aspect, there is provided the use of an afucosylated anti-CD20 antibody with an amount of fucose of 60 % or less of the total amount of oligosaccharides (sugars) at Asn297, for the manufacture of a medicament for the treatment of cancer in combination with bendamustine; wherein said antibody is a humanized B-Ly1 antibody, and the humanized B-Ly1 antibody is characterized in comprising an amino acid sequences of the variable region of the heavy chain (VH) of SEQ ID NO: 7 (B-HH6), and in comprising an amino acid sequences of the variable region of the light chain (VL) of SEQ ID NO: 20(B-KV1); and wherein said cancer is a CD20 expressing B-Cell Non-Hodgkin's lymphoma (NHL).

The disclosure~~invention~~ comprises the use of an afucosylated anti-CD20 antibody with an amount of fucose of 60 % or less of the total amount of oligosaccharides (sugars) at

Asn297, for the manufacture of a medicament for the treatment of cancer in combination with bendamustine.

The disclosure may relate to~~One aspect of the invention is~~ a method of treatment of patient suffering from cancer by administering an afucosylated anti-CD20 antibody with an amount of fucose of 60 % or less of the total amount of oligosaccharides (sugars) at Asn297, in combination with bendamustine, to a patient in the need of such treatment.

The disclosure may relate to~~Another aspect of the invention is~~ an afucosylated anti-CD20 antibody with an amount of fucose of 60 % or less of the total amount of oligosaccharides (sugars) at Asn297, for the treatment of cancer in combination with bendamustine.

In one embodiment, the amount of fucose is between 40 % and 60 % of the total amount of oligosaccharides (sugars) at Asn297.

In another embodiment, the amount of fucose is 0% of the total amount of oligosaccharides at Asn297.

In one embodiment, the afucosylated anti—CD20 antibody is an IgG1 antibody.

In another embodiment, said afucosylated anti-CD20 antibody is humanized B-Ly1 antibody, and said cancer is a CD20 expressing cancer, which in one embodiment is a B-Cell Non-Hodgkin's lymphoma (NHL).

In one embodiment, the humanized B-Ly1 antibody is administered in a dosage of 800 to 1200 mg on day 1, 8, 15 of a 6-week-dosage-cycle and then in a dosage of 800 to 1200 mg on day 1 of up to five 4-week-dosage-cycles, and bendamustine is administered in a dosage of 80 mg/m2 to 110 mg/ m2 on day 1 and 2 of up to six 4-week-dosage-cycles .

One embodiment of the disclosure~~invention~~ is a composition comprising an anti-CD20 afucosylated antibody with an amount of fucose of 60 % or less, and bendamustine for the treatment of cancer.

Detailed Description of the Invention

The invention comprises the use of an afucosylated anti-CD20 antibody of IgG1 or IgG3 isotype (preferably of IgG1 isotype)with an amount of fucose of 60 % or less of the total amount of oligosaccharides (sugars) at Asn297, for the manufacture of a medicament for the treatment of cancer in combination with bendamustine. In one