Rituximab biosimilar (BCD-020)

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General information

Description: Rituximab is a recombinant chimeric murine/human monoclonal antibody, which specifically binds to CD20 protein that is located on the surface of most pre-B lymphocytes and mature B-cells

INN: RITUXIMAB

Internal code: BCD-020

Dosage form: Concentrate for solution for infusion

Indications:

- Non-Hodgkin's lymphoma
- Chronic lymphocytic leukemia
- Rheumatoid arthritis
- Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA)
- Moderate to severe Pemphigus Vulgaris (PV)

Manufacturer: The full manufacturing cycle and quality control are performed by JSC BIOCAD

BIOCAD rituximab biosimilar in the world

Rituximab biosimilar BCD-020 (JSC BIOCAD) was first approved in the Russian Federation on April 4th 2014

- Supplied to and/or registered in **30+**[1] **countries**
- Approval process ongoing in > **18 countries**

Pharmacovigilance data without unexpected efficacy or safety reports on:

> 2 095 500 vials supplied

> 192 000[2] patients treated

1 Number of countries, where the products are supplied to and/or registered, including temporary quarters and emergency tenders
2 Numbers on this page relevant as of November 2023. The calculation is based on the average recommended doses, average patient weight, and the approximate duration of therapy. The approximate rituximab dose for the treatment of one patient (regardless of the indication): 3124 mg

Rituximab Phase I/III Global clinical study
BCD-020-3/ BIORIX

Population: 174 patients with CD20-positive B-cell non-Hodgkin lymphoma

Study groups and treatment

Group 1 (BCD-020) :

- **BCD-020** 375 mg/m^2 on days 1, 8, 15 and 22

Group 2 (reference rituximab*) :

- **Reference rituximab** 375 mg/m^2 on days 1, 8, 15 and 22

Study endpoints

Primary

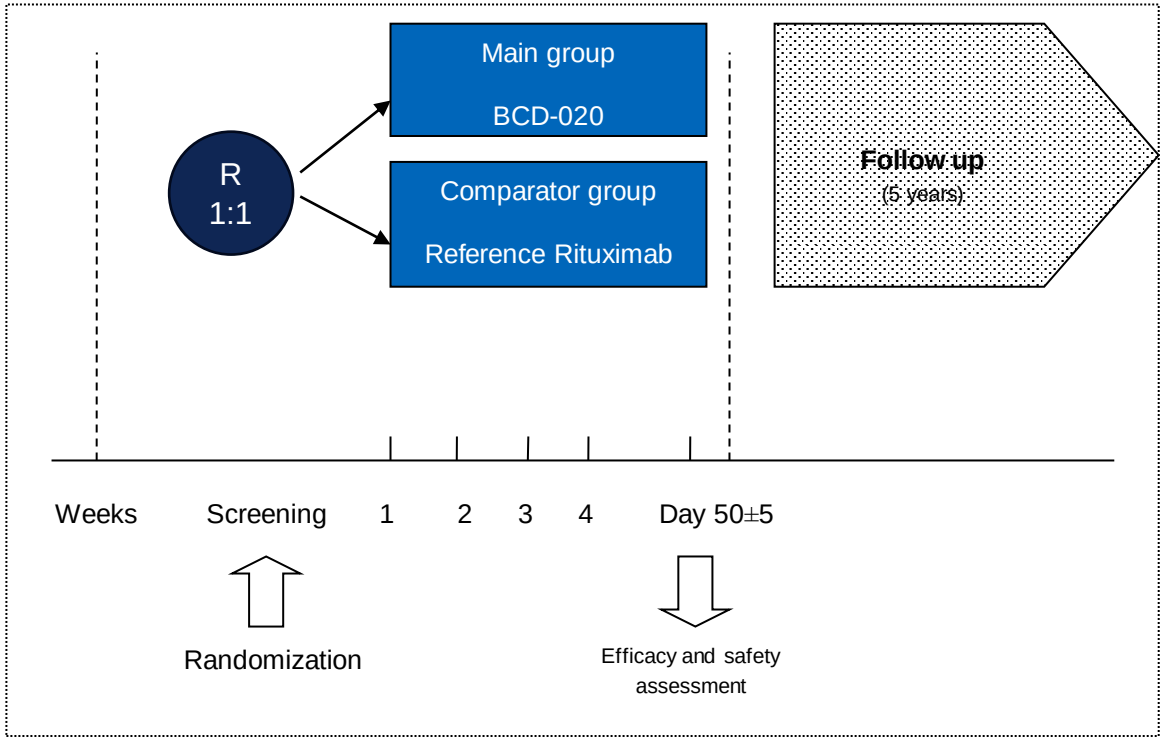
- Overall response rate on day 50±5 after the start of the treatment (reference data obtained from study by Colombat et al[1])
- Changes of rituximab concentrations in blood after single and multiple infusions of BCD-020 or reference rituximab

Secondary

Changes in level of blood CD20+ lymphocytes in blood after infusions of BCD-020 or reference rituximab

Rate of AEs related to monotherapy

Binding and neutralizing antibodies to rituximab



Hypothesis

- BCD-020 has equivalent efficacy (ORR) and safety profile with reference rituximab in patients with CD20-positive B-cell non-Hodgkin lymphoma

Sample size was calculated using the following variables:

- Equivalence margin $|\delta|$ = 0.2*
- Significance level α=0.05
- Power 70%

* Reference rituximab - **MabThera®**

Patient baseline characteristics

Characteristic	BCD-020 n=89 abs. number (%)	Reference rituximab n=85 abs. number (%)	p-value
Age, years (Median [SD])	58±12.19	55±12.74	0.435[1]
– Males	42 (47.2%)	42 (49.4%)	0.888[2]
– Females	47 (52.8%)	43 (50.6%)	0.888[2]
Follicular lymphoma	71 (79.8%)	69 (81.2%)	0.967[2]
– Including FL III-IV stage Ann Arbor	63 (70.8%)	53 (62.4%)	0.307[2]
B-cell marginal zone lymphoma	18 (20.2%)	16 (18.8%)	0.967[2]
– Including MZL III-IV stage Ann Arbor	14 (20.2%)	15 (17.6%)	0.307[2]
High risk by FLIPI	34 (38.2%)	28 (32.9%)	0.571[2]
High risk by IPI	4 (4.5%)	4 (4.7%)	0.74[3]
Positive B-symptoms	28 (31.5%)	28 (32.9%)	0.963[2]

1 Mann-Whitney test; 2 Yates-corrected χ^2 test; 3 Two-tailed Fisher exact test

Study arms were balanced in terms of patient baseline characteristics

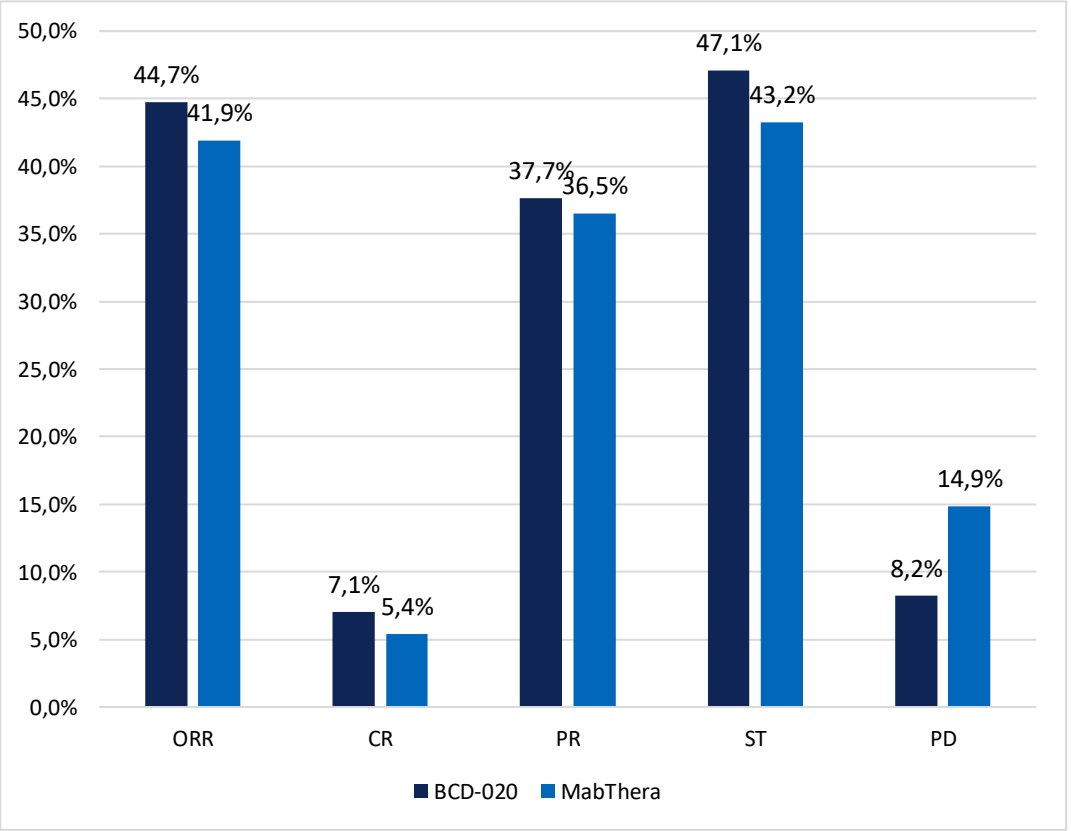
Rituximab Phase I/III Global clinical study (NHL)
Efficacy analysis

Primary efficacy endpoint assessment results

Parameter	BCD-020 (n = 85)		Reference rituximab (n = 74)		p*
	n	%	n	%	
Overall response rate (ORR)	38	44.71	31	41.89	0.721
ORR difference	2.81% (95% CI, −12.62%-18.24%)				

Biosimilarity of BCD-020 to reference rituximab was confirmed

- The ORR (primary endpoint) showed no significant differences between the groups
- 95% CI for ORR difference (-12.62%) − 18.24% was within predetermined equivalence margin
- No differences between the groups in all other efficacy variables

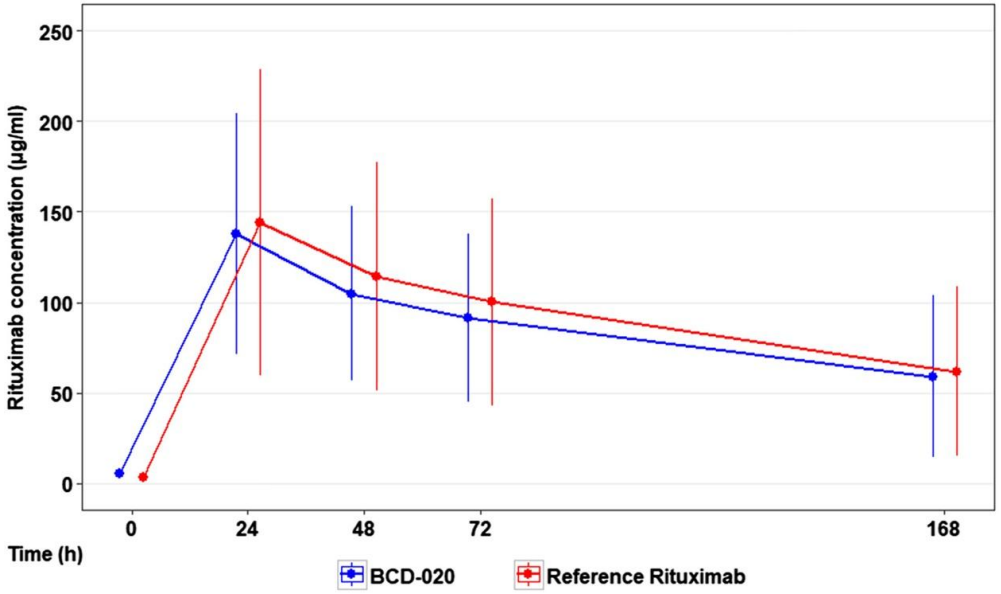


Rituximab Phase I/III Global clinical study (NHL) Pharmacokinetics

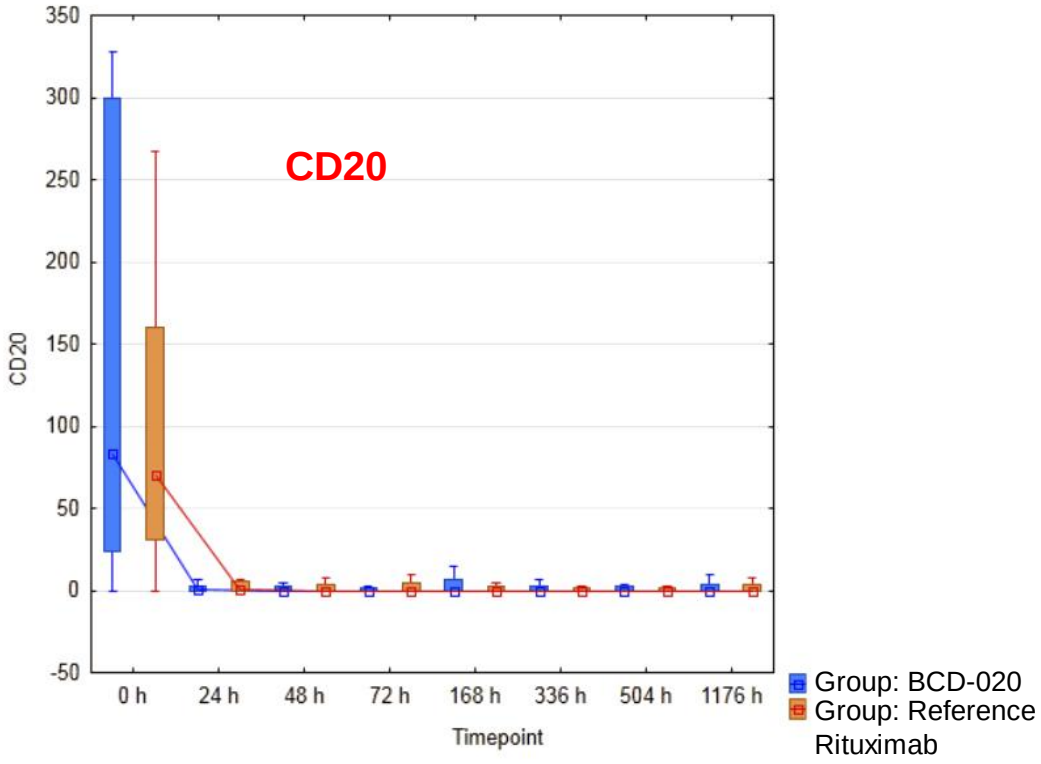
PK analysis after single administration (n=142)

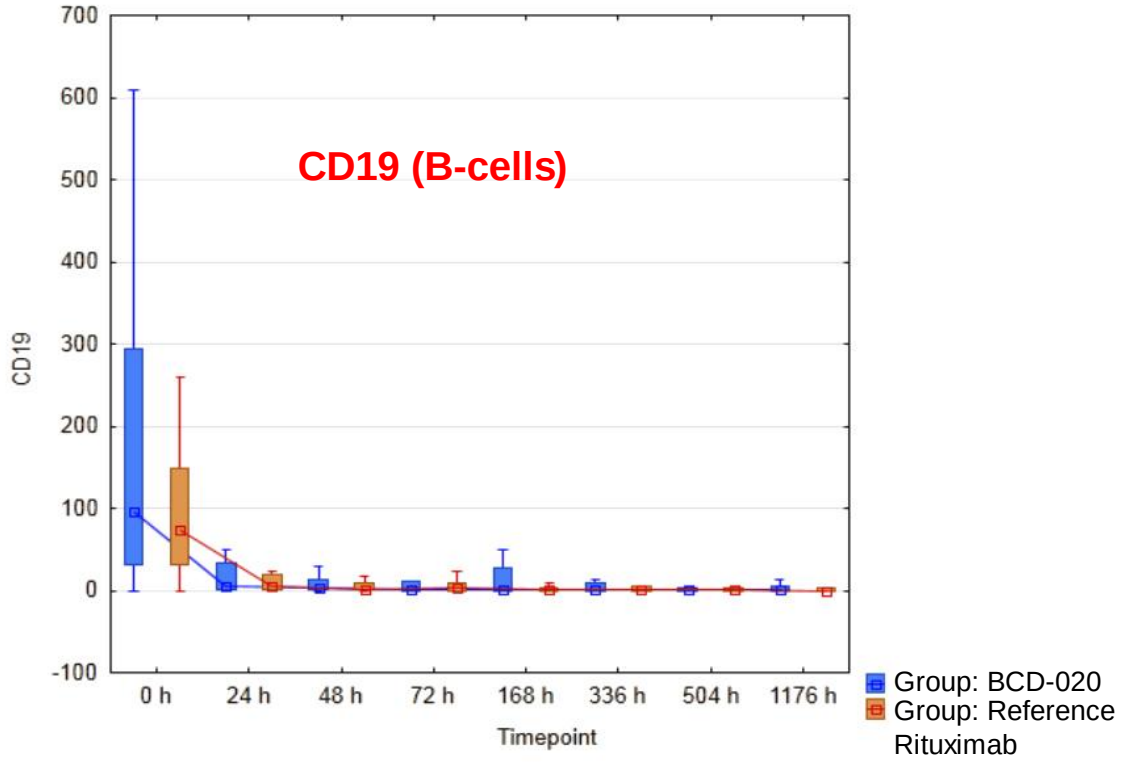
Parameter	90% CI	90% CI equivalence intervals
$AUC_{(0\text{-}168)}$	83.44–121.99%	80% - 125%
C_{max}	88.67-122.03%	80% - 125%

The pharmacokinetics of BCD-020 and reference Rituximab were equivalent



Pharmacodynamics analysis

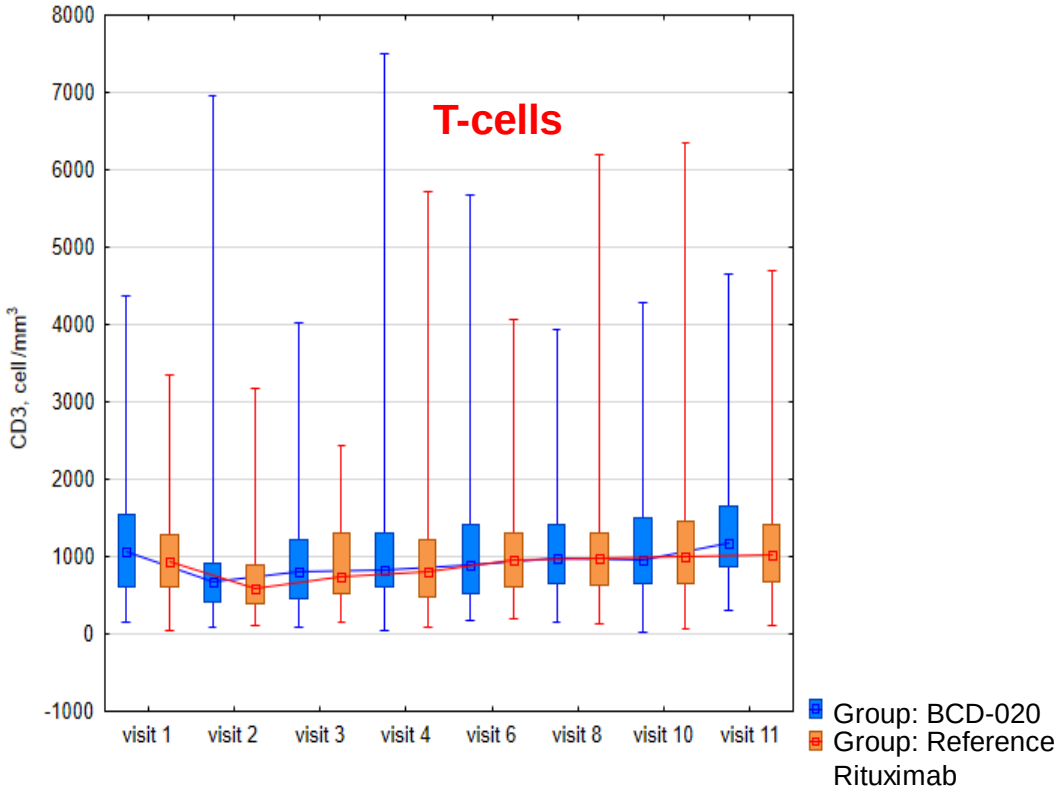




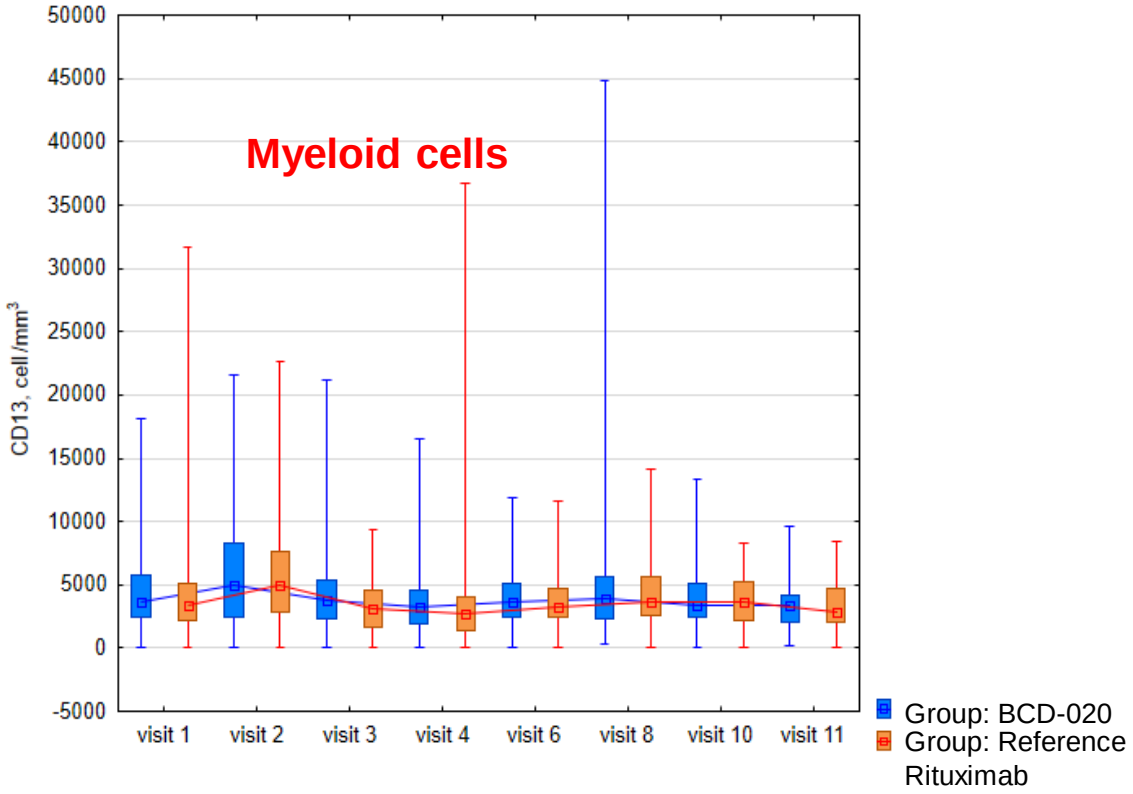
Equal rate of B-cell depletion

Pharmacodynamics analysis

Count of CD3 cells during Rituximab monotherapy



Count of CD13 cells during Rituximab monotherapy



BCD-020 as well as reference rituximab is not toxic to other populations of cells

Rituximab Phase I/III Global clinical study (NHL)
Safety analysis

Parameter	BCD-020 (n = 89)		Reference rituximab (n = 85)		p-value*
	n	%	n	%	
Any AE/SAE	61	68.54	59	69.41	1.000
— **Therapy-related AE**	15	16.85	18	21.18	0.596
— **Therapy-related SAE**	1	1.12	1	1.18	1.0
Courses discontinued due to AE/SAE	1	1.12	3	3.53	0.359
Deaths**	1	1.12	1	1.18	1.0

- The AE profiles of BCD-020 and comparator were similar.
- The rates of all AE (incl. SAE) did not significantly differ between the groups. The most common AE were hematological disorders

*Two-tailed Fisher's exact test/Yates-corrected $\chi 2$ test;
**This tabulation does not include the lethal outcome in patient who was randomized but did not receive a single dose of the study drug

Rituximab Phase I/III Global clinical study (NHL) Immunogenicity analysis

Parameter	BCD-022 (n = 45)		Reference rituximab (n = 45)		p-value*
	n	%	n	%	
Binding antibodies	0	0.00	2	2.73	1.000
Neutralizing antibodies	0	0.00	0	0.00	1.000

Use of rituximab biosimilar did not lead to antidrug antibody formation in any patient

*Two-tailed Fisher's exact test

Conclusions

- Similar efficacy of BCD-020 and reference rituximab was confirmed
- Similar pharmacodynamics and equivalent pharmacokinetics were confirmed
- Similar safety and immunogenicity of BCD-020 compared to reference rituximab was confirmed

BCD-020-3/BIORIX study **publication in** *Hematological Oncology*

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ORIGINAL RESEARCH ARTICLE

Proposed rituximab biosimilar BCD-020 versus reference rituximab for treatment of patients with indolent non-Hodgkin lymphomas: An international multicenter randomized trial

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Reference:

Poddubnaya IV, Alekseev SM, Kaplanov KD, Lukavetskyy LM, Rekhtman GB, Dolai TK, Attili VSS, Bermúdez CD, Isaev AA, Chernyaeva EV, Ivanov RA. Proposed rituximab biosimilar BCD-020 versus reference rituximab for treatment of patients with indolent non-Hodgkin lymphomas: An international multicenter randomized trial. Hematol Oncol. 2020 Feb;38(1):67-73. doi: 10.1002/hon.2693. Epub 2020 Jan 13. PMID: 31724191.

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