GSASA Congress 2018

Dialogue ouvert sur le biosimilaire de rituximab

Chair: Dr. Marco Bissig

- **Biosimilars – general principles explained in a nutshell**
  Prof. Pascal Bonnabry

- **Biosimilars – what clinicians should know**
  Dr. Andreas Jakob

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BIOSIMILARS – GENERAL PRINCIPLES EXPLAINED IN A NUTSHELL

Pr Pascal BONNABRY
Head of pharmacy

GSASA congress
November 15, 2018

Hôpitaux Universitaires Genève

Cartoons from Pécub

UNIVERSITÉ DE GENÈVE
FACULTÉ DES SCIENCES
Section des sciences pharmaceutiques

Costs of biological drugs

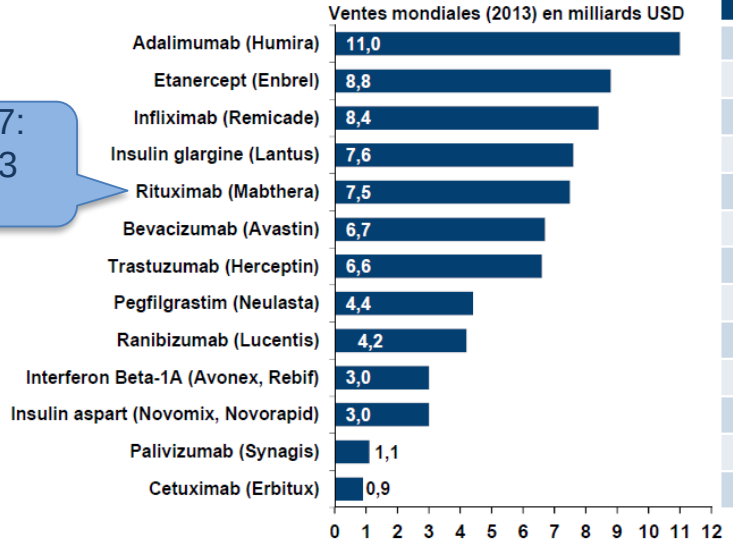
- **Drug worldwide market**
  $ 1000 billions
- **Biological drugs**
  $ 210 billions in 2016

In Switzerland, the price of biosimilar is **at least 25% lower** than originator at the time of registration

- In some countries, many patients **cannot access** to these expensive drugs
- Biosimilars could allow **large savings**:
  - 11.8-33.4 billions euros between 2007 and 2020 (Europe)
  - 44 billions dollars between 2014 and 2024 (USA).

Biosimilars in the coming years

HUG 2017:
CHF ~ 2,3
Mio



Date d'expiration en Europe	Date d'expiration aux Etats-Unis
2018	2016
2015	2028 (prolongée)
Expirée	2018
Expirée	Expirée
Expirée	2016
2019	2017
Expirée	2019
2015	Expirée
2016	2016
Expirée	Expirée
2015	2015
Expirée	2016
2015	2015

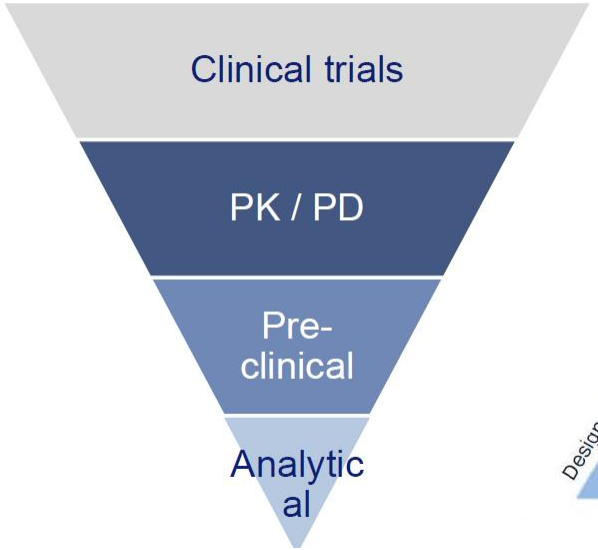
Sources: "Searching for Terra Firma in the Biosimilars and Non-Original Biologics", IMS, 2013 – Evaluate Pharma World Preview 2014, outlook to 2020 – Analyses Smart Pharma Consulting

Similar = not exactly identical

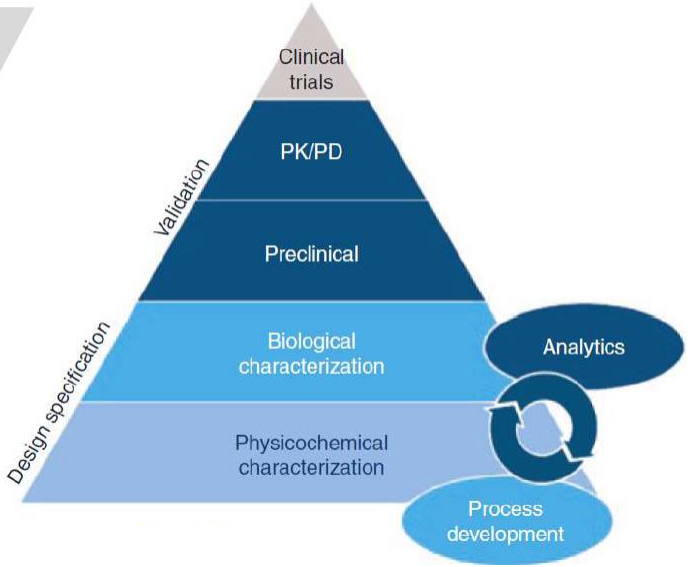
- **Variant** of the original product
  - Same peptidic sequence
  - Slight variations in glycosylation and/or conformation are possible
- Small structural differences **must not induce clinically significant differences in efficacy and safety**

Biosimilars development

Traditionnal

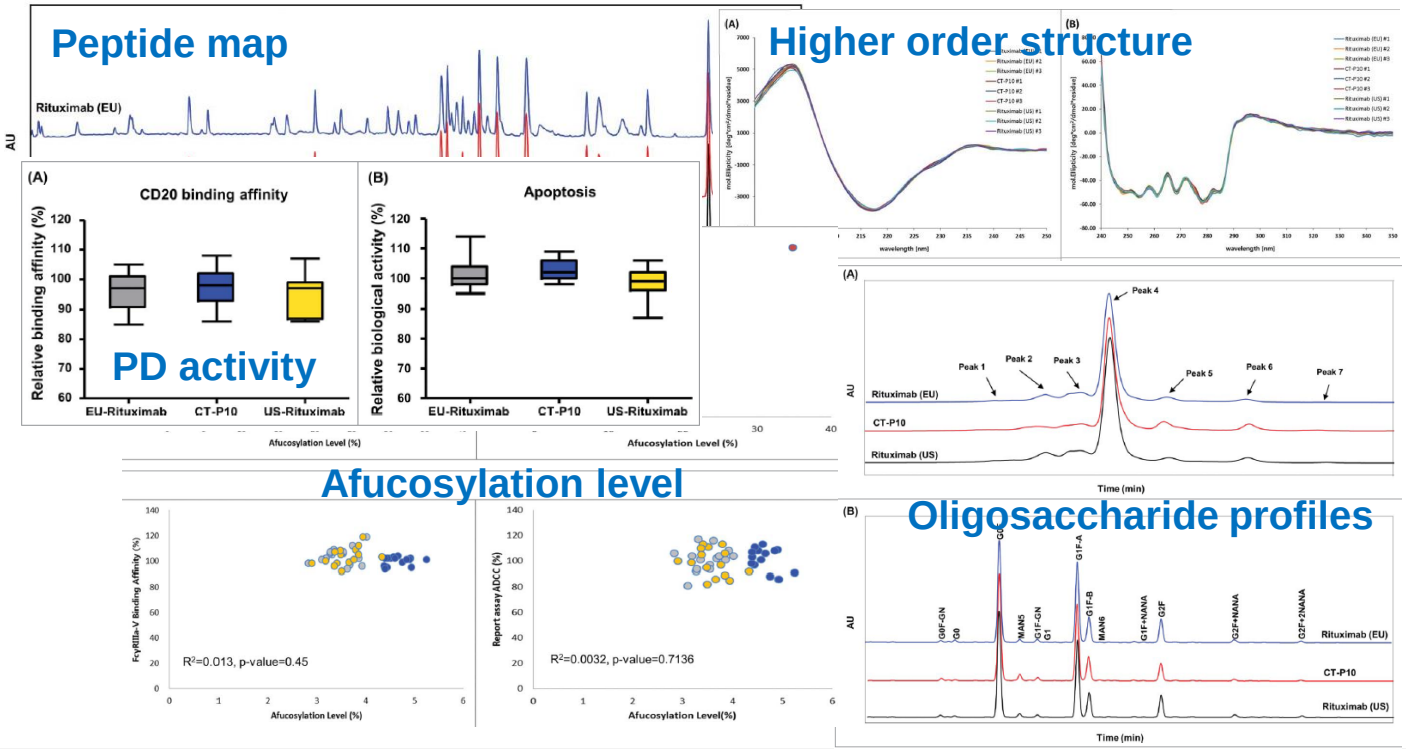


Biosimilar



McCamish M, Clin Pharmacol Ther 2012;91:405

Analytical similarity: rituximab



A production process in continual evolution

- The production of a biosimlar needs a **high expertise** in biological products manipulation
- The final product composition is very sensitive
  - Variabilities in production sources
  - Process changes
- The production process is in continual evolution
  - Increasing demand
  - Process modernization
  - New requirements

Evolution of biologicals production process

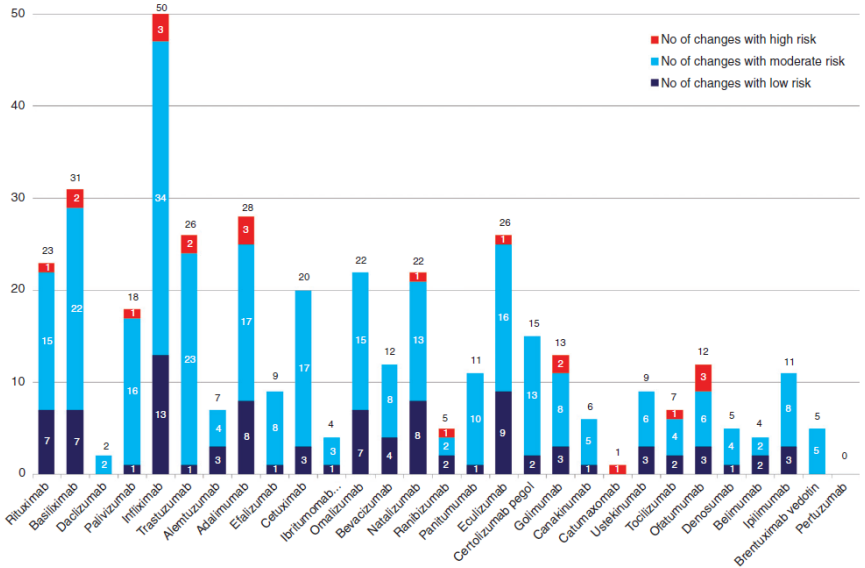
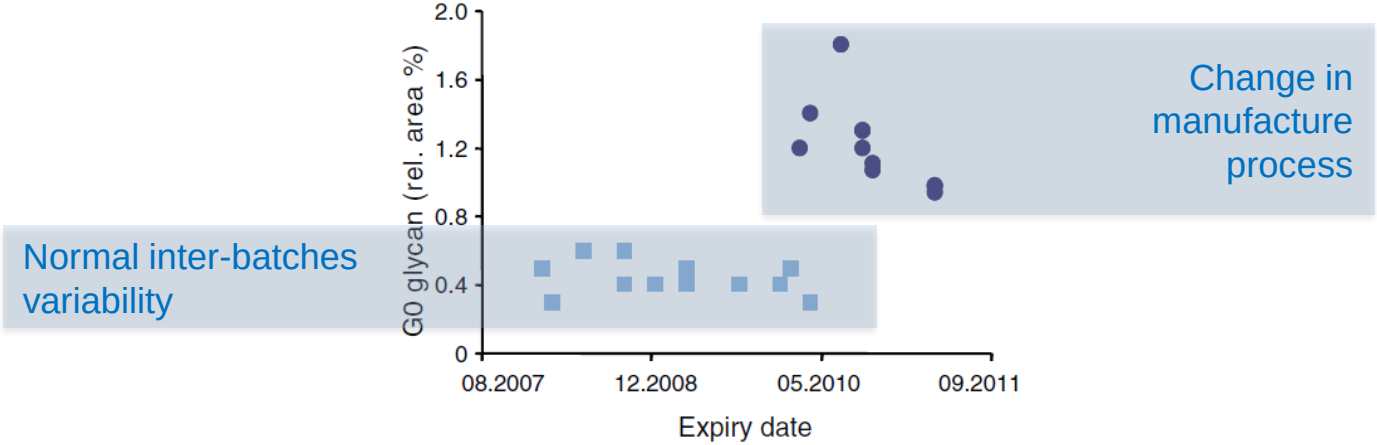


Figure 2. Number of manufacturing changes for monoclonal antibodies in their European Public Assessment Reports according to risk category (during the search period all non-proprietary names relate only to the trade named medicines listed in Table 1).

Today's biologicals are **comparable** but not identical to those at the registration time

Variability of biologics

- **Reference rituximab**
  amount in unfucosylated G0 glycan



The manufacturer has to demonstrate the absence of clinical impact

A clinical development including efficacy studies

- The clinical development of biosimilars is more complex than generics
- The strategy must include the **quality**, the **safety** and the **clinical efficacy**
- A specific development roadmap must be designed, based on scientific arguments, and submitted to the authorities

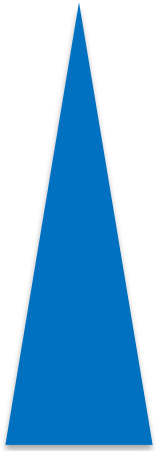
Steps to a successful implementation

- Clinical data
- Approval by authorities
- Pharmacovigilance

- Physicians information
- Patients information

- Price negociation
- Wish to change
- Leadership

Physician’s acceptance depends on the disease ?

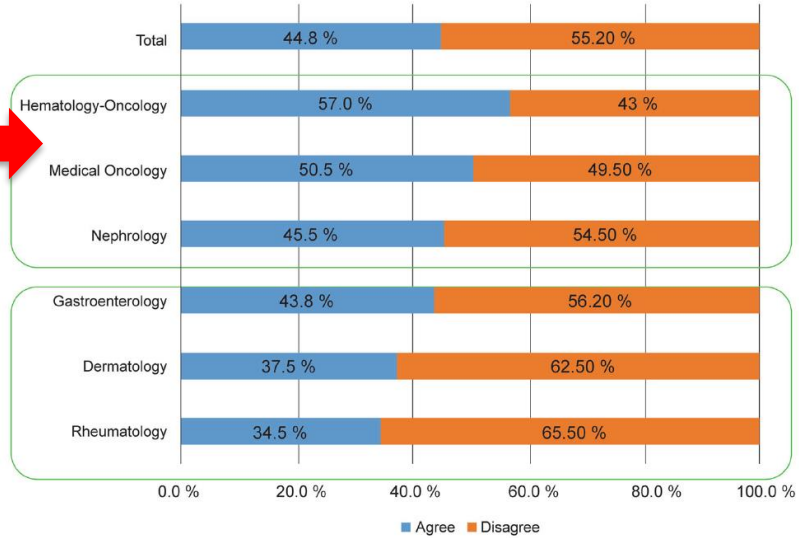


1. Direct biological monitoring of drug efficacy — **Insuline**
2. Clinical monitoring for a non-fatal disease — **Infliximab**
3. Late clinical monitoring for a fatal disease — **Rituximab**

Physicians knowledge

- **Are biosimilars safe and appropriate for use in naive and existing patients ?**

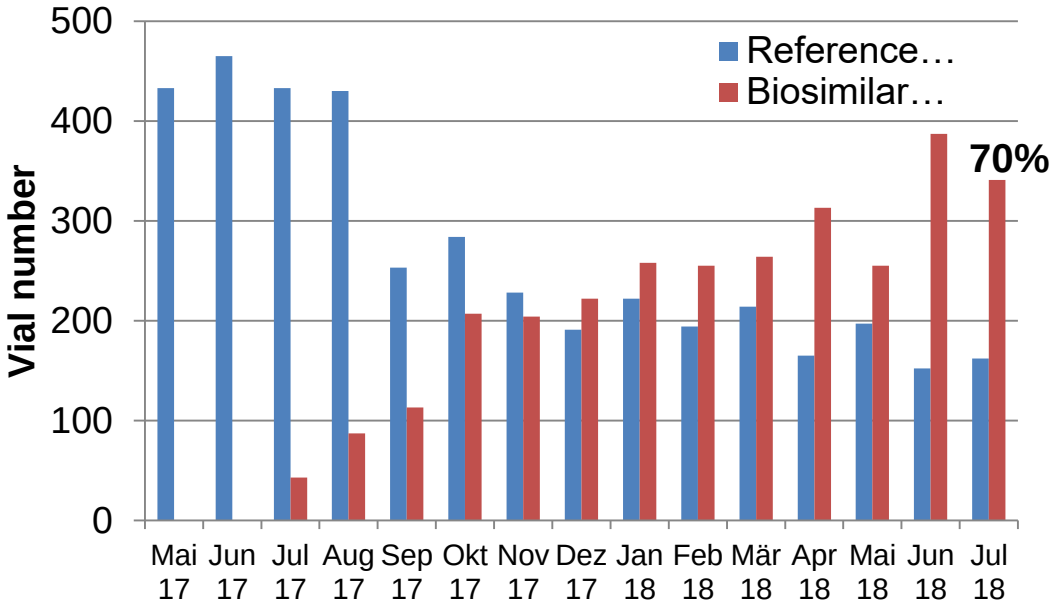
Oncologists



≈ 50:50

Cohen H, Adv Ther 2016;33:2160

Lessons learned: infliximab



Lessons learned: infliximab

- **Real financial impact**

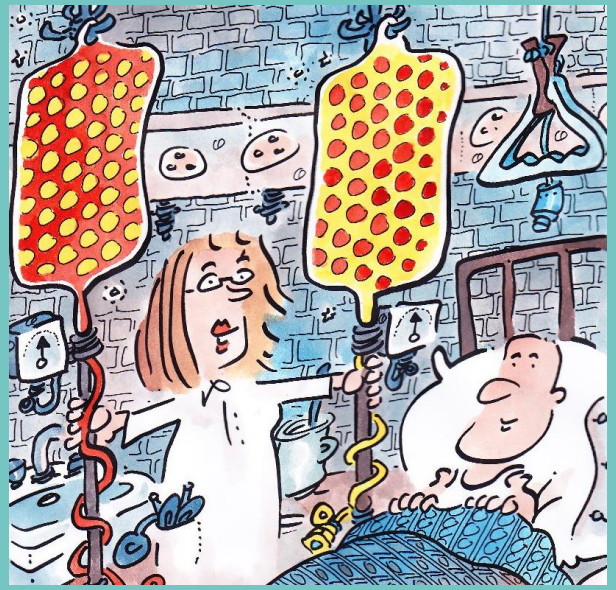
  July 2018 extrapolated over 1 year

  - **Hospitalized patients (~1/3 of use)**
    - Optimisation of purchasing cost — CHF 477’000
  - **Ambulatory patients (~2/3 of use)**
    - Optimisation of margin — CHF 403’000
  - **HUG financial benefit** — **CHF 880’000**
  - **Societal benefit (ambulatory)** — **CHF 550’000**

Finally ?

- The efficacy and safety of biosimilars is comparable to the originators
- Real savings depend on the adoption rate/speed
- The criticity of the disease might impact on the acceptability of biosimilar use
- Educational actions must be developed towards physicians and patients

THANK YOU FOR YOUR ATTENTION



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BIOSIMILARS
WHAT CLINICIANS SHOULD KNOW

- BIOSIMILAR RITUXIMAB IN CLINICAL PRACTICE

LYMPHOMA

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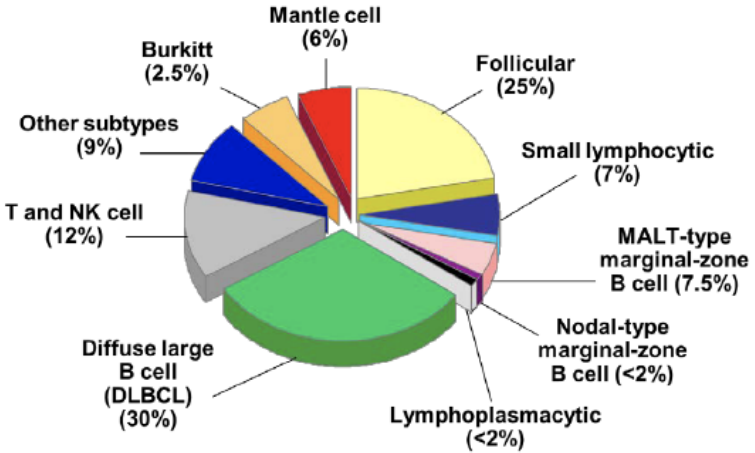
There are nearly 100 types of lymphoma



Goals of therapy vary by histology and expected clinical behavior:

- ❑ **Curative intent**
- ❑ **Palliative intent**

- Most of the lymphomas are B-cell lymphomas and express CD 20

WHO Classification of Lymphoid Malignancies 2008, 2016 update

Introduction
Reference Rituximab

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- Rituximab is a chimeric murine/human monoclonal IgG1 kappa antibody[1]
- It exerts its effects through several mechanisms of action, including ADCC, CDC and apoptosis[2]
- It is approved as the first therapeutic antibody for treating B-cell lymphoma and leukemia in the US and EU[1]
- Rituximab is an integrated treatment for NHL since more than 10 years and is indicated for the use in NHL and CLL in combination with chemotherapy or as monotherapy[3,4]
- Rituximab with chemotherapy significantly increased the overall survival rate compared with chemotherapy alone in FL[5]

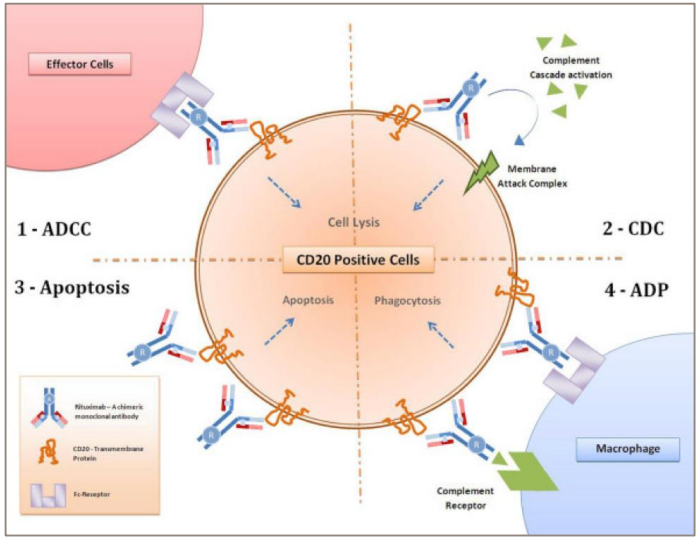

Fig: Mechanism of action of Rituximab

ADCC: antibody-dependent cellular cytotoxicity, CDC: complement-dependent cytotoxicity CLL: Chronic lymphocytic leukemia, EU: European union, NHL: non-Hodgkin's Lymphoma, US: United states

[1]Pescovitz MD. Am J Transplant. 2006 May;6(5 Pt 1):859–66; [2]Weiner GJ. Semin Hematol 2010;47:115–23; [3]Engelhard M.Clin Immunol. 2016 pii: S1521-6616(16)30273-X; [4]http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000165/WC500025821.pdf
[5]Papaioannou D, et al. Health Technol Assess. 2012;16(37):1–253, iii-iv

Global Health Challenges: Access to Affordable Care Is Not Just a Problem for Poorer Nations

- Without a sustained investment for innovation in cancer care the advances in precision therapy will slow or halt[1]

Publications > The Journal of Targeted Therapies in Cancer > 2016 > April 2016 >

Cost of Biologics Therapy Soars Above Other Cancer Expenses

Tony Hagen
Published Online: Jul 08 2016

10-year cost rises[2]

Biologics 485%

Cytotoxics 101%

Radiotherapy 66%

Our greatest challenge for 2018?

Affordable acce to healthcare

1. Thomas R et al. Delivering Affordable Cancer Care a Value Challenge to Health Systems. Report of the WISH Delivering Affordable Cancer Care Forum 2015. http://www.wish.org.qa/wp-content/uploads/2018/01/WISH_Cancer_Forum_08.01.15_WEB.pdf. 2. Hagen T. Cost of Biologics Therapy Soars Above Other Cancer Expenses. *J Targ Ther in Cancer*. 2016. http://www.targetedonc.com/publications/targeted-therapies-cancer/2016/april-2016/cost-of-biologics-therapy-soars-above-other-cancer-expenses. Both Accessed 14 June 2018.

COSTS

REFERENCE RITUXIMAB VERSUS SANDOZ BIOSIMILAR RITUXIMAB

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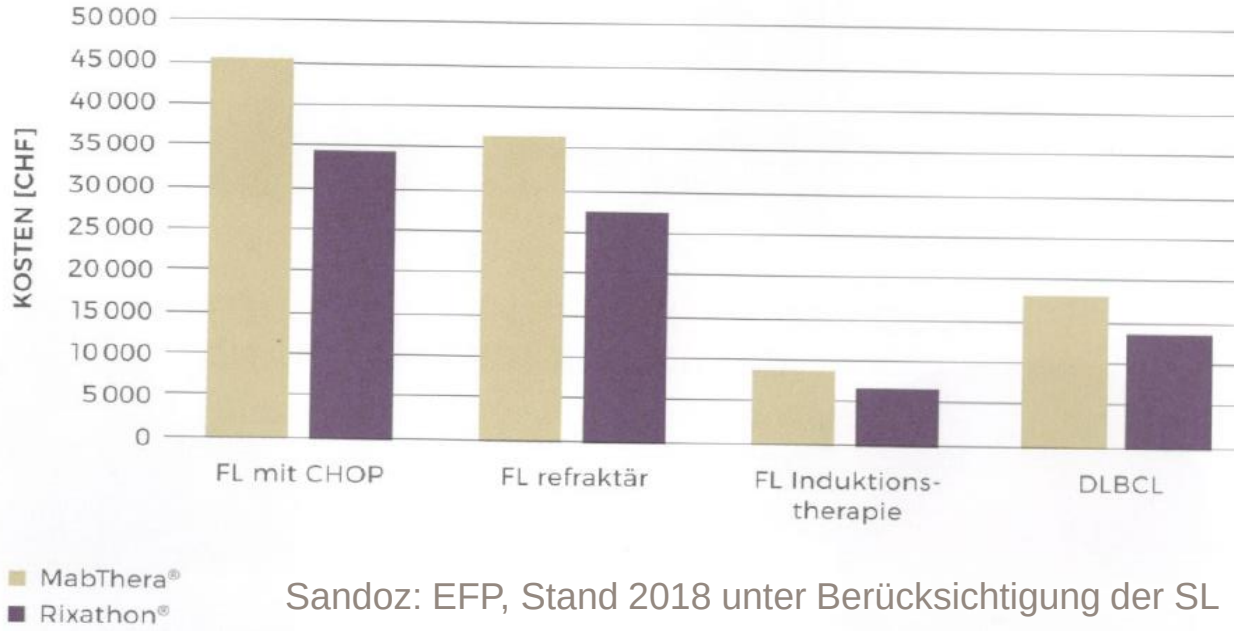

Sandoz: EFP, Stand 2018 unter Berücksichtigung der SL

CONCERNS ABOUT BIOSIMILARS

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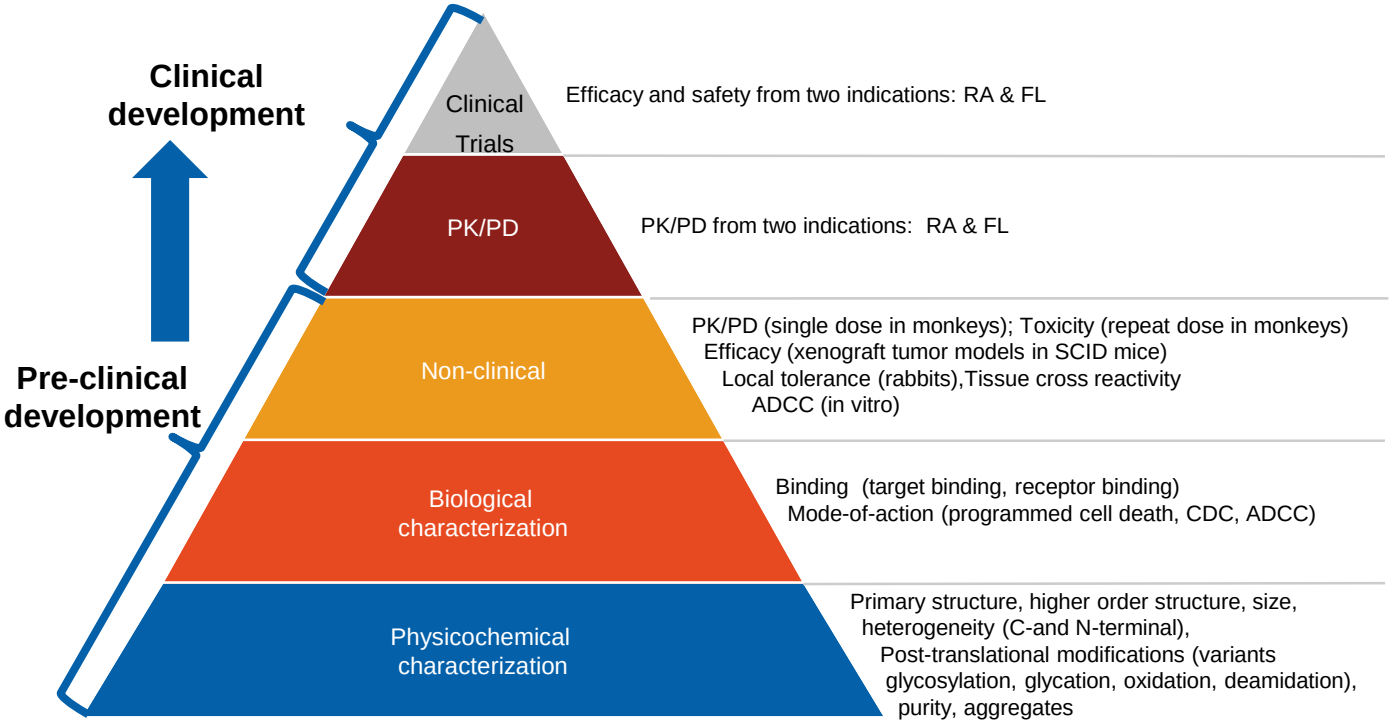
- Similar but not identical: uncertainties about manufacturing process and in vivo biological behaviour
- Lower quality
- Drug safety and tolerability?
- Immunigenicity?
- Efficacy in different populations?
- Is extrapolation appropriate?
- Do we have enough clinical data?

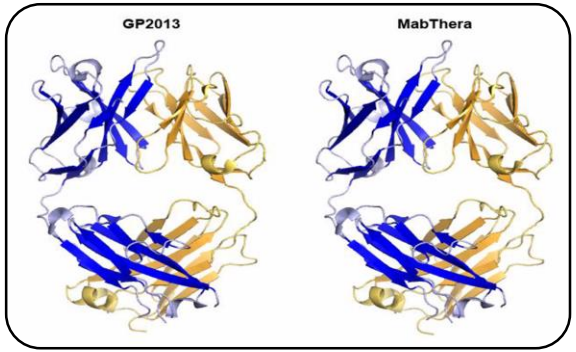
GP2013 development program



ADCC: antibody-dependent cellular cytotoxicity, CDC: complement-dependent cytotoxicity ,
FL: Follicular Lymphoma, PD: pharmacodynamics, PK: pharmacokinetic, RA: Rheumatoid arthritis,
SCID: severe combined immune deficiency

GP2013 & rituximab: structural and functional comparability

- GP2013 has been characterized in great detail using an extensive set of state-of-the-art analytical technologies
- GP2013 was highly similar to reference drug rituximab at the level of
  - primary and higher-order structure
  - post-translational modifications (e.g. glycans, charge and size variants)
  - biological properties



The high level of structural and functional similarity provides confidence that subsequent tailored preclinical and clinical studies will also reveal a comparable safety and efficacy profile

Visser J, et al., BioDrugs 2013;27:495–507

GP2013 & rituximab: pharmacological and functional similarity

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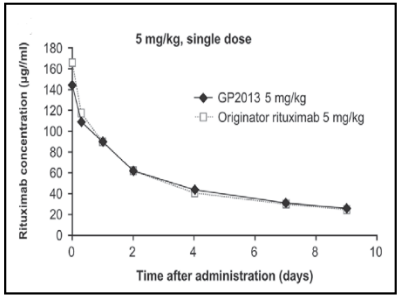
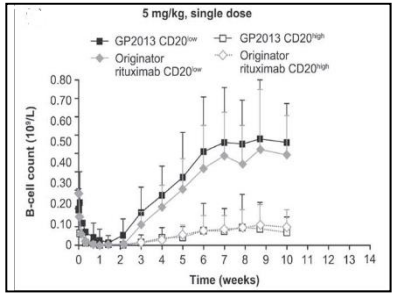
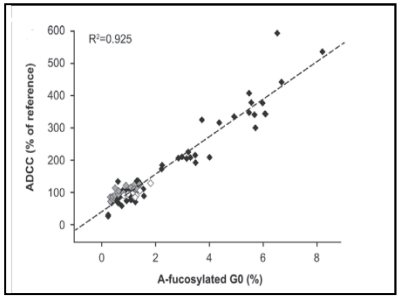
- GP2013 is pharmacokinetically similar to the reference drug rituximab in preclinical studies
- GP2013 is pharmacodynamically similar to the reference drug rituximab, it displays similar B-cell depletion in preclinical *in vivo* studies
- GP2013 displays similar *in vitro* ADCC potency activity as the reference drug rituximab







ADCC: antibody-dependent cellular cytotoxicity

da Silva A, et al. Leuk Lymphoma 2014;55:1609–17

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GP2013 & rituximab: functional similarity (ADCC potency)

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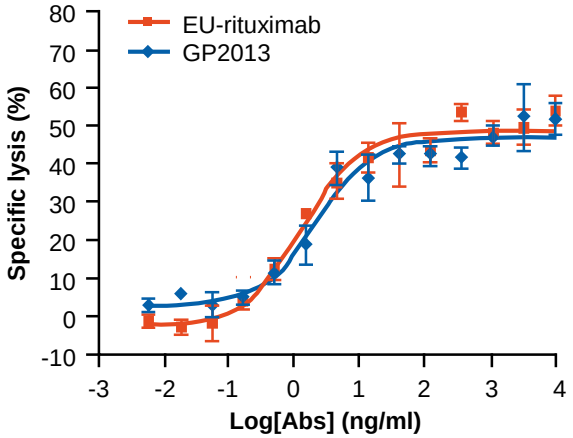
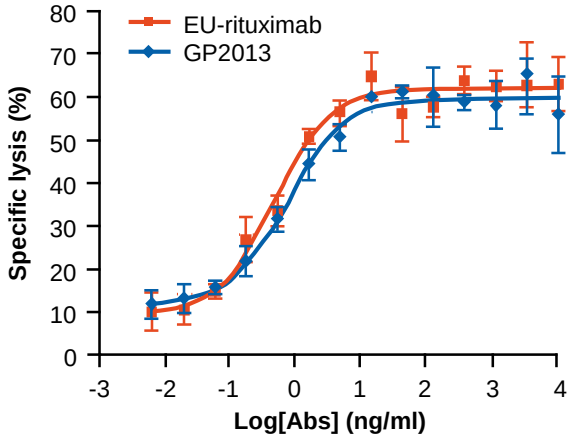
- Both, GP2013 and rituximab have similar ADCC potency across multiple concentrations tested using SU-DHL-4 and Daudi target cells

SU-DHL4 & fresh effector cells



Comparative assessment of ADCC potency against SU-DHL-4 (diffuse large B-cell Lymphoma) cells

Daudi cell line & fresh effector cells



Comparative assessment of ADCC potency against Daudi (Burkitt lymphoma) cells

ADCC: antibody-dependent cellular cytotoxicity

da Silva A, et al. Leuk Lymphoma 2014;55:1609–17

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GP2013 & rituximab: functional similarity (tumor growth)

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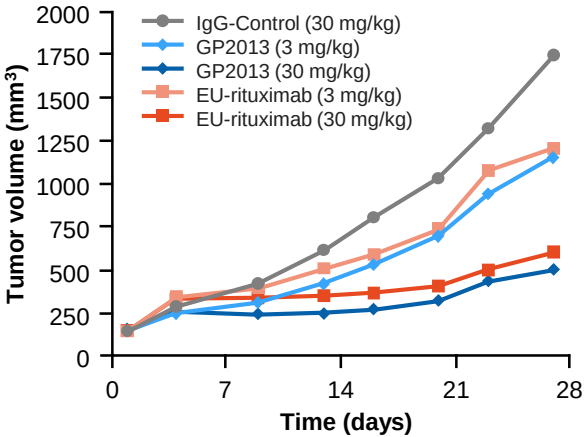
- Both GP2013 and rituximab inhibit tumor growth to a similar extent, including at the sensitive mid-dose levels tested in SU-DHL-4 model and Jeko-1 model

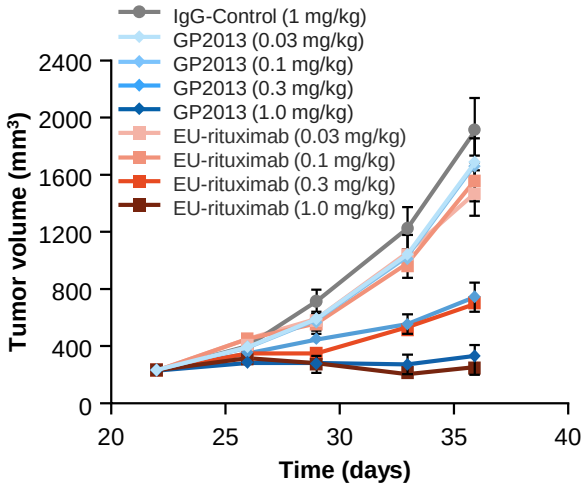
SU-DHL-4 model



In vivo comparability in two mouse xenograft models of non-Hodgkin lymphoma SU-DHL-4 (diffuse large B-cell Lymphoma) model

da Silva A, et al. Leuk Lymphoma 2014;55:1609–17

Jeko-1 model



In vivo comparability in two mouse xenograft models of non-Hodgkin lymphoma. Jeko-1 model

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Results – *PK*

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Timepoint	PK parameter	GP2013-CVP N=119	R-CVP N=120
Cycle 4, Day 1	C_{max} (µg/mL), mean (SD)	356.03 (121.612)	350.99 (116.797)
	C_{max} (µg/mL), geometric mean ratio, (90% CI)	1.00 (0.925; 1.090)	
	C_{trough} (µg/mL), mean (SD)	66.42 (47.593)	82.13 (61.526)
Cycle 8, Day 1	C_{max} (µg/mL), mean (SD)	391.11 (111.561)	391.30 (125.511)
	C_{trough} (µg/mL), mean (SD)	123.10 (59.048)	127.19 (76.346)
		GP2013-CVP N=27	R-CVP N=22
Cycle 4	$AUC_{0–21d}$ (µg*day/mL), mean (SD)†	3320 (872)	3500 (1020)
	AUC_{all} (µg*day/mL), mean (SD)†	2820 (1250)	2950 (1510)

The clinical PK profile was similar between GP2013 and reference rituximab, with a ratio of geometric means of C_{max} at Cycle 4 Day 1 of 1.00

†$AUC_{0–21d}$ and AUC_{all} were calculated for cycle 4 in a subgroup of patients undergoing extended PK/PD sampling
CI: confidence interval; C_{max}: maximum (peak) observed serum drug concentration at the end of infusion dose administration; C_{trough}: minimum observed serum drug concentration which is measured right before the next infusion dose administration; CVP: cyclophosphamide, vincristine, prednisone; PD: pharmacodynamics; PK: pharmacokinetics, SD: standard deviation
Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

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Moving a Biosimilar Into the Clinic: Equivalent Pharmacokinetics is the First Critical Hurdle

- Molecules that have been demonstrated to be ‘highly similar’ in preclinical evaluation need to be evaluated in the clinic
- Showing of biosimilar PK, within predefined equivalence margins, should be the first clinical ‘go/no go’ step for biosimilars
- The biosimilar concept implies the same dose, strength, and route of administration
- PK is a critical measure in assessing bioavailability of ‘highly similar’ structure

Product class-specific PK equivalence margins will be important to extrapolation decisions that occur later in the development program

FDA. Scientific considerations in demonstrating biosimilarity to a reference product: guidance for industry. April 2015.
Isakov L, et al. Am J Ther. 2016;23:e1903-e1910.

GP2013 clinical development

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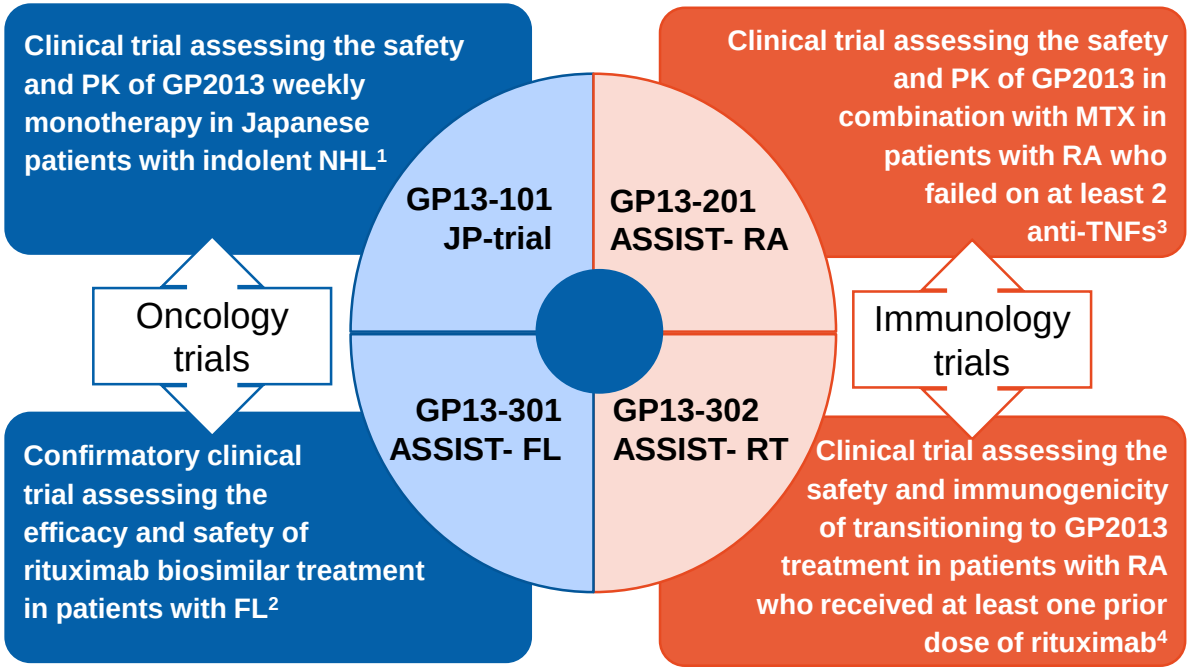

FL: follicular lymphoma, JP: Japanese patients, NHL: non-Hodgkin's lymphoma, PK: pharmacokinetics, RA: Rheumatoid arthritis, TNF: Tumor necrosis factor

ClinicalTrials.gov Identifier: [1]NCT01933516, [2]NCT01419665, [3]NCT01274182, [4]NCT02514772 https://clinicaltrials.gov

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ASSIST-FL: Methods
Study design and setting

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- A prospective, multi-center, randomized, double-blind, active-controlled, parallel-group, confirmatory, phase III trial was conducted in 629 patients, across 159 centers from 26 countries

Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

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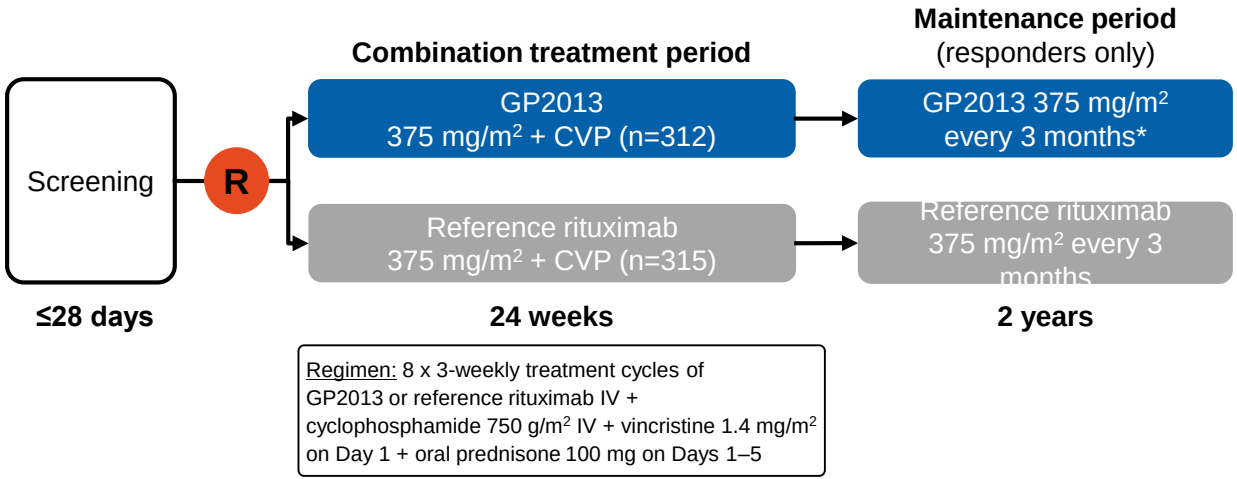
Methods
Study design

- Patients were randomized 1:1 to GP2013 or reference rituximab combined with CVP, stratified by FLIPI risk group and geographical region
- The study consisted of a combination treatment phase over 24 weeks and a maintenance treatment phase over 2 years – those responding (CR or PR) at the end of the combination treatment period were enrolled in the maintenance phase.



*Except in Italy, where maintenance therapy was administered every 2 months
CR, complete response; CVP, cyclophosphamide, vincristine and prednisone; FLIPI, follicular lymphoma international prognostic index; IV, intravenous; PR, partial response; R, randomization; WHO, World Health Organization
Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

Methods
Study objectives

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Primary objective

- To demonstrate equivalence in terms of overall response rate (ORR) during the combination phase of the study

Secondary objectives

- Descriptive assessments of rates of best overall response (BoR), progression-free survival (PFS) and overall survival (OS)
- Safety and tolerability of GP2013 in comparison with reference rituximab, in combination with CVP or as monotherapy

Additional endpoints

- Immunogenicity (ADA formation against GP2013 and reference rituximab)
- Pharmacology
  - PK of GP2013 and reference rituximab
  - PD marker evaluation (peripheral B-cell counts)

ADA: anti-drug antibody, CVP: cyclophosphamide, vincristine, prednisone,
PD: pharmacodynamics, PK: pharmacokinetic
Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

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ASSIST-FL: ORR as a suitable and sensitive endpoint

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- **Justification of ORR → ORR appropriate endpoint**
  - Primary endpoint that was appropriately powered to demonstrate similarity[1]
  - PFS or OS may not be suitable endpoints for demonstrating biosimilarity[2]
  - ORR accepted by regulatory authorities as a suitable endpoint for biosimilar studies in oncology[2]
  - Large effect size with rituximab on ORR in follicular lymphoma
    - Add on effect of rituximab for ORR to CVP chemotherapy is 24% (ORR 57% with CVP vs 81% with R-CVP)[3]

→ Therefore, ORR is the most sensitive endpoint for biosimilar development

CVP, cyclophosphamide, vincristine and prednisone;
ORR, overall response rate; OS, overall survival; PFS, progression-free survival

1. Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]; 2. EMA Guideline on Similar Biological Medicinal Products containing Monoclonal Antibodies (May 2012); 3. Marcus R, et al. Blood 2005;105:1417–23.

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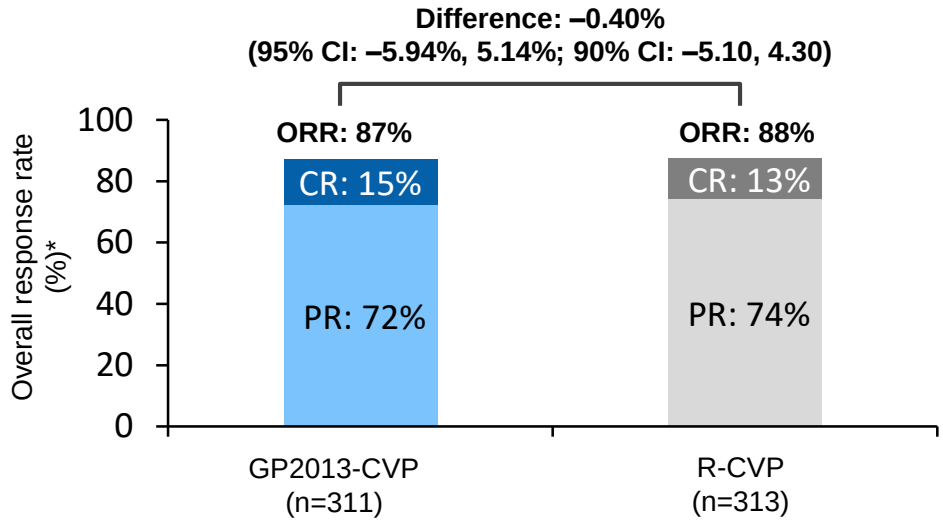
Results

Primary efficacy results – ORR at Week 24



- **The primary endpoint was met, with equivalence demonstrated in ORR for GP2013 and reference rituximab when combined with CVP**
- Both 95% and 90% CI lay entirely within predefined margin of equivalence (–12% to +12%)

*Centrally-assessed ORR in the per-protocol population (all patients who received at least one (partial or complete) dose of investigational treatment and who did not have any major protocol deviations)
CI: confidence interval; CR: complete response; R-CVP: reference rituximab, cyclophosphamide, vincristine, prednisone; PR: partial response; ORR: overall response rate.
Adapted from Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

Results

Secondary efficacy results – PFS and OS

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Outcome†	GP2013-CVP N=312 n (%)	R-CVP N=315 n (%)	Hazard ratio (90% CI)*
PFS			
Event, n (%)	94 (30)	76 (24)	1.31 (1.02, 1.69)
Censored events, n (%)	218 (70)	239 (76)	
Kaplan-Meier estimate, median	Not reached	Not reached	
OS			
Event, n (%)	23 (7)	29 (9)	0.77 (0.49, 1.22)
Censored events, n (%)	289 (93)	286 (91)	
Kaplan-Meier estimate, median	Not reached	Not reached	

Data cut-off: 31 December 2016; Median follow-up: 23.8 months

- **ASSIST-FL was not powered to evaluate comparability in terms of PFS and OS – these endpoints are not intended to be used to confirm biosimilarity**
- **Data are currently immature, with a high-proportion of patients censored (~70–90%)**
- **The observed hazard ratios for PFS and OS are inconsistent, suggesting that current results are likely due to random variation and not actual treatment differences**

*Obtained by fitting Cox regression model with treatment allocation as a covariate and FLIPI score as a stratification factor; †Full-analysis set data, including all patients to whom investigational treatment had been assigned by randomization and who received at least one (partial or complete) dose of investigational treatment
CVP: cyclophosphamide, vincristine, prednisone; OS: overall survival; PFS: progression-free survival
Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

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Results

Safety – AEs during combination phase

	GP2013-CVP N=312 n (%)	R-CVP N=315 n (%)
Any AE	289 (93)	288 (91)
Most frequent AEs		
Neutropenia	80 (26)	93 (30)
Constipation	70 (22)	63 (20)
Nausea	51 (16)	42 (13)
Grade of AEs experienced		
1–2 (mild/moderate)	280 (90)	277 (88)
3	127 (41)	132 (42)
4	39 (13)	47 (15)
AE leading to discontinuation of study drug*	23 (7)	22 (7)
Serious AEs	71 (23)	63 (20)
Deaths‡	4 (1)	7 (2)

- **Safety profiles of GP2013 and reference rituximab were similar when combined with CVP, with comparable incidences of AEs, SAEs, AEs leading to discontinuations, and deaths**
- **Most AEs were mild or moderate in severity**

*Discontinuation of GP2013, reference rituximab or any component of CVP; ‡excludes death events occurring 30 days after treatment discontinuation (n=1 patient in the GP2013-CVP treatment arm)
AE: adverse event; CVP: cyclophosphamide, vincristine, prednisone
Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

Results

*Safety – drug-related infusion reactions**

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	GP2013-CVP N=312 n (%)	R-CVP N=315 n (%)
Any potential infusion-related reaction AEs (≥2% of all patients)*	154 (49)	152 (48)
Infusion-related reaction	41 (13)	37 (12)
Nausea	34 (11)	35 (11)
Fatigue	26 (8)	18 (6)
Asthenia	21 (7)	22 (7)
Vomiting	16 (5)	14 (4)
Pyrexia	11 (4)	16 (5)
Diarrhoea	12 (4)	14 (4)
Myalgia	11 (4)	11 (3)
Abdominal pain	12 (4)	9 (3)
Headache	9 (3)	11 (3)
Pruritus	9 (3)	10 (3)
Abdominal pain, upper	9 (3)	8 (3)
Dyspnoea	10 (3)	7 (2)
Rash	8 (3)	7 (2)
Dyspepsia	6 (2)	7 (2)

Frequency of infusion-related reactions was similar with GP2013 and reference rituximab when combined with CVP

*During combination phase
AE: adverse event; CVP: cyclophosphamide, vincristine, prednisone
Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

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Results
Additional results – immunogenicity

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Development of ADAs during study*	GP2013 N=268 n (%)	Reference rituximab N=283 n (%)
ADAs developed	5 (2)	3 (1)
Neutralizing ADAs developed	2 (1)	2 (1)

Immunogenicity data support the similarity between GP2013 and reference rituximab, with similar incidences of ADAs reported in each arm

*Results reported for immunogenicity analysis set, including all patients exposed to study drug with a pre- and post-baseline immunogenicity sample
ADA: anti drug antibodies
Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

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Conclusion

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- GP2013 is a monoclonal antibody that has been developed as a biosimilar to the reference drug rituximab
- ASSIST-FL is an ongoing, multi-center, randomized, double-blind, confirmatory phase III trial being conducted in patients with untreated advanced stage FL[1]
- Results from ASSIST-FL to date demonstrate:[1]
  - Equivalent **efficacy** with GP2013 and reference rituximab
  - Similar **safety profiles** of GP2013 and reference rituximab
  - Superimposable **PK and PD profiles** of GP2013 and reference rituximab
  - Comparable incidences of **ADAs** with GP2013 and reference rituximab
- These results complement prior data demonstrating physicochemical, functional, biological and pharmacokinetic similarity between GP2013 and reference rituximab[2,3]

ADA: anti-drug antibodies; AE: adverse event; CI: confidence intervals; ORR: overall response rate; PD: pharmacodynamic; PK: pharmacokinetic

[1]Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]; [2]Visser J, et al. BioDrugs 2013;27:495–507;
[3]da Silva A, et al. Leuk Lymphoma 2014;55:1609–17.

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What a Clinician Wants Before They Feel Comfortable With Extrapolation

- PK analysis is essential to show equivalent drug exposure
  - PK can differ by the clinical context (eg, rituximab for lymphoma vs rheumatoid arthritis)
- Monitoring for anti-drug antibodies is a major safety measure
- Clinical efficacy should be demonstrated in appropriate patient populations
  - Independent trials in NHL and non-malignant diseases (for rituximab)
  - Single-agent activity in first-line follicular lymphoma as a sensitive indicator of activity (for rituximab)

RITUXIMAB BIOSIMILARS IN GERMANY

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Erhebung	Elektronische Datenerhebung mit der Software „oncotrace“
Zeitraum	01.07.2017 – 30.06.2018
Datenquelle	Niedergelassene onkologisch tätige Fachärzte deutschlandweit
Datengrundlage	Anonymisierte in den teilnehmenden Zentren dokumentierte Behandlungsdaten von Krebspatienten
Anzahl der verordnenden Ärzte	61
Teilnehmende Zentren	19
Patientendaten	1140 erfasste Therapiezyklen
Auswertung	Deskriptive statistische Auswertung mit der Software SPSS

- Otremba et al. DGHO Wien 10/2018

BIOSIMILARS IN LYMPHOMA

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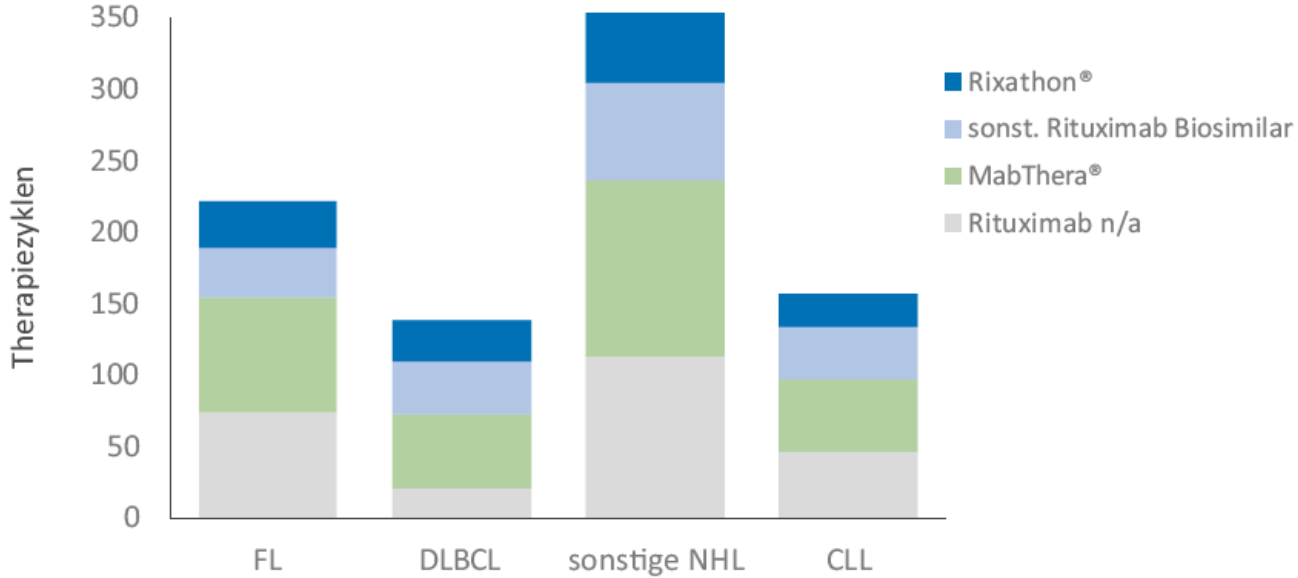

Otremba et al. DGHO Wien 10/2018

BIOSIMILARS IN LYMPHOMA

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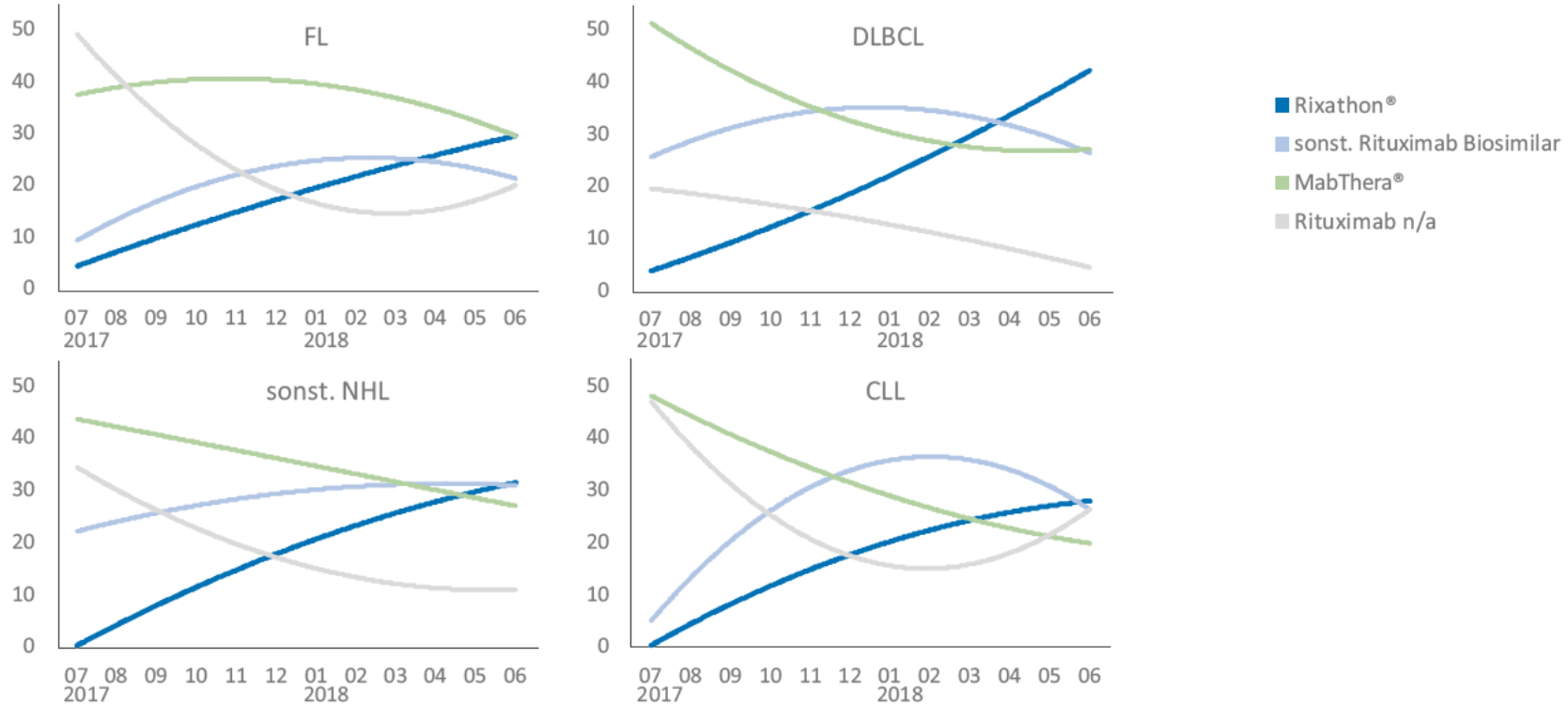

Otremba et al. DGHO Wien 10/2018

IMPLEMENTING BIOSIMILARS

MY EXPERIENCE

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- **Information and education** of prescriber and patient:
  Acceptance depends on good information and experience
- **Oncologists must be aware of PK-data, immunogenicity and clinical trial results**
- **Most often patients do what their oncologist recommends**
- So far I haven`t seen more **infusion reactions**
- So far I haven`t seen more **AE**
- So far I haven`t seen a **change in efficacy**
- **Surveillance and real world data will be collected!**

Die Privatklinikgruppe Hirslanden:

Hirslanden Klinik Aarau - Klinik Beau-Site, Bern - Klinik Permanence, Bern - Praxiszentrum am Bahnhof, Bern - Salem-Spital, Bern - AndreasKlinik, Cham Zug - Klinik Am Rosenberg, Heiden - Clinique la Colline, Genève - Clinique Bois-Cerf, Lausanne - Clinique Cecil, Lausanne - Klinik St. Anna, Luzern - St. Anna am Bahnhof, Luzern - Hirslanden Klinik Meggen - Klinik Birshof, Münchenstein Basel - Klinik Belair, Schaffhausen - Klinik Stephanshorn, St. Gallen - Klinik Hirslanden, Zürich - Klinik Im Park, Zürich

www.hirslanden.ch

Thank you

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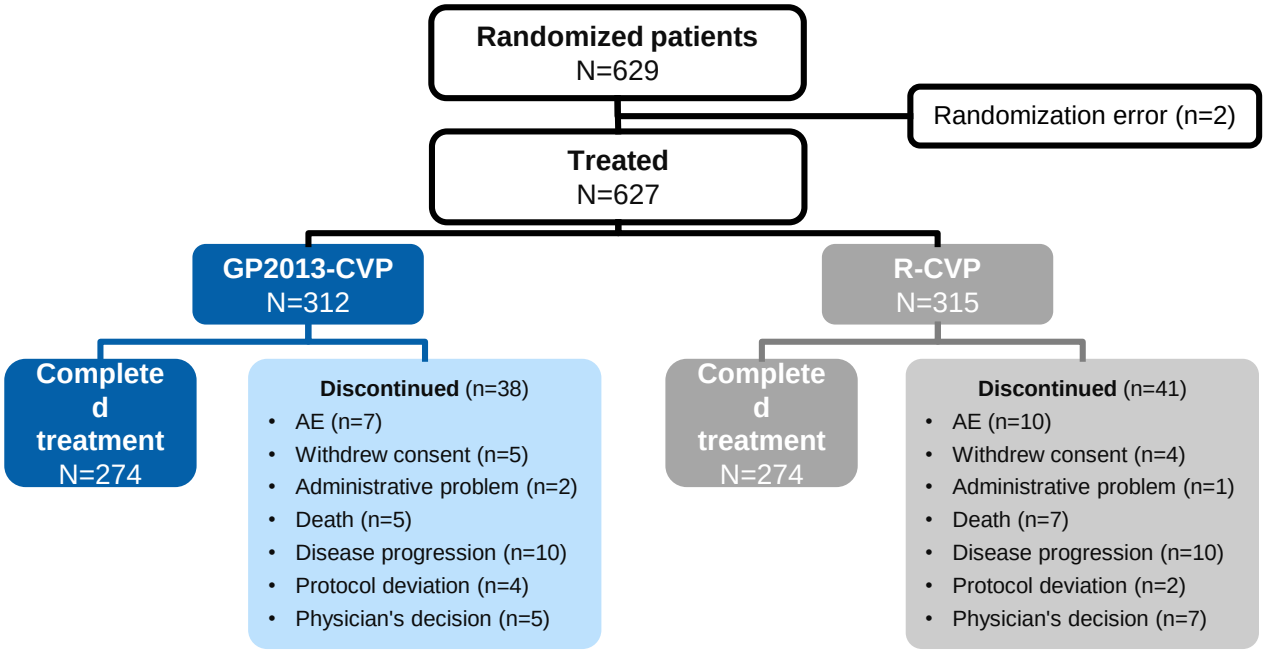
BACK-UP SLIDES

Results

Patient disposition – combination phase



AE: adverse event; CVP: cyclophosphamide, vincristine, prednisone
Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

Results

Demographics and baseline characteristics

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Demographics, baseline and disease characteristics*	GP2013-CVP N=312	R-CVP N=315
Age (years), mean (SD)	57.5 (11.86)	56.4 (11.72)
Age category (years), n (%)		
<60	163 (52)	175 (56)
≥60	149 (48)	140 (44)
Female	181 (58)	169 (54)
Body mass index, mean (SD)	26.4 (4.89)	26.0 (4.82)
ECOG performance status, n (%)		
0: no restrictions	179 (57)	175 (56)
1: only light work	125 (40)	123 (39)
2: only self care	5 (2)	13 (4)
Missing	3 (1)	4 (1)

Baseline characteristics were well balanced between the arms

*Full analysis set population, including all patients to whom investigational treatment had been assigned by randomization and who received at least one (partial or complete) dose of investigational treatment
CVP: cyclophosphamide, vincristine, prednisone; ECOG: Eastern Cooperative Oncology Group; SD: standard deviation
Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

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