Disclosures

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Advisory Boards :

Sandoz Novartis, Roche, Janssen, Acerta, Abbvie, TG Therapeutics, Teva, Takeda, Spectrum, NovoNordisk, Mundipharma,

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Celgene, Abbvie, Gilead, TgTherapeutics, Janssen, Acerta,, Merck, Begene, Pharmacyclics, Pfizer, Roche, Sandoz – Novartis, Takeda, Teva, Servuier, Eisai.

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Najbardziej obiecujące terapie lekami biopodobnymi - Hematologia

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Przeciwciała monoklonalne w leczeniu chłoniaków - wszystko zaczęło się od Rytuksymabu

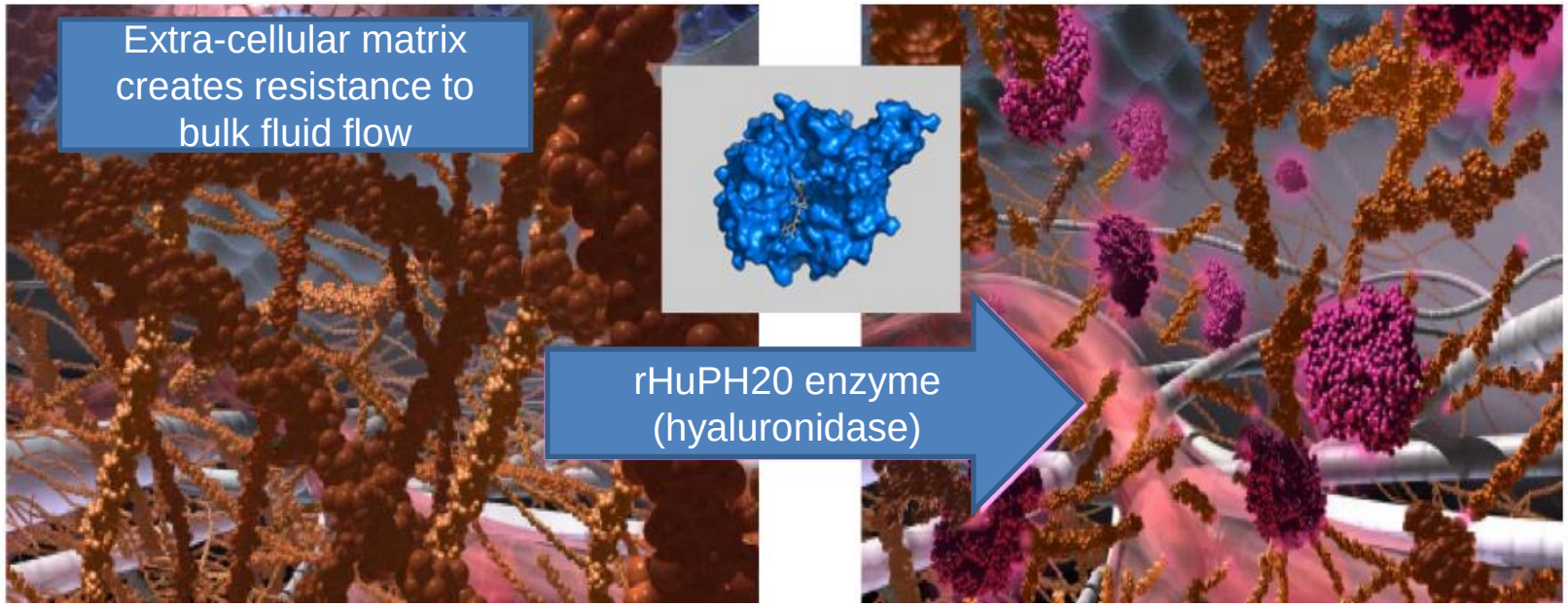
Development and registration of original particle (Roche)

Subcutaneous Rituximab (Roche)

Rituximab biosimilars:

- **CT-P10 (Celltrion)**
- **GP2013 (Sandoz Novartis)**

Jedyną konkurencją dla biosymilarów Rytuksymabu jest … poskórna postać Rytuksymabu

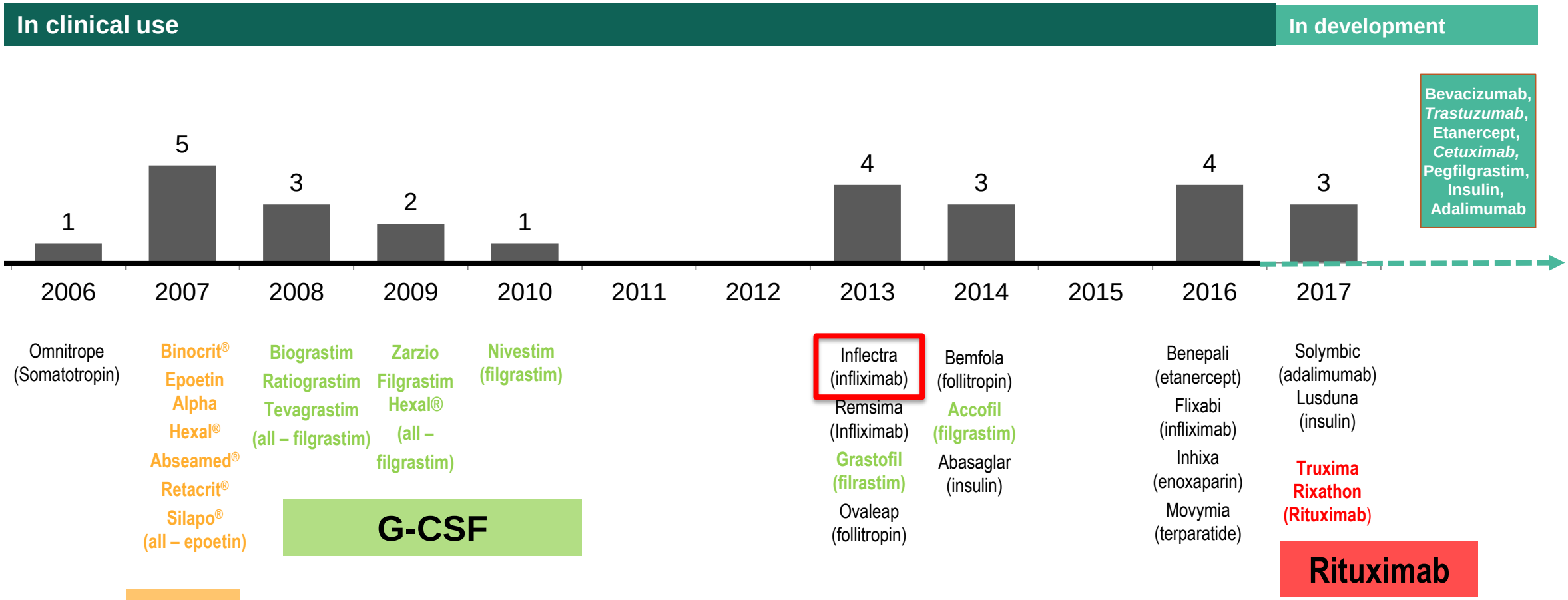


Registration, lab tests, patient assessment	Drug preparation in pharmacy	IV line	IV rituximab infusion + observation
Registration, lab tests, patient assessment	Drug preparation	“Saved” time with SC rituximab	
	SC administration		

IV: intravenous; SC; subcutaneous.

Based on: Aguiar-Bujanda D et al. *Cancer Manag Res*. 2015;7:319–330.

Biosymilary zarejestrowane przez EMA

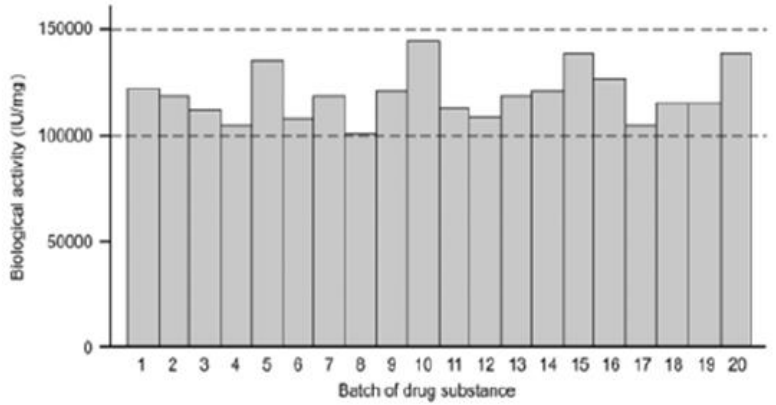


G-CSF: Granulocyte-colony stimulating factor; EMA: European Medicines Agency; EPO: epoetin.

EMA website. http://www.ema.europa.eu/ema/. Accessed 7 June 2017

Każda wytworzona partia leków biologicznych, różni się nieznacznie

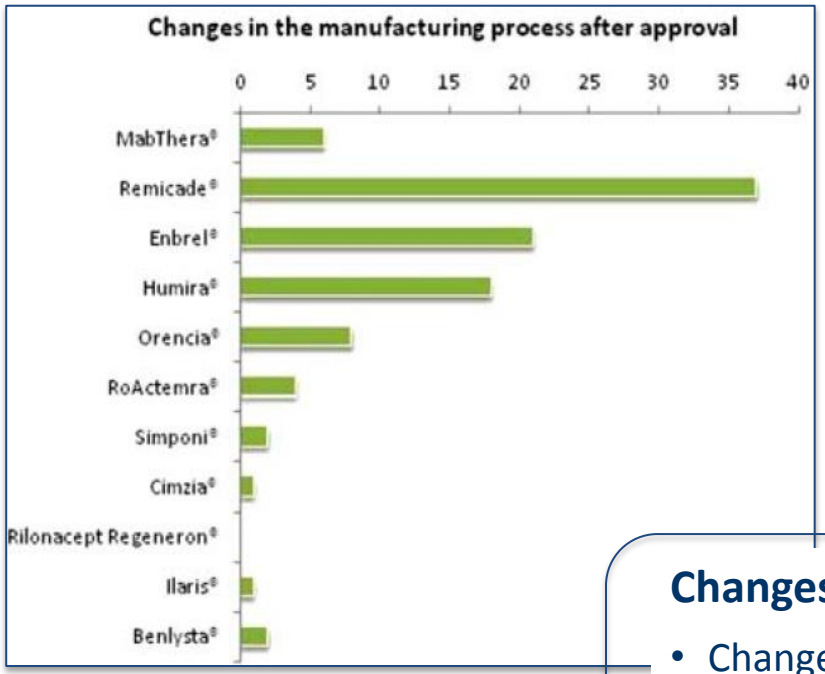
- „Non-identicality“ is a normal principle in biotechnology.
- No batch of any biological is „identical“ to the others



- The „art“ is to demonstrate that the biosimilar is as close as possible to its reference product in all relevant functional and structural aspects, within current technical and scientific limitations (inherent variability)

C Schneider, Ann Rheum Dis 2013 Vol 72 No 3

Lekarze nie są informowani o zmianach leku biologicznego, po jego rejestracji

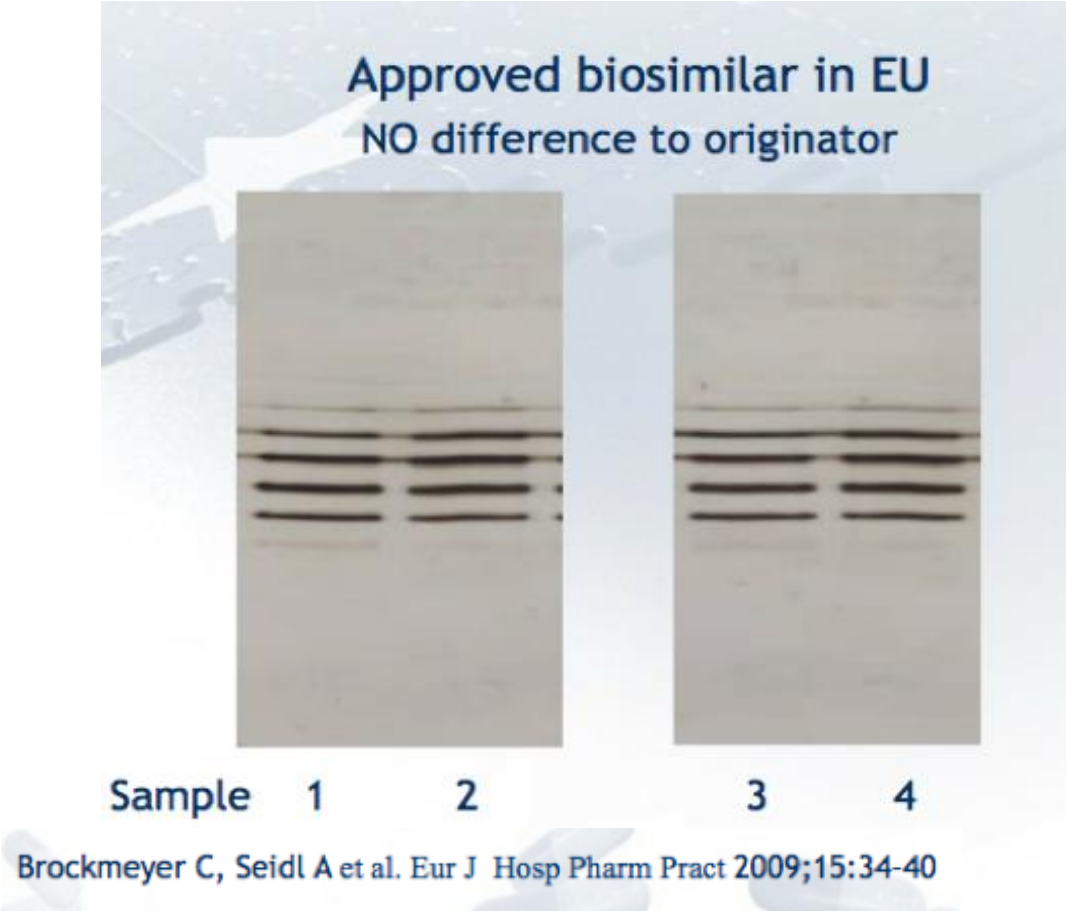


Changes include e.g.

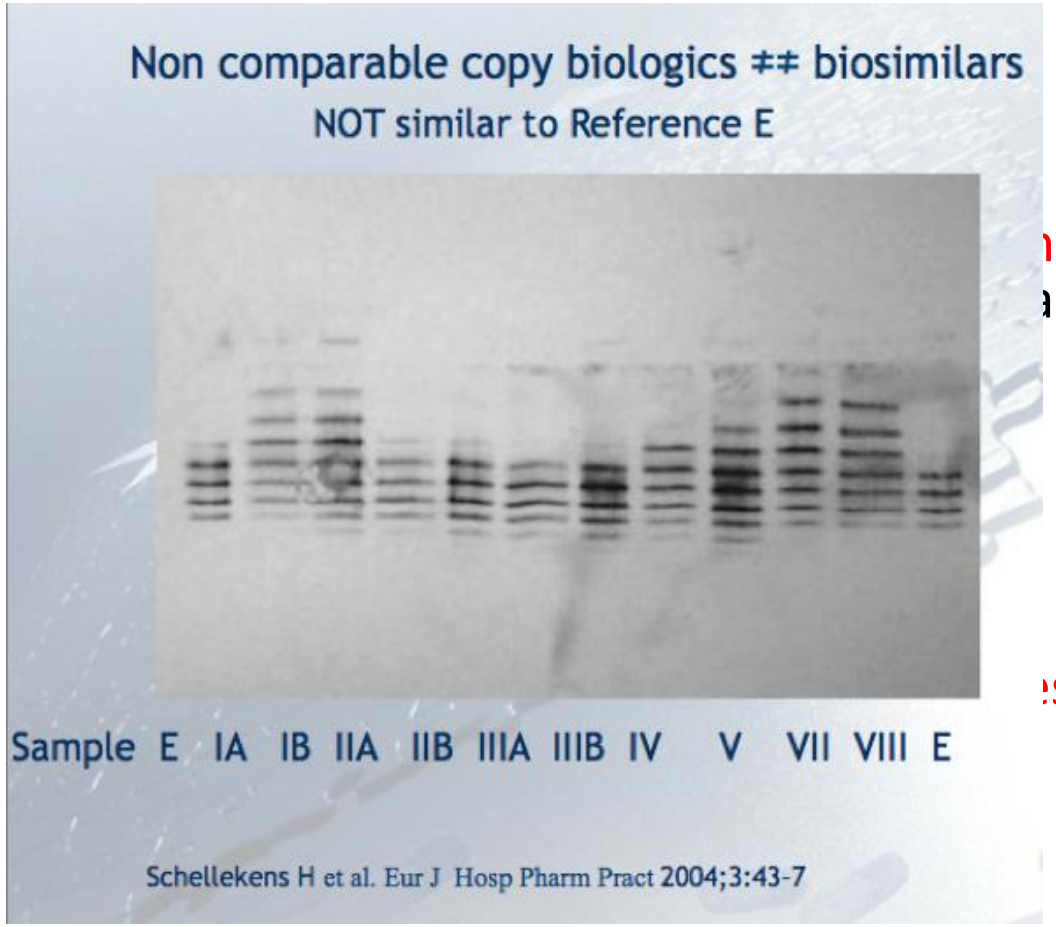
- Change in the supplier of a cell culture media
- New purification methods
- New manufacturing sites

C Schneider, Ann Rheum Dis 2013 Vol 72 No 3

Ścieżka rejetracji biosymilarów EMA/ FDA



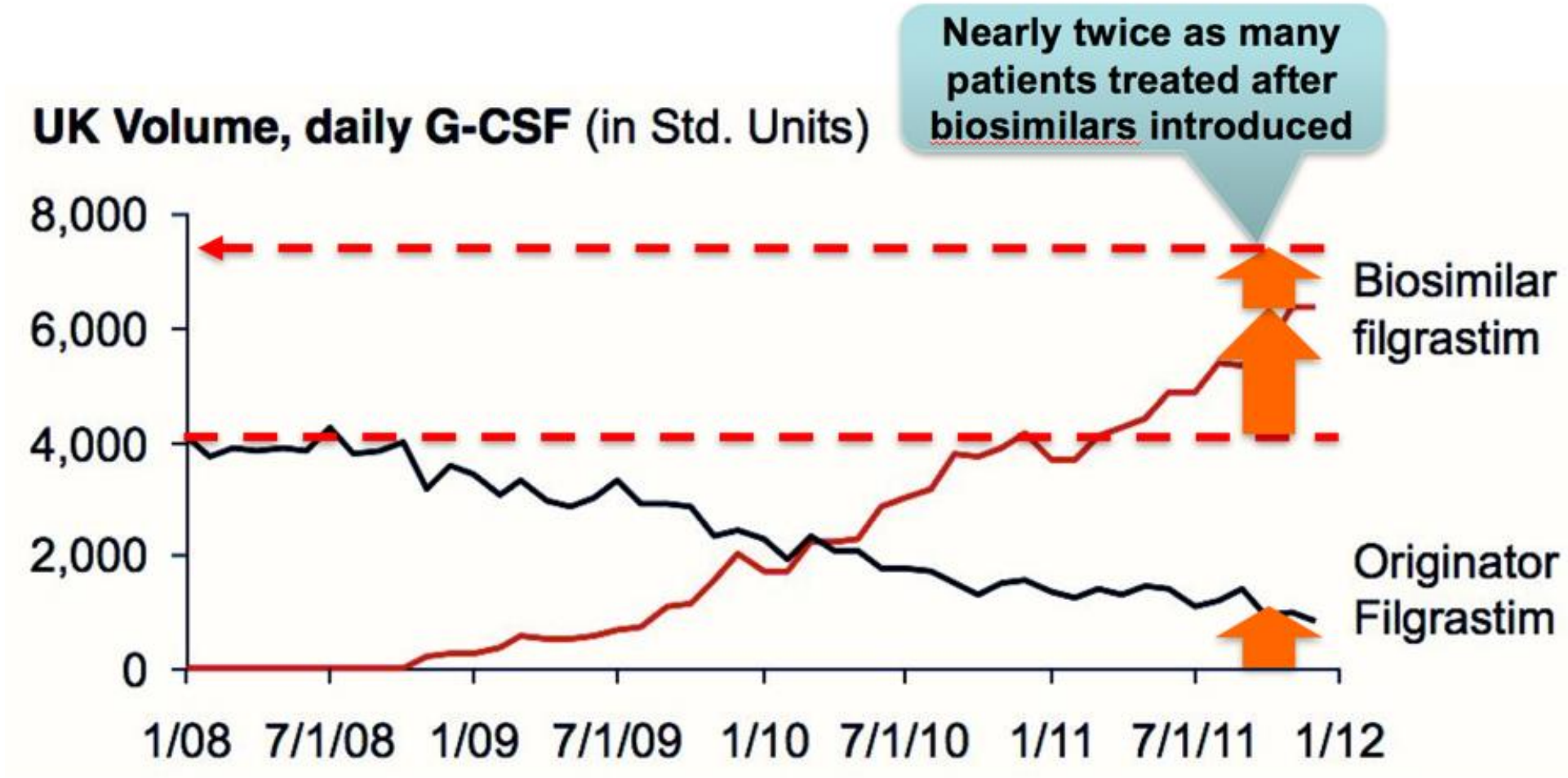
“Copy-biologic”



Rejestracja biosymilarów przynosi znaczne oszczędności

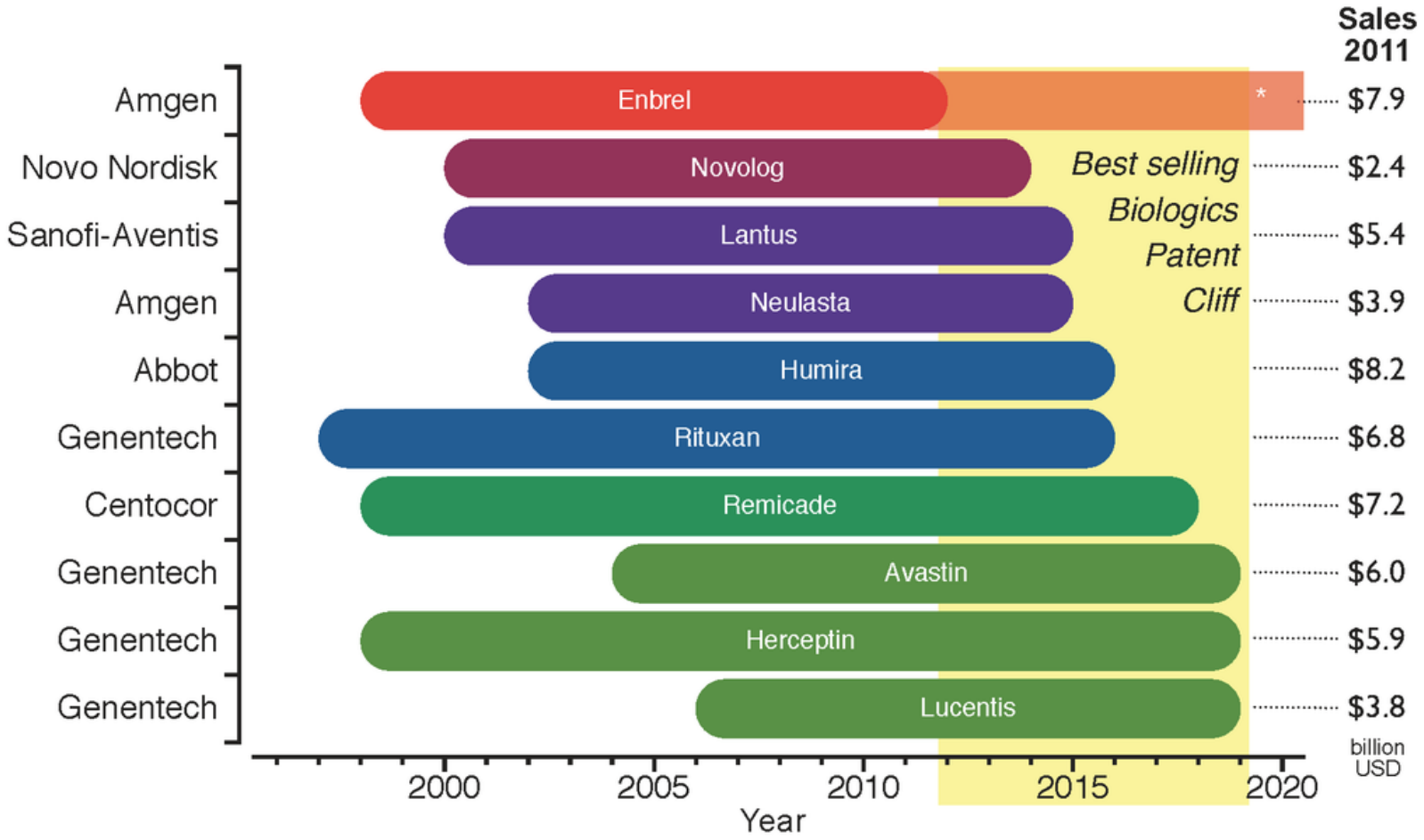
"Biosymilars – symilar but not identical"

Rejestracja biosymilarów zwiększa dostępność leku



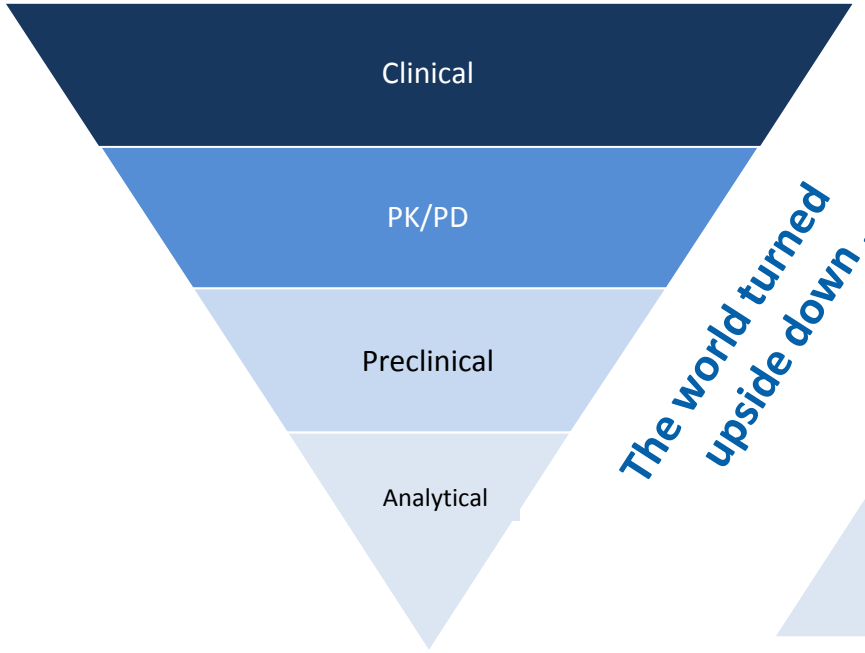
Walsh K.: Biosimilar Medicines 11th EGA International Symposium, 2013

W najbliższych latach większość leków biologicznych, będzie miała swoje biosymilary



Różnice pomiędzy rejestracją leku oryginalenego i biosymilaru

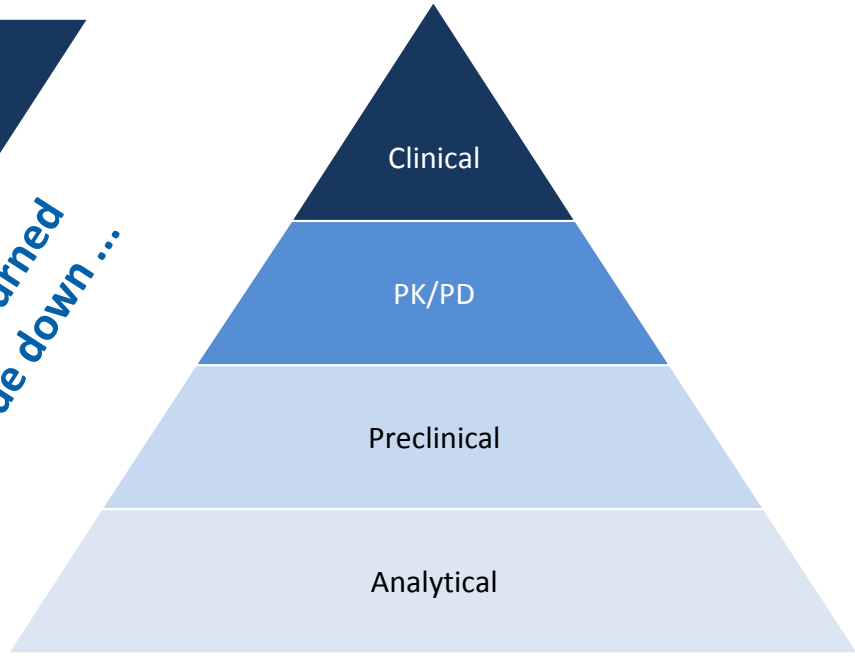
Reference medicine



Major goal is to
determine the clinical effect

The world turned upside down …

Biosimilar



Major goal is **to determine similarity**;
establishment of the scientific bridge
to the clinical experience of the originator

In the end, both approaches provide the same level of confidence with regard to safety and efficacy of the medicine

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Różnice pomiędzy rejestracją leku oryginalenego i biosymilaru

	Originator	Biosimilar
Patient population	Any	Sensitive and homogeneous
Clinical design	**Superiority versus standard of care**	**Comparative versus innovator** (therapeutic equivalence studies)
Study endpoints	Clinical outcomes data (**OS & PFS**) or accepted/established surrogates	**Pharmacokinetic and Pharmacodynamic** markers; objective **response rate (RR)**
Safety	**Acceptable risk/benefit profile** versus standard of care	**Similar safety profile** to innovator
Immunogenicity	**Acceptable risk/benefit profile** versus standard of care	**Similar immunogenicity profile** to innovator
Extrapolation	**Not allowed**	**Possible** if justified

prIME Podcast Series 2013: A Focus on Biosimilar Antibodies, Reference Slidk [online]. Available at: https://www.youtube.com/watch?v=VwNWUzyuJuw [Accessed 2016 March 22].

Biosymilary Rytuksymabu

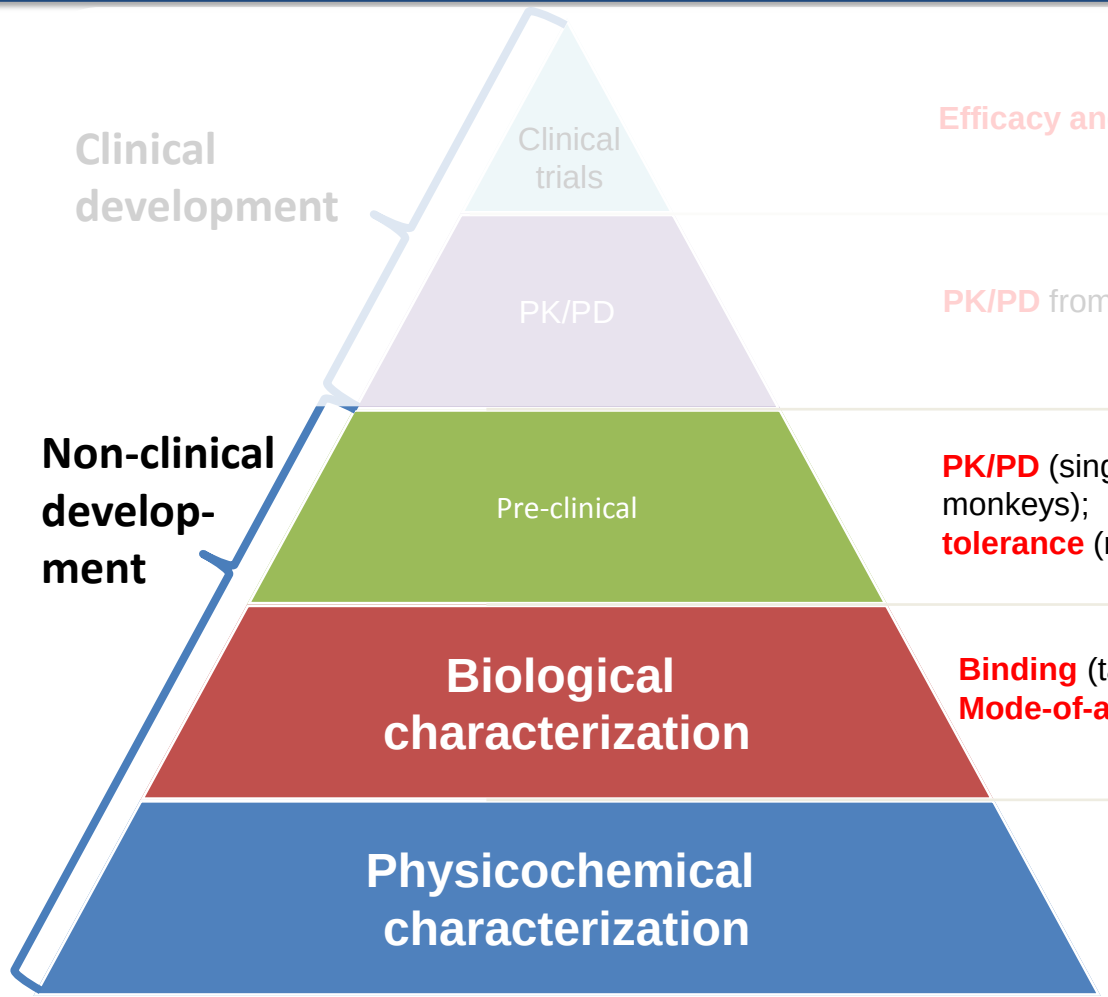
CELLTRION

CT-P10
Registered by EMA

SANDOZ
a Novartis company

GP2013
Being assessed by EMA

Rejestracja biosymilarów Rytusymabu



Efficacy and safety from two indications: RA & FL

PK/PD from two indications: RA & FL

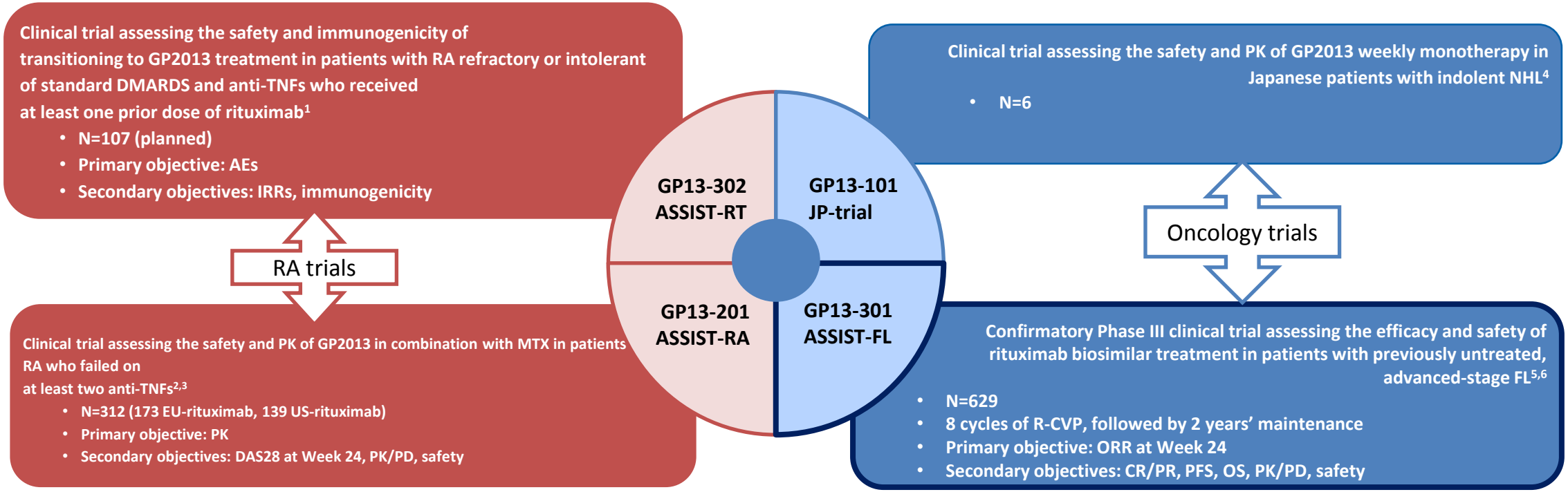
PK/PD (single dose in monkeys); **toxicity** (repeat dose in monkeys); **Efficacy** (xenograft tumor models in SCID mice); Local **tolerance** (rabbits); **Tissue cross reactivity**, **ADCC** (in vitro)

Binding (target binding, receptor binding)
Mode-of-action (programmed cell death, CDC, ADCC)

Primary structure, higher order structure, size, **heterogeneity** (C-and N-terminal),**post-translational modifications** (variants glycosylation, glycation, oxidation, deamidation).
Purity, **Aggregates**

ADCC, antibody-dependent cellular cytotoxicity; CDC, complement-dependent cytotoxicity; FL, follicular lymphoma; PD, pharmacodynamics; PK, pharmacokinetics; RA, rheumatoid arthritis; SCID, severe combined immunodeficiency

Badania kliniczne z GP2013



Total safety data: c. 1000 patients (500 receiving GP2013), efficacy data: 312 (RA) + 629 (FL) patients

AE, adverse event; CR, complete response ; CVP, cyclophosphamide, vincristine, prednisolone; DAS, disease activity score; FL, follicular lymphoma; IRR, infusion-related reaction; JP, Japanese patients; MTX, methotrexate; NHL, non-Hodgkin's lymphoma; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PK, pharmacokinetics; PR, partial response; R, rituximab; RA, rheumatoid arthritis; TNF, tumor necrosis factor

1. Clinicaltrials.gov (NCT02514772); 2. Clinicaltrials.gov (NCT01274182); 3. Smolen et al. Ann Rheum Dis 2017;76:1598–1602; 4. Clinicaltrials.gov (NCT01933516); 5. Clinical trials.gov (NCT01419665); 6. Jurczak W, et al. Lancet Haematol 2017 Jul 13 [Epub ahead of print]

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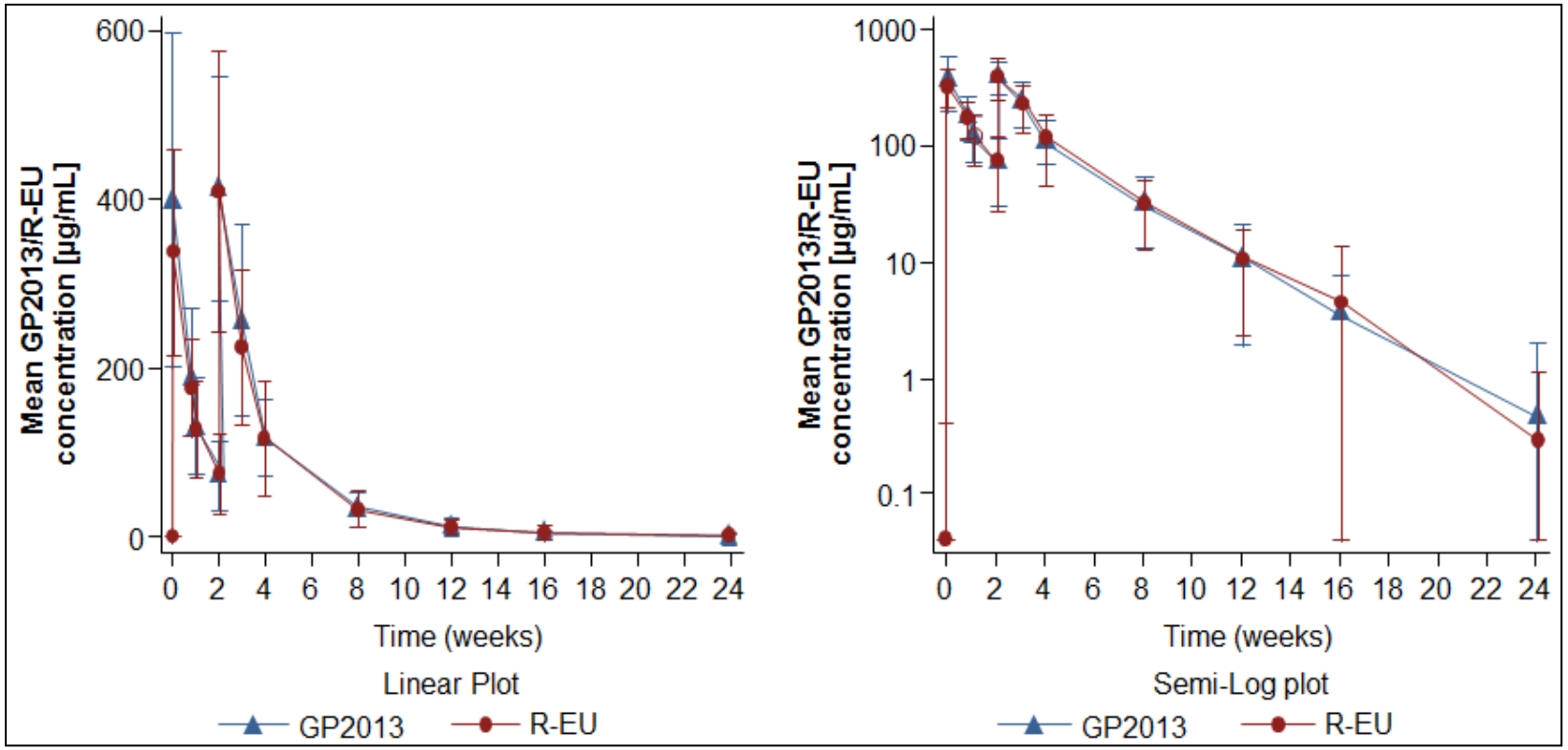
Badania Kliniczne z CTP-10

Study	Indication	Primary Endpoint	Sample size	Status
1.1 **1.3** (1.1 Extension Study)	RA	**PK equivalence** Long term safety and efficacy	154 58	Completed
3.2	RA	▪ Part 1: **PK equivalence** ▪ Part 2: **Therapeutic equivalence**	372	Study Ongoing Week 48 results available
3.3	AFL	▪ Part 1: **PK equivalence** ▪ Part 2: **Therapeutic non-inferiority**	140	Study Ongoing Week 24 results available
3.4	LTBFL	**Therapeutic equivalence**	174**	**Recruiting**

Safety Data: 650 (325 in CT-P10), Efficacy data: 372 (RA)+ 140 (FL)

Farmakokinetyka - ($AUC_{(0\text{-}inf)}$)- (PAS)

Arithmetic mean (SD) serum PK concentration-time profile over 24 weeks by treatment (PK analysis set*)



Serum concentration-time profiles for the two treatments were similar up to week 24

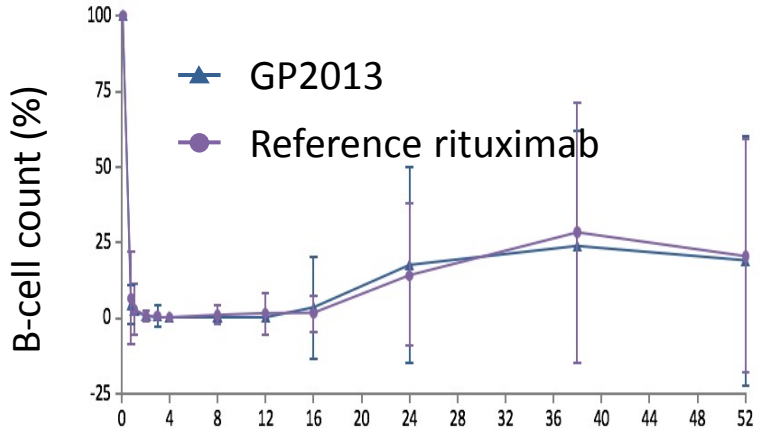
$AUC_{(0\text{-}inf)}$, The area under the concentration-time curve from time zero to infinity; FAS, full analysis set; PK, pharmacokinetics; SD, standard deviation
*The PK analysis set was a subset of the FAS and consisted of patients who did not have any major protocol deviations

Smolen J et al., EULAR congress, 8-11 June, London UK: FRI0222

Farmakodynamika (deplecja limfocytów B)

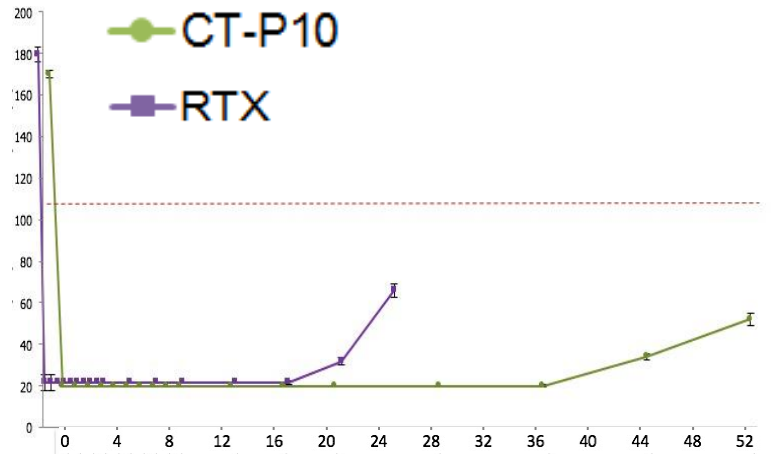
ASSIST-RA
Affordable Efficacy & Safety from Rituximab Biosimilar Treatment

Geometric mean ratio in $AUEC_{0-14d}$
1.019 (95% CI: 0.997, 1.042)



CT-P10 3.2 RA

Median (±SE) B-cell Kinetics (cells/µL)



ASSIST-RA
Affordable Efficacy & Safety from Rituximab Biosimilar Treatment

Profil bezpieczeństwa GP2013

n (%)	GP2013 (n=86)	Rituximab reference (n=87)
Deaths	1 (1.16)	0 (0.0)
Other non-fatal SAEs	10 (11.63)	14 (16.09)
Leading to discontinuation	2 (2.33)	4 (4.60)
Any AE	56 (65.1)	57 (65.5)
Leading to study drug discontinuation	2 (2.33)	3 (3.45)
AEs by most frequent SOCs		
Infections and infestations	27 (31.4)	31 (35.6)
Musculoskeletal	16 (18.6)	14 (16.1)
Gastrointestinal disorders	13 (15.1)	15 (17.2)
General disorders	12 (14.0)	9 (10.3)
Skin and subcut. tissue	9 (10.5)	11 (12.6)
Injury and poisoning	9 (10.5)	11 (12.6)
Resp., thoracic, mediastinal	7 (8.1)	12 (13.8)
Vascular disorders	7 (8.1)	10 (11.5)
Nervous system disorders	7 (8.1)	10 (11.5)
Potential infusion related reaction	32 (37.2)	37 (42.5)

CT-P10 3.2 RA

Profil bezpieczeństwa CTP-10

Events, n (%)	CT-P10 (N=161)	US-RTX (N=151)	EU-RTX (N=60)	RTX (N=211)
AE	122 (75.8)	96 (63.6)	37 (61.7)	133 (63.0)
- Related	73 (45.3)	47 (31.1)	25 (41.7)	72 (34.1)
SAE	13 (8.1)	14 (9.3)	2 (3.3)	16 (7.6)
- Related	0	5 (3.3)	1 (1.7)	6 (2.8)
Infection	61 (37.9)	53 (35.1)	17 (28.3)	70 (33.2)
- Related	27 (16.8)	25 (16.6)	6 (10.0)	31 (14.7)
IRR	33 (20.5)	12 (7.9)	13 (21.7)	25 (11.8)
Malignancy	0	2 (1.3)	1 (1.7)	3 (1.4)
Discontinuation due to AEs	3 (1.9)	7 (4.6)	2 (3.3)	9 (4.3)
- Related	2 (1.2)	5 (3.3)	1 (1.7)	6 (2.8)

Equivalent Efficacy of a Biosimilar Rituximab and Reference Rituximab in Previously Untreated Advanced Follicular Lymphoma: Extended Results of ASSIST-FL, a Confirmatory Phase III Study

Wojciech Jurczak; Ilidia Moreira; Kanaka Setty Govindbabu; Eduardo Munhoz; Maria-Asuncion Echeveste; Pratyush Giri; Nelson Castro; Juliana Pereira; Luiza Akria; Sergey Alexeev; Dzhalil Osmanov; Peijuan Zhu; Siyka Alexandrova; Angela Zubel; Olof Harlin; Jutta Amersdorffer

Jurczak et al, ESMO 2017, Lancet Hematol 2017

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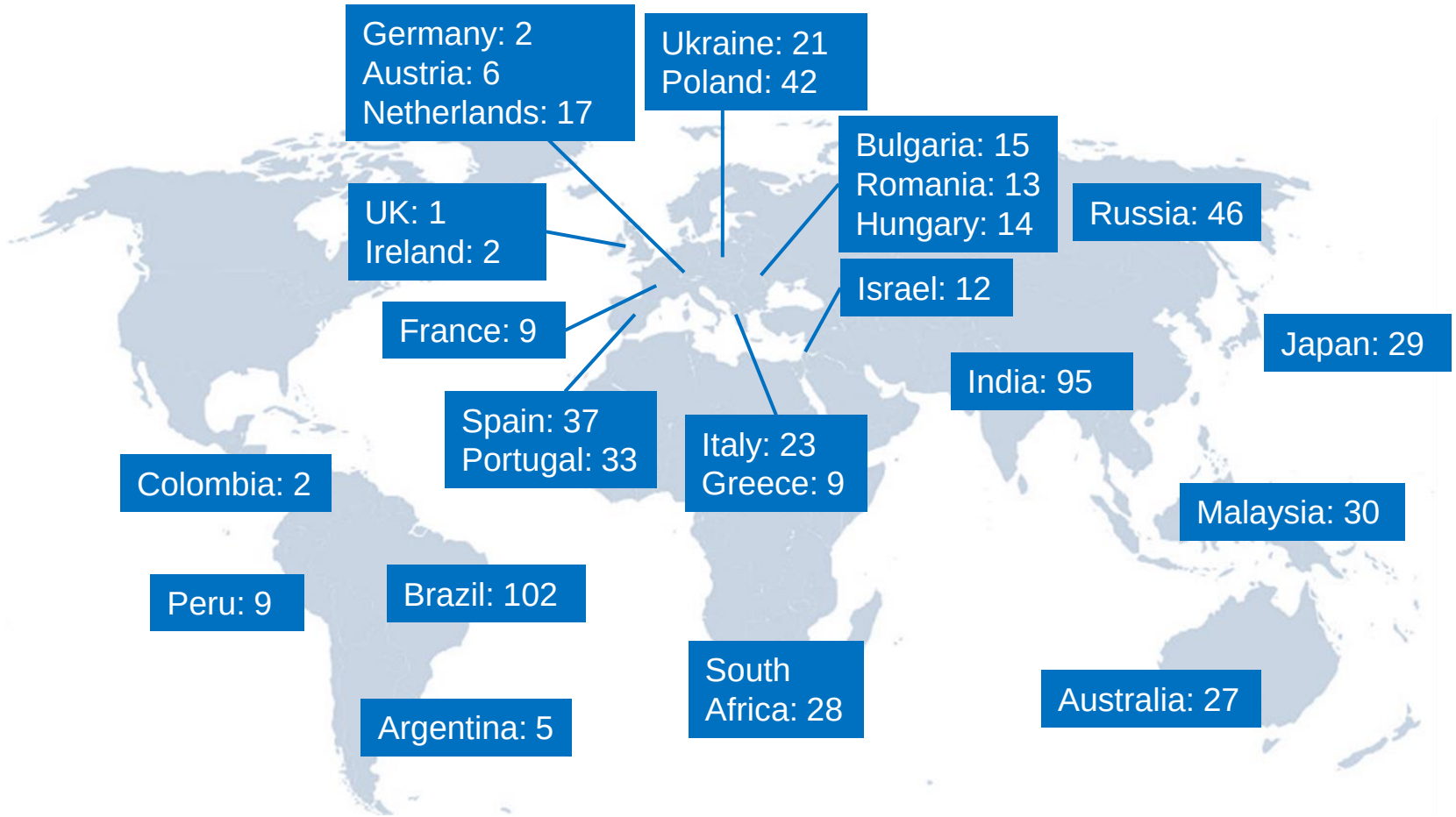
(GP13-301): 629 chorych, w 22 krajach



Jurczak et al, ESMO 2017, Lancet Hematol 2017

ASSIST-FL: prospektywne, randomizowane badanie fazy III

N=629

- ≥18 years of age
- Treatment-naïve, advanced-stage, CD20-positive, stage III/IV FL (Ann Arbor classification)
- WHO histologic grade 1, 2 or 3a FL
- At least one measurable lesion
- ECOG performance status 0–2

Screening ≤28 days

R 1:1

Stratification: FLIPI risk group and geographical region

GP2013
375 mg/m^2 + CVP (n=312‡)

GP2013 375 mg/m^2
every 3 months*

Reference rituximab
375 mg/m^2 + CVP (n=315)

Reference rituximab
375 mg/m^2 every 3 months*

Combination treatment period

24 weeks (8 cycles)

Maintenance period (responders only)

2 years

‡2 patients were mis-randomized;
*Except in Italy, where maintenance therapy was administered every 2 months
CVP, cyclophosphamide, vincristine, prednisone; ECOG, Eastern Cooperative Oncology Group; FL, follicular lymphoma; FLIPI, Follicular Lymphoma International Prognostic Index; WHO, World Health Organization

Jurczak et al, ESMO 2017, Lancet Hematol 2017

ASSIST-FL
Clinical Trial Assessing the Efficacy and Safety of a Rituximab Biosimilar Treatment

Cele badania

Efficacy

- **Efficacy assessments:**
  - **primary endpoint:**
    - **Overall response rate (ORR)**
  - **Secondary endpoints:**
    - Complete response (CR)
    - Partial response (PR)
    - Progression free survival (PFS)
    - Overall survival (OS)

Safety

(secondary endpoints)

- **Safety assessments:** AEs, SAEs, with their severity and relationship to study drug, pregnancies, monitoring of hematology, blood chemistry and urine, vital signs, performance status, ECG, and body weight
- **Immunogenicity:** ADA formation

PK/PD

(secondary endpoints)

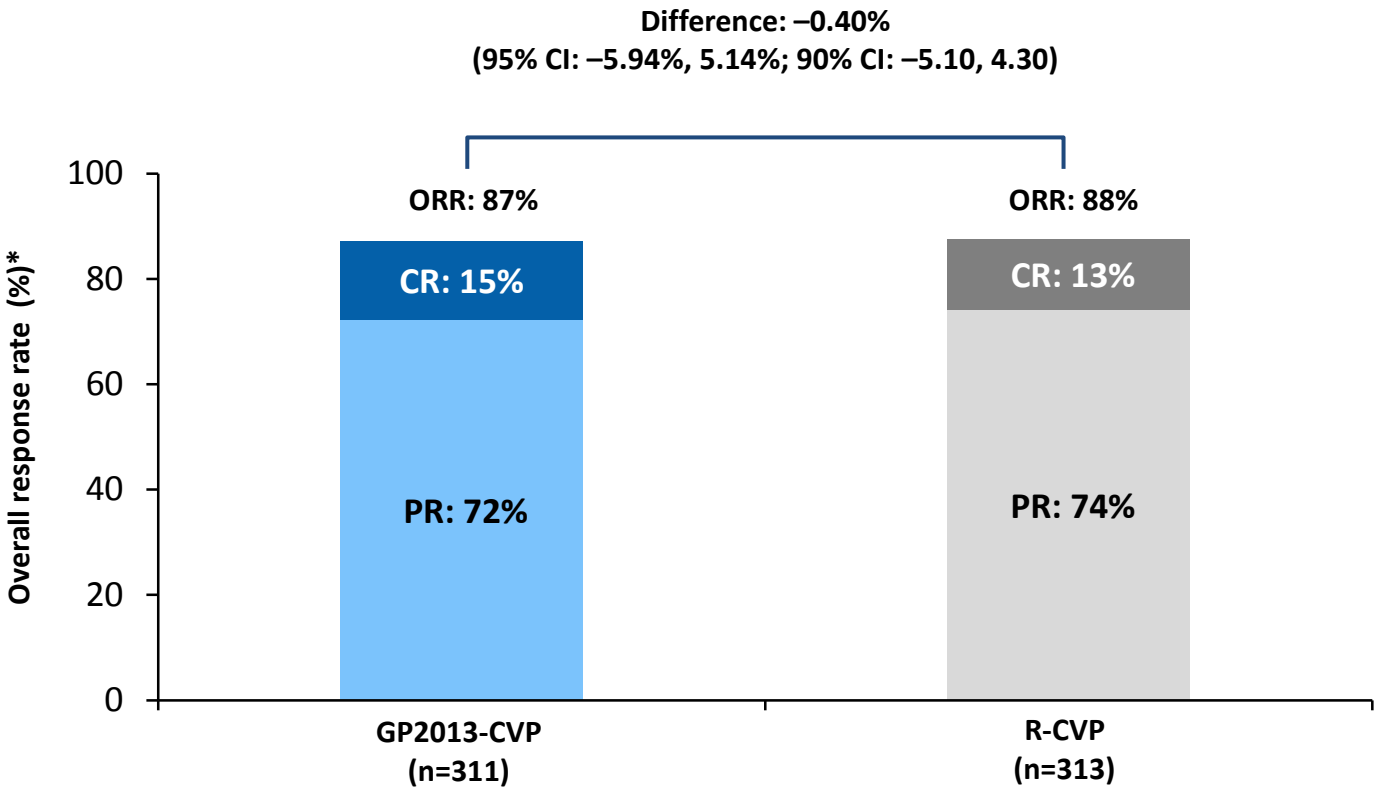
- **PK:** C_{max}, C_{trough}, $AUC_{(0-t)}$, and AUC_{all}
- **PD:** peripheral CD19+ B cell counts (absolute and relative to baseline) and $AUEC_{(0-21)}$ in Cycle 1

CT-P10 3.3 AFL
PK being the primary target, ***ORR the secondary target***

Jurczak W, et al. Abstract 1809 presented at the 58th ASH San Diego, USA, 3–6 December 2016.
Coiffier B ,et al Abstract 1807presented at the 58th ASH, San Diego, USA, 3–6 December 2016.

ASSIST-FL
Clinical Trial Assessing the Efficacy and Safety of a Rituximab Biosimilar Treatment

ORR - cel pierwszorzędowy



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; CVP, cyclophosphamide, vincristine, prednisone; PR, partial response; ORR, overall response rate; R-CVP, rituximab-CVP

Jurczak et al, ESMO 2017, Lancet Hematol 2017

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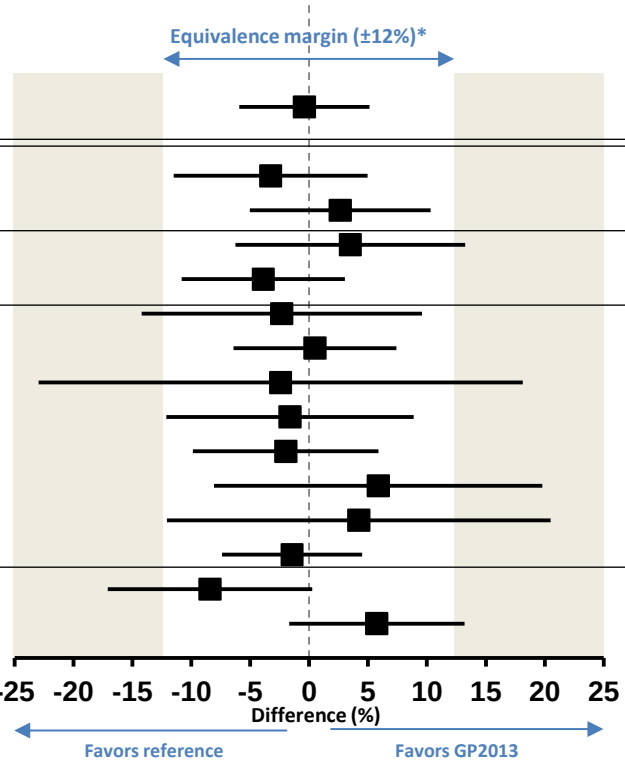
Clinical Trial Assessing the Efficacy and Safety of a Rituximab Biosimilar Treatment

Analiza ORR w podgrupach chorych

Population	GP2013-CVP n (%)	R-CVP n (%)	Difference in ORR, % (95% CI)
Overall	271 (87.1)	274 (87.5)	–0.4 (–5.94, 5.14)
Age <60 years	136 (83.4)	150 (86.7)	–3.27 (–11.49, 4.95)
Age ≥60 years	135 (91.2)	124 (88.6)	2.64 (–5.02, 10.31)
Male	113 (86.3)	120 (82.8)	3.50 (–5.74, 12.75)
Female	158 (87.8)	154 (91.7)	–3.89 (–10.82, 3.04)
Asian	61 (85.9)	75 (88.2)	–2.32 (–14.21, 9.57)
Caucasian	186 (87.3)	178 (86.8)	0.49 (–6.42, 7.41)
Other	24 (88.9)	21 (91.3)	–2.42 (–22.97, 18.14)
Asia-Pacific	77 (87.5)	82 (89.1)	–1.63 (–12.13, 8.87)
Europe	143 (86.1)	141 (88.1)	–1.98 (–9.86, 5.90)
Latin America	51 (89.5)	51 (83.6)	5.87 (–8.07, 19.80)
Bulky disease – yes	38 (86.4)	46 (82.1)	4.22 (–12.07, 20.51)
Bulky disease – no	233 (87.3)	228 (88.7)	–1.45 (–7.40, 4.50)
FLIPI score 0–2	111 (82.8)	125 (91.2)	–8.41 (–17.09, 0.28)
FLIPI score 3–5	160 (90.4)	149 (84.7)	5.74 (–1.70, 13.17)



CVP, cyclophosphamide, vincristine, prednisone; FLIPI, Follicular Lymphoma International Prognostic Index; ORR, overall response rate; R-CVP, rituximab-CVP

*The predefined equivalence margin was powered only for the primary endpoint of overall response rate in the full population, and not for subgroup analyses

Jurczak et al, ESMO 2017, Lancet Hematol 2017

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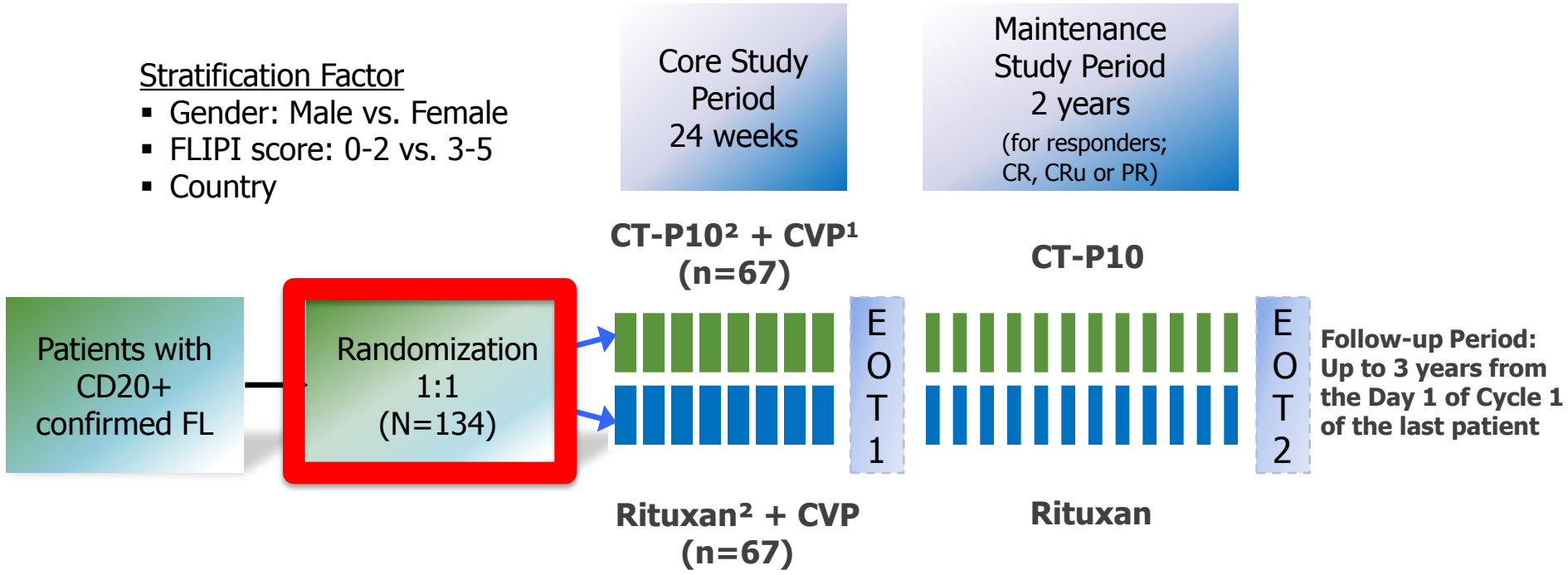
CT-P10 3.2 RA prospektywne, randomizowane badanie fazy III



1. CVP: Cyclophosphamide 750 mg/m², Vincristine 1.4 mg/m² [max 2mg], Prednisone or prednisolone 40 mg/m²
2. Rituximab: 375 mg/m² (Core study: 3-weekly, Maintenance study: every 2 months)

Abbreviations: FL, Follicular Lymphoma; EOT, End of Treatment; FLIPI, Follicular Lymphoma International Prognostic Index

Coiffier B ,et al ASH 2017, Lancet Hematology 2017

CT-P10 3.2 RA

ORR – cel II rzędowy

ITT Population			
Response	**CT-P10 (N=70)**	**Rituxan (N=70)**	**Difference [lower bound of 95% CI]**
ORR[1]	**67 (95.7%)**	**63 (90.0%)**	**5.7% [-3.41%]**
CR	21 (30.0%)	15 (21.4%)	-
CRu	6 (8.6%)	8 (11.4%)	-
PR	40 (57.1%)	40 (57.1%)	-

The difference between the groups lies on the positive side of -7%.
lower bound of 95% CI of differences lies on the positive side of -7%.

Coiffier B ,et al ASH 2017, Lancet Hematology 2017

ASSIST-FL
Clinical Trial Assessing the Efficacy and Safety of a Rituximab Biosimilar Treatment

CT-P10 3.2 RA

: Podsumowanie

1. **ORR** with GP2013 and CT-P10 equivalent to reference rituximab
2. **PK (C_{max})** of GP2013 and CT-P10 equivalent to reference rituximab
3. Medians not yet reached for PFS and OS
4. **PD (B-cell depletion)** with GP2013 and CT-P10 equivalent to reference rituximab
5. **No clinical meaningful differences** between GP2013 or CT-P10 and reference rituximab in safety, tolerability or immunogenicity
6. **Registered by EMA**

Jurczak et al, ESMO 2017, Lancet Hematol 2017
Coiffier B ,et al ASH 2017, Lancet Hematology 2017

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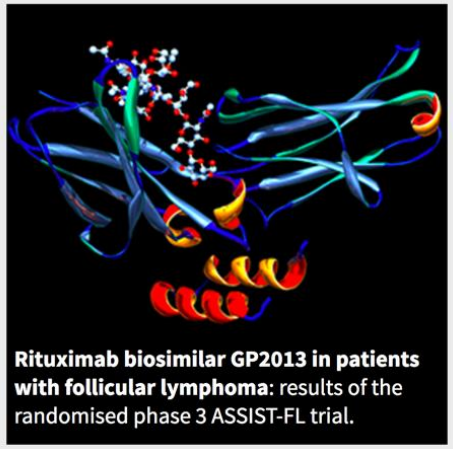
17 lipca 2017 był ważną datą dla rozwoju biosymilarów

Editor's Choice



Research on Biosimilars: pivotal trials and principles
Wojciech Jurczak, Arnold G Vulto, Jutta Amersdorffer, Won S Kim, Bertrand Coiffier
The Lancet Haematology, Vol. 4, No. 9, e409–e410 Published: September, 2017

Rituximab biosimilar and reference rituximab in patients with previously untreated advanced follicular lymphoma (ASSIST-FL): primary results from a confirmatory phase 3, double-blind, randomised, controlled study
Wojciech Jurczak, Ilídia Moreira, Govind Babu Kanakasetty, Eduardo Munhoz, Maria Asunción Echeveste, Pratyush Giri, and others
The Lancet Haematology, Vol. 4, No. 8, e350–e361Published: July 13, 2017

Rituximab biosimilars: introduction into clinical practice
Shinichi Makita, Kensei Tobinai
The Lancet Haematology, Vol. 4, No. 8, e342–e343 Published: July 13, 2017

Efficacy, pharmacokinetics, and safety of the biosimilar CT-P10 compared with rituximab in patients with previously untreated advanced-stage follicular lymphoma: a randomised, double-blind, parallel-group, non-inferiority phase 3 trial
Won Seog Kim, Christian Buske, Michinori Ogura, **Wojciech Jurczak**, Juan-Manuel Sancho, Edvard Zhavrid, and others
The Lancet Haematology, Vol. 4, No. 8, e362–e373 Published: July 13, 2017

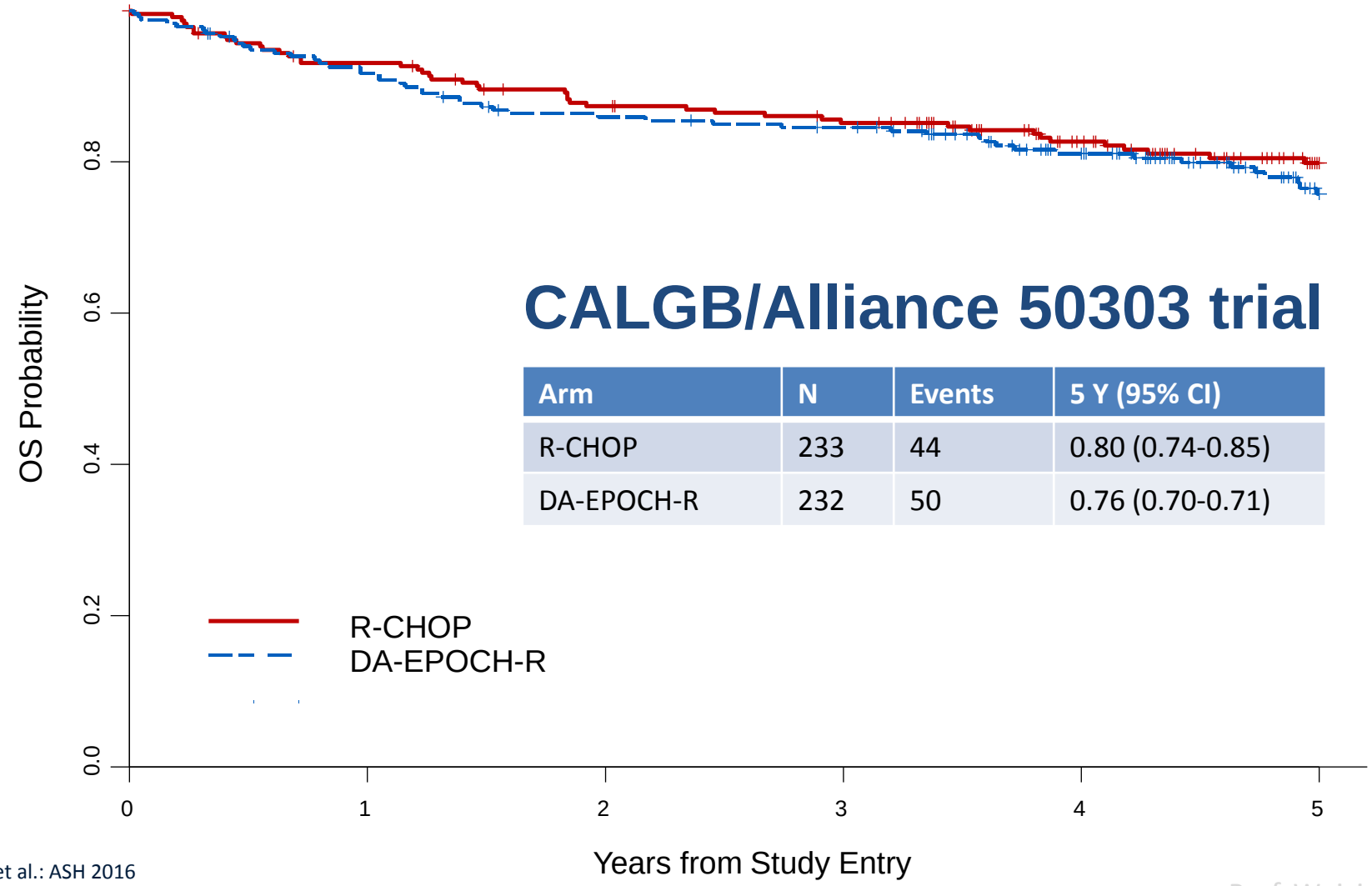
Rytuksymab jest niezaprzeczalnym standardem leczenia I linii chłoniaków B-komórkowych

Lymphoma Subtype	I line induction	I line maintenance
Aggresive Lymphomas	*yes*	*No*
MCL	*yes*	*yes*
Indolent lymphomas	*yes*	*?*
CLL	*yes*	*yes*

With new MoAb and small particles, Rituximab role in relapsing / refractory NHL may be disputable

Rytuksymab jest "*A Great Equaliser*" dla różnych schematów chemioterapii

CHOP
CHOP-14
CHOEP
DA-EPOCH



CALGB/Alliance 50303 trial

Arm	N	Events	5 Y (95% CI)
R-CHOP	233	44	0.80 (0.74-0.85)
DA-EPOCH-R	232	50	0.76 (0.70-0.71)

Wilson WH, et al.: ASH 2016

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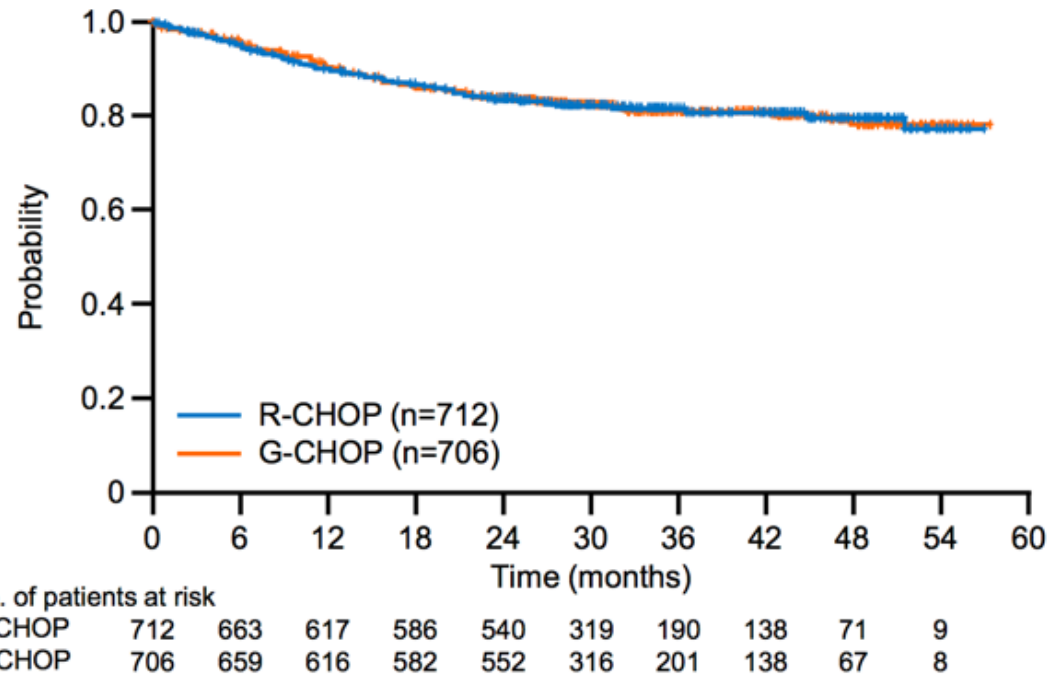
Chemioterapia może być *"A Great Equaliser"* dla różnych przeciwciał monoklonalnych

Rituximab
Obinutuzumab
MOR 208 ?

OS in previously untreated DLBCL patients (GALLIUM trial)

Kaplan-Meier plot of OS by treatment arm



	R-CHOP, n=712	*G-CHOP, n=706*
Pts with event, n (%)	126 (17.7)	126 (17.8)
1-yr OS, %	89.9	90.7
2-yr OS, %	83.7	83.9
3-yr OS, %	81.4	81.2
HR (95% CI), p-value*	1.00 (0.78, 1.28), p=0.9982	

Median follow-up: 29 months

Vitolo et al.: 2016

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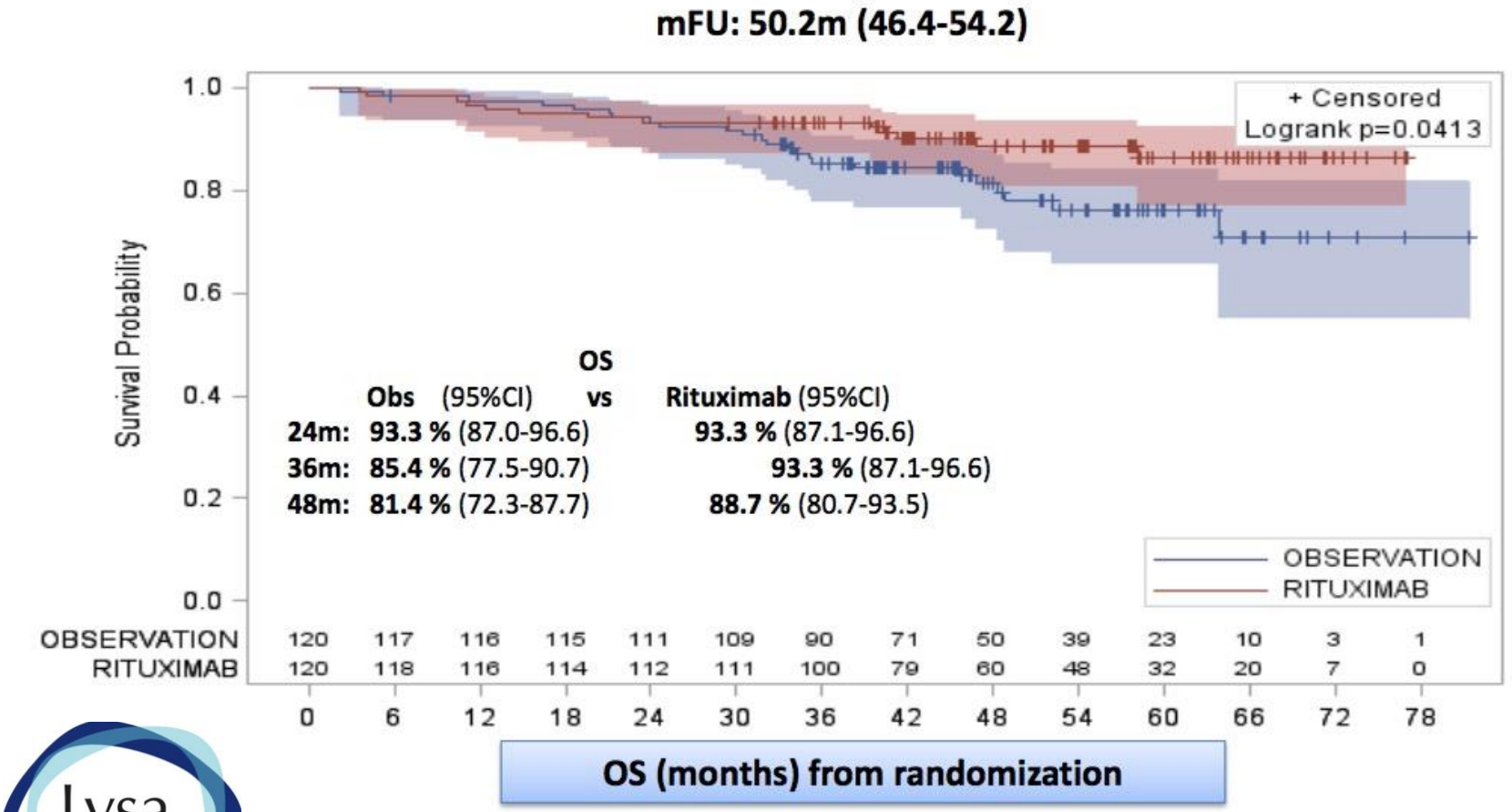
Rytuksymab jest standardem w leczeniu indukującym i podtrzymującym u chorych z MCL *(‡)*

	Young Patients (<65)	Elderly Patients (>65)	"Compromised"
1st Line	Dose-intensified (R-CHOP + R-high dose Ara-C ASCT) + **Rituximab Maintenance**	Conventional Immunochemotherapy (eg, R-CHOP, VR-CAP, BR) + **Rituximab maintenance**	Best supportive care R-Chlorambucil, R-CVP, BR (dose reduced) + **Rituximab maintenance**
1st Relapse	Immunochemotherapy (eg, R-BAC, BR) or **targeted approaches** Discuss: Rituximab maintenance Allo-SCT	Immunochemotherapy (eg, R-BAC, BR) or **targeted approaches** Discuss: Rituximab maintenance Radioimmunotherapy Autologous SCT	Immunochemotherapy (eg, BR) or **targeted approaches**
Higher Relapse	**Targeted approaches** (Ibrutinib, Lenalidomide, Temsirolimus, Bortezomib (preferably in Combinations); Alternatively – repeat previous therapy if in long remissions		

Dreyling M et al. *ESMO, MCL guidelines.* 2017. In press.

MCL – wyniki randomizowanego badania LyMa *(≠)*



LE GOUILL et al.: ASH 2013/2014/2015/2016

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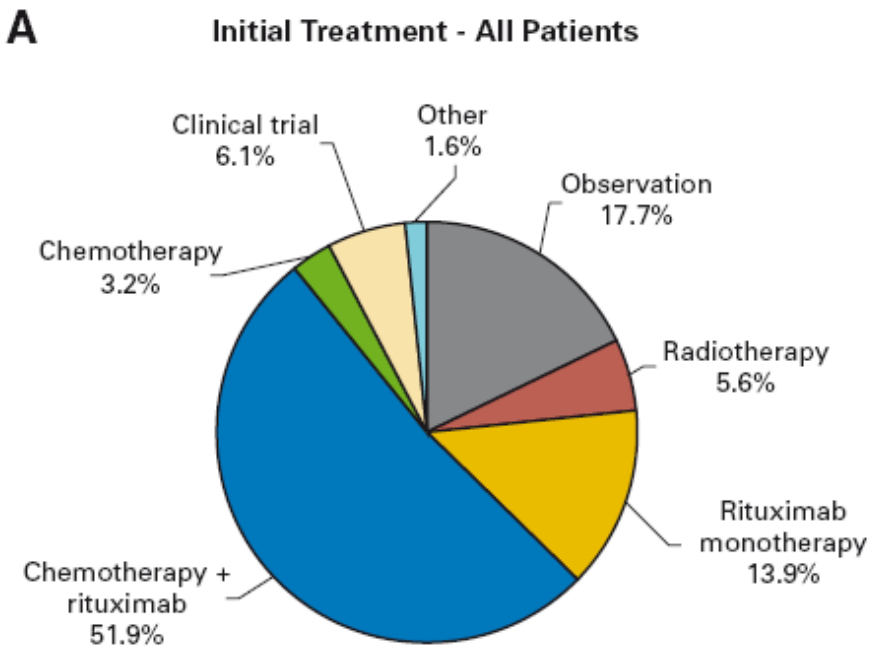
Chłoniaki Indolentne

W ciągu całego życia chorych poddaje się 5-8 liniom leczenia...

Chemioterapii bez przciwciał monoklonalnych
nie stosuje się już w praktycze klinicznej

USA clinical practice – SEER data
FL, N= 2728, years 2004-2007

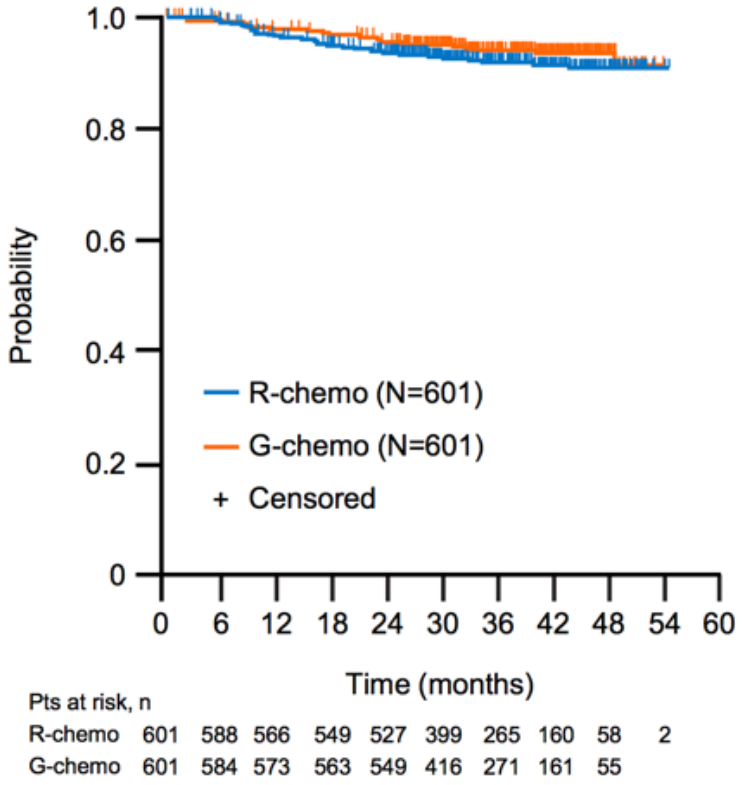


Friedberg, et al.: JCO 2009

Standardem są różne schematy immuno-chemioterapii

Chemioterapia może być *"A Great Equaliser"* dla różnych przeciwciał monoklonalnych

OS in previously untreated FL patients (GALLIUM trial)



	R-chemo, n=601	*G-chemo, n=601*
Pts with event, n (%)	46 (7.7)	35 (5.8)
3-yr OS, % (95% CI)	92.1 (89.5, 94.1)	94.0 (91.6, 95.7)
HR (95% CI), p-value*	0.75 (0.49, 1.17), p=0.21	

Median follow-up: 34.5 months

Marcus et al.: 2016

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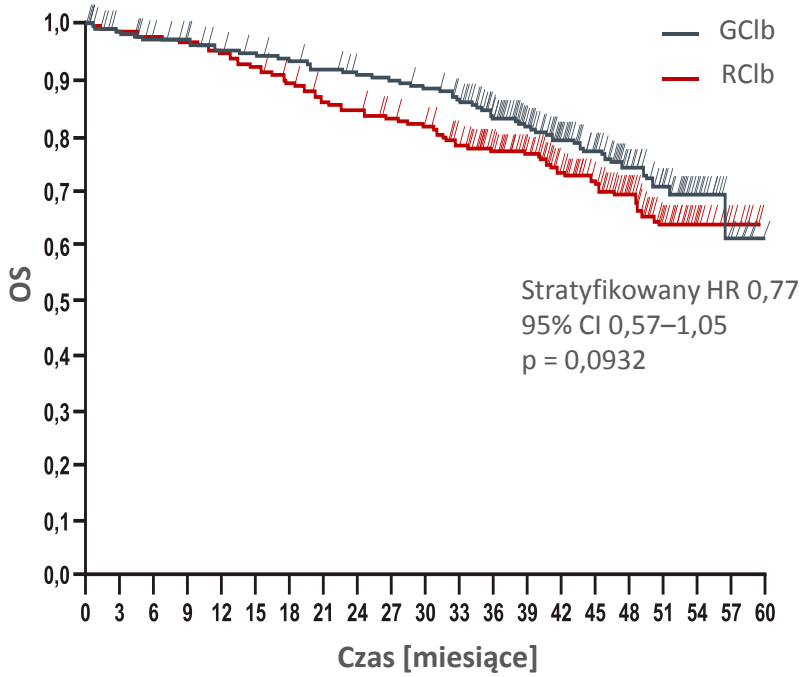
Chemioterapia może być *"A Great Equaliser"* dla różnych przeciwciał monoklonalnych

Rituximab
Obinutuzumab
MOR 208 ?

Unless it is chlorambucil ?

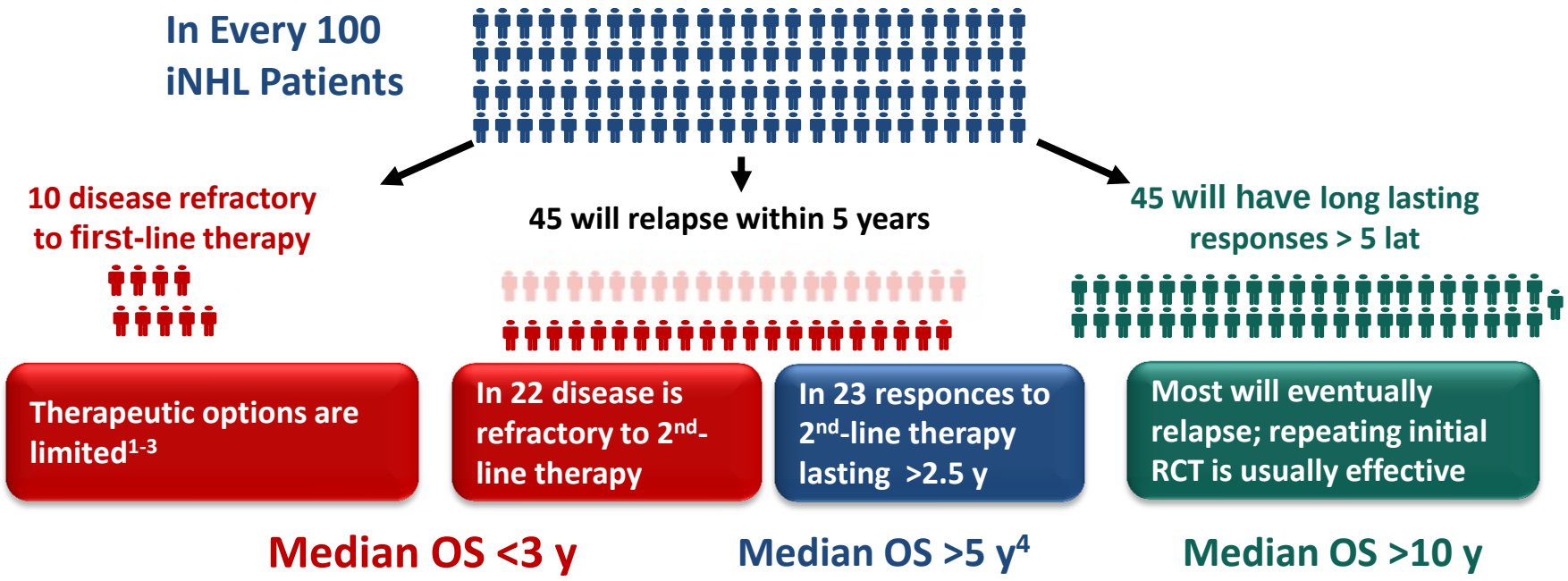
OS in previously untreated elderly CLL patients (CLL-11 trial)



	Clb Alone (n = 118)	RClb (n = 233)	O-Clb (n = 238)
ORR	32%	65%	78%
CR	0	7%	21%
Median PFS	11 months	16 months	27 months

Geode et al.: 2014

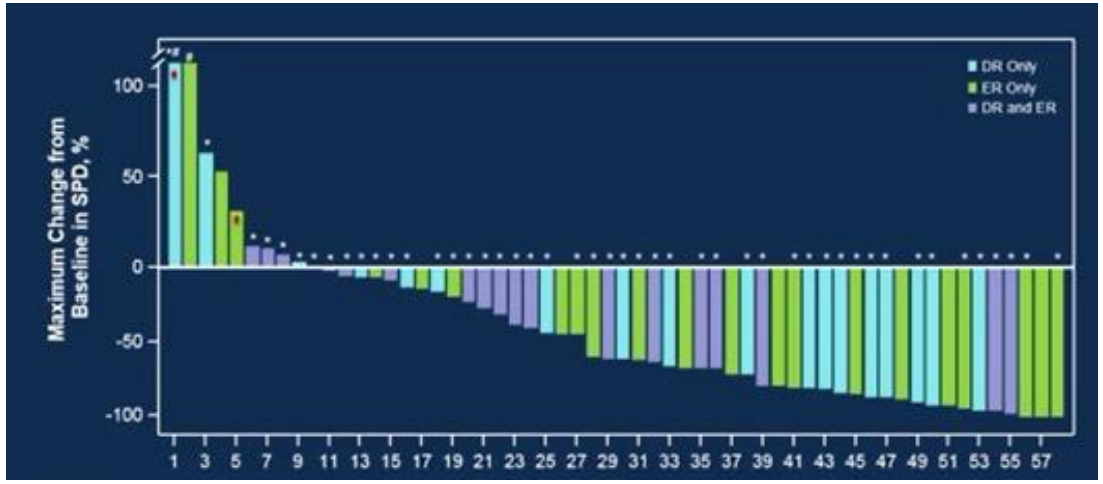
Część z chorych pozostaje oporna na immunochemioterapię

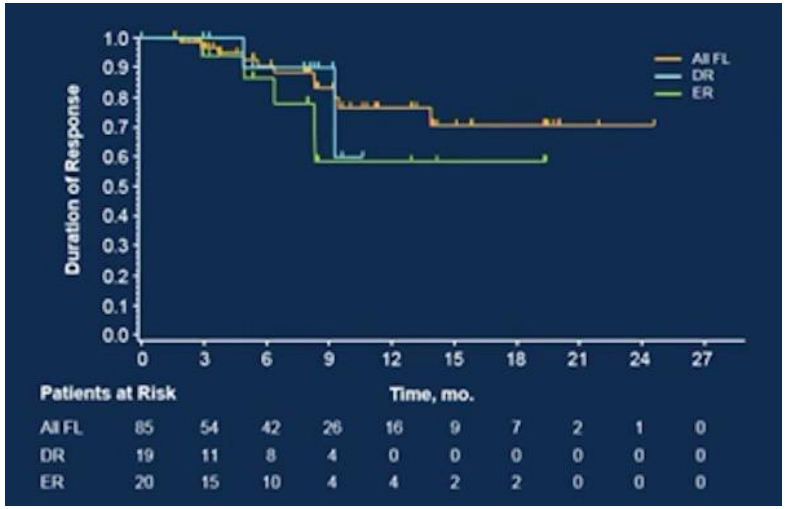


1. Kahl B et al. *Cancer.* 2010;116:106-114; 2. Horning SJ et al. *J Clin Oncol.* 2005;23:712-719;
3. Czuczman MS et al.:*Blood.* 2012;119:3698-3704; 4. Van Oers MH et al. *J Clin Oncol*. 2010;28:2853-2858.

Lenalidomide + Rituximab u chorych z iNHL ze wznową/ opornością *(‡)*

MAGNIGY Phase 3 Trial: Lenalidomide Plus Rituximab (R^2) Followed by Lenalidomide Versus Rituximab Maintenance for Relapsed/Refractory Follicular, Marginal Zone or Mantle-Cell Lymphoma (N = 117)





Andorsky DJ et al. ASCO 2017. Abstract 7502.

Lenalidomid z przeciwciałamia anty CD20 w nawrotowych/opornych DLBCL *(≠)*

Single-agent lenalidomide (Phase II/III)[1]

No. of patients	N=51
ORR	28%
CR	10%
Median PFS, weeks	13.6

Lenalidomide **+ rituximab** (Phase II)[2]

No. of patients	N=32
ORR	28%
CR	22%
Median PFS, months	3.7

Lenalidomide **+ obinutuzumab** (Phase II)[3]

No. of patients	N=71
ORR	45%
CR	16%
Median PFS, months	4.1

Lenalidomide **+ MOR208** (Phase II; preliminary data)[4]

No. of patients	N=34
ORR	56%
CR	32%
Median PFS, months	N/A

1. Czuczman MS, et al. Clin Cancer Res 2017; doi: 10.1158/1078-0432.CCR-16-2818; **2.** Wang M, et al. Leukemia 2013;27:1902–1909;
3. Morschhauser F, et al. ASH 2016; **4.** Maddocks KJ, et al. ASCO 2017.

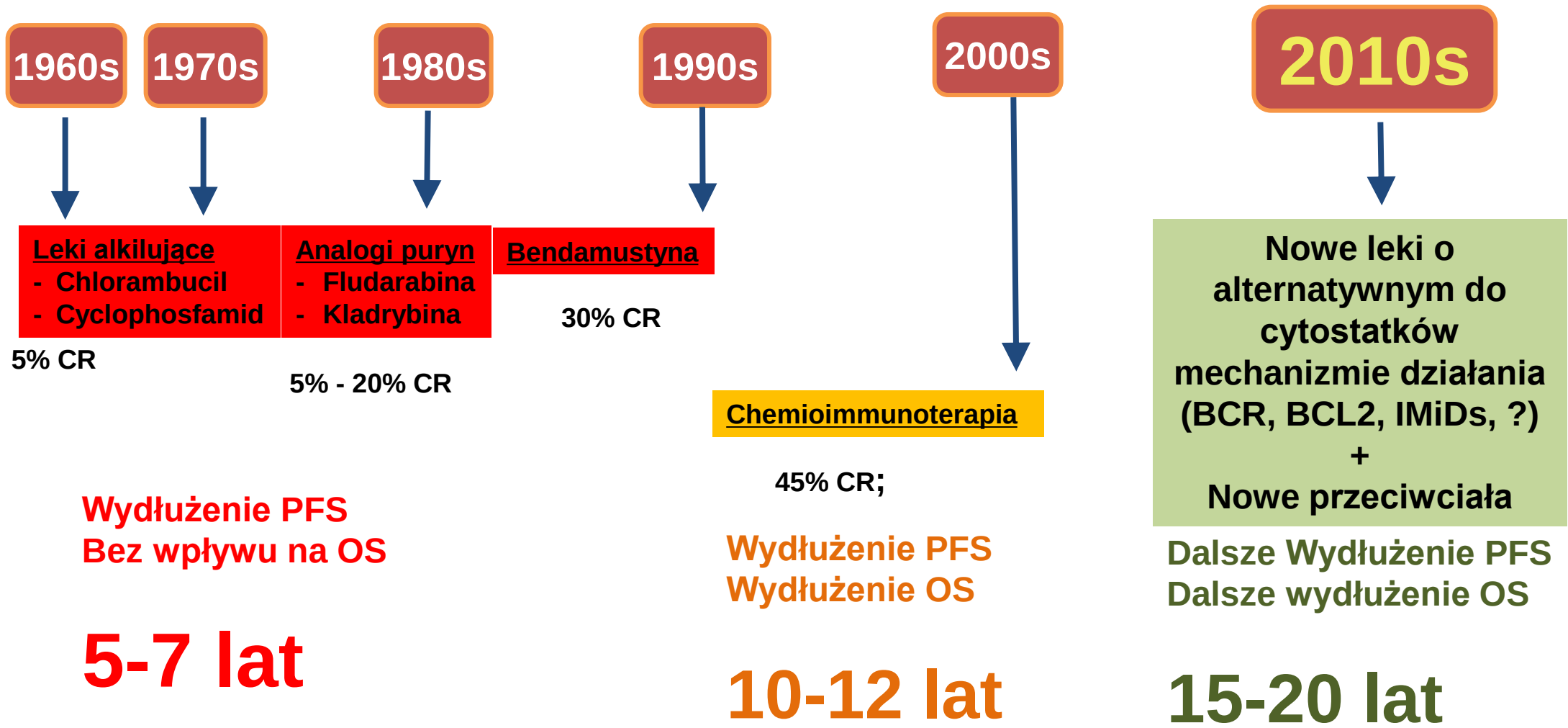
Podsumowanie :

- **Rituximab biosimilars** are good quality MoAb with a safety and efficacy profile identical to their originator
- Their similarity to Rituximab was determined by extensive pre-clinical analyses, and finally confirmed by clinical trials, with **nearly 2000 participating patients**
- **Subcutaneous Rituximab** **is the only** competitor to Rituximab biosimilars in the I line B cell NHL therapy
- **Chlorambucil + Obinutuzumab** **is the only** protocol, with novel anti CD20 MoAb, better to Rituximab based I line immuno-chemotherapy regimens

Biosymilary to duże oszczędności dla NFZ i budżetu Państwa

”Bio-similar for Bio-better”

CLL – najczęstszy chłoniak w Polsce - długość życia chorych



Dostępność w Polsce leków zarejestrowanych przez EMA I FDA w leczeniu chłoniaków

Leki dostępne **Leki częściowo dostępne** **Leki Niedostępne**

Inhibitory knazy Brutona
(Ibrutinib)

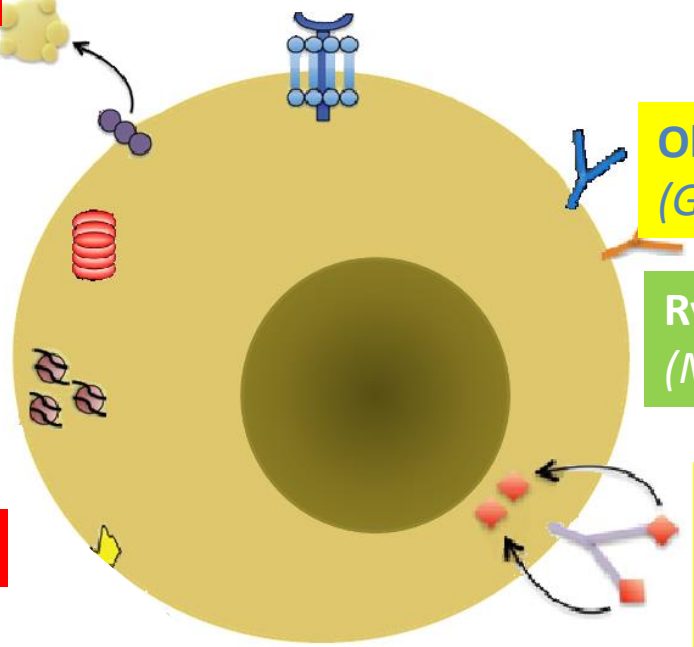
Inhibitory kinazy IP3
(Idelalisib)

Inhibitory bcl-2
(Venetoclax)

Belinostat

Inhibitory Proteasomu
(Bortezomib)

Leki Immunomodulujące
(Lenalidomid)
(Nivolumab)



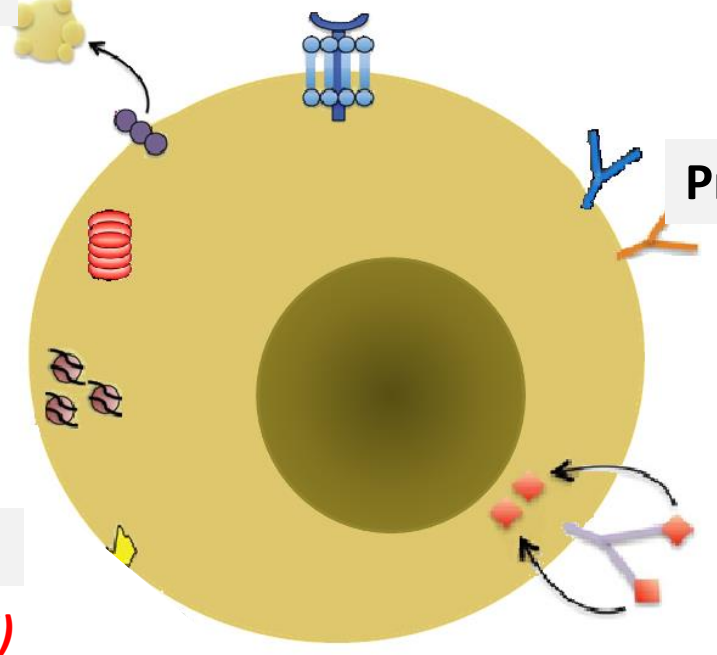
Obinutuzumab
(Gazyvaro)

Rytuksymab
(Mabthera)

Biosymilary Rituximabu
(Truxima, Rixathon)

Brentuximab Vedotin
(Adcetris)

Leki zarejestrowane przy współudziale zespołu Kl.Hematologii UJCM



Inhibitory knazy Brutona
(Ibrutinib)

Inhibitory kinazy IP3
(Idelalisib)

Inhibitory bcl-2
(Venetoclax)

Belinostat

Leki Immunomodulujące
(Lenalidomid)

Przeciwciała monoklonalne

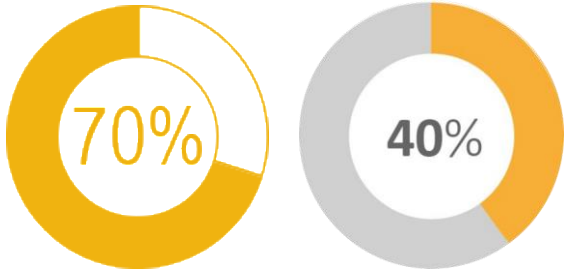
Biosymilary
Rituximabu
(Truxima, Rixathon)

Brentuximab
Vedotin
(Adcetris)

Chłoniaki o dużej dynamice – duża szansa na całkowite wyleczenie choroby

Chłoniaki o niepewnym rokowaniu
- Chłoniak z komórek płaszcza
- Szpiczak mnogi
- Chłoniaki z komórek T

Chłoniaki agresywne
- Chłoniak rozlany z dużych komórek B
- Chłoniak limfoblastyczny



Chłoniaki indolentne
- Przewlekła białaczka limfatyczna
- Chłoniak grudkowy
- Chłoniak strefy brzeżnej, MALT

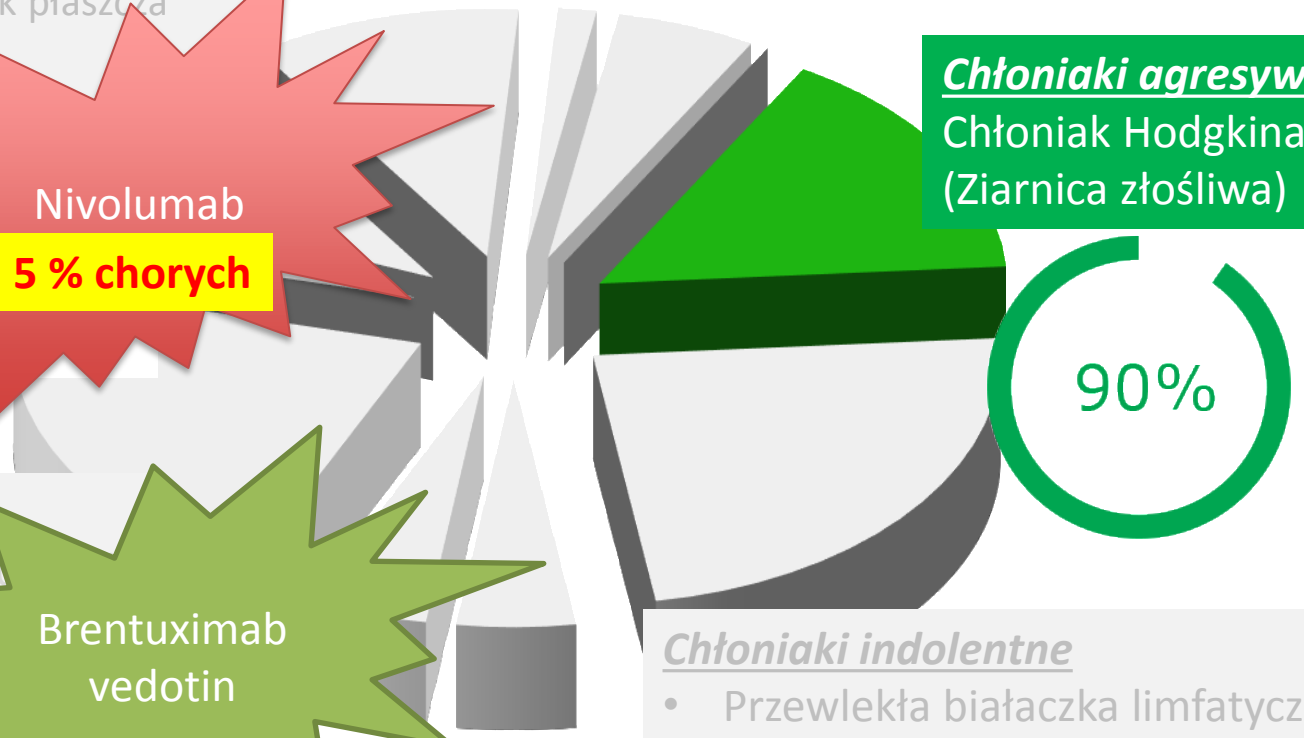
Chłoniaki o dużej dynamice – duża szansa na całkowite wyleczenie choroby

Chłoniaki o niepewnym rokowaniu
- Chłoniak z komórek płaszcza
- Szpiczak mnogi
- Chłoniaki z komór

Nivolumab
5 % chorych

Chłoniaki agresywne
- Chłoniak rozlany z komórek B
- Chłoniak li

Brentuximab vedotin



Chłoniaki agresywne
Chłoniak Hodgkina
(Ziarnica złośliwa)

Chłoniaki indolentne
- Przewlekła białaczka limfatyczna
- Chłoniak grudkowy
- Chłoniak strefy brzeżnej, MALT

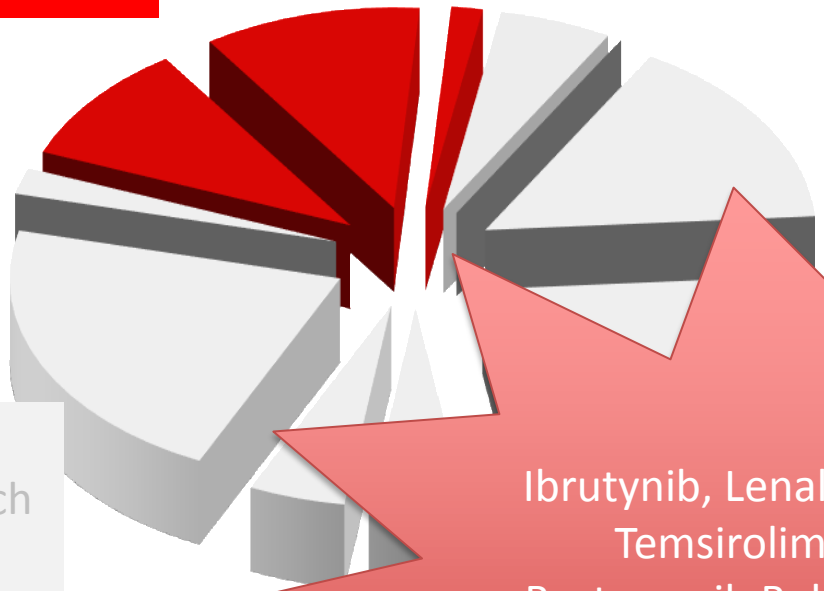
Chłoniaki indolentne (ok 4 000 / rok) – kolejne wznowy są naturalnym przebiegiem choroby

Wg. Rejestru Patologów PLRG

Chłoniaki o niepewnym rokowaniu – szybkie pojawienie się oporności na chemioterapię

Chłoniaki o niepewnym rokowaniu
- Chłoniak z komórek płaszcza
- Chłoniaki z komórek T

Chłoniaki agresywne
Chłoniak Hodgkina
(Ziarnica złośliwa)



Chłoniaki agresywne
- Chłoniak rozlany z dużych komórek B
- Chłoniak limfoblastyczny

Ibrutynib, Lenalidomid,
Temsirolimus,
Bortezomib Belinost, …

90% chorych

…yczna

…efy b… …żnej, MALT

Badania Kliniczne w Polsce

- Szansa na skuteczne leczenie w przypadkach opornych
- Coraz częściej jedyna możliwość leczenia zgodne z europejskim standardem
- Inne niż chemioterapia skutki działań niepożądanych
- Znaczne oszczędności dla NFZ i budżetu Państwa

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