

悪性リンパ腫

治療の変遷

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発表者のCOI開示

演題発表内容に関連し、発表者に開示すべき
COI関係にある企業などはありません。

病理分類の変遷

ホジキンリンパ腫 (ホジキン病) : リンパ腫の5-10%

1832年 Thomas Hodgkinにより提唱

1865年 Hodgkin病の初めての報告

1947年 Jackson and Parker分類

1966年 Rye分類 (LP, NS, MC, LD)

1994年 REAL分類 (NLPHLとclassical HLに分けられる)

2001年 WHO分類 (内容は変更なし)

非ホジキンリンパ腫

1900年頃 R-S細胞の有無でホジキン病と区別されるようになる。

1966年 NHLとして独立概念となる。

Rappaport分類 (米国, 増殖patternを重視, 濾胞性, びまん性, 組織球性, リンパ球性, 混合型...)

1970年 Kiel分類 (欧州, 細胞形態を重視, リンパ球型, リンパ形質細胞, 濾胞中心芽球型, 免疫芽球型...)

1978年 LSG分類 (日本のみ, 濾胞性 vs びまん性, 細胞の大きさ)

1982年 Working Formulation分類 (米国, 増殖pattern + 形態, B 14, T/NK 6)

1988年 up-date Kiel分類 (欧州, 細胞形態 B 13, T/NK 11)

1994年 REAL分類 (B 12, T/NK 11)

2023年 WHO分類改定第5版 (B 77?, T/NK 39?)

2001年 WHO分類第3版

2008年 WHO分類第4版

2017年 WHO分類改定第4版

(B 20, T/NK 17)

(B 44, T/NK 23)

(B 67, T/NK 35)

REAL分類

Table 1. List of Lymphoid Neoplasms Recognized by the International Lymphoma Study Group

-
- B-Cell Neoplasms
- I. Precursor B-cell neoplasm: Precursor B-lymphoblastic leukemia/lymphoma
 - II. Peripheral B-cell neoplasms
 1. B-cell chronic lymphocytic leukemia/prolymphocytic leukemia/small lymphocytic lymphoma
 2. Lymphoplasmacytoid lymphoma/immunocytoma
 3. Mantle cell lymphoma
 4. Follicle center lymphoma, follicular
Provisional cytologic grades: I (small cell), II (mixed small and large cell), III (large cell)
Provisional subtype: diffuse, predominantly small cell type
 5. Marginal zone B-cell lymphoma
Extranodal (MALT-type +/- monocytoid B cells)
Provisional subtype: Nodal (+/- monocytoid B cells)
 6. Provisional entity: Splenic marginal zone lymphoma (+/- villous lymphocytes)
 7. Hairy cell leukemia
 8. Plasmacytoma/plasma cell myeloma
 9. Diffuse Large B-cell lymphoma*
Subtype: Primary mediastinal (thymic) B-cell lymphoma
 10. Burkitt's lymphoma
 11. Provisional entity: High-grade B-cell lymphoma, Burkitt-like*

T-Cell and Putative NK-Cell Neoplasms

- I. Precursor T-cell neoplasm: Precursor T-lymphoblastic lymphoma/leukemia
- II. Peripheral T-cell and NK-cell neoplasms
 1. T-cell chronic lymphocytic leukemia/prolymphocytic leukemia
 2. Large granular lymphocyte leukemia (LGL)
T-cell type
NK-cell type
 3. Mycosis fungoides/Sezary syndrome
 4. Peripheral T-cell lymphomas, unspecified*
Provisional cytologic categories: medium-sized cell, mixed medium and large cell, large cell, lymphoepithelioid cell
Provisional subtype: Hepatosplenic $\gamma\delta$ T-cell lymphoma
Provisional subtype: Subcutaneous panniculitic T-cell lymphoma
 5. Angioimmunoblastic T-cell lymphoma (AILD)
 6. Angiocentric lymphoma
 7. Intestinal T-cell lymphoma (+/- enteropathy associated)
 8. Adult T-cell lymphoma/leukemia (ATL/L)
 9. Anaplastic large cell lymphoma (ALCL), CD30⁺, T- and null-cell types
 10. Provisional entity: Anaplastic large-cell lymphoma, Hodgkin's-like

Hodgkin's Disease

- I. Lymphocyte predominance
- II. Nodular sclerosis
- III. Mixed cellularity
- IV. Lymphocyte depletion
- VI. Provisional entity: Lymphocyte-rich classical HD

* These categories are thought likely to include more than one disease entity.

WHO分類第5版 (案)

WHO Classification, 5th edition
<i>Tumour-like lesions with B-cell predominance</i>
Reactive B-cell-rich lymphoid proliferations that can mimic lymphoma
IgG4-related disease
Unicentric Castleman disease
Idiopathic multicentric Castlemans disease
KSHV/HHV8-associated multicentric Castleman disease
Precursor B-cell neoplasms
<i>B-cell lymphoblastic leukaemias/lymphomas</i>
B-lymphoblastic leukaemia/lymphoma, NOS
B-lymphoblastic leukaemia/lymphoma with high hyperdiploidy
B-lymphoblastic leukaemia/lymphoma with hypodiploidy
B-lymphoblastic leukaemia/lymphoma with iAMP21
B-lymphoblastic leukaemia/lymphoma with <i>BCR::ABL1</i> fusion
B-lymphoblastic leukaemia/lymphoma with <i>BCR::ABL1</i> -like features
B-lymphoblastic leukaemia/lymphoma with <i>KMT2A</i> rearrangement
B-lymphoblastic leukaemia/lymphoma with <i>ETV6::RUNX1</i> fusion
B-lymphoblastic leukaemia/lymphoma with <i>ETV6::RUNX1</i> -like features
B-lymphoblastic leukaemia/lymphoma with <i>TCF3::PBX1</i> fusion
B-lymphoblastic leukaemia/lymphoma with <i>IGH::IL3</i> fusion
B-lymphoblastic leukaemia/lymphoma with <i>TCF3::HLF</i> fusion
B-lymphoblastic leukaemia/lymphoma with other defined genetic abnormalities
Mature B-cell neoplasms
<i>Pre-neoplastic and neoplastic small lymphocytic proliferations</i>
Monoclonal B-cell lymphocytosis
Chronic lymphocytic leukaemia/small lymphocytic lymphoma (Entity deleted)
<i>Splenic B-cell lymphomas and leukaemias</i>
Hairy cell leukaemia
Splenic marginal zone lymphoma
Splenic diffuse red pulp small B-cell lymphoma
Splenic B-cell lymphoma/leukaemia with prominent nucleoli
<i>Lymphoplasmacytic lymphoma</i>
Lymphoplasmacytic lymphoma
<i>Marginal zone lymphoma</i>
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue
Primary cutaneous marginal zone lymphoma
Nodal marginal zone lymphoma
Paediatric marginal zone lymphoma
<i>Follicular lymphoma</i>
In situ follicular B-cell neoplasm
Follicular lymphoma
Paediatric-type follicular lymphoma
Duodenal-type follicular lymphoma

<i>Cutaneous follicle centre lymphoma</i>
Primary cutaneous follicle centre lymphoma
<i>Mantle cell lymphoma</i>
In situ mantle cell neoplasm
Mantle cell lymphoma
Leukaemic non-nodal mantle cell lymphoma
<i>Transformations of indolent B-cell lymphomas</i>
Transformations of indolent B-cell lymphomas
<i>Large B-cell lymphomas</i>
Diffuse large B-cell lymphoma, NOS
T-cell/histiocyte-rich large B-cell lymphoma
Diffuse large B-cell lymphoma/ high grade B-cell lymphoma with <i>MYC</i> and <i>BCL2</i> rearrangements
ALK-positive large B-cell lymphoma
Large B-cell lymphoma with <i>IRF4</i> rearrangement
High-grade B-cell lymphoma with 11q aberrations
Lymphomatoid granulomatosis
EBV-positive diffuse large B-cell lymphoma
Diffuse large B-cell lymphoma associated with chronic inflammation
Fibrin-associated large B-cell lymphoma
Fluid overload-associated large B-cell lymphoma
Plasmablastic lymphoma
Primary large B-cell lymphoma of immune-privileged sites
Primary cutaneous diffuse large B-cell lymphoma, leg type
Intravascular large B-cell lymphoma
Primary mediastinal large B-cell lymphoma
Mediastinal grey zone lymphoma
High-grade B-cell lymphoma, NOS
<i>Burkitt lymphoma</i>
Burkitt lymphoma
<i>KSHV/HHV8-associated B-cell lymphoid proliferations and lymphomas</i>
Primary effusion lymphoma
KSHV/HHV8-positive diffuse large B-cell lymphoma
KSHV/HHV8-positive germinotropic lymphoproliferative disorder
<i>Lymphoid proliferations and lymphomas associated with immune deficiency and dysregulation</i>
Hyperplasias arising in immune deficiency/dysregulation
Polymorphic lymphoproliferative disorders arising in immune deficiency/dysregulation
EBV-positive mucocutaneous ulcer
Lymphomas arising in immune deficiency / dysregulation
Inborn error of immunity-associated lymphoid proliferations and lymphomas

<i>Hodgkin lymphoma</i>
Classic Hodgkin lymphoma
Nodular lymphocyte predominant Hodgkin lymphoma
Plasma cell neoplasms and other diseases with paraproteins
<i>Monoclonal gammopathies</i>
Cold agglutinin disease
IgM monoclonal gammopathy of undetermined significance
Non-IgM monoclonal gammopathy of undetermined significance
Monoclonal gammopathy of renal significance
<i>Diseases with monoclonal immunoglobulin deposition</i>
Immunoglobulin-related (AL) amyloidosis
Monoclonal immunoglobulin deposition disease
<i>Heavy chain diseases</i>
Mu heavy chain disease
Gamma heavy chain disease
Alpha heavy chain disease
<i>Plasma cell neoplasms</i>
Plasmacytoma
Plasma cell myeloma
Plasma cell neoplasms with associated paraneoplastic syndrome
-POEMS syndrome
-TEMPI syndrome
-AESOP syndrome

Tumour-like lesions with T-cell predominance
Kikuchi-Fujimoto disease
Indolent T-lymphoblastic proliferation
Autoimmune lymphoproliferative syndrome
Precursor T-cell neoplasms
<i>T-lymphoblastic leukaemia/lymphoma</i>
T-lymphoblastic leukaemia / lymphoma, NOS
Early T-precursor lymphoblastic leukaemia / lymphoma (Entity deleted)
Mature T-cell and NK-cell neoplasms
<i>Mature T-cell and NK-cell leukaemias</i>
T-prolymphocytic leukaemia
T-large granular lymphocytic leukaemia
NK-large granular lymphocytic leukaemia
Adult T-cell leukaemia/lymphoma
Sezary syndrome
Aggressive NK-cell leukaemia
<i>Primary cutaneous T-cell lymphomas</i>
Primary cutaneous CD4-positive small or medium T-cell lymphoproliferative disorder
Primary cutaneous acral CD8-positive lymphoproliferative disorder
Mycosis fungoides
Primary cutaneous CD30-positive T-cell lymphoproliferative disorder: Lymphomatoid papulosis
Primary cutaneous CD30-positive T-cell lymphoproliferative disorder: Primary cutaneous anaplastic large cell lymphoma
Subcutaneous panniculitis-like T-cell lymphoma
Primary cutaneous gamma/delta T-cell lymphoma
Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma
Primary cutaneous peripheral T-cell lymphoma, NOS
<i>Intestinal T-cell and NK-cell lymphoid proliferations and lymphomas</i>
Indolent T-cell lymphoma of the gastrointestinal tract
Indolent NK-cell lymphoproliferative disorder of the gastrointestinal tract
Enteropathy-associated T-cell lymphoma
Monomorphic epitheliotropic intestinal T-cell lymphoma
Intestinal T-cell lymphoma, NOS
<i>Hepatosplenic T-cell lymphoma</i>
Hepatosplenic T-cell lymphoma
<i>Anaplastic large cell lymphoma</i>
ALK-positive anaplastic large cell lymphoma
ALK-negative anaplastic large cell lymphoma
Breast implant-associated anaplastic large cell lymphoma
Nodal T-follicular helper (TFH) cell lymphoma
Nodal TFH cell lymphoma, angioimmunoblastic-type
Nodal TFH cell lymphoma, follicular-type
Nodal TFH cell lymphoma, NOS
<i>Other peripheral T-cell lymphomas</i>
Peripheral T-cell lymphoma, not otherwise specified
<i>EBV-positive NK/T-cell lymphomas</i>
EBV-positive nodal T- and NK-cell lymphoma

Extranodal NK/T-cell lymphoma
<i>EBV-positive T- and NK-cell lymphoid proliferations and lymphomas of childhood</i>
Severe mosquito bite allergy
Hydroa vacciniforme lymphoproliferative disorder
Systemic chronic active EBV disease
Systemic EBV-positive T-cell lymphoma of childhood

実臨床では？

低悪性度リンパ腫 (indolent lymphoma)

年単位の進行

ただし原則根治は困難

代表的疾患：B細胞性ではFL, MZL, LPL, SLLなど(旧来はMCLも)

中等度～高悪性度リンパ腫 (aggressive lymphoma)

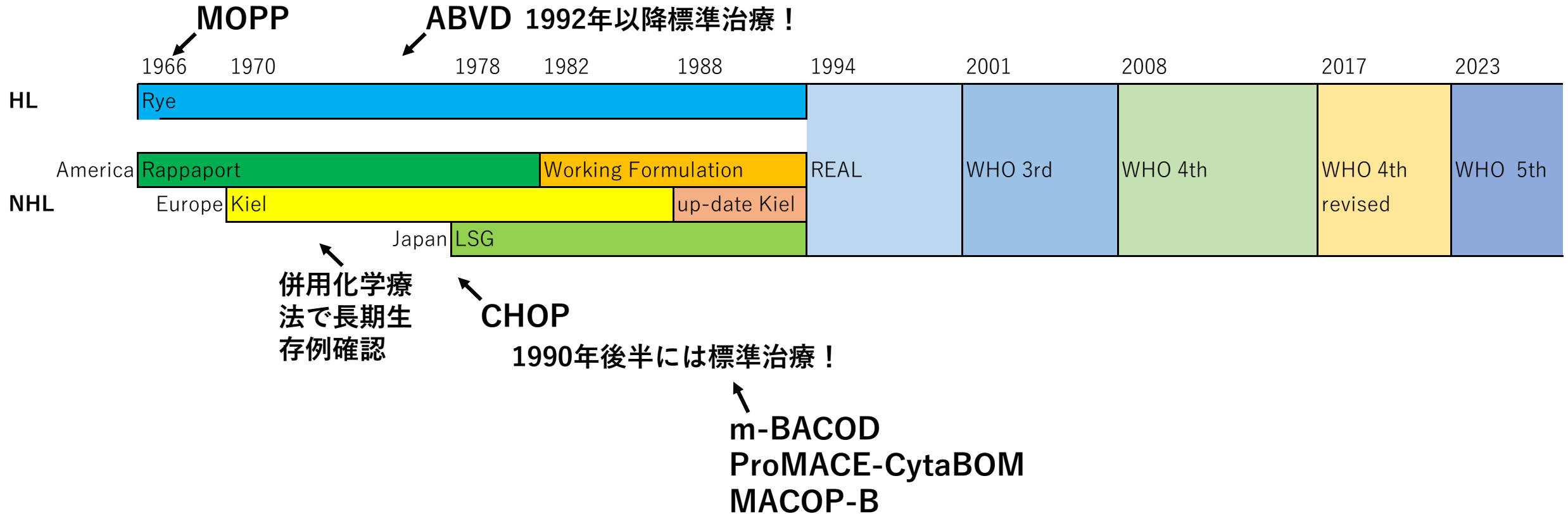
月～日単位の進行

ただし根治可能

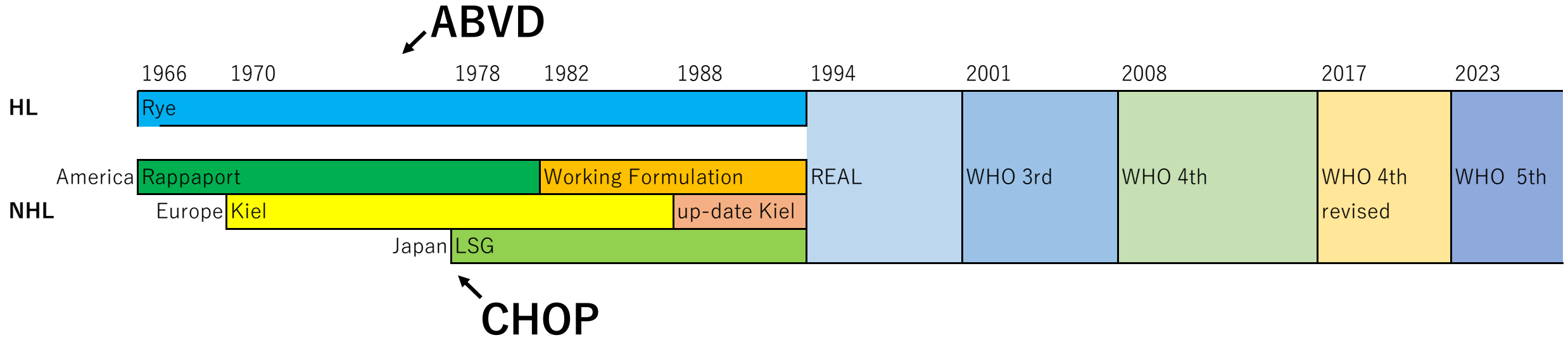
代表的疾患：B細胞性ではDLBCL、T細胞性ではPTCL-NOS, ALCL, AITLなど

FL：濾胞性リンパ腫, MZL：辺縁帯リンパ腫, LPL：リンパ形質細胞性リンパ腫, SLL：小リンパ球性リンパ腫, MCL：マントル細胞リンパ腫,
DLBCL：びまん性大細胞型B細胞リンパ腫
PTCL-NOS：末梢性T細胞リンパ腫, 分類不能型, ALCL：未分化大細胞型リンパ腫, AITL：血管免疫芽球性T細胞リンパ腫

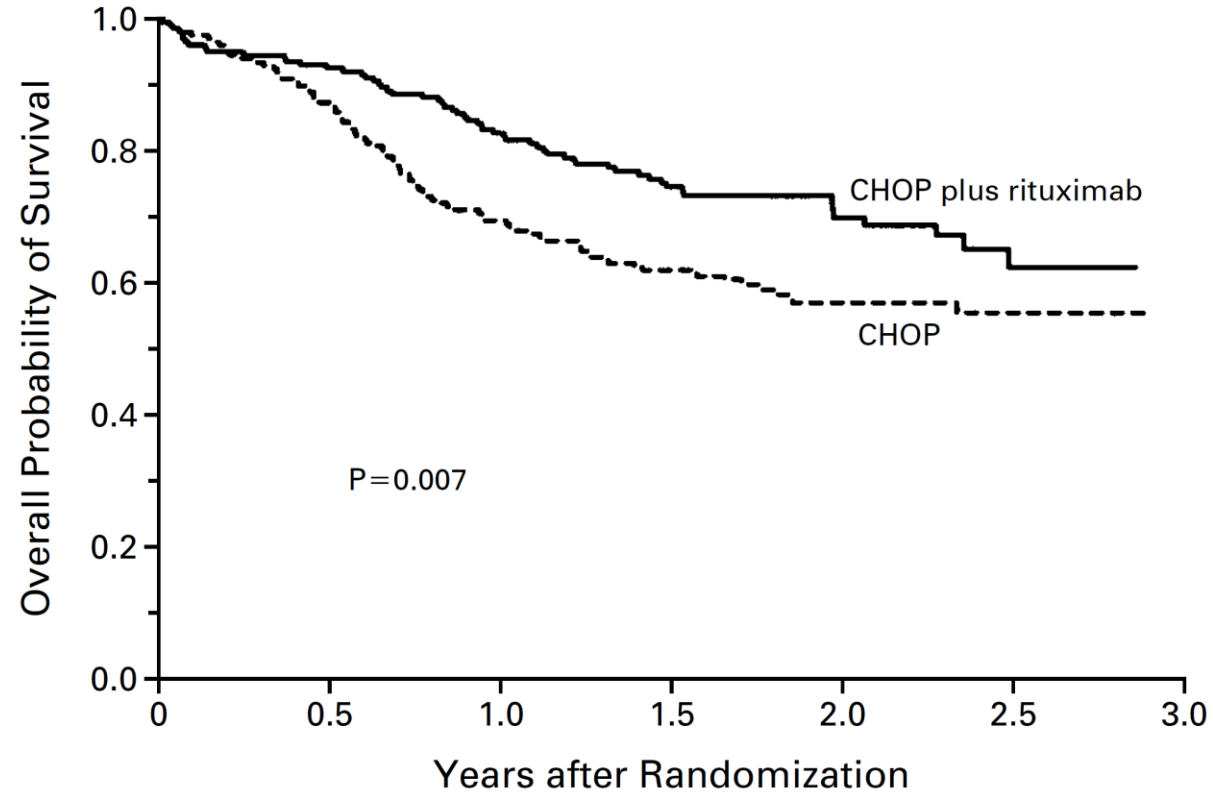
病理分類の変遷



レジメンの変遷



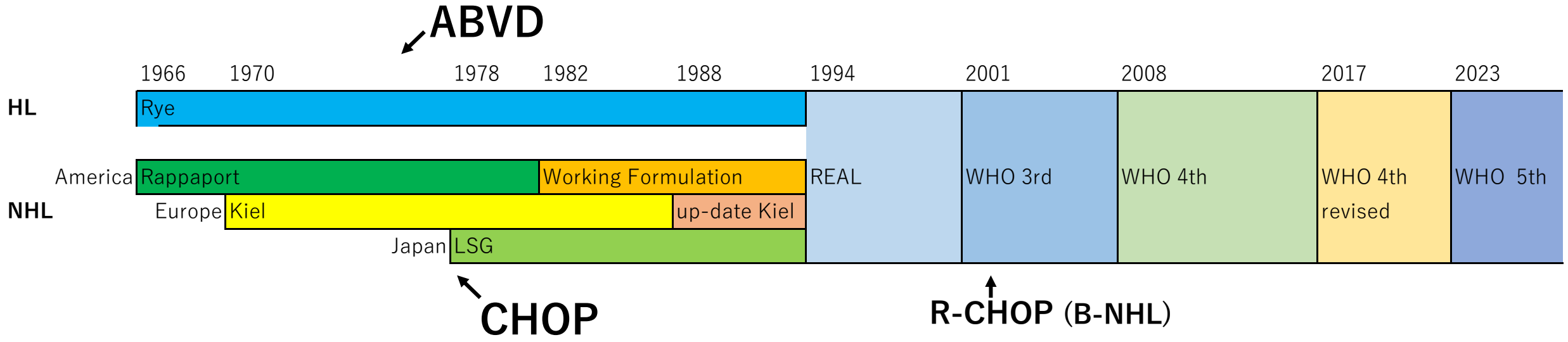
R-CHOP vs CHOP for DLBCL



No. AT RISK						
CHOP plus rituximab	202	187	167	118	64	21
CHOP	197	171	136	96	58	16

Figure 2. Overall Survival among 399 Patients Assigned to Chemotherapy with Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (CHOP) or with CHOP plus Rituximab.

レジメンの変遷



BR (Bendamustine + R) vs R-CHOP for indolent NHL

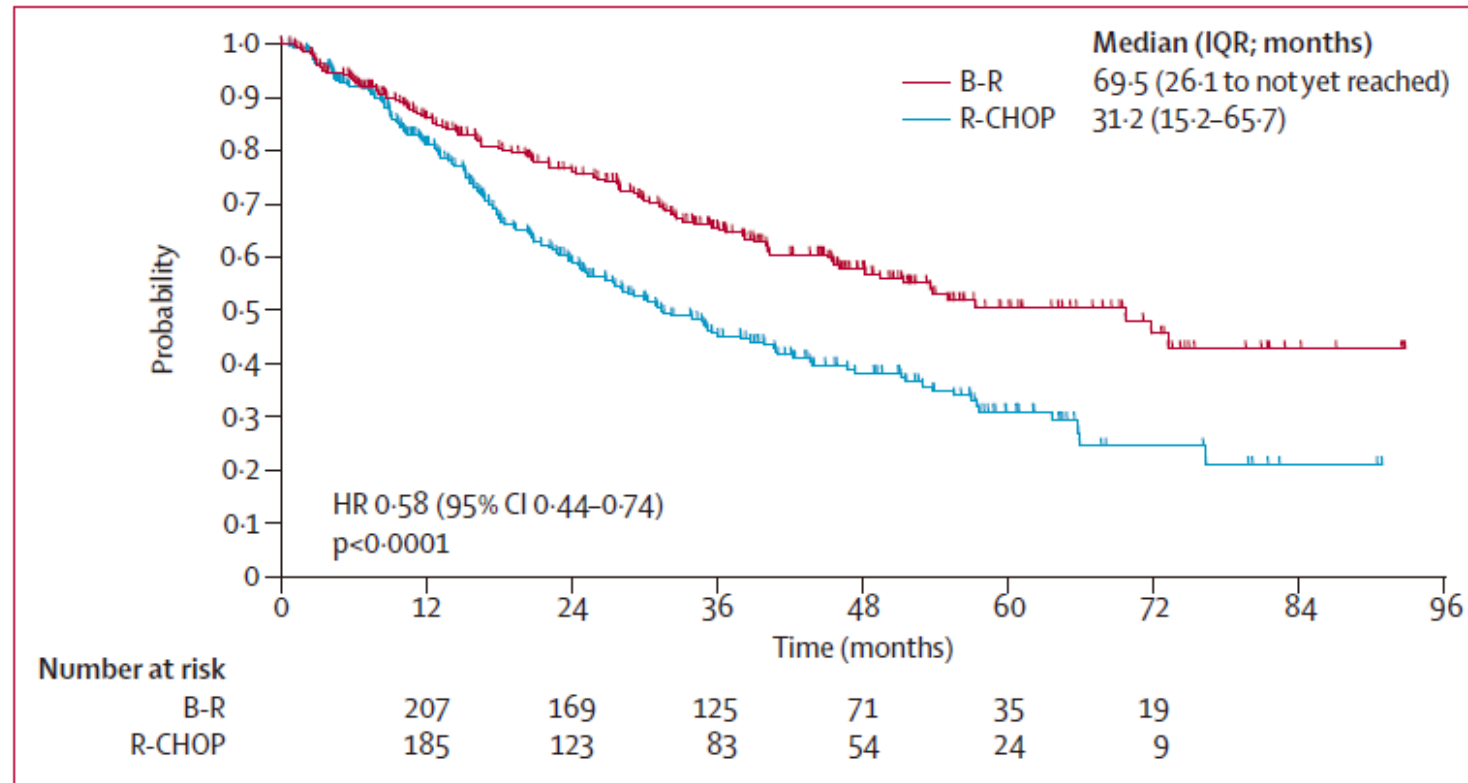
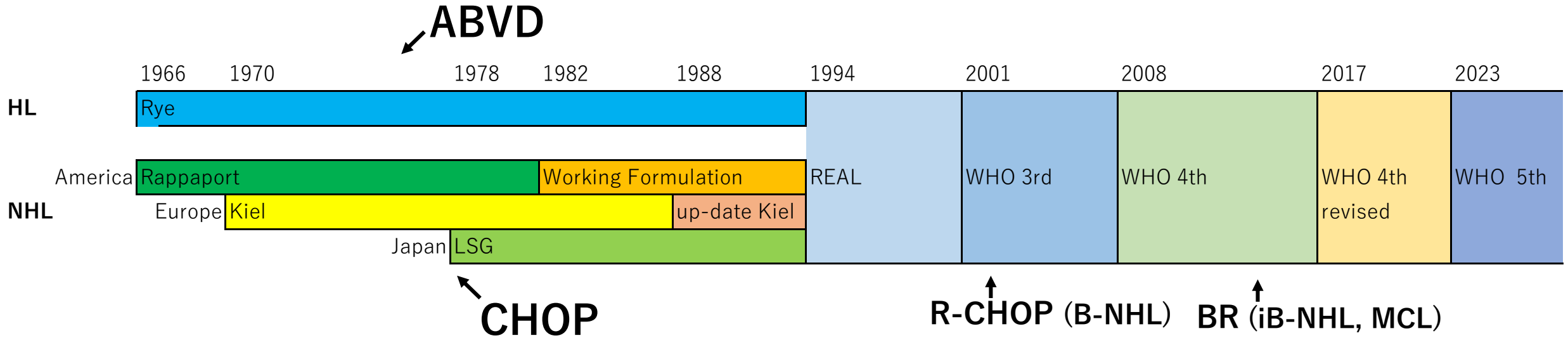


Figure 2: Progression-free survival

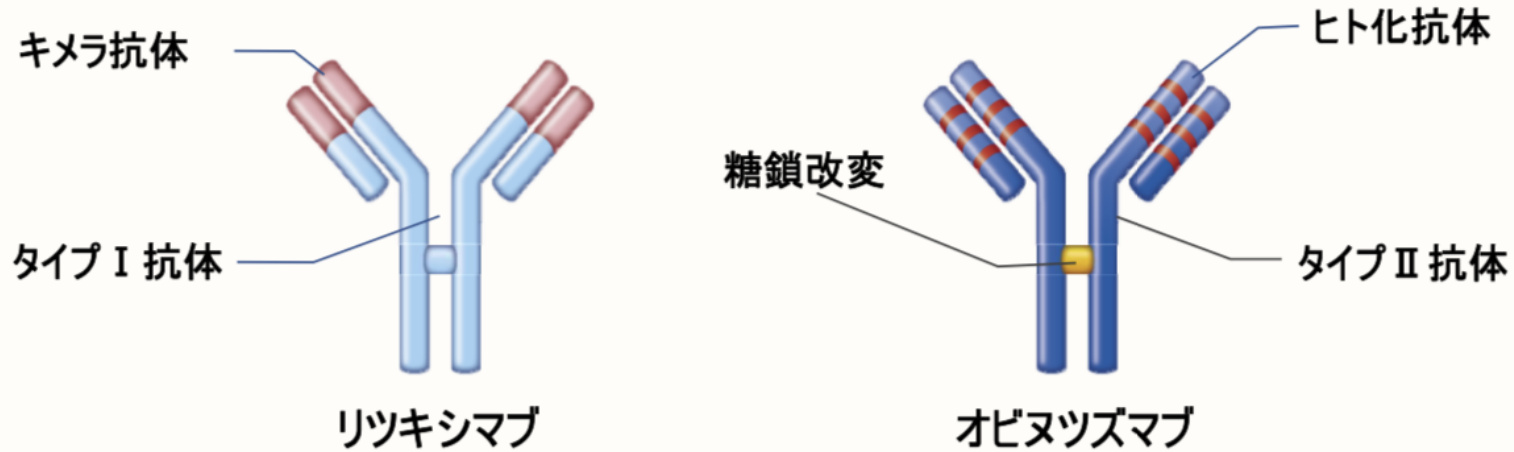
B-R=bendamustine plus rituximab. R-CHOP=CHOP plus rituximab.

レジメンの変遷



Obinutuzumab

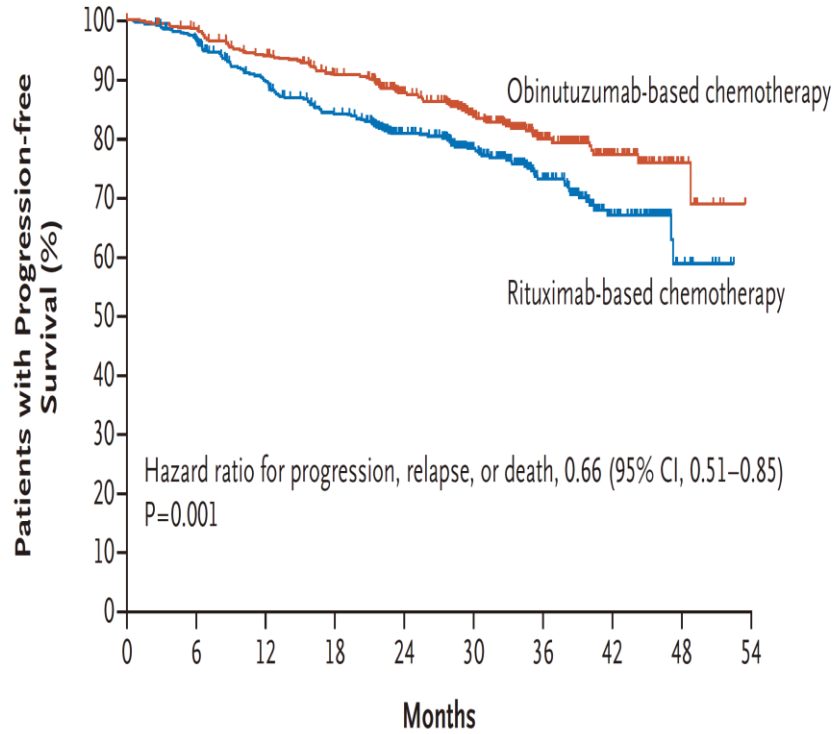
	タイプ I / タイプ II 抗体による違い		糖鎖改変による違い
	直接的な細胞死の誘導活性* 細胞死が認められた細胞の割合 (%)	CDC 活性* EC ₅₀ 値 (μg/mL)	ADCC 活性* EC ₅₀ 値 (ng/mL)
リツキシマブ	6.5 ~ 36.5	0.027 ~ 0.062	4.32 ~ 26.18
オビヌツズマブ	19.1 ~ 73.5	2.7 ~ 12	0.459 ~ 2.471



* 各種B-NHL由来細胞株に対するオビヌツズマブおよびリツキシマブの活性

GB, G-CHOP for FL

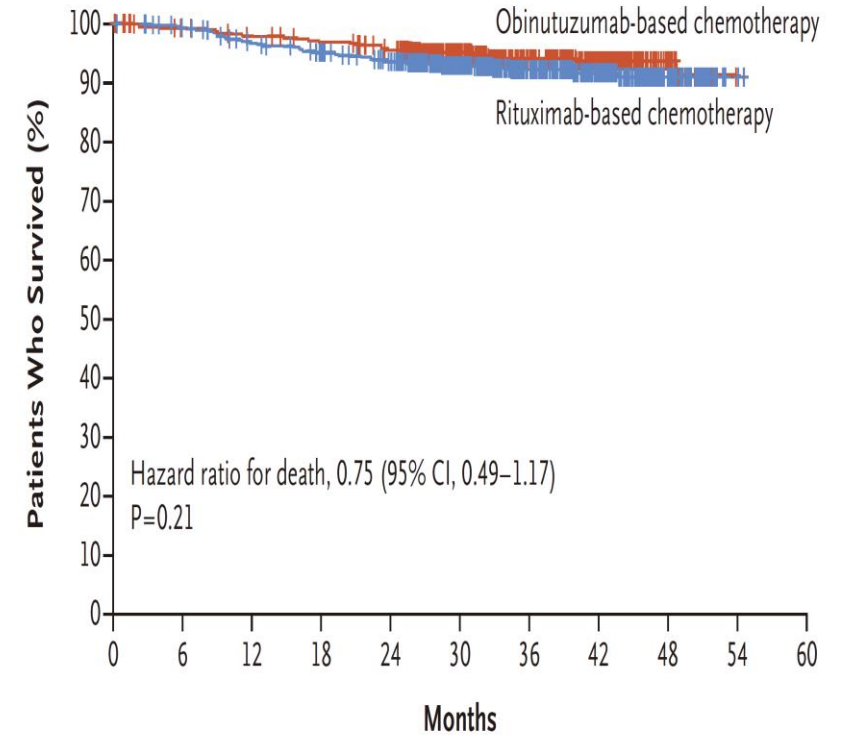
A Progression-free Survival



No. at Risk

Obinutuzumab-based chemotherapy	601	570	536	502	405	278	168	75	13	0
Rituximab-based chemotherapy	601	562	505	463	378	266	160	68	10	0

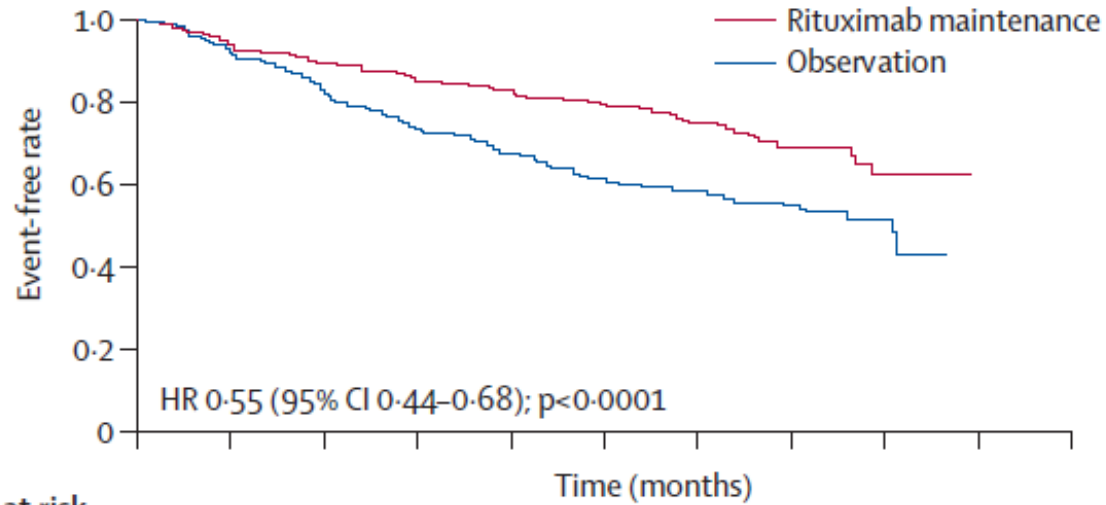
B Overall Survival



No. at Risk

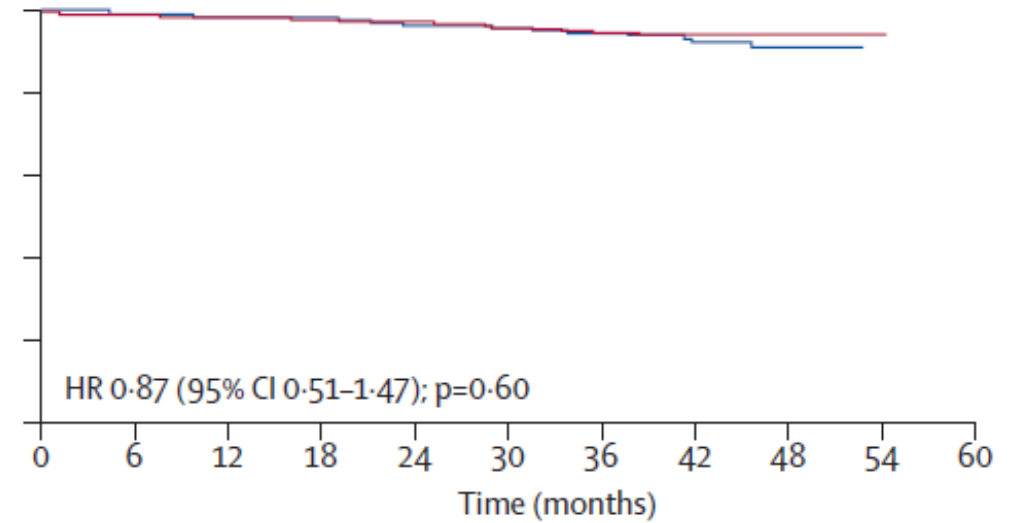
Obinutuzumab-based chemotherapy	601	584	573	563	549	416	271	161	55	0	0
Rituximab-based chemotherapy	601	588	566	549	527	399	265	160	58	2	0

Maintenance therapy with Rituximab



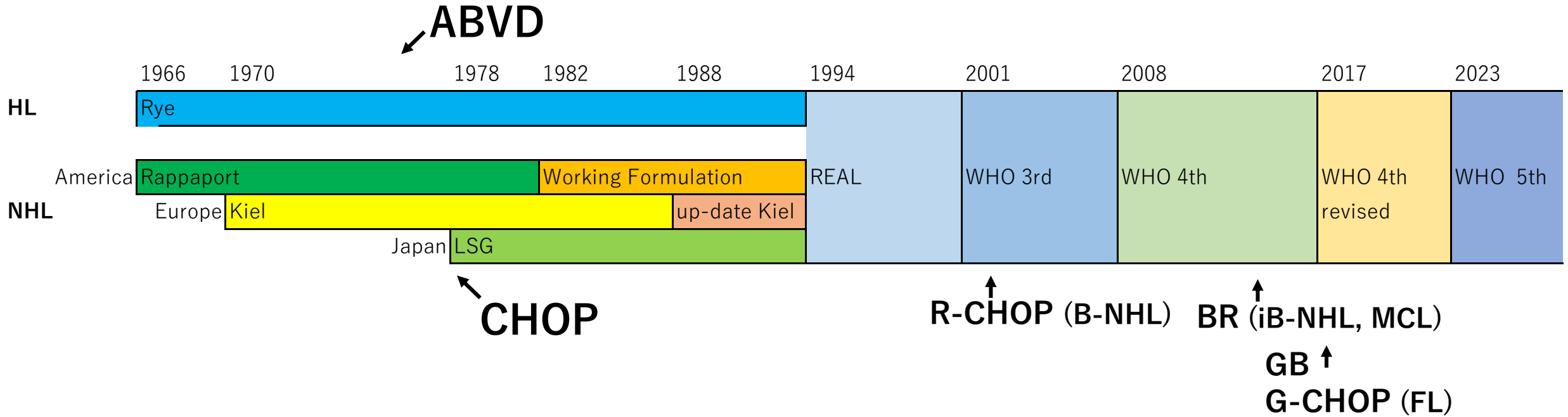
Number at risk

	0	6	12	18	24	30	36	42	48	54
Rituximab	505	472	445	423	404	307	207	84	17	0
Observation	513	469	415	367	334	247	161	70	16	0

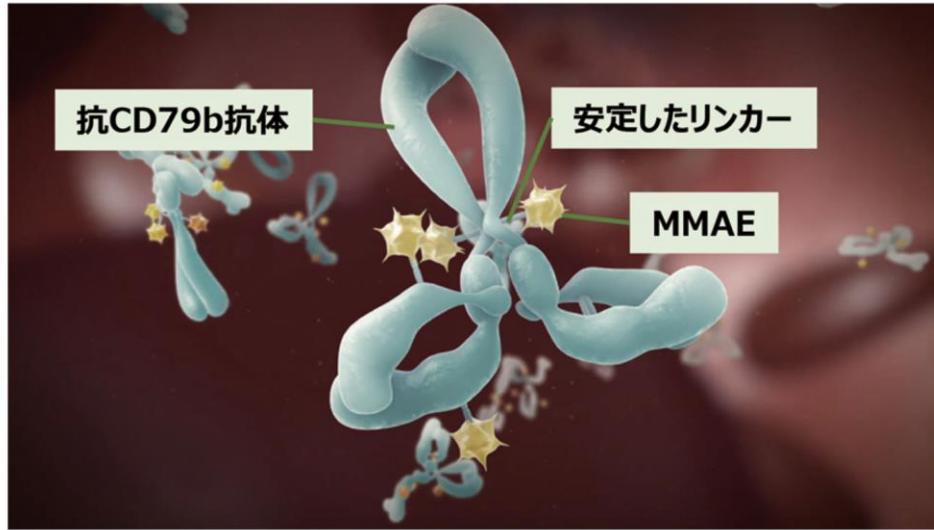


	0	6	12	18	24	30	36	42	48	54
Rituximab	505	499	492	483	474	365	246	108	22	1
Observation	513	507	501	492	472	381	243	97	26	0

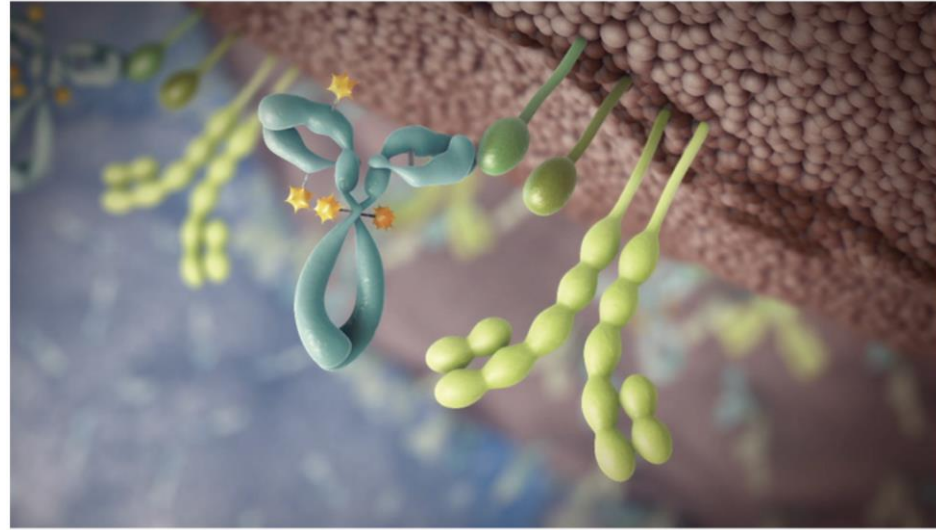
レジメンの変遷



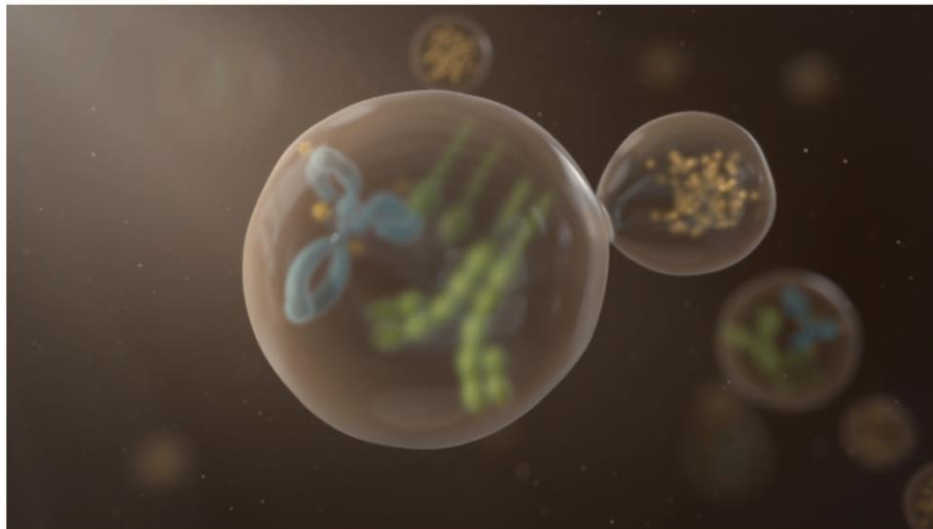
Polatuzumab vedotin



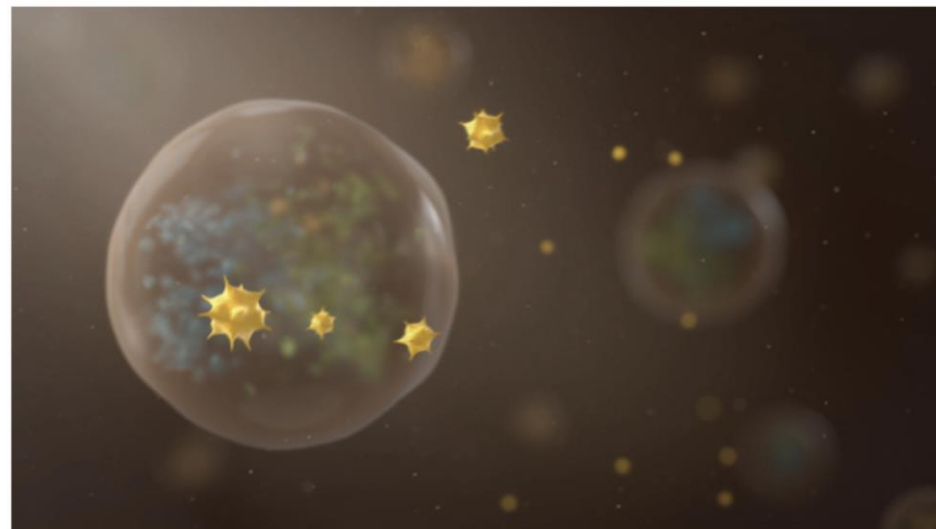
ポラツズマブ ベドチンは、抗CD79bヒト化IgG1モノクローナル抗体と有糸分裂阻害剤のMMAEをプロテアーゼ切断性リンカーを介して共有結合させた抗体薬物複合体（ADC）である¹⁾。



(1) ポラツズマブ ベドチンは、CD79bに特異的に結合すると、速やかに細胞内に移行する²⁻⁴⁾。

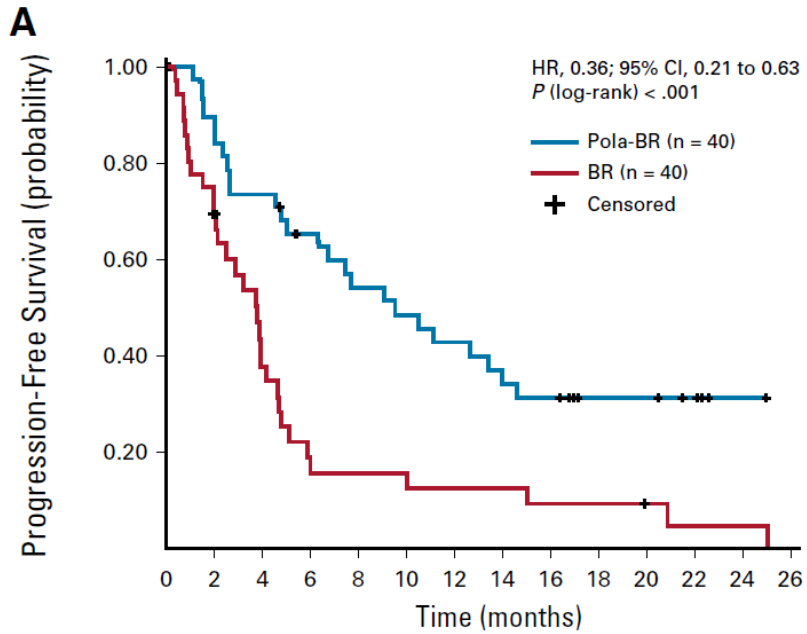


(2) リンカーはリソソームプロテアーゼにより切断され、MMAEが細胞内に放出される⁵⁾。



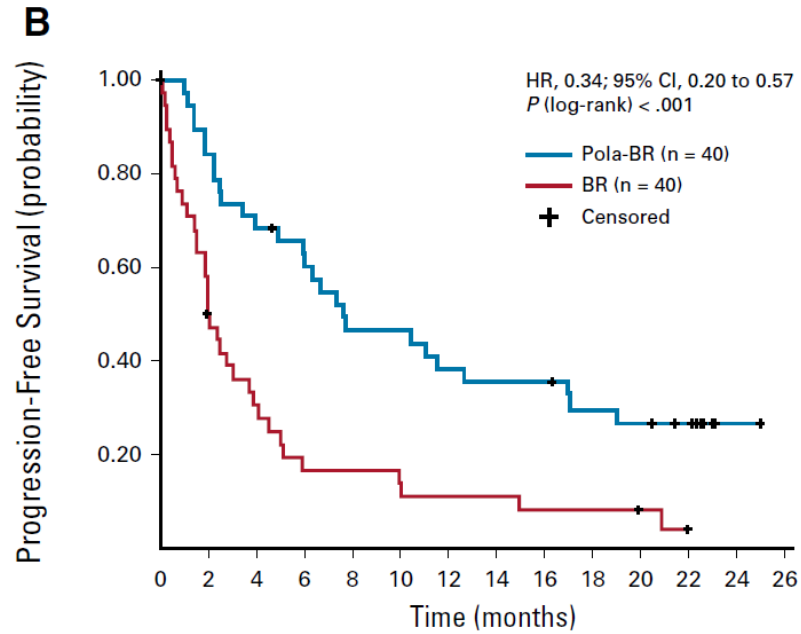
(3) 放出されたMMAEは微小管に結合し、細胞分裂を阻害してアポトーシスを誘導する⁶⁻⁸⁾。

Pola-BR vs BR for relapsed/refractory DLBCL



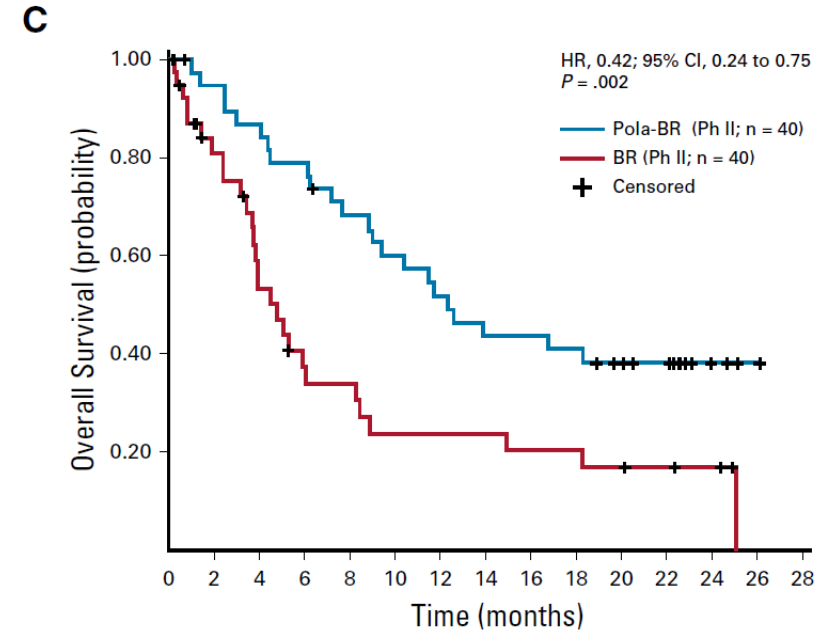
No. at risk:

Pola-BR (Ph II)	40	38	32	28	28	24	23	21	19	19	17	16	15	14	12	11	11	8	7	7	6	5	1	1	
BR (Ph II)	40	28	23	18	12	8	5	5	5	5	4	4	4	4	4	3	3	3	3	3	2	1	1	1	1



No. at risk:

Pola-BR (Ph II)	40	38	32	28	26	24	23	20	17	17	16	14	13	13	13	11	10	10	9	8	7	3	1
BR (Ph II)	40	28	20	14	11	9	6	6	6	6	5	4	4	4	4	3	3	3	3	2	1		

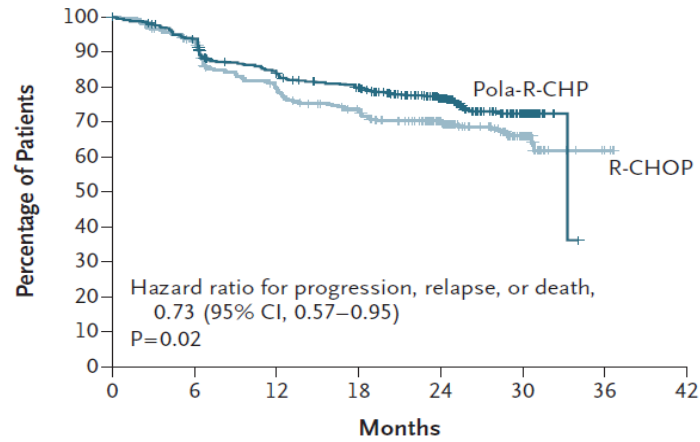


No. at risk:

Pola plus BR (Ph II)	40	38	36	34	33	30	30	27	25	24	22	21	19	17	16	16	16	15	15	13	12	9	5	3	2	1
BR (Ph II)	40	33	27	25	17	15	11	10	10	7	7	7	7	7	6	6	6	6	5	5	4	4	3	3	1	

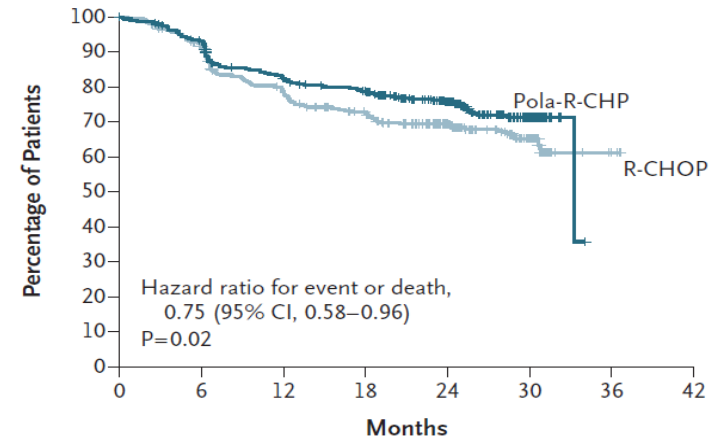
Pola-R-CHP vs R-CHOP for newly diagnosed DLBCL

A Investigator-Assessed Progression-free Survival



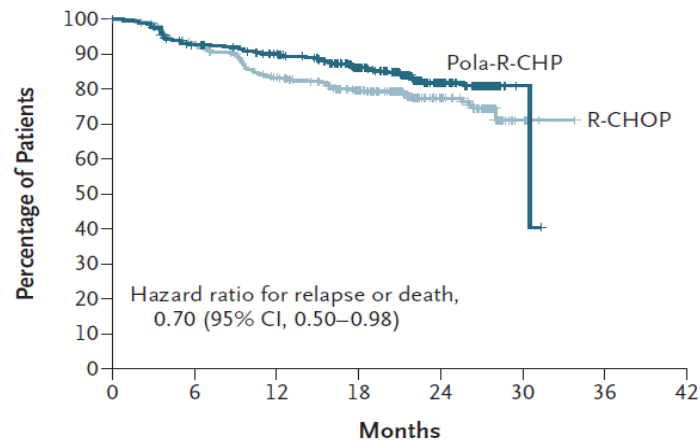
No. at Risk								
Pola-R-CHP	440	404	353	327	246	78	NE	NE
R-CHOP	439	389	330	296	220	78	3	NE

B Investigator-Assessed Event-free Survival



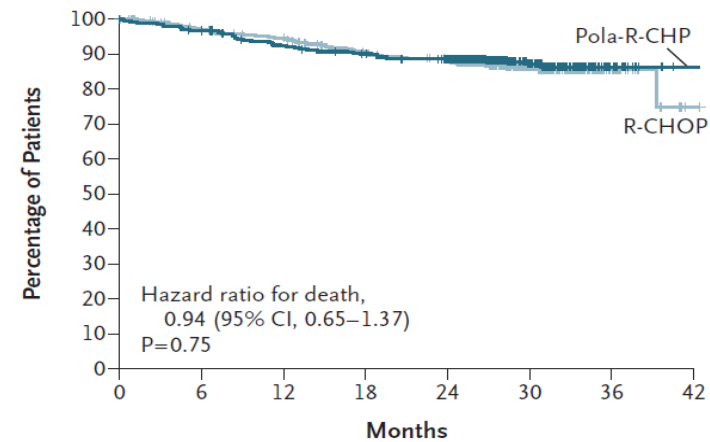
No. at Risk								
Pola-R-CHP	440	402	348	323	243	78	NE	NE
R-CHOP	439	386	327	294	218	78	3	NE

C Investigator-Assessed Disease-free Survival



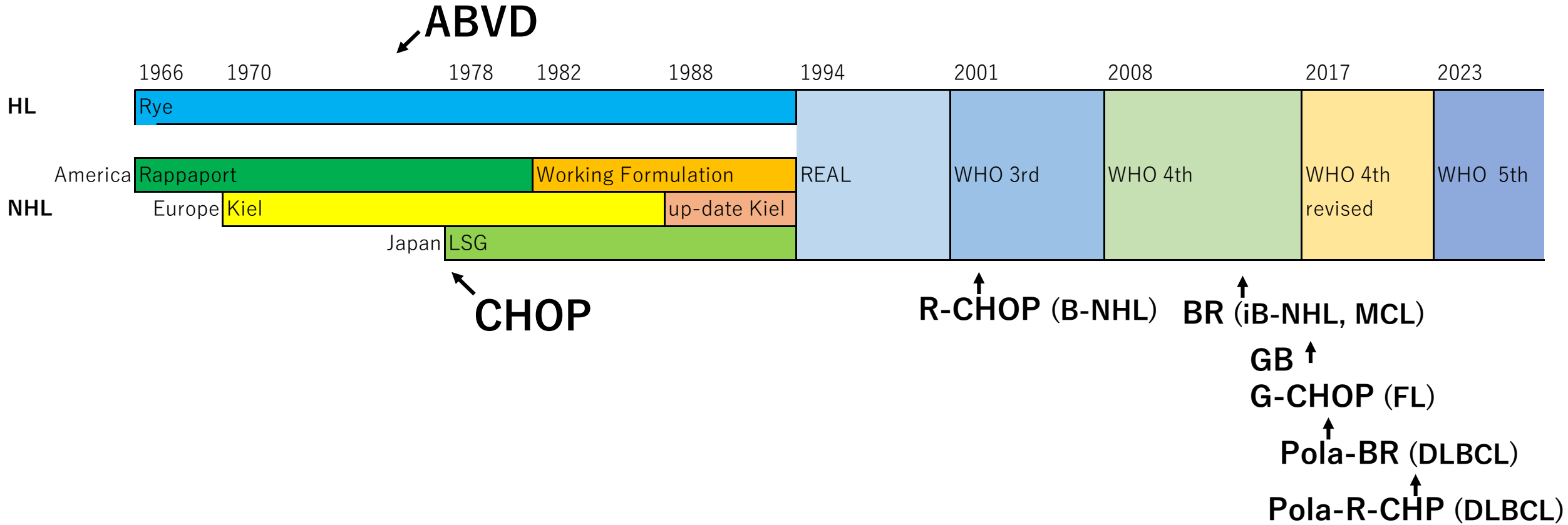
No. at Risk								
Pola-R-CHP	381	342	322	266	106	2	NE	NE
R-CHOP	363	326	282	238	96	5	NE	NE

D Overall Survival

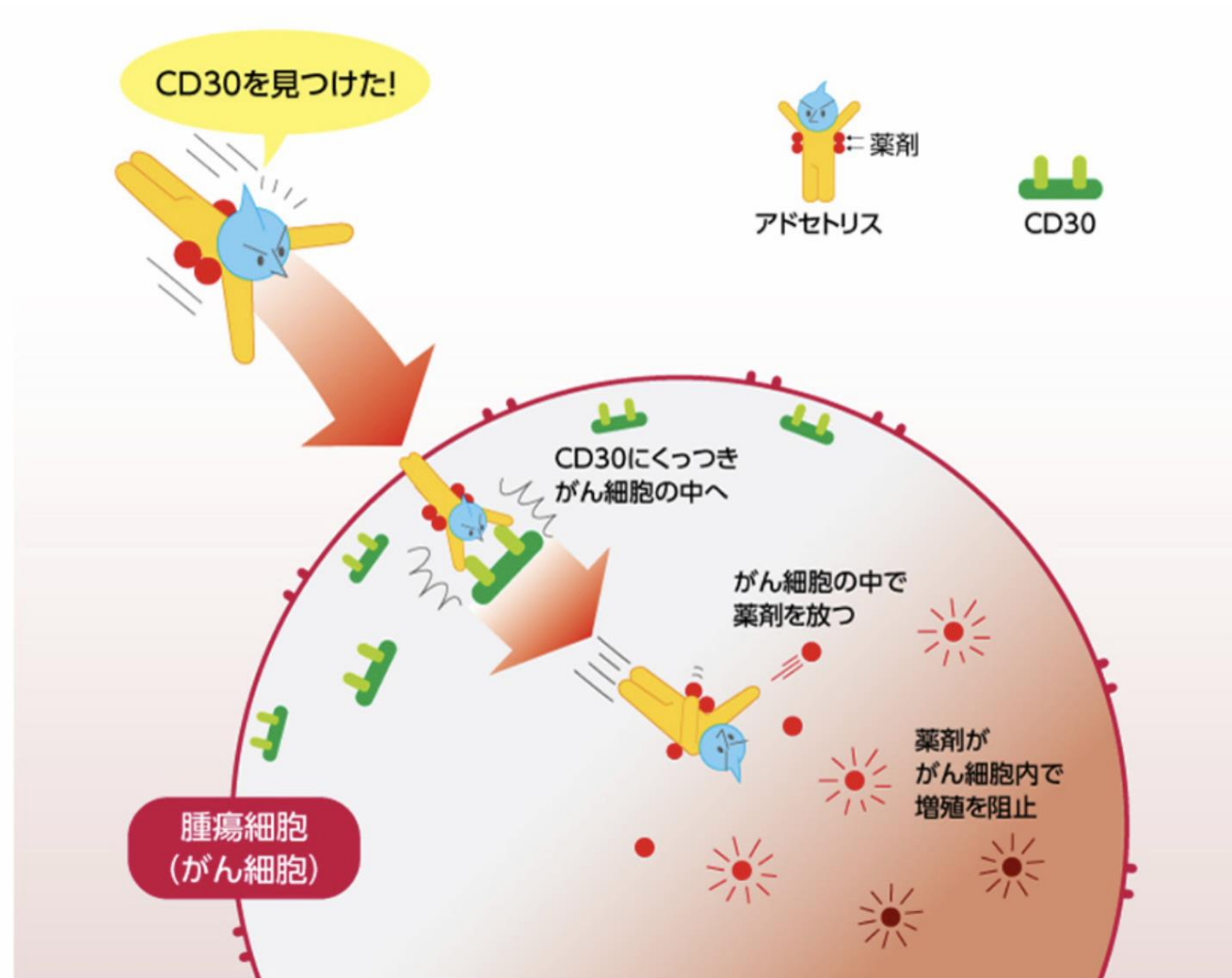


No. at Risk								
Pola-R-CHP	440	423	397	384	362	140	15	1
R-CHOP	439	414	401	376	355	132	20	1

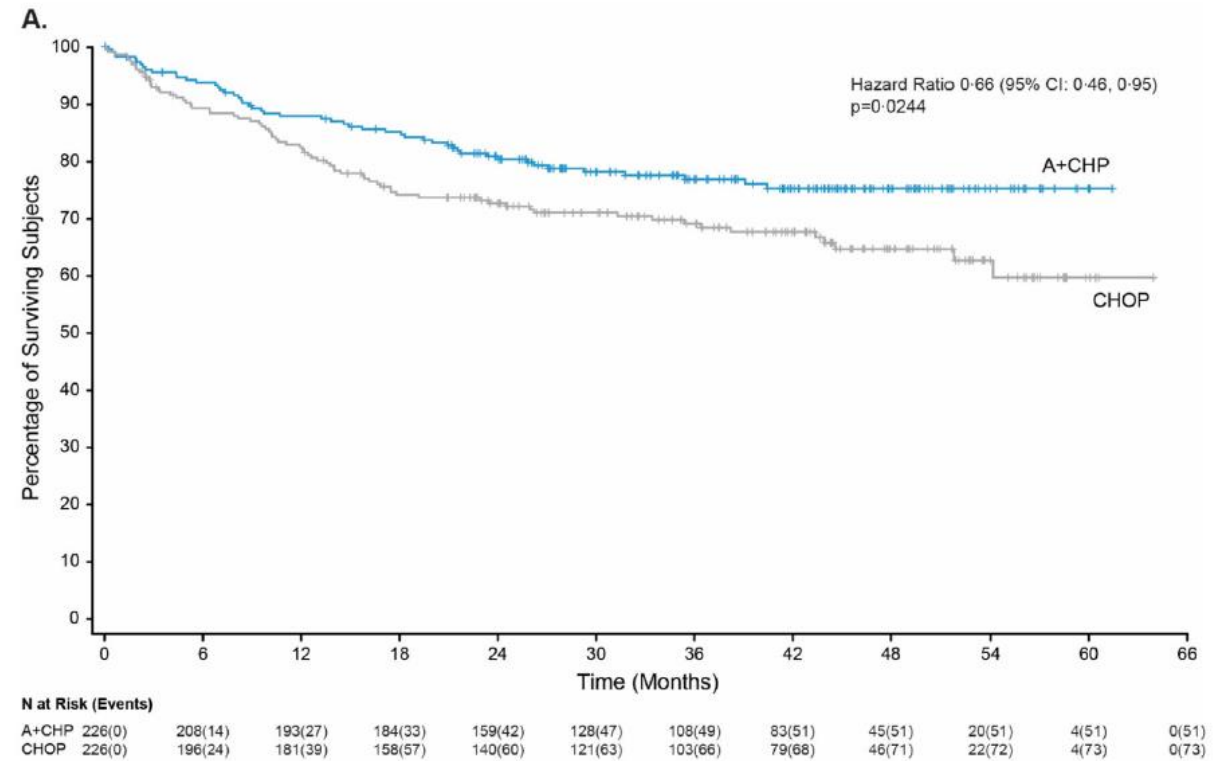
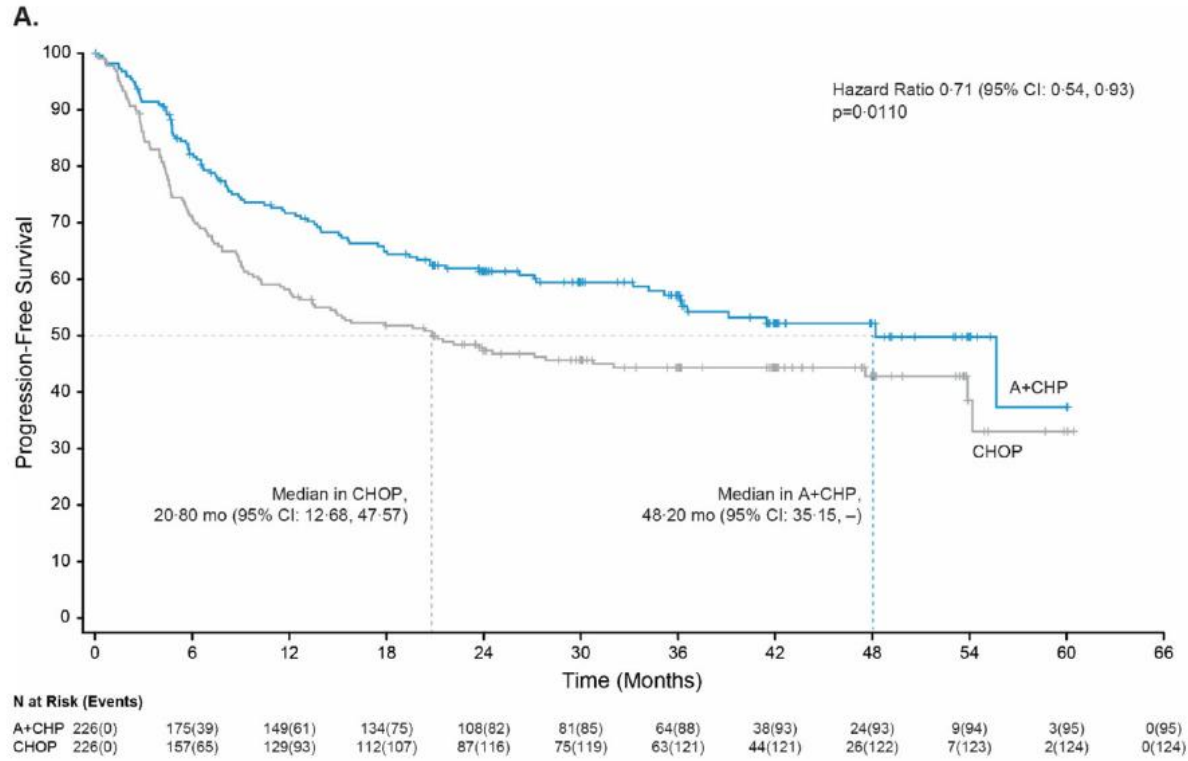
レジメンの変遷



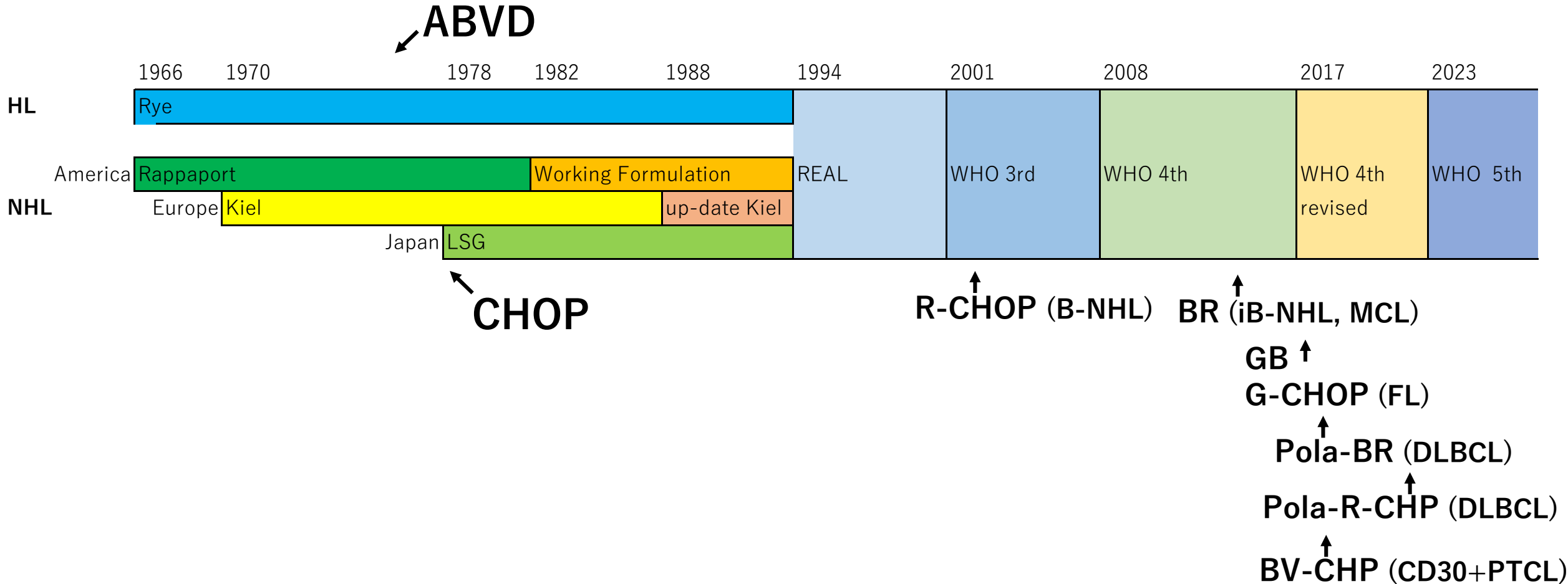
Brentuximab vedotin



BV-CHP vs CHOP for CD30+PTCL



レジメンの変遷



SUGGESTED TREATMENT REGIMENS^a
PTCL-NOS; EATL; MEITL^f

SECOND-LINE THERAPY AND SUBSEQUENT THERAPY (INTENTION TO PROCEED TO TRANSPLANT)	SECOND-LINE AND SUBSEQUENT THERAPY (NO INTENTION TO PROCEED TO TRANSPLANT)
<ul style="list-style-type: none"> • Clinical trial preferred Preferred regimens • Single agents (alphabetical order) <ul style="list-style-type: none"> ▶ Belinostat ▶ Brentuximab vedotin for CD30+ PTCL^{d,g} ▶ Pralatrexate ▶ Romidepsin • Combination regimens (alphabetical order) <ul style="list-style-type: none"> ▶ DHA (dexamethasone and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) ▶ ESHAP (etoposide, methylprednisolone, and cytarabine) + platinum (cisplatin or oxaliplatin) ▶ GDP (gemcitabine, dexamethasone, and cisplatin) ▶ GemOx (gemcitabine and oxaliplatin) ▶ ICE (ifosfamide, carboplatin, and etoposide) Other recommended regimens • Single agents (alphabetical order) <ul style="list-style-type: none"> ▶ Bendamustine^d ▶ Duvelisib^k ▶ Gemcitabine ▶ Lenalidomide^d ▶ Ruxolitinib (category 2B) • Combination regimen <ul style="list-style-type: none"> ▶ GVD (gemcitabine, vinorelbine, and liposomal doxorubicin)^p 	<ul style="list-style-type: none"> • Clinical trial preferred Preferred regimens (alphabetical order) • Belinostat • Brentuximab vedotin for CD30+ PTCL^{d,g} • Pralatrexate • Romidepsin Other recommended regimens (alphabetical order) • Alemtuzumab^l • Bendamustine^d • Bortezomib^j (category 2B) • Cyclophosphamide and/or etoposide (IV or PO) • Duvelisib^k • Gemcitabine • Lenalidomide^d • RT^l • Ruxolitinib (category 2B) <p>See First-line Therapy on PTCL-B 1 of 7. See Second-line and Subsequent Therapy: AITL, including nodal PTCL, TFH, and FTCL (PTCL-B 4 of 7) ALCL (PTCL-B 5 of 7)</p> <p>^j Activity has been demonstrated in small clinical trials and additional larger trials are needed. ^k In the phase II study, the preferred dosing regimen of duvelisib was 75 mg BID for 2 cycles followed by 25 mg BID for long-term disease control. ^l See Principles of Radiation Therapy (TCLYM-D). ^p Data suggest there may be excessive pulmonary toxicity with GVD (gemcitabine, vinorelbine, and liposomal doxorubicin) regimen when used in combination with unconjugated anti-CD30 monoclonal antibodies for the treatment of Hodgkin lymphoma (Blum KA, et al. Ann Oncol 2010;21:2246-2254). A similar regimen, gemcitabine and liposomal doxorubicin, may be used for mature T-cell lymphoma; however, it is recommended to wait 3 to 4 weeks following treatment with brentuximab vedotin before initiation.</p>

^a See references for regimens on [PTCL-B 6 of 7](#) and [PTCL-B 7 of 7](#).

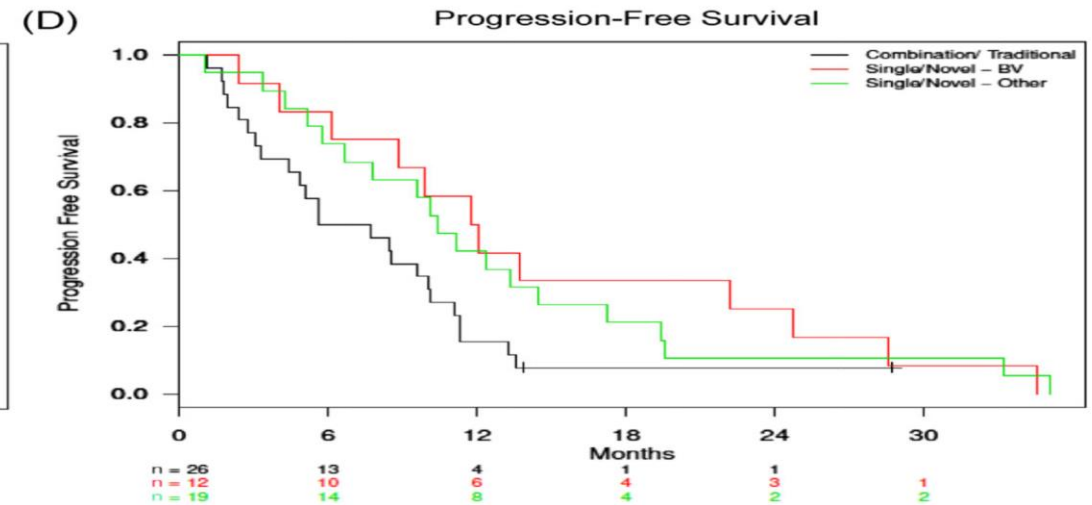
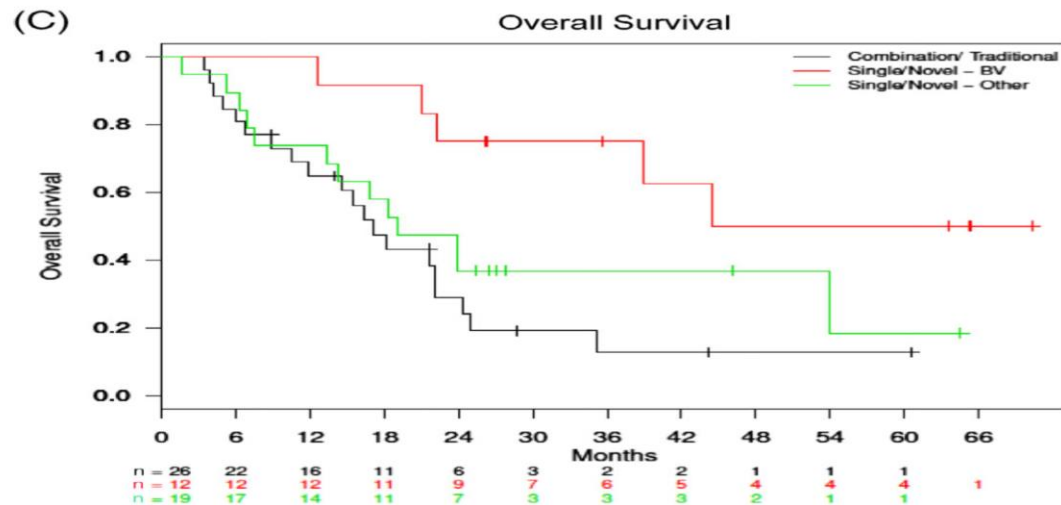
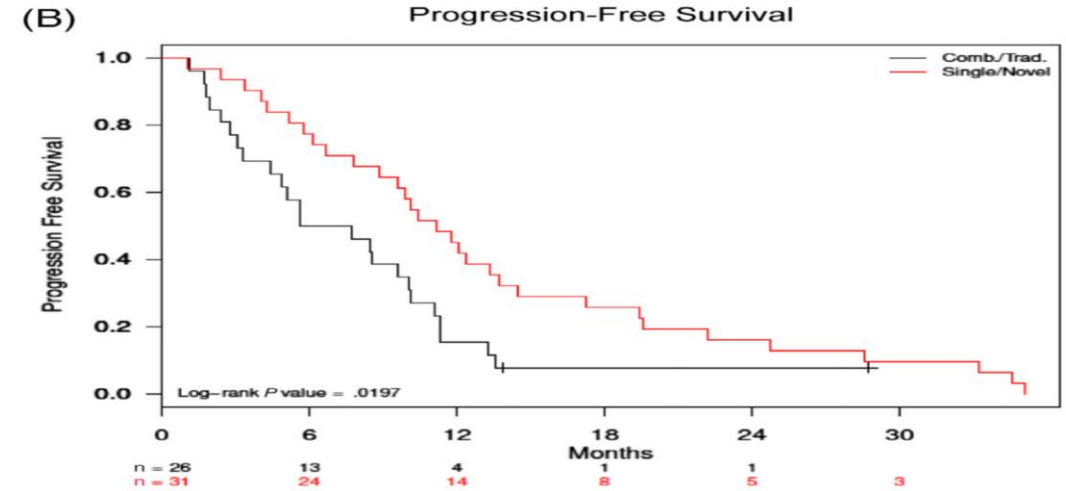
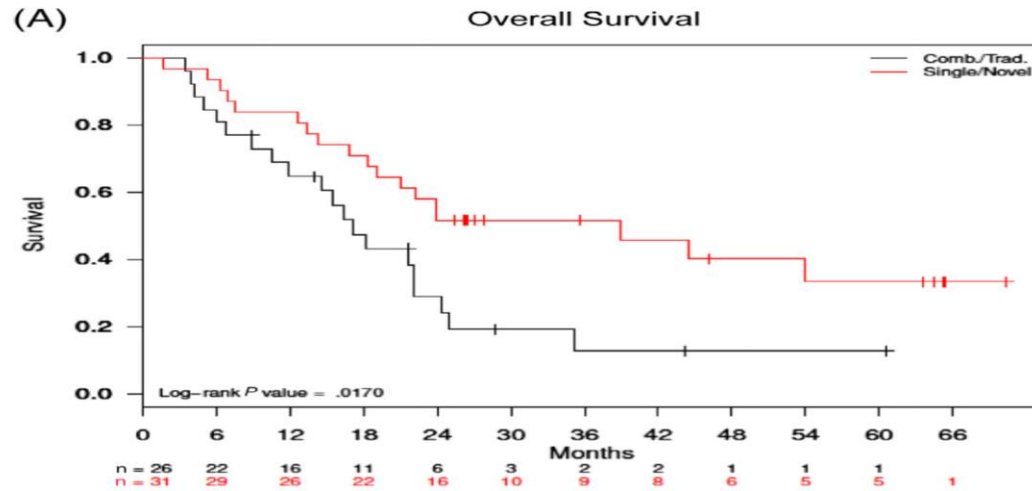
^d See Supportive Care (TCLYM-B).

^f MEITL has only recently been separated as its own entity and optimal treatment has not been defined.

^g Interpretation of CD30 expression is not universally standardized. Responses have been seen in patients with a low level of CD30-positivity.

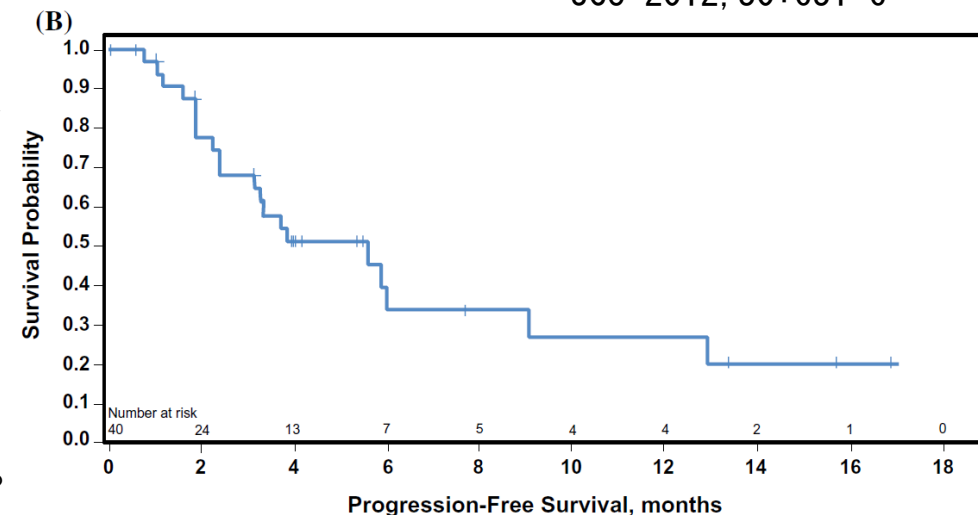
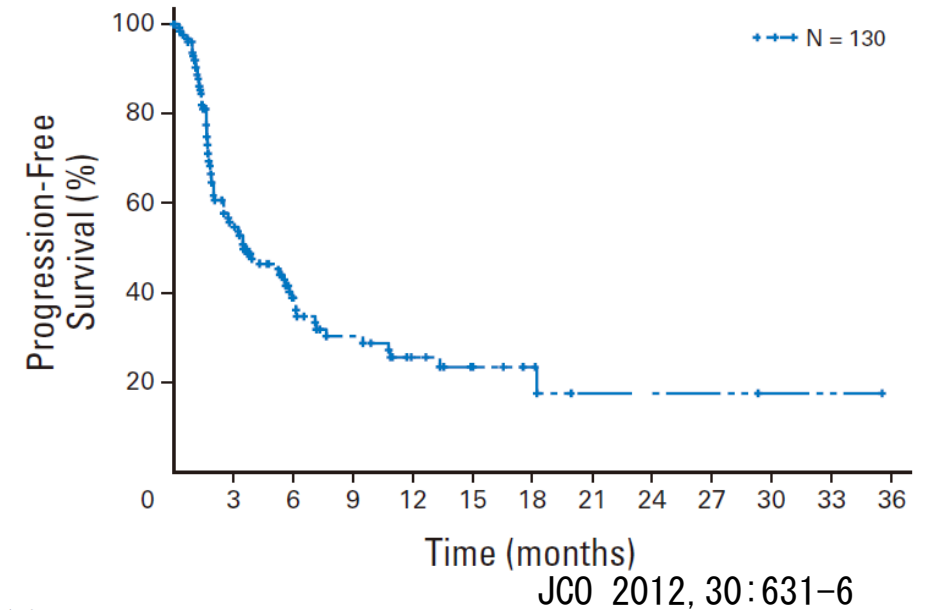
^l While alemtuzumab is no longer commercially available, it may be obtained for clinical use. CMV monitoring or prophylaxis is recommended. (See TCLYM-B).

single agent vs combination chemotherapy for R/R PTCL

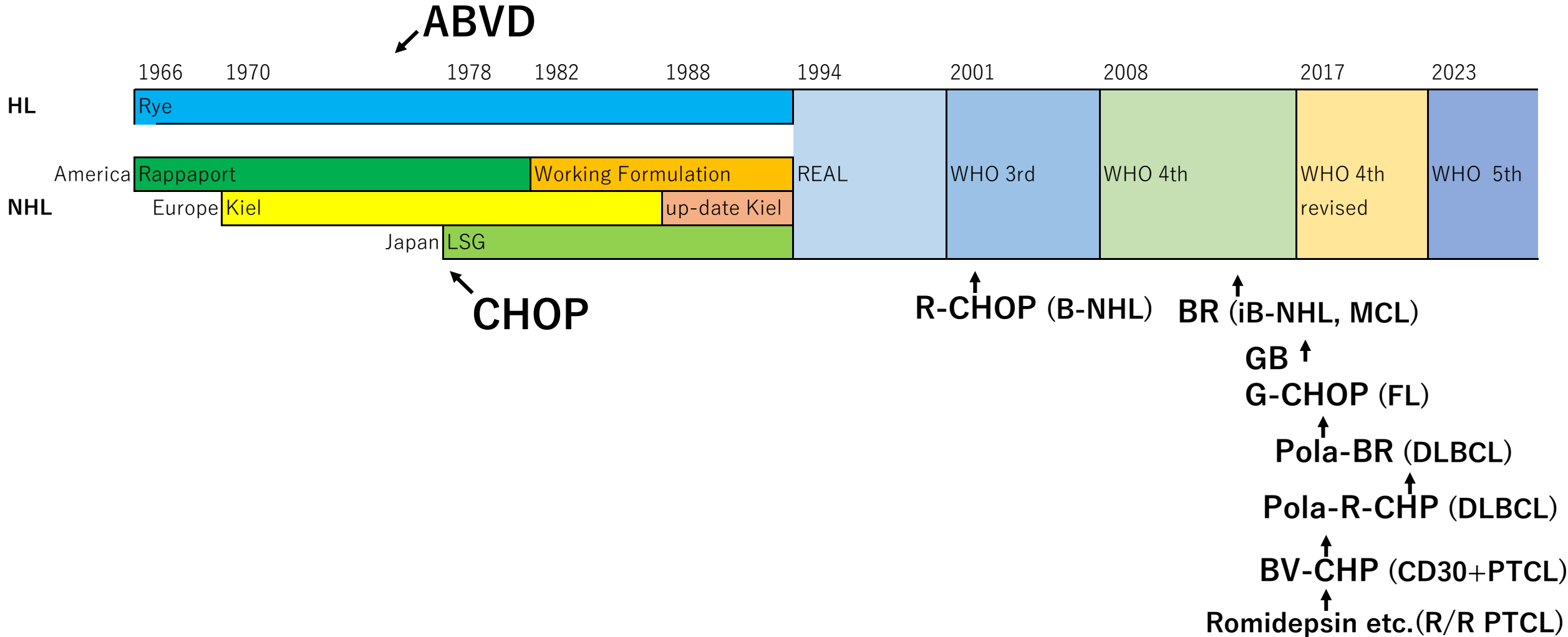


Romidepsin for R/R PTCL

- ヒストン脱アセチル化酵素(HDAC)阻害剤：癌抑制遺伝子発現を促し、腫瘍の増殖抑制、細胞周期制御、apoptosisなどを介し作用。
- 再発難治PTCL(PCL-NOS, AITL, ALK-ALCL含む)に対して単剤でORR 25%, CR/CRu rate 15%, median PFS 4ヶ月(海外)、ORR 43%, CR/CRu rate 25%, median PFS 5.6ヶ月(国内)。
- Objective responseまでの期間が1.8ヶ月と短く、CR/CRu例でのmedian DORが17ヶ月, 11.1ヶ月(海外, 国内)と、有効例で長期効果が持続。
- AITLなどfollicular helper T由来のものに特に有効。
- 国内臨床試験では26%が有害事象(血球減少、不整脈など心合併症)のため治療中断となったが、治療関連死亡はごく少数。

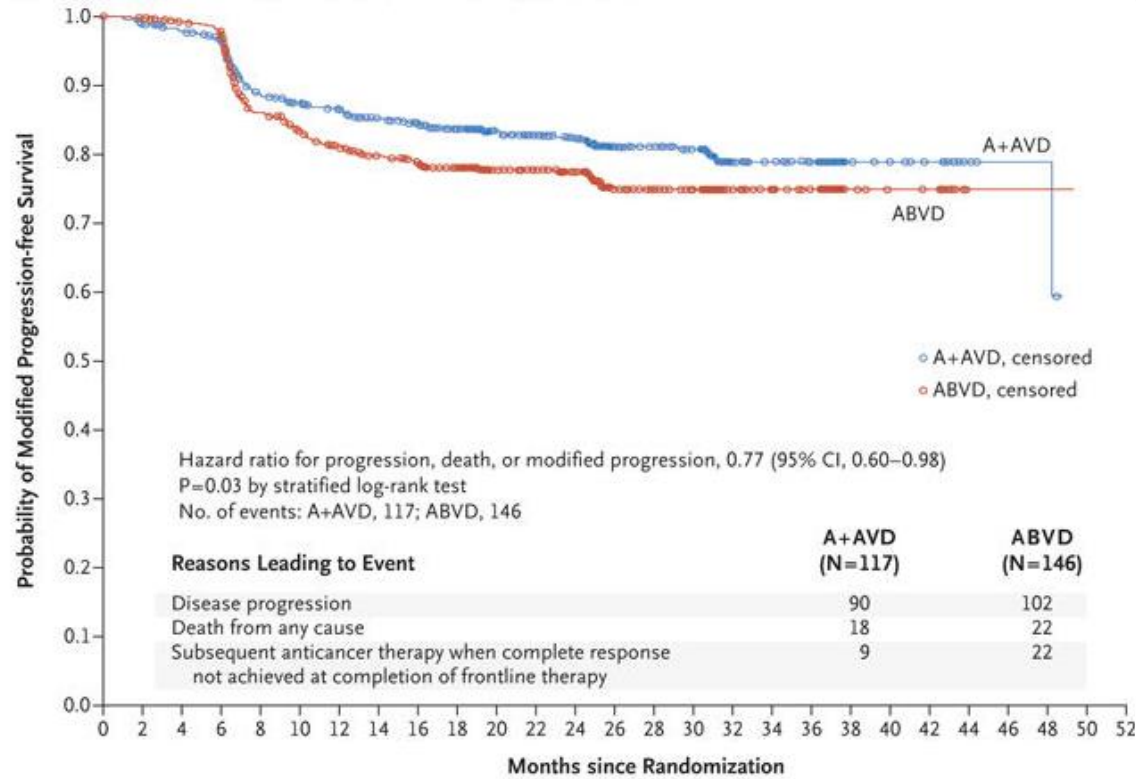


レジメンの変遷



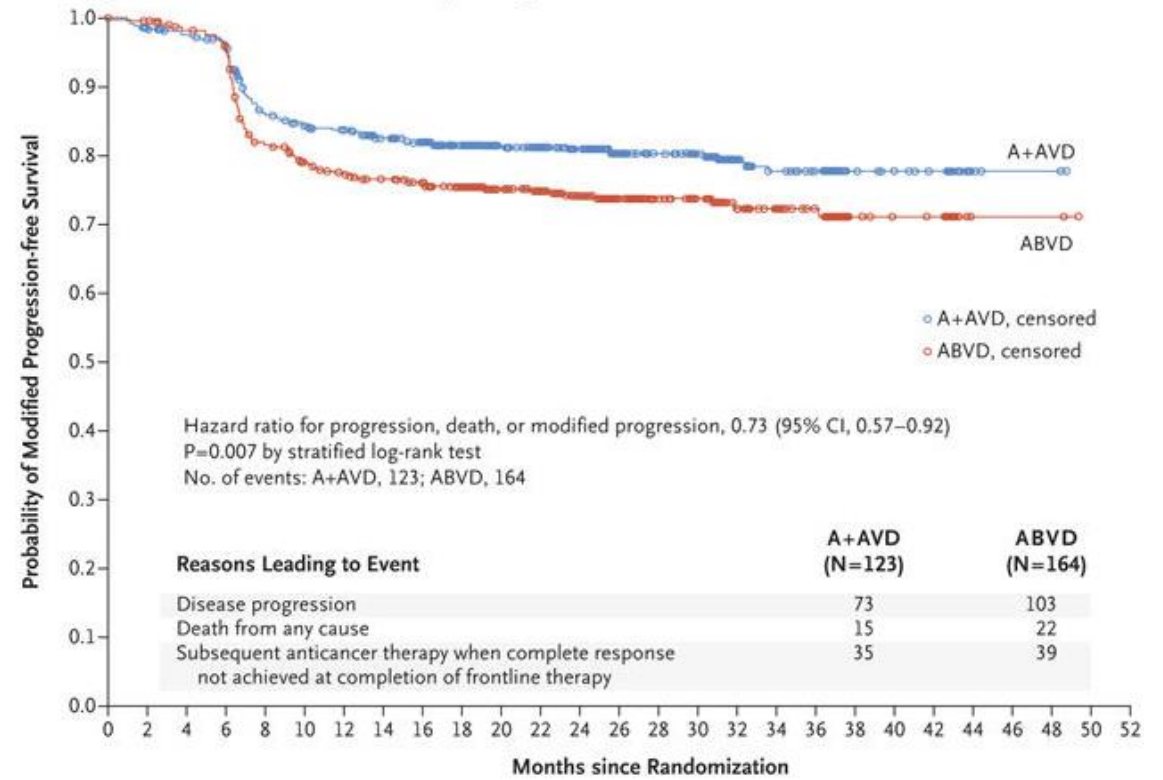
A+AVD vs ABVD for cHL

A Modified Progression-free Survival as Assessed by Independent Review Committee



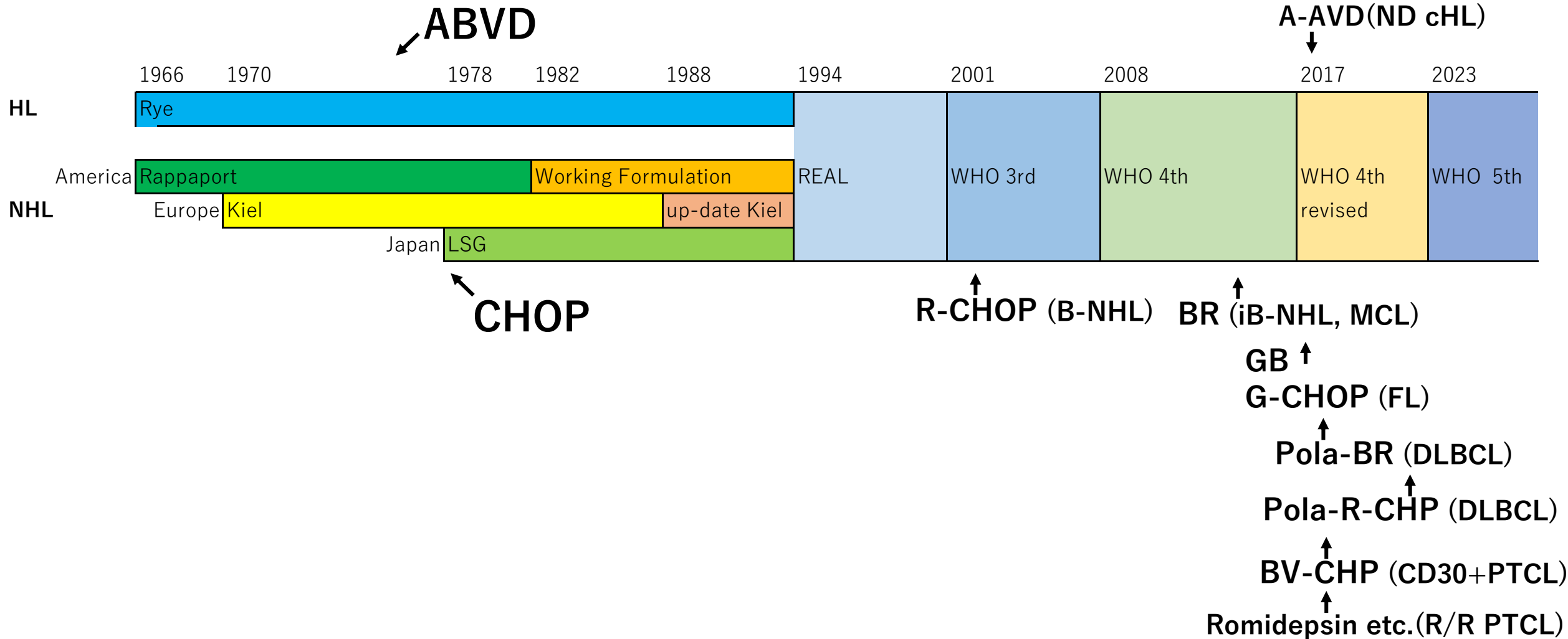
No. at Risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
A+AVD	664	640	623	606	544	530	516	496	474	447	350	334	311	200	187	174	99	85	77	27	24	21	6	4	4	0	0
ABVD	670	644	626	613	522	496	476	459	439	415	328	308	294	179	168	153	78	68	62	16	13	12	1	1	1	0	0

B Modified Progression-free Survival as Assessed by Investigator



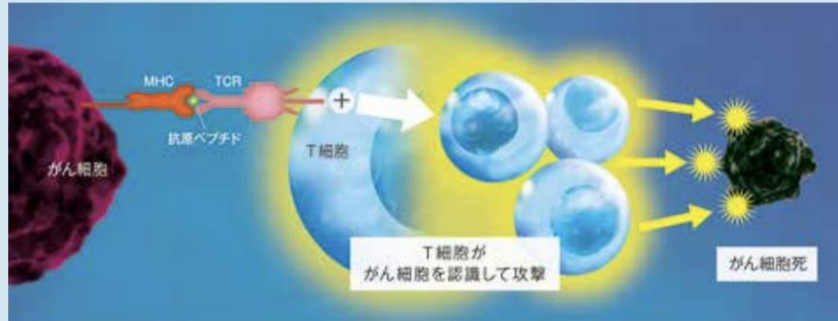
No. at Risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
A+AVD	664	643	626	613	540	524	516	497	479	456	361	347	325	206	192	180	102	87	79	28	24	21	5	3	3	0	0
ABVD	670	643	628	611	514	492	476	463	448	426	343	319	299	186	171	157	82	71	63	16	13	12	2	2	2	0	0

レジメンの変遷



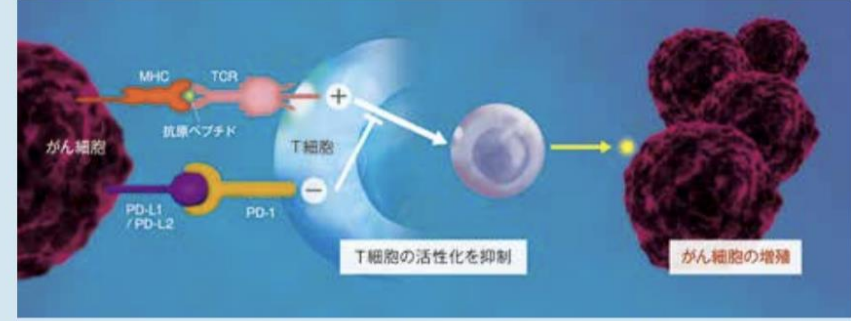
Nivolumab

● 免疫監視機構



T細胞は抗原提示しているがん細胞を認識し、細胞傷害活性を発揮する

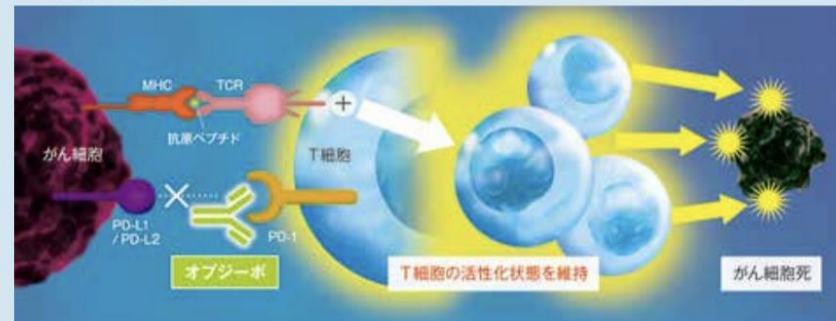
● がんの免疫逃避



がん細胞はPD-L1及びPD-L2を発現して、活性化されたT細胞に発現するPD-1と結合し、T細胞に抑制性シグナルを伝達する

オプジーボの作用

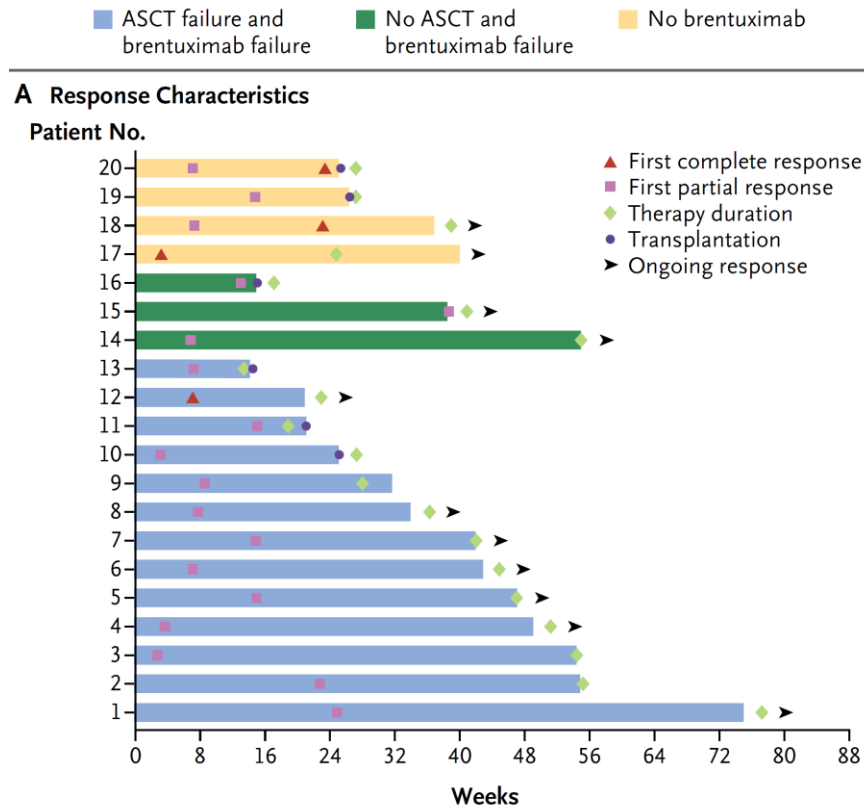
● T細胞の免疫応答維持



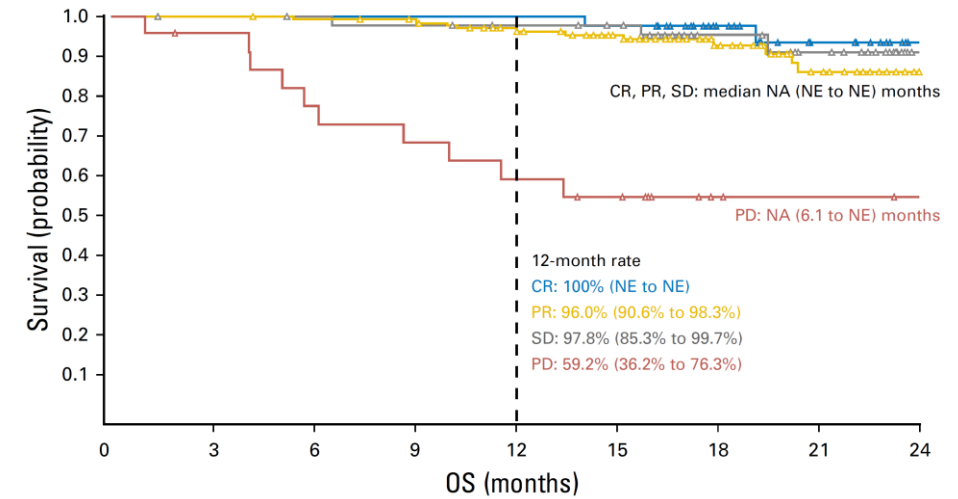
オプジーボは、PD-L1及びPD-L2とPD-1との結合を阻害し、T細胞への抑制性シグナルを減少させる

MHC：主要組織適合遺伝子複合体 TCR：T細胞受容体

Nivolumab for R/R cHL

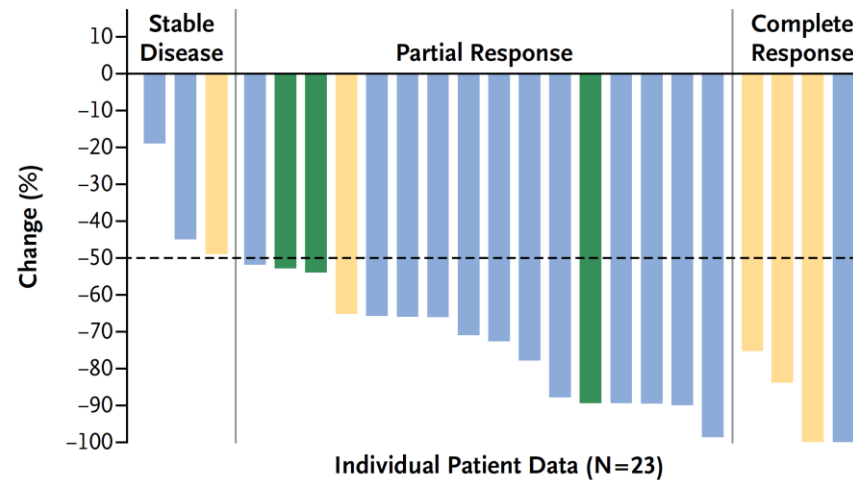


NEJM 2015, 372:311-9



No. at risk:	0	3	6	9	12	15	18	21	24
CR	40	40	40	40	40	39	26	16	7
PR	128	128	126	123	113	97	59	34	10
SD	47	46	45	44	42	39	25	16	3
PD	23	21	17	15	13	11	5	4	3

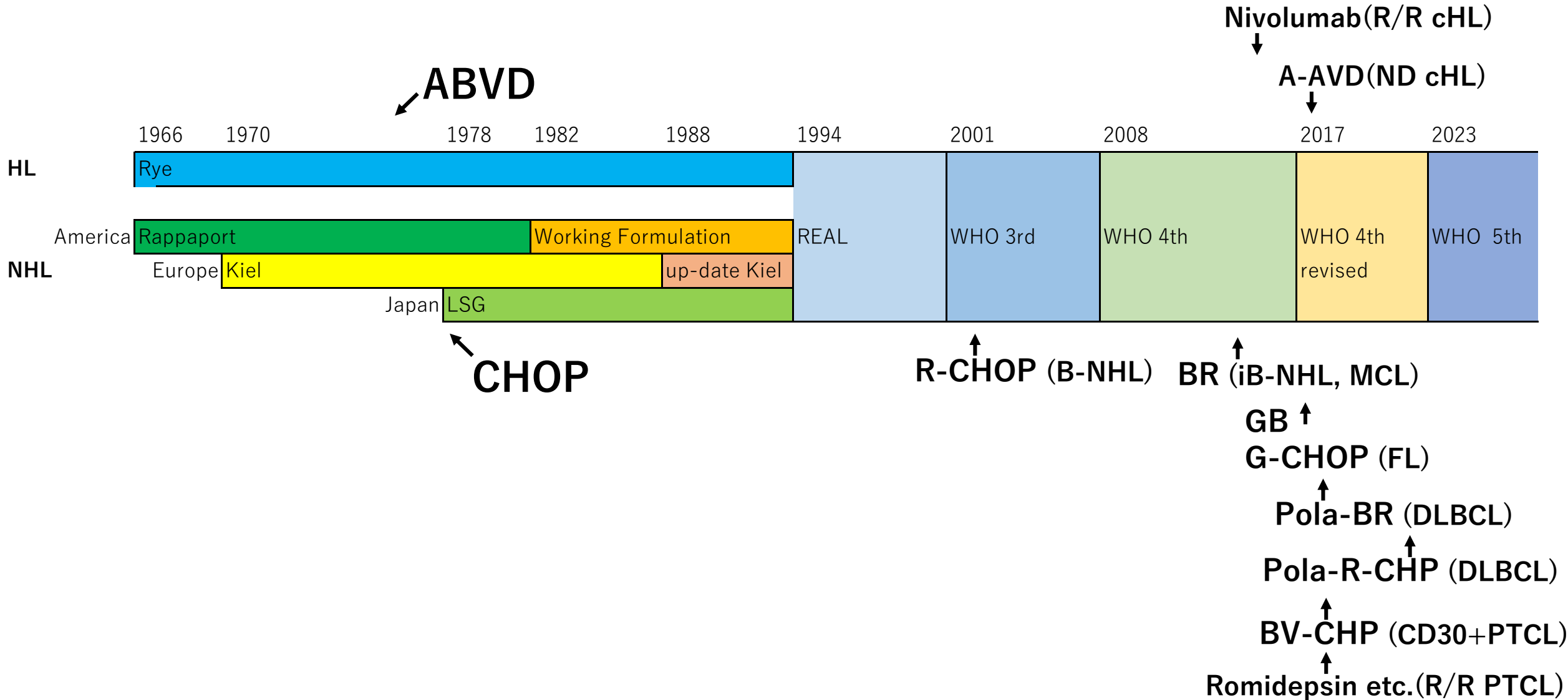
B Change in Tumor Burden



JCO 2018, 36:1428-39

Figure 1. Response Characteristics and Changes in Tumor Burden in Patients with Hodgkin's Lymphoma Receiving Nivolumab.

レジメンの変遷



結 語

- 悪性リンパ腫はHLとNHLに分けられ、現在は形態のみならず、免疫形質、遺伝子検査などからさらに詳細な亜型に分類されるようになったが、治療方針決定などの際には悪性度が重要。
- 1990年代にABVD, CHOP療法が初発HL, NHLの標準療法として確立され、以後も基本の治療である。
- 2000年代以降様々な分子標的薬剤や、旧来からあるBendamustineなどの薬剤を組み込んだregimenが開発され、支持療法の進歩もあり、徐々に治療成績は改善してきている。
- ただし、初発のCD30陰性中悪性度T/NK細胞リンパ腫はいまだにCHOP療法が標準治療であり成績の向上が見られないため、今後の展開が待たれる。