新CD20单抗治疗淋巴瘤的临床研究

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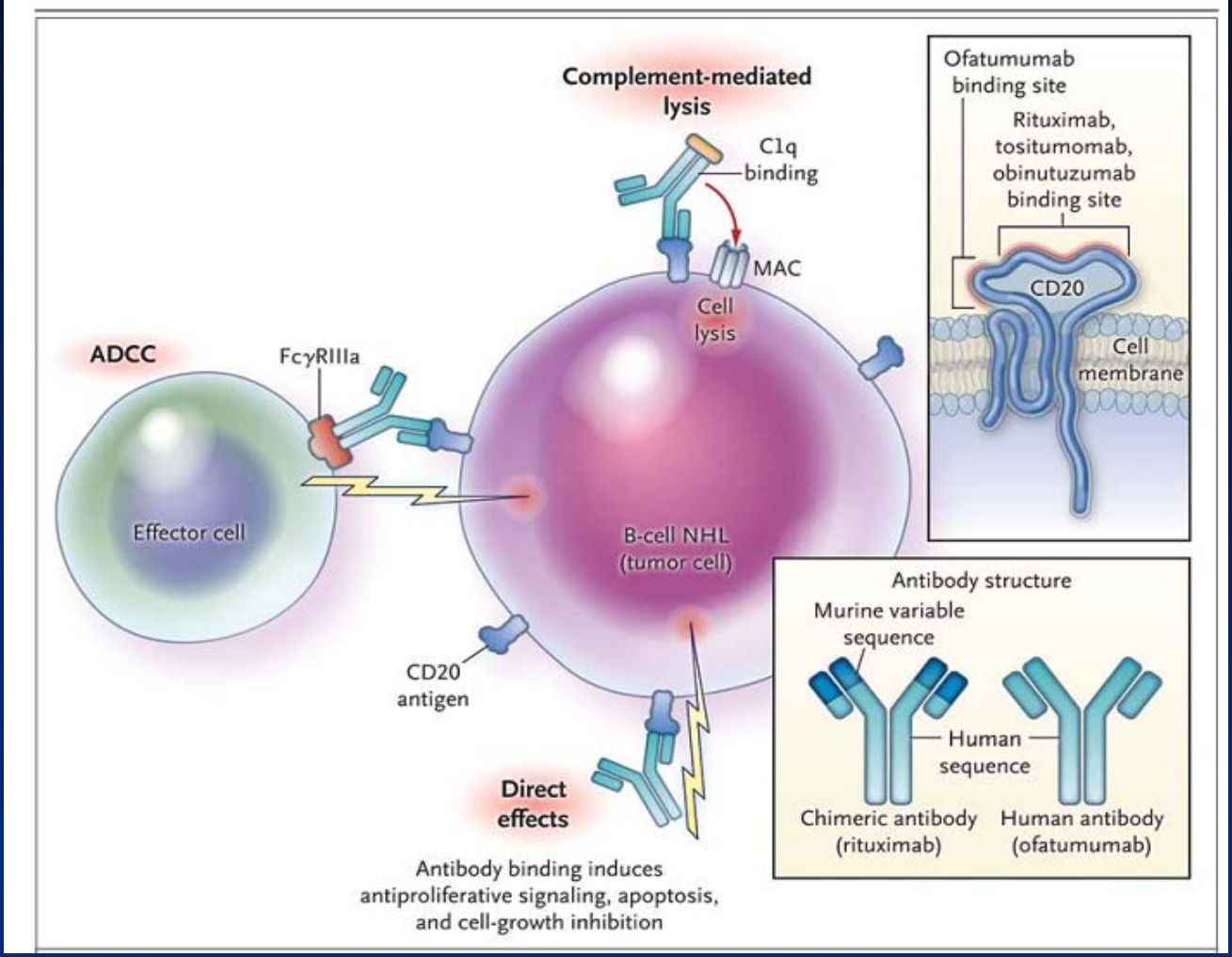
CD20抗体


Complement-mediated lysis
C1q binding
MAC
Cell lysis
ADCC
FcγRIIIa
Effector cell
B-cell NHL (tumor cell)
CD20 antigen
Direct effects
Antibody binding induces antiproliferative signaling, apoptosis, and cell-growth inhibition
Ofatumumab binding site
Rituximab, tositumomab, obinutuzumab binding site
CD20
Cell membrane
Antibody structure
Murine variable sequence
Human sequence
Chimeric antibody (rituximab)
Human antibody (ofatumumab)

不同CD20抗体的生物学特性

Nom	Compagnie	Type	ADCC	CDC	Apoptose
Rituximab	Roche/Genentech	chIgG1	++	++	+
Ocrelizumab	Roche/Genentech	huIgG1	++	+/-	+
Veltuzumab	Immunomedics	huIgG1	++	++	+
Ofatumumab	GenMab/GSK	huIgG1	++	**+++**	0
AME-133	Lilly	huIgG1	**+++**	++	+
PRO131921	Genentech	huIgG1	**+++**	+/-	+
GA101	Roche/Glycart	huIgG1	**+++**	0	**+++**
EMAB-6	LFB	huIgG1	**+++**	++	+
KM3065	Kyowa	huIgG1	**+++**	++	+
Others	Macogenics, Biolex				

Adapted from G. Cartron

Figure 1. Antibody-dependent cellular cytotoxicity in target cells after treatment with GA101, rituximab, or ofatumumab

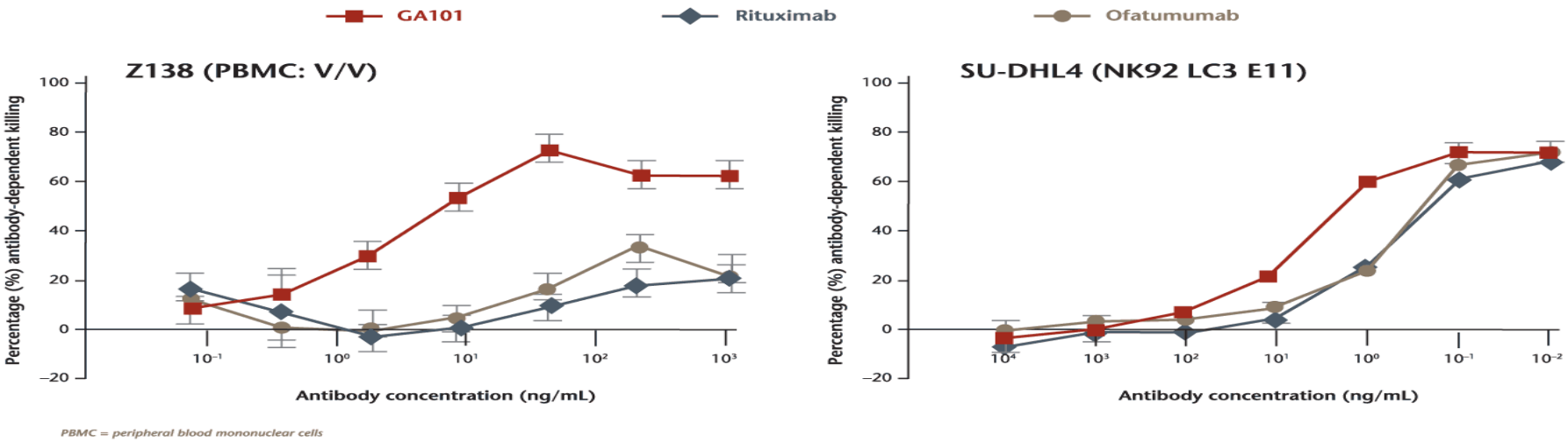


Figure 2. Complement-dependent cytotoxicity in target cells after treatment with GA101, rituximab, or ofatumumab

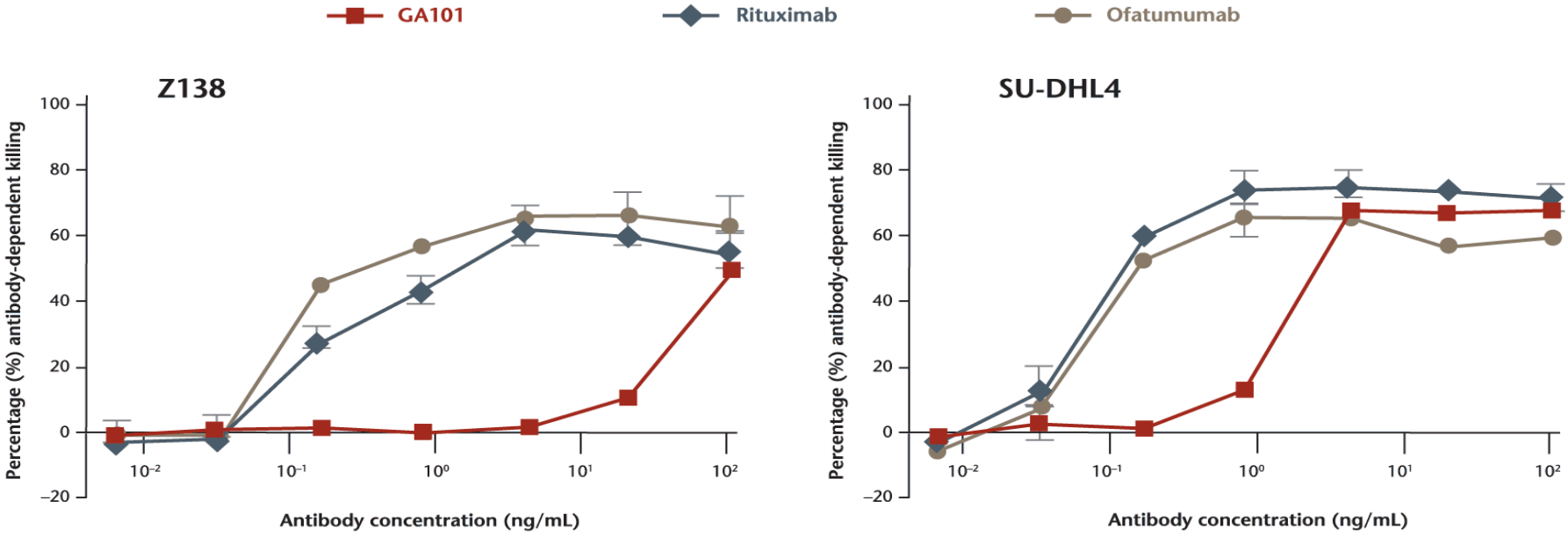
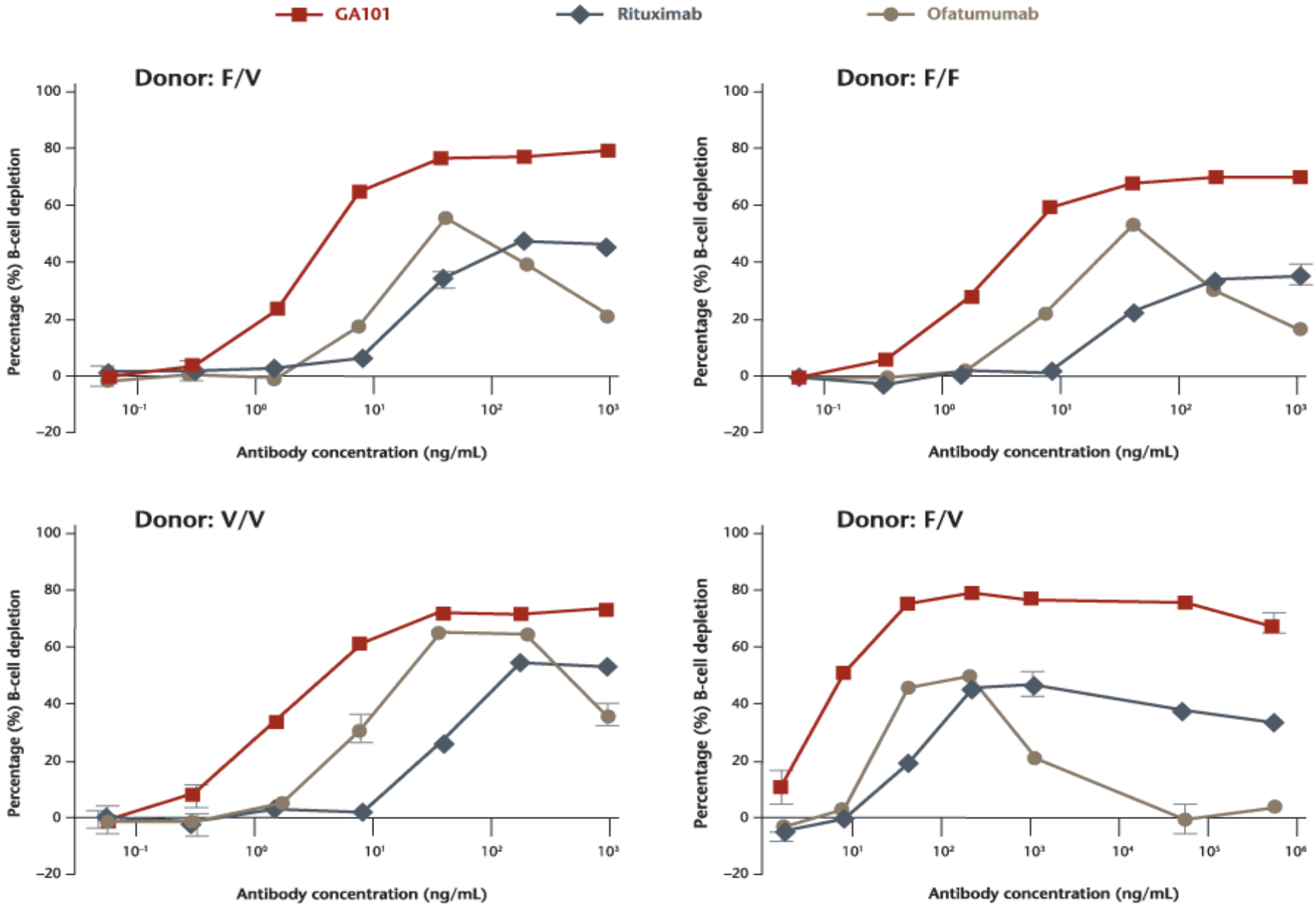
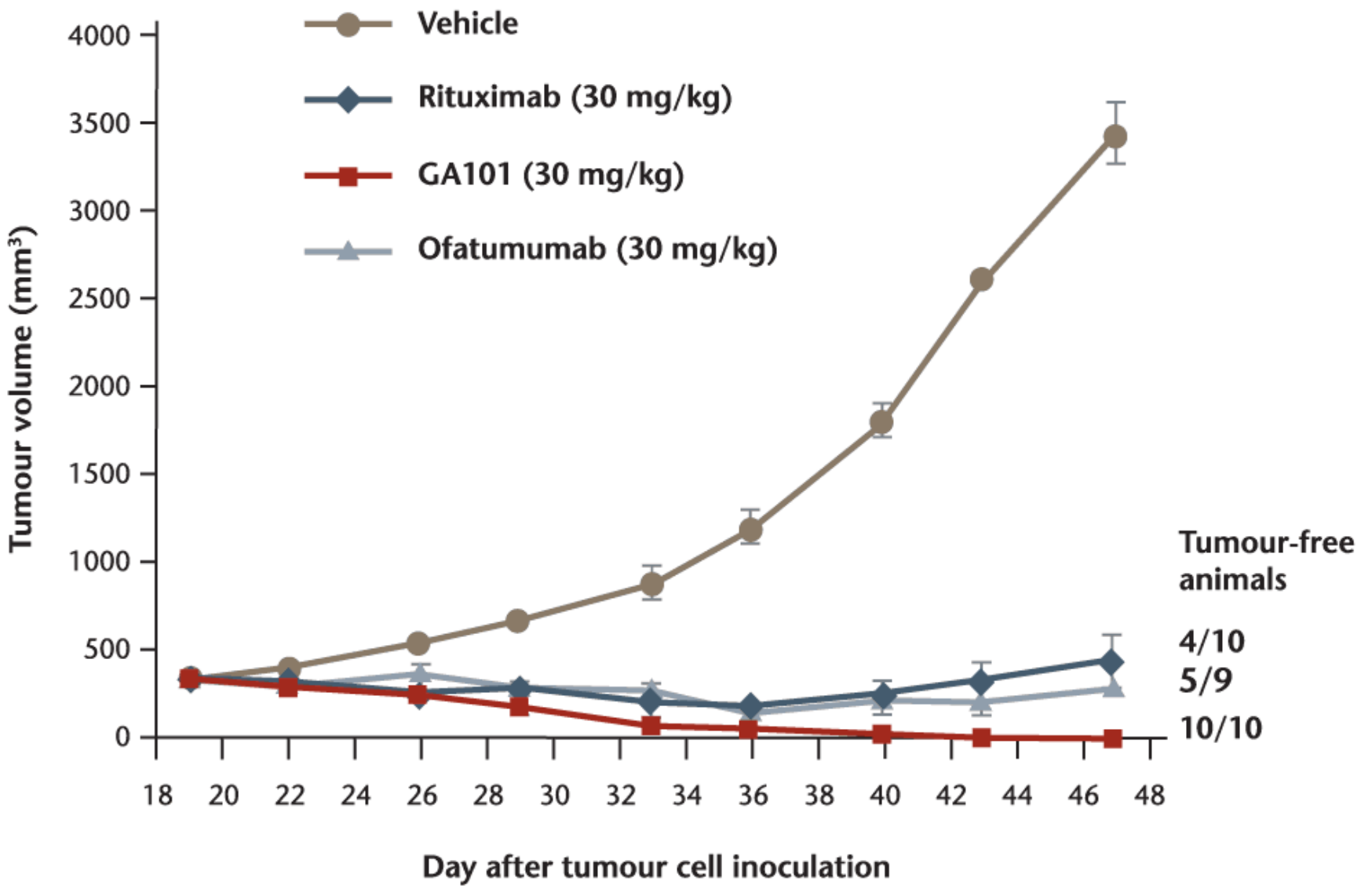


Figure 3. Whole blood B-cell depletion in an integrated assay of ADCC, CDC, and direct cell death mechanisms



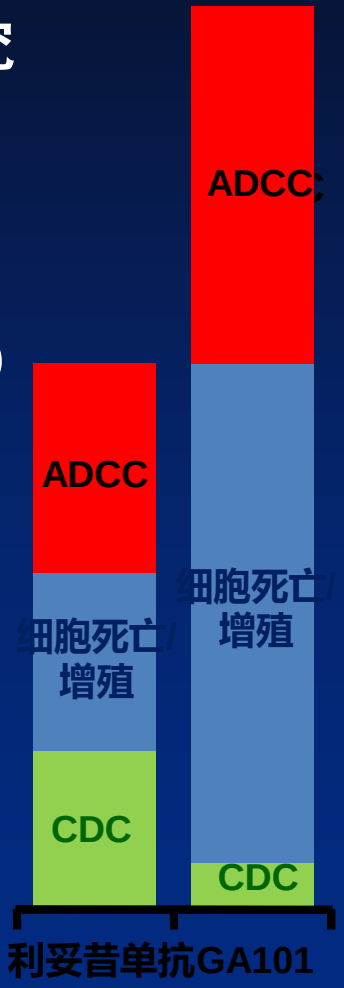
ADCC = antibody-dependent cellular cytotoxicity; CDC = complement-dependent cytotoxicity

Figure 4. Mean anti-tumoral activity in SU-DHL xenografts after treatment with GA101, rituximab, or ofatumumab



Obinutuzumab (GA101)

- GA101单药治疗RR-iNHL的I/II期 GAUGUIN(BO20999)研究
- GA101+CHOP或FC治疗RR-FL的Ib期GAUDI研究
- GA101 vs Rituximab治疗CD20+ iNHL的III期GAUSS研究
- GA101+CHOP方案一线治疗DCBCL的III期GATHER(GAO4915g)研究
- GA101+化疗 vs R+化疗用于初治晚期iNHL的III期GALLIUM (BO21223)研究
- GA101+Chl vs R-Chl用于初治CLL的III期CLL11研究



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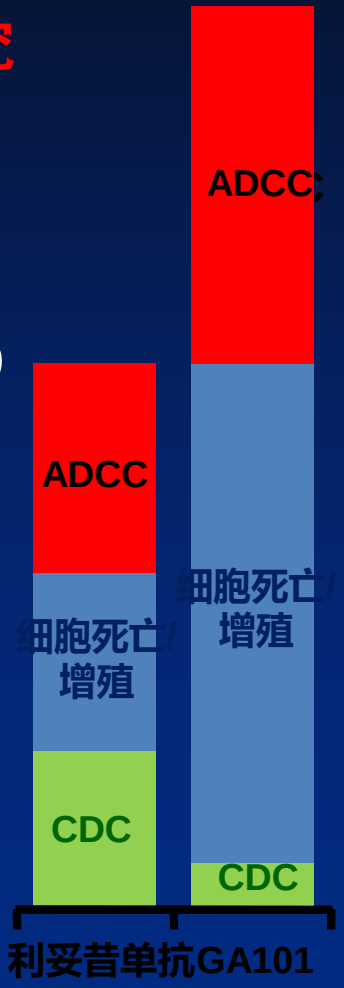
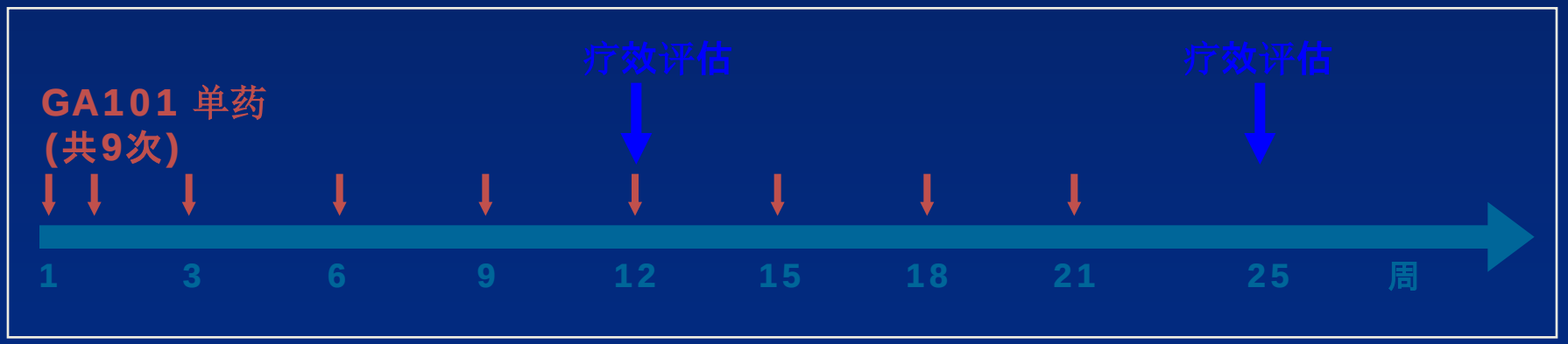


GA101治疗复发难治NHL(BO20999 Ⅰ期)

- 入选标准: 复发难治的 CD20+ 惰性NHL ：
  滤泡淋巴瘤: n = 13,
  小淋巴细胞淋巴瘤: n = 1
  淋巴浆细胞淋巴瘤: n = 1
  巨球蛋白血症： n = 1
- 非随机，剂量爬坡设计



Salles GA et al. *Proc ASH* 2011;Abstract 268.

GA101治疗复发难治NHL(B020999 Ⅰ期)

Cohort (n = 3/group)	GA101 剂量 (mg) Dose 1/doses 2-9
1	50/100
2	100/200
3	200/400
4	400/800
5	800/1,200
6	1,200/2,000
7	1,600/1,600/800*

* Dose 1/dose 2/dose 3-9

Salles GA et al. *Proc ASH* 2011;Abstract 268.

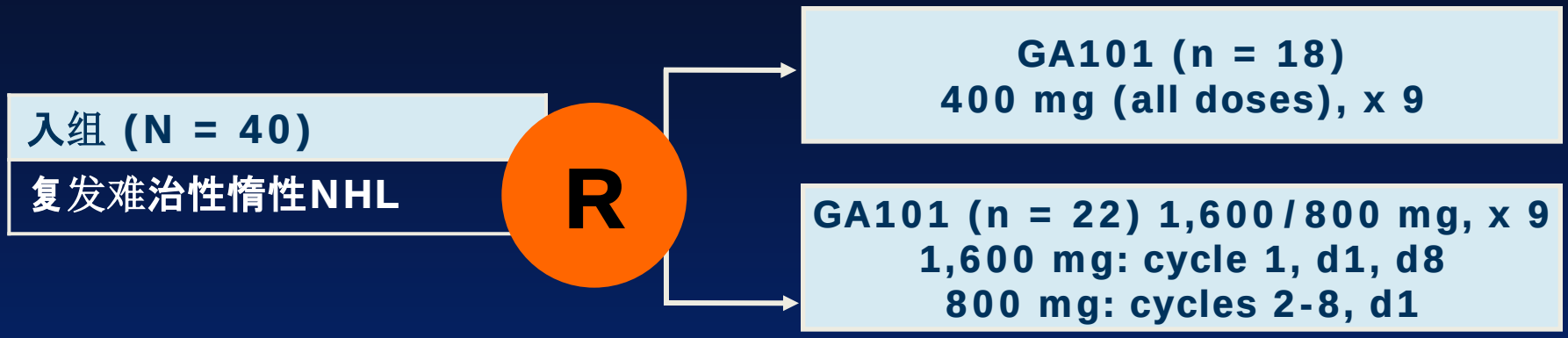
GA101治疗复发难治NHL(BO20999 Ⅰ期)

	最佳疗效	治疗结束时
总有效率 (ORR)	56%	44%
完全缓解 (CR)	31%	25%
部分缓解 (PR)	25%	19%

- 所有剂量水平均有效
  - 剂量疗效无明确对应关系
- 中位有效时间: 32 个月

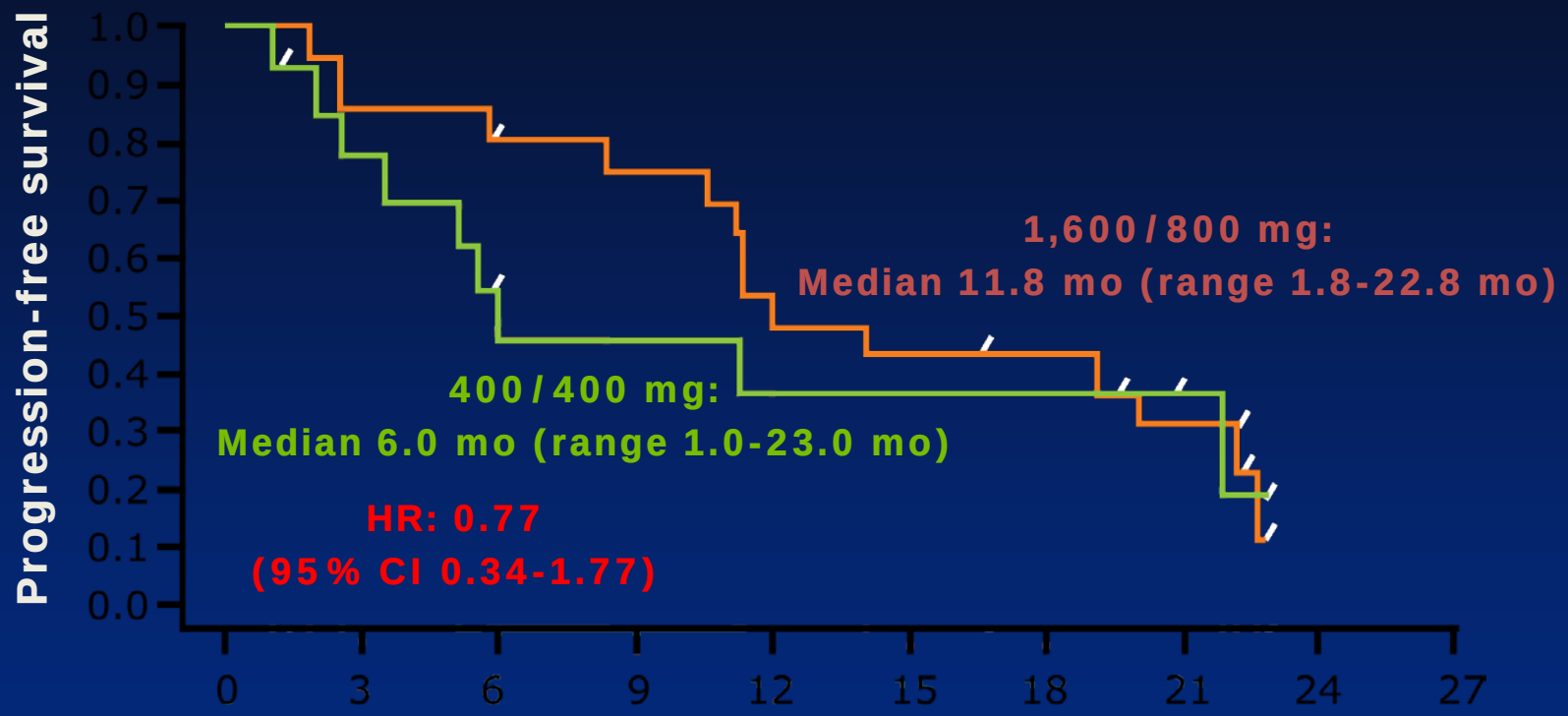
Salles GA et al. *Proc ASH* 2011;Abstract 268.

GAUGUIN II期临床研究



所有患者	400/400 mg (n = 18)	1,600/800 mg (n = 22)
ORR	17%	55%
CR/CRu	—	9%
PR	17%	45%
SD	33%	27%
PD	50%	18%
Rituximab耐药患者	(n = 12)	(n = 10)
ORR	8%	50%
CR/CRu	—	10%
PR	8%	40%
SD	33%	30%
PD	58%	20%

FL患者PFS



Patients at risk, n										
400/400 mg	14	10	5	5	4	4	4	2	0	0
1,600/800 mg	20	17	15	14	9	8	7	5	0	0

中位随访时间：23.1月

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3/4度不良反应

不良反应	400/400 mg (n = 18)	1,600/800 mg (n = 22)
血小板减少	0%	5%
淋巴细胞减少	6%	9%
粒缺/发热性粒缺	0%	19%
感染	0%	5%
输液反应	0%	9%
哮喘	0%	5%
肝损害	0%	5%

根据以上数据和药代动力学结果， 推荐1000 mg作为后续研究剂量

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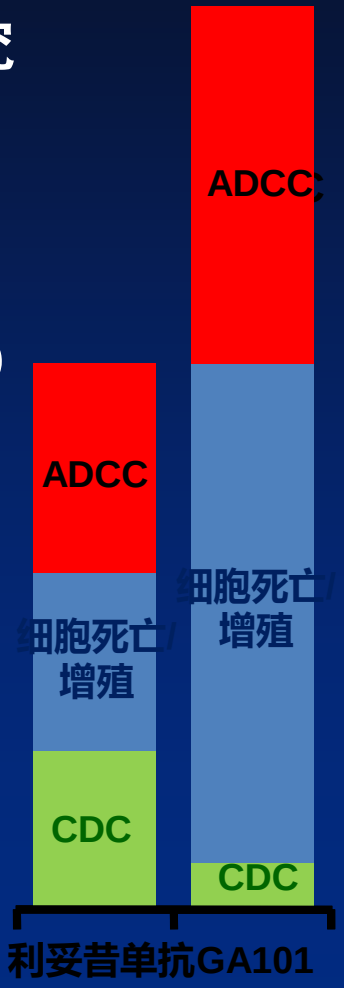
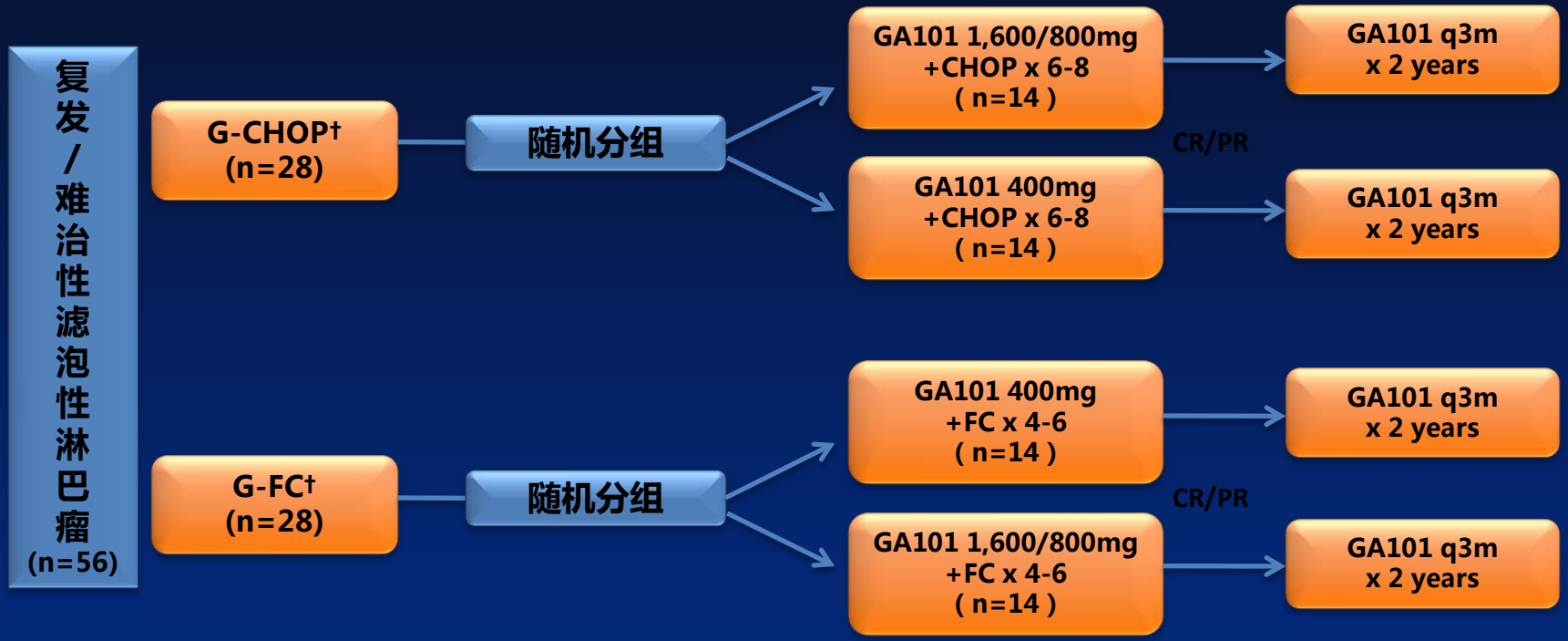


GAUDI Ib期研究
GA 101联合FC或CHOP治疗复发难治FL



	G-CHOP n=28	G-FC n=28
ORR	27 96.4%	26 92.9%
CR	11 39.3%	14 50.0%
PR	16 57.1%	12 42.9%

GA101治疗复发难治FL(GAUDI Ib期)

不良事件	G-CHOP (n = 28)	G-FC (n = 28)
给药相关反应 (IRR)* 任何级别 3/4级	 64% 7%	 79% 7%
中性粒细胞减少 (3/4级)	39%	50%
由于血液学毒性或感染引起的疗程推迟	6%	10%
由于毒性引起的化疗减量	29%	36%

* IRRs 主要发生在第1次给药时. G = GA101

- 没有证据表明 1,600/800-mg剂量组较400/400 mg剂量组毒性增加
- G-CHOP组：28/28例患者； G-FC 组：22/28例患者完成全部治疗

Radford J et al. *Proc ASH* 2011;Abstract 270.

GA101治疗复发难治FL(GAUDI Ib期)

疗效*	G-CHOP (n = 28)	G-FC (n = 28)
ORR	96.4%	92.9%
CR	39.3%	50.0%
PR	57.1%	42.9%
SD	3.6%	0%
PD	0%	3.6%

* 按照IWG标准， CRu纳入PR

- G-FC组中3.6%的患者未评价.
- 经匹配性分析， G-CHOP组有效率优于EORTC 20981 研究中R-CHOP治疗组

Radford J et al. *Proc ASH* 2011;Abstract 270.

GA101治疗复发难治FL(GAUDI Ib期)结论

- GA101 联合化疗治疗 FL安全性可，同时有效率优于历史研究对照
- 多数病人可耐受G-CHOP每3周给药方式
- G-FC 方案的耐受性差于 G-CHOP
- 根据以上结果，GA101 可以与CHOP或其他化疗方案联合，在进一步的随机III 期临床试验中与标准方案R-CHOP进行比较 (NCT01287741)

Radford J et al. *Proc ASH* 2011;Abstract 270.

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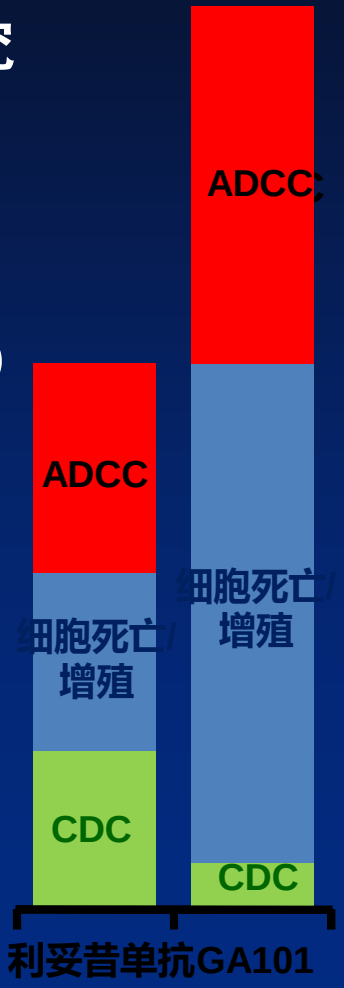
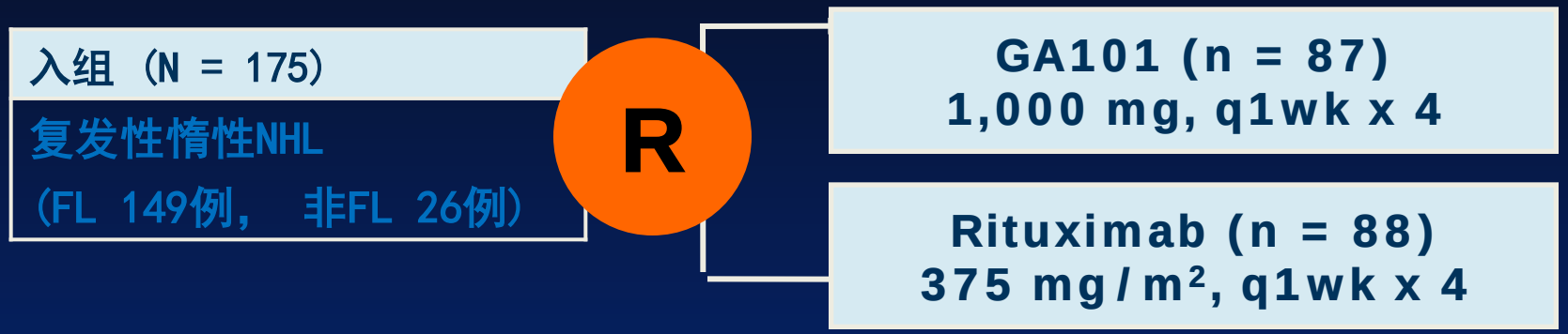


GA101治疗复发难治iNHL(GAUSS Ⅱ期)



诱导治疗后无进展者每2月维持治疗2年

不良反应	GA101(n = 88)	Rituximab (n = 87)
输注反应(IRR) 任何 3/4度	 72% 11%	 49% 5%
疲乏	23%	17%
背痛	7%	2%
食欲下降	7%	2%
失眠	5%	0%

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GA101治疗复发难治iNHL(GAUSS Ⅱ期)

	FL患者			
	GA101 (n = 74)		R (n = 75)	
肿瘤缓解	INV	IRF	INV	IRF
ORR	43.2%	43.2%	38.7%	28%
CR/CRu	10.8%	NR	6.7%	NR
PD	20.3%		17.3%	
	全部患者			
	GA 101 (n = 88)		R (n = 87)	
ORR	43.2%	42.0%	35.6%	24.1%

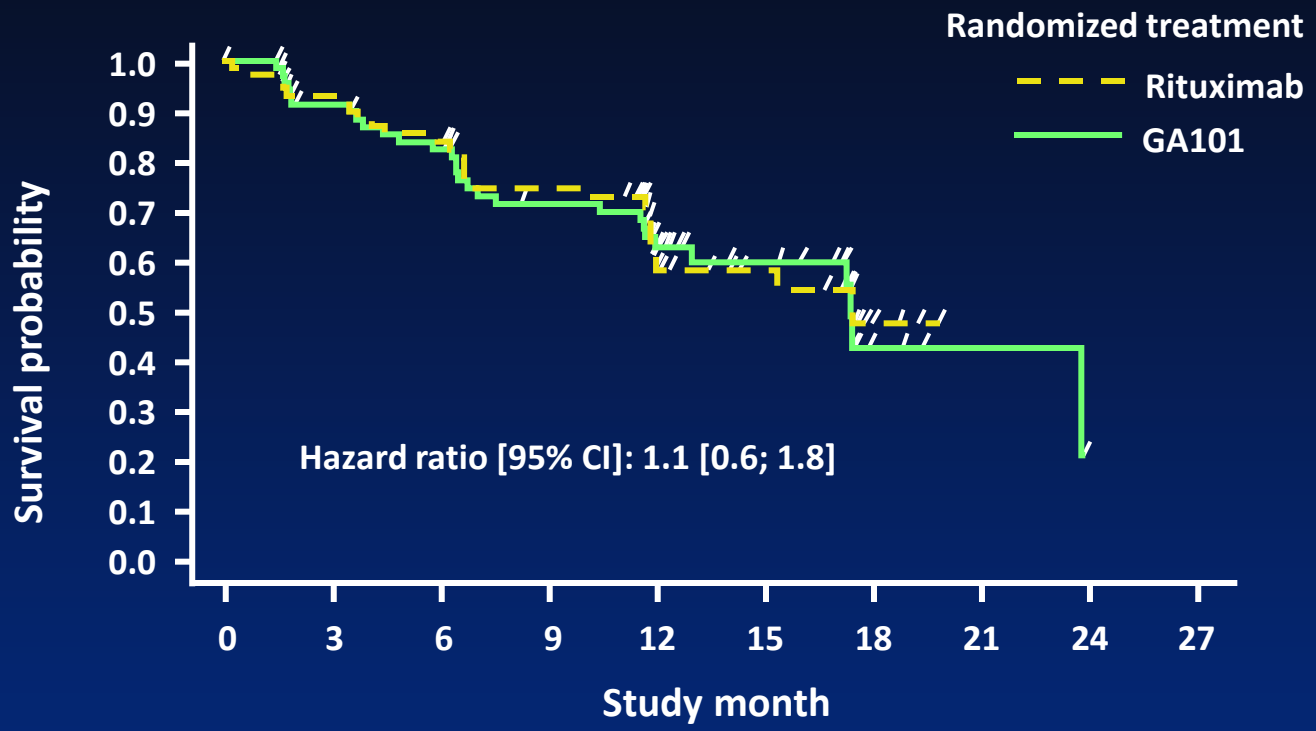
GA101治疗复发难治iNHL(GAUSS Ⅱ期)

不良事件	GA101 (n = 88)	Rituximab (R) (n = 87)
给药相关反应 (IRR) 任何级别 3/4级	 72% 11%	 49% 5%
疲乏 (任何级别, ≥5%)	23%	17%
背痛 (任何级别, ≥5%)	7%	2%
食欲下降 (任何级别, ≥5%)	7%	2%
失眠 (任何级别, ≥5%)	5%	0%

- 严重不良事件: GA101 组(n = 5) ，分别为IRR (n = 2), 中性粒细胞减少性发热 (n = 1), 胸腔积液 (n = 1), 肾结石(n = 1); R 组(n = 9)
- 死亡: GA101 (n = 1) ，分别为 肺曲霉病 R (n = 1) 导致心跳呼吸骤停
- 停药: GA101 (n = 4, 3 例由于 IRR, 1 例由于体位性低血压), R (n = 7)

Sehn LH et al. *Proc ASH* 2011;Abstract 269.

PFS Assessed by Investigators in FL Pts



Patients at risk, n

Rituximab	75	63	56	48	20	15	3	0	0	0
GA101	74	61	55	45	26	19	4	2	0	0

	Rituximab (n = 75)	GA101 (n = 74)
Patients with an event, n (%)	26 (34.7)	29 (39.2)
Median time to event, mo	17.4	17.3
95% CI for median time to event	[11.8; –]	[13.0; –]

Sehn et al. ASH 2011.

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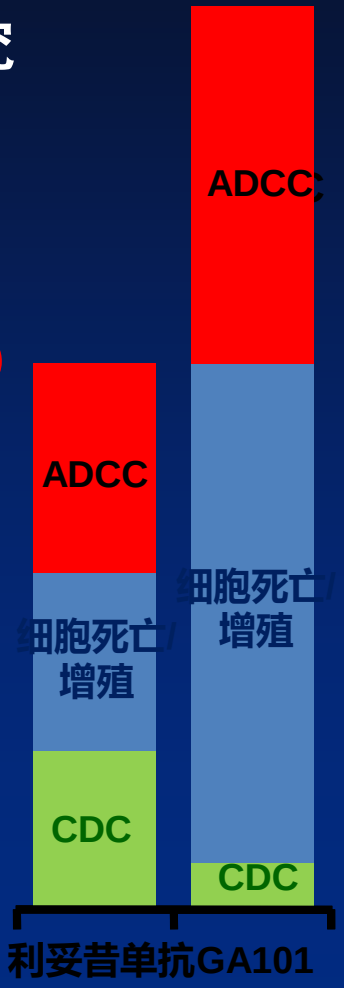
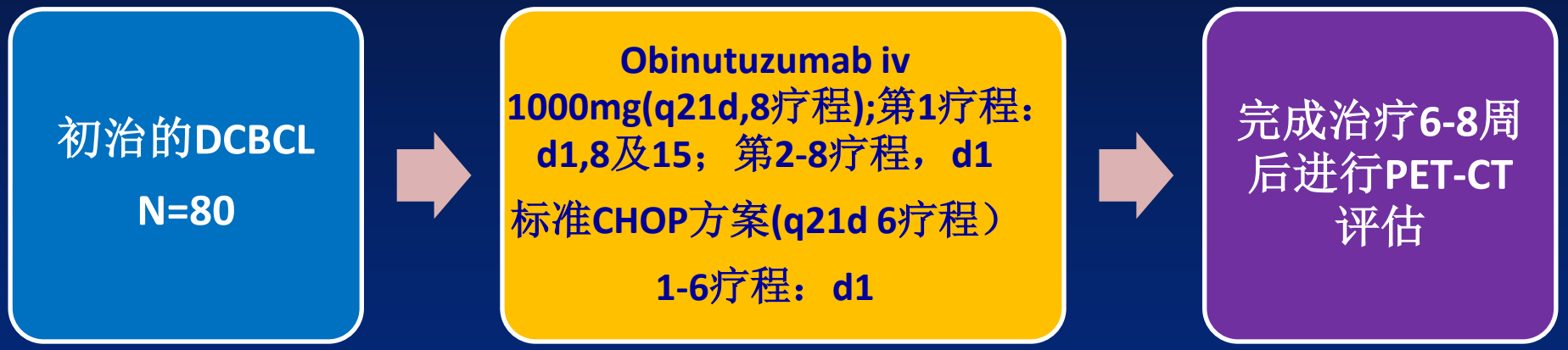


Obinutuzumab（GA101）联合CHOP方案在一线治疗DCBCL的安全性以及疗效
II期 GATHER研究（GAO4915g)



主要终点

疗效：ORR及治疗完成时研究者及独立审查委员会评估的CR

次要终点：

根据细胞来源亚型在治疗完成时的ORR（ABC或者GCB型）

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基线特征

基线	N=80
中位年龄，岁（范围）	61（24-80）
≥69岁，n(%)	41（51.3）
男，n(%)	47（58.8）
种族，n(%)	
亚洲	3（3.8）
黑人	9（11.3）
白人	64（80.0）
其他	4（5.0）
B症状，m(%)	43（53.8）

基线特征

基线	N=80
Ann Arbor 临床分期，n(%)	
II(巨块)	11(13.8)
III	28(35.0)
IV	41(51.3)
IPI评分，n(%)	
低危	9(11.3)
低中危	34(42.5)
中高危	21(26.3)
高危	16(20.0)
ECOG PS，n(%)	
0	28(35.0)
1	46(57.5)
2	6(7.5)

总安全性

- 所有患者均遇到至少1级AE（1251 事件）
- 根据研究者评估62例患者（77.5%）出现与obinutuzumab相关毒性
- ½级注射反应是obinutuzumab最常见的AE
- 严重的AES出现在26例患者（32.5%），7（8.8%）与obinutuzumab相关
- 治疗过程中死亡：
- AE相关：2例
- 疾病进展：3例

≥3级AE事件

AE, n(%)	患者（n=80）
3级	25（43.8）
粒细胞减少	6（7.5）
分叶粒细胞减少	5（6.3）
贫血	4（5.0）
低钾	3（3.8）
低磷	3（3.8）
晕厥	3（3.8）
腹泻	3（3.8）
肺炎	3（3.8）
4级	28（35.0）
粒细胞减少	17（21.3）
分叶粒减少	6（7.5）
血小板减少	4（5.0）
脓毒症	2（2.5）
5级	2（2.5）
心血管问题	1（1.3）
颅内感染	1（1.3）

注射持续时间缩短

- 在头20例患者使用常规注射时间注射GA101证实其安全性后，缩短注射持续时间（SDI）为120分钟及90分钟
- 如果在注射obinutuzumab注射前出现外周淋巴细胞数＜5,000/ul及在第一周期并未出现严重和/或≥3级注射相关AEs，患者在第二周期是可以SDI
- 总共288次SDIs (24例 120min 及 264例 90min)给53例患者
- SDIs仅发生3例注射相关性AEs，没有大于2级的相关事件
- 1例患者出现2级乏力，1例出现1级呕吐，1例出现1级注射相关反应及恶心。

疗效

缓解率，n(%) (95%CI)	研究者评估	独立审查复核
有效缓解(CR+PR)	66(82.5) (72.4-90.1)	63(78.8) (68.2-87.1)
CR	44(55.0) (43.5-66.2)	48(60.0) (48.4-70.8)
PR	22(27.5) (18.1-38.6)	15(18.8) (10.9-29.0)
SD	-	2(2.5) (0.3-8.7)
PD	9(11.3) (5.3-20.3)	9(11.3) (5.3-20.3)
未能评估	1(1.3) (0.03-6.8)	-
数据丢失	4(5.0) (1.4-12.3)	6(7.5) (2.8-15.6)

原始资料中的细胞类型

- 61例能获得原始资料中的细胞类型（无丢失数据个案）
  - 活化B细胞样（ABC）：19例患者（31.1%）
  - 生长中心 B细胞

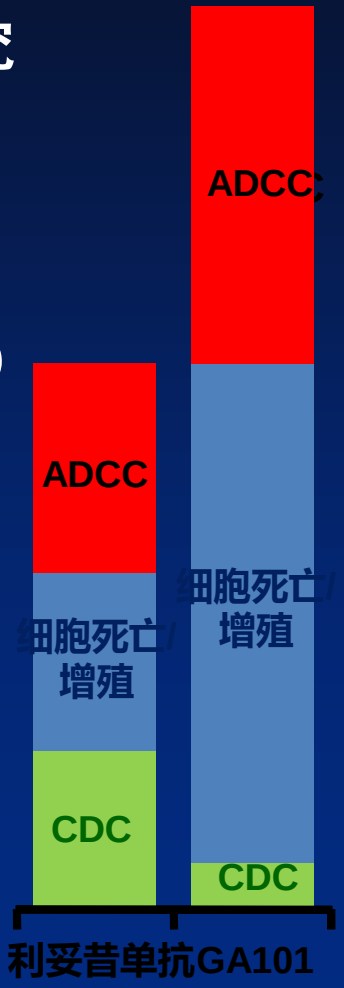
有效率，n(%)(95% CI)	ABC N=19	GBC N=33
有效率(CR+PR)	17(78.9) (54.4-94.0)	28(84.8) (68.1-94.9)
CR	9(47.4) (24.5-71.1)	21(63.6) (45.1-79.6)
PR	6(31.6) (12.6-56.5)	7(21.2) (9.0-38.9)
PD	3(15.8) (3.4-39.6)	3(9.1) (1.9-24.3)
数据丢失	1（5.3） （0.1-26.0）	2（6.1） （0.7-20.2）

结论

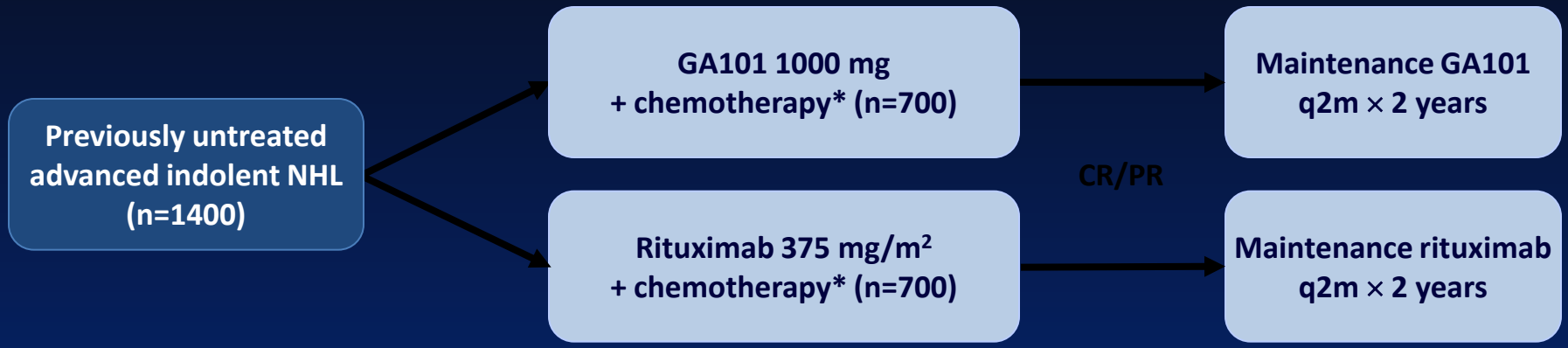
- G-CHOP在初治DLBCL中是安全的，同时在治疗过程中CHOP方案为剂量强化方案
- 注射相关的AES在第一次注射时经常出现但是一般为轻中度，在症状改善后患者可以继续注射
- SDI在符合的患者中是安全的
- 最重要的AE是粒细胞减少及分叶粒细胞减少，但是这些可以使用GCSF预防
- 初步的疗效实在预测范围内，进一步次要终点评估正在进行
- 这些数据为正在进行的G-CHOP vs R-CHOP在DLBCL的III期研究（NCT01287741）提供进一步合理参考

Obinutuzumab (GA101)

- GA101单药治疗RR-iNHL的I/II期 GAUGUIN(BO20999)研究
- GA101+CHOP或FC治疗RR-FL的Ib期GAUDI研究
- GA101 vs Rituximab治疗CD20+ iNHL的III期GAUSS研究
- GA101+CHOP方案一线治疗DCBCL的III期GATHER(GAO4915g)研究
- GA101+化疗 vs R+化疗用于初治晚期iNHL的III期GALLIUM (BO21223)研究
- GA101+Chl vs R-Chl用于初治CLL的III期CLL11研究



GALLIUM (BO21223) Phase III: Study design



***FL:** Each site to choose 1 of 3 chemotherapy regimens (CHOP, CVP, or bendamustine) which will; then be administered to all patients
Non-FL: CHOP, CVP, or bendamustine selected on a patient-by-patient basis

Experimental arm	GA101 1000 mg d1, d8, d15 cycle 1; d1 cycles 2-8 q21d + CHOP, CVP or cycles 2–6 q28d + bendamustine
Control arm	Rituximab 375 mg/m^2 on d1 cycles 1-8 q21d + CHOP, CVP or cycles 1-6 q28d + bendamustine
Primary endpoint	Investigator-assessed PFS
Extended treatment	Patients achieving CR, PR or SD, may continue induction therapy every 2 months for up to 2 years

www.clinicaltrials.gov; NCT01332968

Obinutuzumab (GA101)

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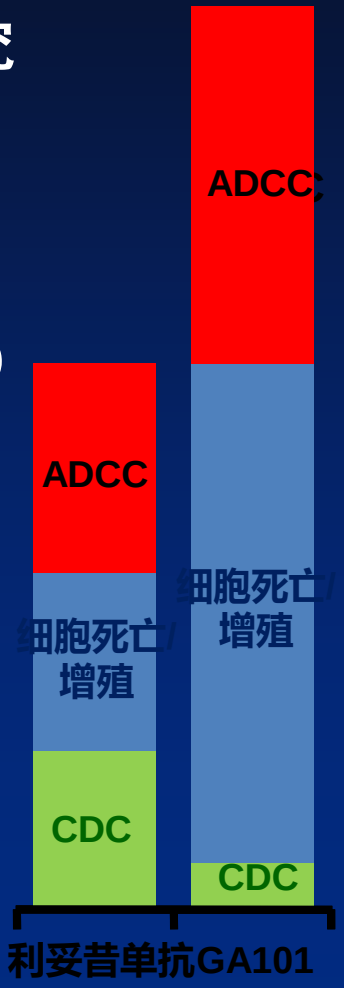
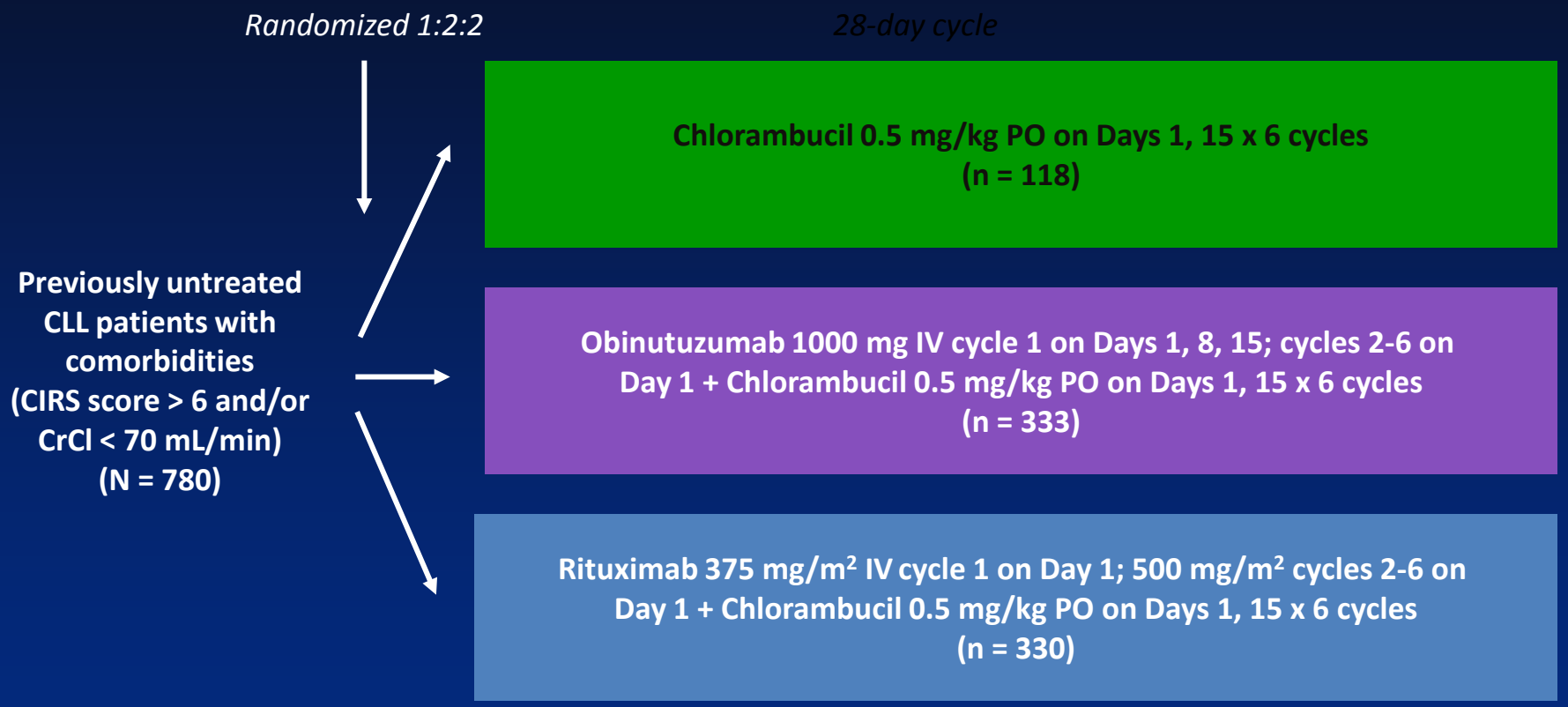
- GA101+Chl vs R-Chl用于初治CLL的III期CLL11研究

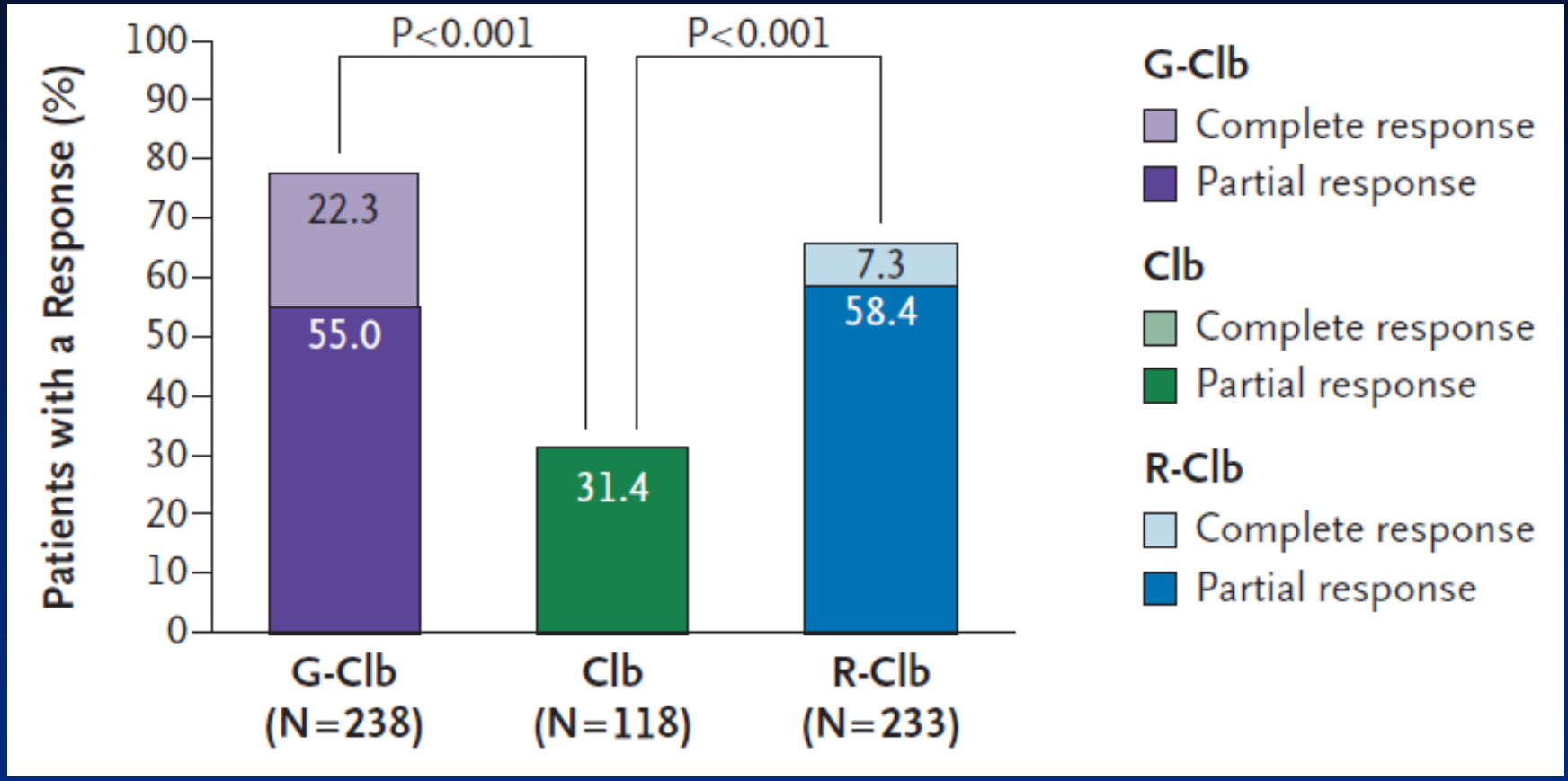


CLL11 Trial:
Obinutuzumab + Chl v Rituximab + Chl



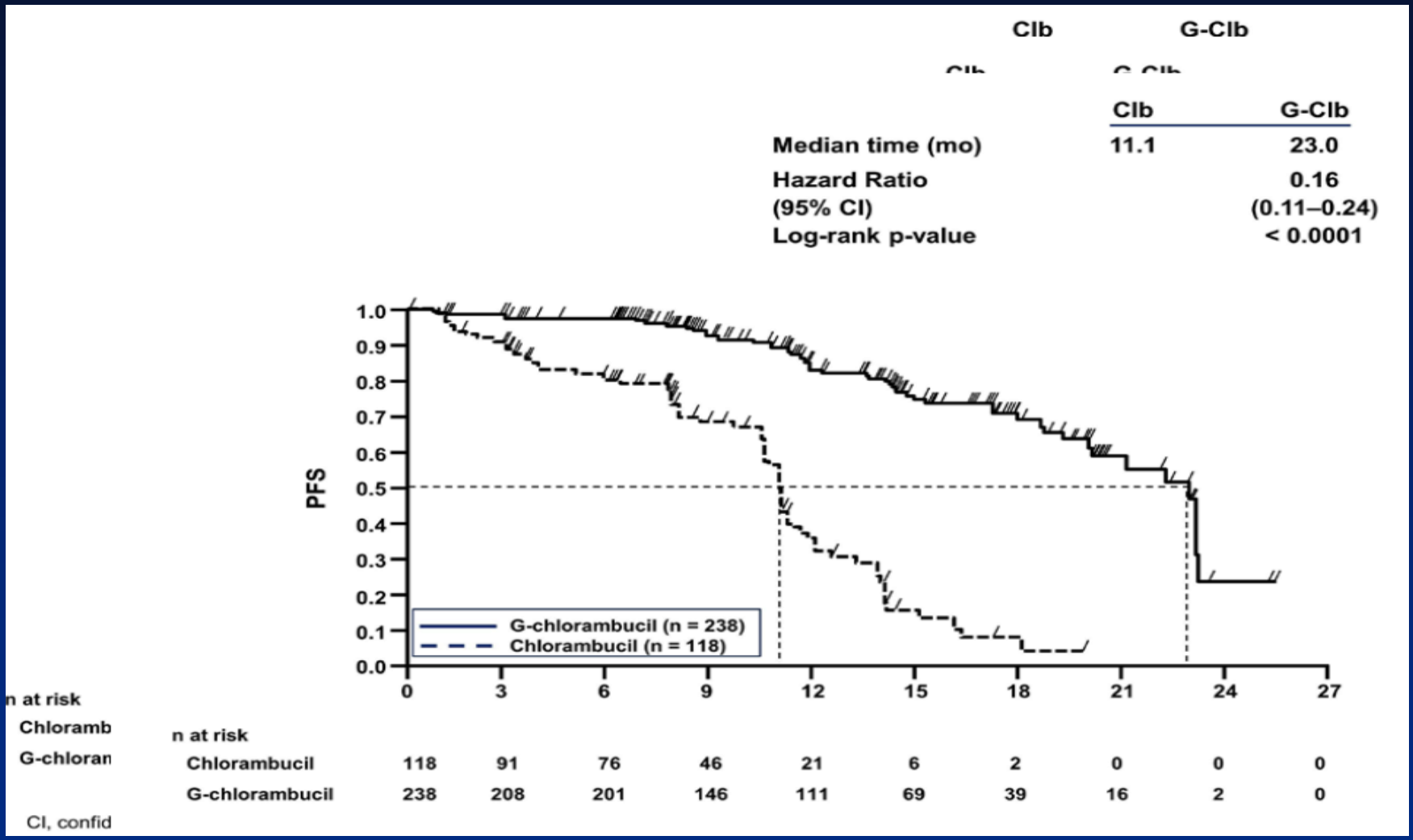
Goede V, et al. ASH 2013. Abstract 6.; Goede V, et al. *NEJM* 2014 [Epub ahead of print]

CLL11 Trial:
Obinutuzumab + Chl v Rituximab + Chl



Goede V, et al. ASH 2013. Abstract 6.; Goede V, et al. *NEJM* 2014 [Epub ahead of print]

CLL11 Trial:
Obinutuzumab + Chl vs Chl



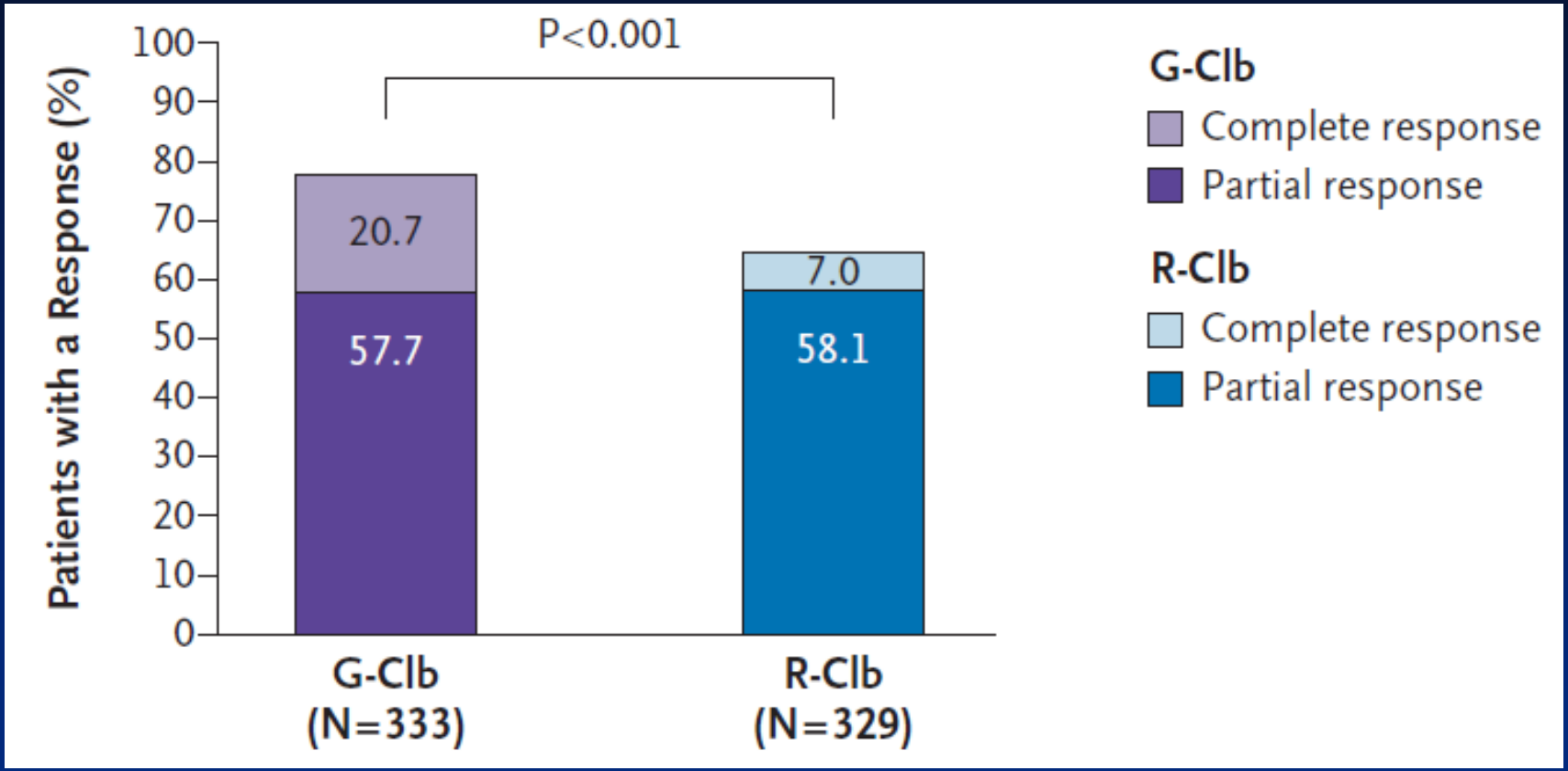
CLL11 Trial:
Obinutuzumab + Chl vs Rituximab + Chl

Grade ≥ 3, %	Obinutuzumab + Chlorambucil, n = 336*	Rituximab + Chlorambucil, n = 321*
Any	70	55
Infusion-related reaction	20	4
Neutropenia	33	28
Anemia	4	4
Thrombocytopenia	10	3
Infection	12	14
Pneumonia	4	5

*Includes 5 patients randomized to who mistakenly received obinutuzumab-chlorambucil.

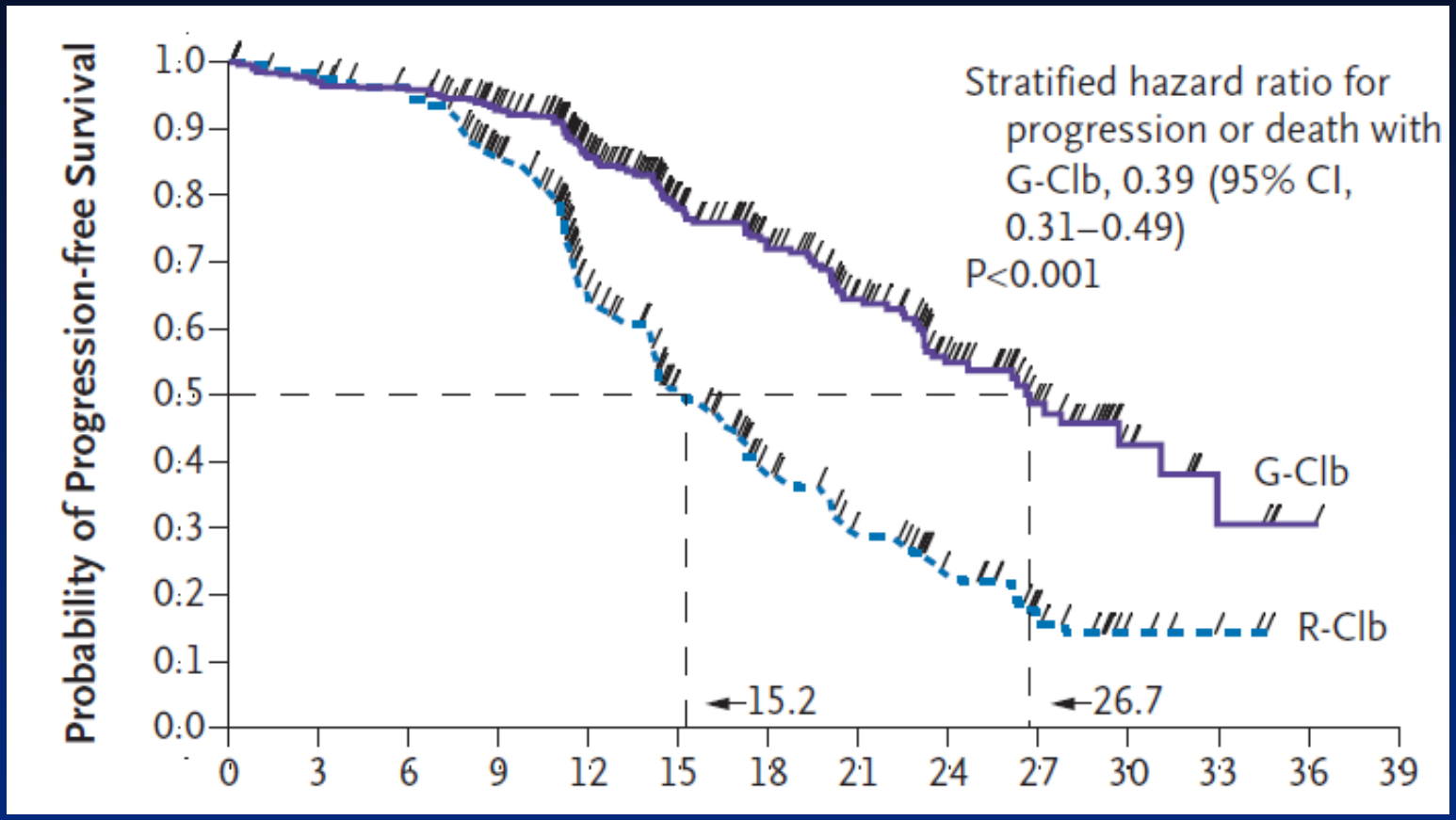
Goede V, et al. ASH 2013. Abstract 6.; NEJM 2014 [Epub ahead of print]

CLL11 Trial:
Obinutuzumab + Chl vs Rituximab + Chl



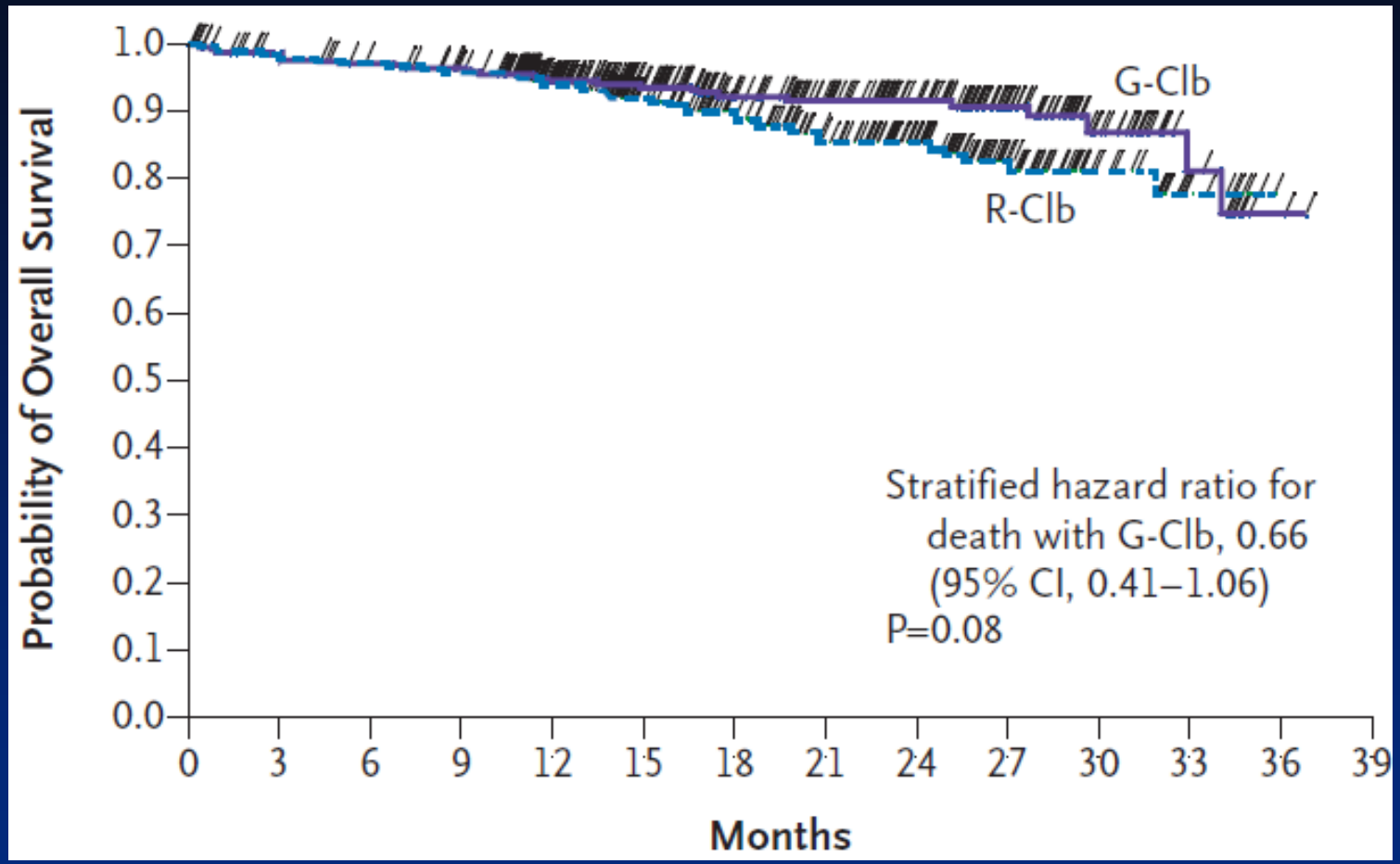
Goede V, et al. ASH 2013. Abstract 6.; *NEJM* 2014 [Epub ahead of print]

CLL11 Trial (G-Chl v. R-Chl) PFS



Goede V, et al. ASH 2013. Abstract 6.; NEJM 2014 [E-pub ahead of print]

CLL11 Trial (G-Chl v. R-Chl) OS



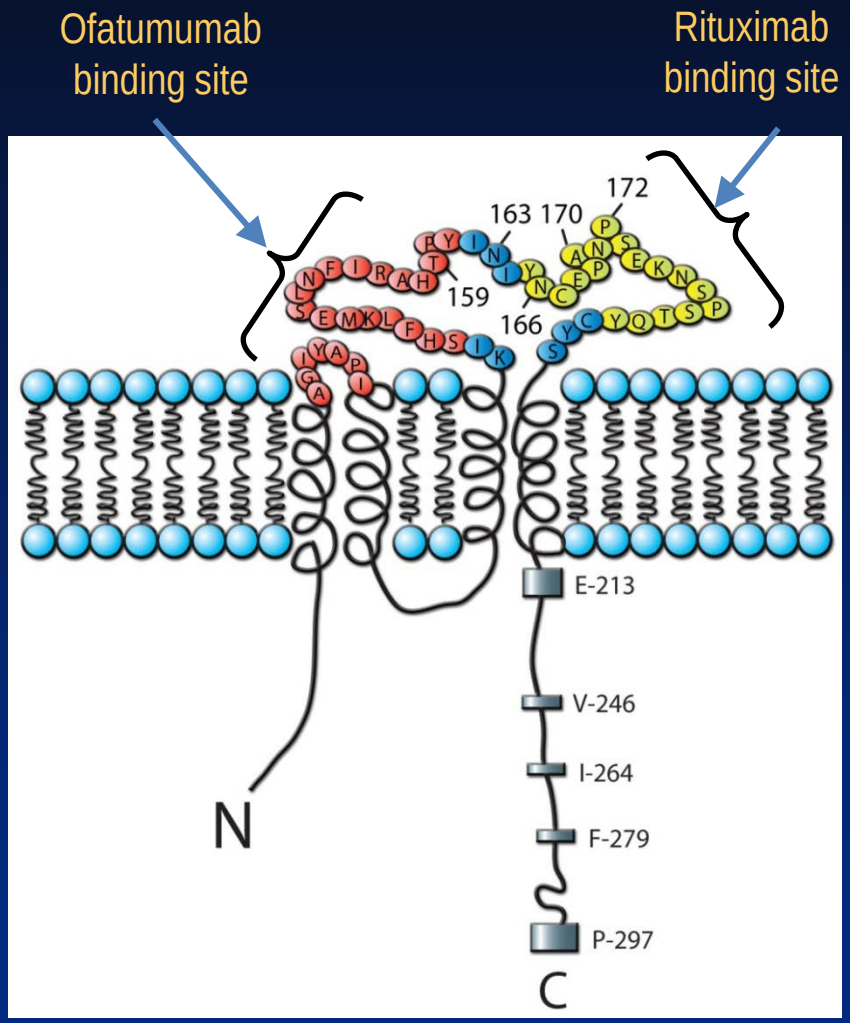
Goede V, et al. ASH 2013. Abstract 6.; NEJM 2014 [E-pub ahead of print]

Obinutuzumab

Monoclonal Ab	Ig type	Patients	Regimen	Overall response rate	Adverse events
Obinutuzumab (GA-101)	IgG1	21	Obinutuzumab (Refractory B cell NHL) 1600/800 mg 400/400 mg	60% 35%	Infusion related reaction, neutropenia, anemia, thrombocytopenia, tumor lysis syndrome
		28	G-CHOP (Relapsed or refractory FL) 1600/800 mg 400/400 mg	94%	Infusion related reaction, neutropenia, neuropathy, infection
		28	G-FC (Relapsed or refractory FL) 1600/800 mg 400/400 mg	93%	Infusion related reaction, neutropenia, rash, infection

JHO 2012

Ofatumumab

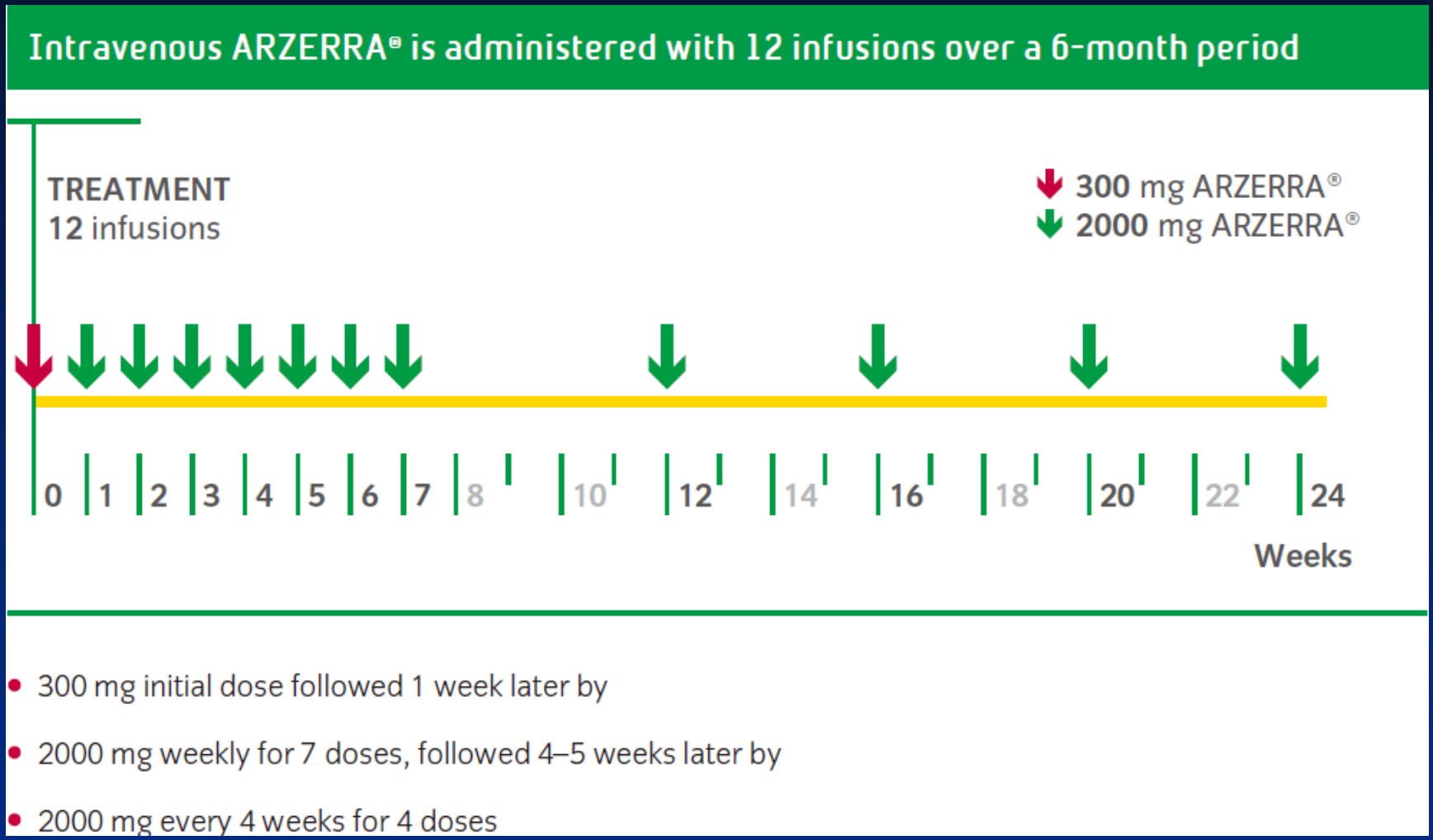


- Human CD20 monoclonal antibody that binds to membrane-proximal epitope encompassing both the small loop and large loop of CD20[1,2]
- Approved in refractory CLL
- Phase I/II study in relapsed or refractory FL[3]
  - ORR: 42%
  - Median duration of response: 30 months
  - ORR in prior rituximab-treated patients: 64%

1. Teeling et al. *J Immunol* .2006;177:362.
2. Teeling JL et al. *Blood.* 2004;104:1793-1800.
3. Hagenbeek A et al. *Blood.* 2008;111(12):5486-5495.

CLL = chronic lymphocytic leukemia.

Ofatumumab


Intravenous ARZERRA® is administered with 12 infusions over a 6-month period
TREATMENT
12 infusions
300 mg ARZERRA®
2000 mg ARZERRA®
0 1 2 3 4 5 6 7 8 10 12 14 16 18 20 22 24
Weeks
300 mg initial dose followed 1 week later by
2000 mg weekly for 7 doses, followed 4–5 weeks later by
2000 mg every 4 weeks for 4 doses

Ofatumumab

Pre-medication schedule

To reduce the risk of infusion-related adverse drug reactions (ADRs) patients should receive the following pre-medications 30 minutes to 2 hours prior to every ARZERRA® dose according to the following schedule:

ARZERRA® Infusion Number	Intravenous corticosteroid dose	Analgesic dose	Antihistamine dose
1 (300 mg)	Equivalent to 100 mg prednisolone	Equivalent to 1000 mg paracetamol	Equivalent to 10 mg cetirizine
2 (2000 mg)	Equivalent to 100 mg prednisolone		
3–8 (2000 mg)	Equivalent to 0–100 mg prednisolone†		
9 (2000 mg)	Equivalent to 100 mg prednisolone		
10–12 (2000 mg)	Equivalent to 50–100 mg prednisolone‡		

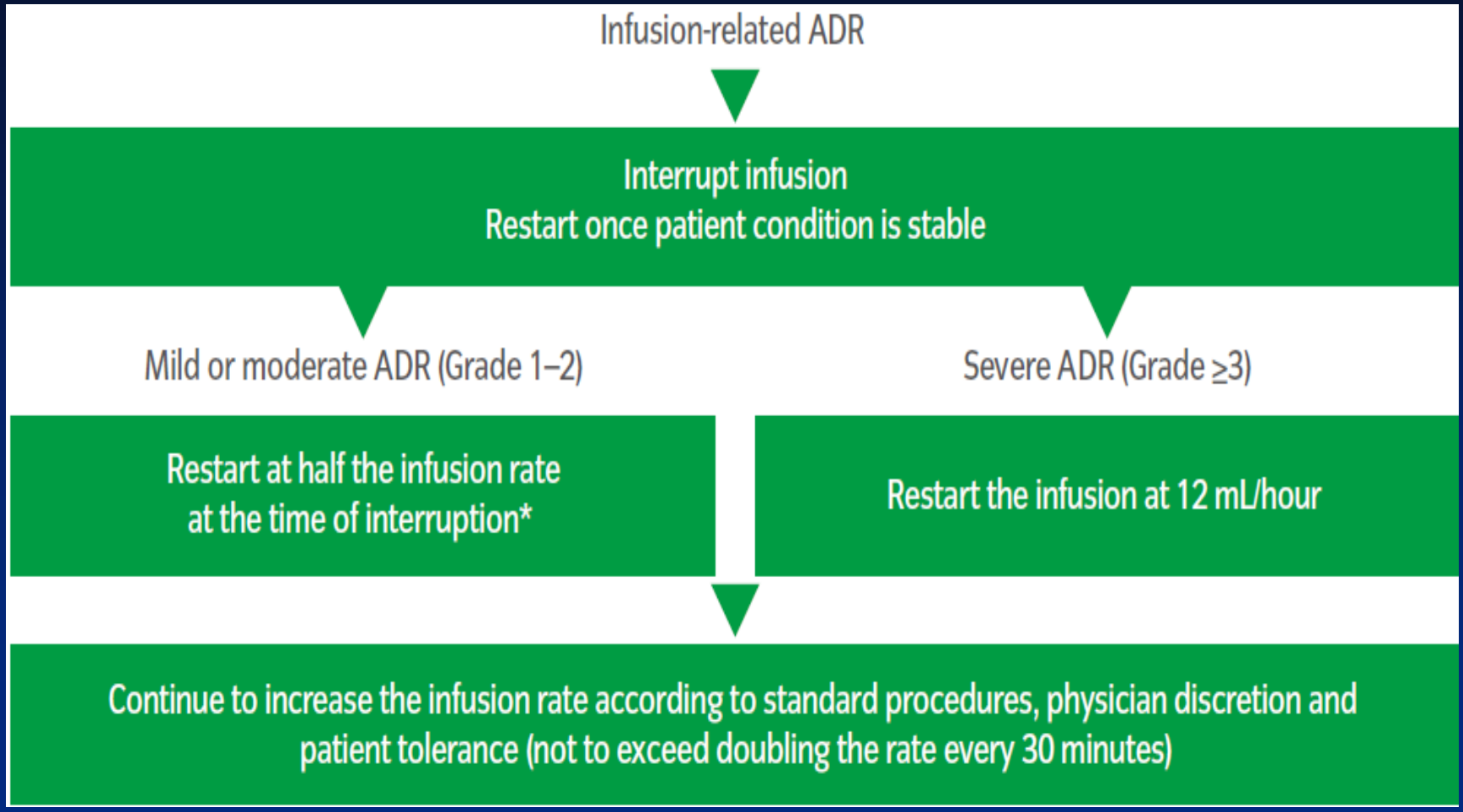
Ofatumumab

Infusion schedule

- The first and second ARZERRA® infusions should be administered over 6.5 hours and the remaining infusions (3–12) should be administered over 4 hours*

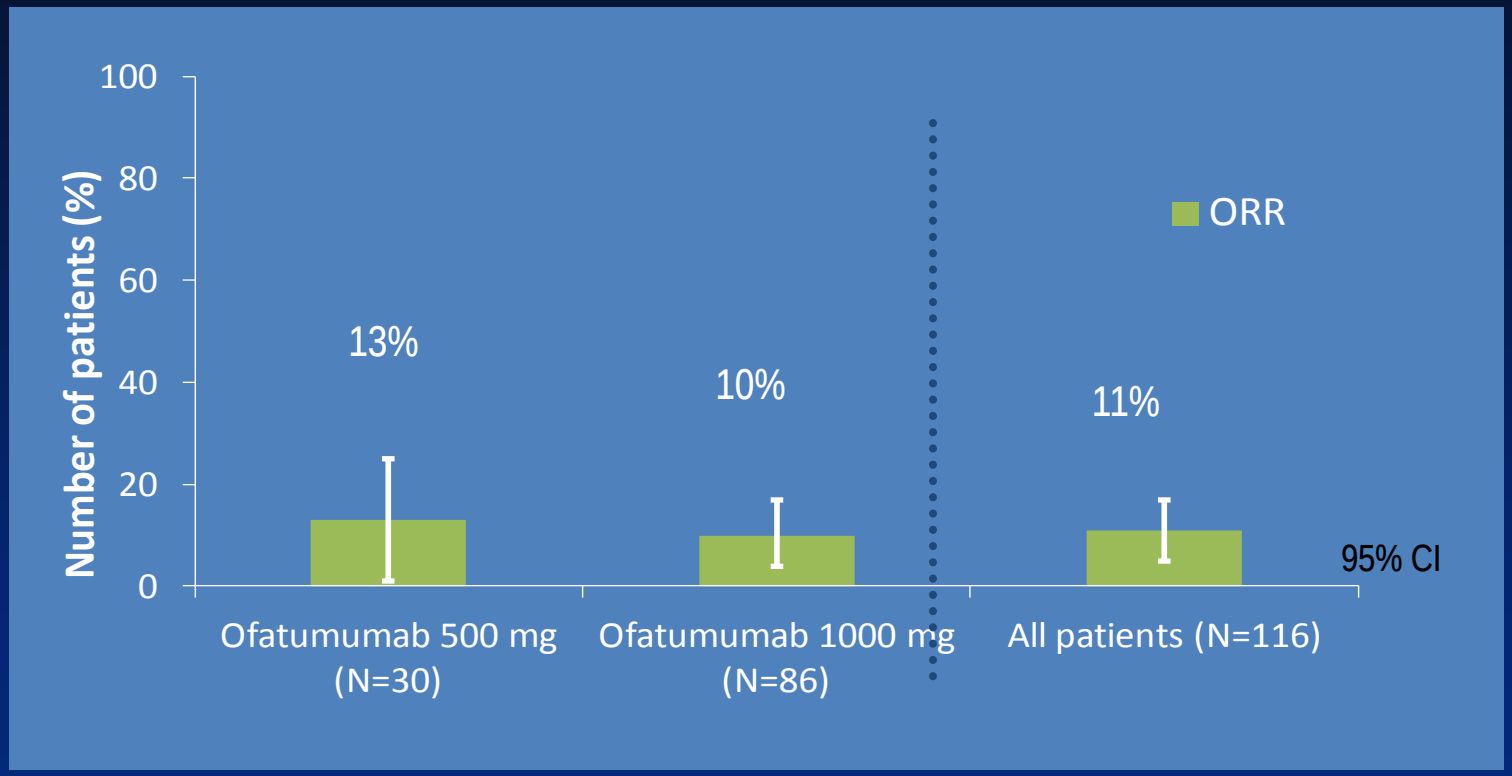
	Infusion rate (mL/hour)	
Time (minutes)	Infusions 1 and 2	Infusions 3 to 12*
0–30	12	25
31–60	25	50
61–90	50	100
91–120	100	200
121 +	200	400

Ofatumumab


Infusion-related ADR
Interrupt infusion
Restart once patient condition is stable
Mild or moderate ADR (Grade 1–2)
Severe ADR (Grade ≥3)
Restart at half the infusion rate at the time of interruption*
Restart the infusion at 12 mL/hour
Continue to increase the infusion rate according to standard procedures, physician discretion and patient tolerance (not to exceed doubling the rate every 30 minutes)

ORGAN SITE	SIDE EFFECT
	Clinically important side effects are in ***bold, italics***
blood and lymphatic system/ febrile neutropenia	anemia (16-17%, severe 5-8%)
	neutropenia (15-42%)[3,4]; may be prolonged (≥1 week)[4]
	thrombocytopenia, may be prolonged (≥1 week)
cardiac	hypertension (5-8%)
	hypotension (3-5%)
	tachycardia (5-7%, severe ≤2%)
gastrointestinal	*emetogenic potential:* rare[5]
	diarrhea (16-19%)[3,4]
	intestinal obstruction
	nausea (11-12%)
general disorders and administration site conditions	*extravasation hazard:* none[6]
	chills (8-10%)
	edema, peripheral (8-9%, severe ≤2%)
	fatigue (15%)
	infusion reactions (38-44% with first infusion; 29% with second infusion; 7% at 12th infusion)[3,4]; see paragraph following **Side Effects** table
	pyrexia (15-25%, severe 3-5%)[3,4]
infections and infestations	bronchitis (11-19%, severe ≤2%)
	Herpes zoster (6-7%, severe 1-2%)
	Hepatitis B virus infection or reactivation
	nasopharyngitis (8%)
	pneumonia (23-25%, severe 14-15%)
	sepsis (8-10%, severe 8-10%)
	sinusitis (3-5%, severe 2%)
	upper respiratory tract infections (3-11%)
musculoskeletal and connective tissue	back pain (8-12%, 1-2%)
	muscle spasms (3-5%)
nervous system	headache (6-7%)
psychiatric	insomnia (7-10%)
respiratory, thoracic and mediastinal	cough (18-19%)[3,4]
	dyspnea (13-19%; severe 2-5%)[3,4]
skin and subcutaneous tissue	hyperhidrosis (5%)
	rash (10-17%, severe ≤2%)[3,4]
	urticaria (5-8%)

Ofatumumab in Relapsed/Refractory FL—Response Rates



- 87% and 91% of patients in the 500-mg and 1000-mg groups, respectively, completed all 8 infusions of ofatumumab
- No difference in primary endpoint (ORR) between the 500-mg and 1000-mg groups; thus, 2 groups were combined for secondary endpoint analyses

Hagenbeek et al, ASH 2009.

Ofatumumab

Monoclonal Ab	Ig type	Patients	Regimen	Overall response rate(%)	Adverse events
Ofatumumab (OFA)	IgG1 Kappa	116	Ofatumumab (Refractory FL) 500 mg 1000mg	13% 10%	Infections, rash, urticaria, pruritis, neutropenia, anemia, thrombocytopenia
		59	O-CHOP (untreated FL) 500 mg 1000 mg	90% 100%	Leucopenia, neutropenia
		61	O-FC (Frontline therapy for CLL) 500 mg 1000 mg	77% 73%	Neutropenia, thrombocytopenia, anemia, infection

JHO 2012

我中心相关的国际多中心III期研究

- 比较GA101(RO5072759)联合CHOP (G-CHOP)与利妥昔单抗联合CHOP (R-CHOP)在初治的CD20 阳性的DLBCL患者中疗效的III期、多中心、开放的、随机临床试验
- 在以往未治疗的晚期惰性非霍奇金淋巴瘤患者中评价在GA101(RO5072759)+化疗相对利妥昔单抗+化疗后再接受GA101或利妥昔单抗维持疗法获益的一项多中心、开放性、随机的Ⅲ期临床研究
- OMB113676随机、开放性Ⅲ期研究：含利妥昔单抗方案治疗后复发的滤泡性淋巴瘤患者接受Ofatumumab单药治疗与利妥昔单抗单药治疗的对比
- OMB110928 复发或难治性弥漫性大B细胞淋巴瘤用Ofatumumab或利妥昔单抗进行挽救性化学免疫治疗后再进行ASCT的疗效对比

G-CHOP vs R-CHOP in untreated DLBCL

- N=10，6例已评价疗效，CR 2例，正在治疗的患者2或4程后CR 2例，PR2例
- 预处理：提前半小时苯海拉明40mg im，加合百服宁565mg po，地塞米松 20mg iv drip
- 输液反应3例（CTCAE 1-2度），出现输液反应后给予暂停输注，可给与吸氧、非那根或再次给予地米，患者症状缓解后按暂停前滴注速率的一半重新开始滴注，无因滴注反应中断治疗或转入ICU的病例
- 第一疗程后4例出现3-4度发热性粒缺，第一疗程后给予预防性G-CSF治疗的患者5例中仅1例再次出现3-4度发热性粒缺，调整剂量化疗后未再发现上述情况

谢谢