®

Rituximab Injection

Lituoxi Dankang Zhusheye

80 37%

CD20 III-IV ,

CD20 B DLBCL CHOP

8

FC /

CLL

100 /10

500 /50

/

0.9% 5%

1mg/ml

24

X

50 mg/h 30 50 mg/h

400 mg/h

100 mg/h 30 100 mg/h 400 mg/h

375 mg/m^2 BSA

22 4

375 mg/m^2 BSA 8

1

375mg/m^2 BSA 8 12

375 mg/m2 BSA 4

1 4

B

B CHOP

375mg/m^2 BSA

48

> 25 x10^9/L /

100mg /

FC 28 6 1

375mg/m2 BSA 500mg/m2 BSA FC 1

ADRs

2%

≥1/10 ≥1/100--<1/10 ≥1/1000--<1/100

/

1 356

671

R-CHOP R-CVP R-FCM 2

12 1

1. N=356

N=671

	≥ 10%	≥ 1% - < 10%	≥ 0.1% - < 1%
		+ + + +	

2

/ / 202 R-CHOP DLBLC 234 162 R-CHOP R-CVP 397 CLL 274 / CLL R-FC

2. R-CHOP DLBCL N=202 N=234 R-CVP N=162 R-FC CLL N 397 / CLL N 274 ≥ 3

	≥ 10%	≥ 1% - <10%
		*

* R-FC / CLL ≥ 3 NCI

/ /

R-FC

<2%

MCP CHVP-IFN

CVP CHOP FC

-4

50%

NHL *R-CVP* *DLBCL* *R-CHOP* *CLL* *R-FC*

12%

1%

90 *f-NHL* *R-CVP* *DLBCL* *R-CHOP*

90

U4391g 363 90 2 /

3-4 1.1% 95% CI [0.3%, 2.8%] 90

2-8 3-4 2.8% 95% CI [1.3%, 5.0%]

-4

70% 80% B

356 30.3%

3.9% 3/4

2 *NHL*

3-4 2

NHL *R-CVP* *DLBCL* *R-CHOP* *CLL* *R-FC*

R-CVP

12.3% CVP 16.4% R-CVP 4.3% CVP 4.4%

R-CHOP R-CHOP 2-4 45.5% CHOP 42.3%

R-CHOP 2-4 R-CHOP 4.5% vs CHOP 2.6%

R-CHOP 2-4 4.5%

CHOP 1.5% 2-4 / R-

CHOP 55.4% CHOP 51.5%

CLL 3 4 R-FC FC

2% 0%

-4

4.2% 3 4 1.1%

1.7%

2 NHL

3-4 2% vs 5%

4% vs 10% 3-4

1% vs <1% B

B 12

NHL R-CVP DLBCL R-CHOP CLL R-FC

3/4 R-CHOP

88% CHOP 79% R-FC 23% FC 12% (

R-CVP 24% CVP 14% R-CHOP 97% CHOP 88%, R-FC

30% FC 19%)

/

FC

3-4 CLL

4% R-FC 7% FC 3/4 7% R-FC

10% FC 3/4 / CLL R-FC

3/4 12% FC 13% R-FC 3/4

11% FC 9%

-4

18.8%

3 4

2 NHL

3-4 <1% 3%

1% 1%

<1% <1%

NHL R-CVP DLBCL R-CHOP CLL R-FC

R-CHOP R-CHOP 6.9% 3-4 CHOP 1.5%

/

,

3 4

R-CHOP CHOP

CLL 3 4 R-FC 4%

FC 3% / R-FC 4% FC 4%

IgG

2 NHL

IgG <7g/L

IgG

2 IgG

0.8/100

2.05/100

/

-

PRES RPLS

PRES/RPLS

PRES/RPLS

/

CMV - JC

PML

* s *

HIV

IgM IgM

4

/

30 2

50% 100 mg/h 50 mg/h

>25 × 10^9/L CLL

25 × 10^9/L

/

X-

1 2

CD20

TLS

LDH

>25 × 10^9/L CLL

TLS

TLS

/

12

<1.5 × 10^9/L / <75 × 10^9/L

ç ő

13 25

HBV

HBsAg HBcAb

PML

PML PML

-

NHL

KLH

16% vs 81% 4% vs 76% 2

A

6

:

:

12

IgG

B

B

IgG

B

HAMA HACA

15 25

1000mg

5000mg 2250mg/m^2

B

166

375mg/m^2 BSA 4

48% CI $_{95\%}$ 41%-56% 6% 42%

13.0

IWF B C D ORR

IWF A 58% vs 12% 5cm

7cm 53% vs 38%

3 50% vs 22%

78% 43%

LDH Fisher

40%

4

39 B

375mg/m^2 BSA 4

36% $CI_{95\%}$ 21%-51% CR 3% PR 33%

9.6 4.5-26.8

4

58

B 375mg/m^2 BSA

4

60 38% $CI_{95\%}$ 26%-51% CR 10% PR 28%

17.8 5.4-26.6

12.4

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322 B

CVP 750 mg/m^2 1.4 mg/m^2 1

2 mg 1 5 40 mg/m^2/ 3 8

375 mg/m^2 BSA CVP R-CVP

321 162 R-CVP 159 CVP

53 R-CVP CVP

27 vs7 p<0.0001 log-rank CR Cru PR

R-CVP 80.9% CVP 57.2% R-CVP 33.6

CVP 14.7 p 0.0001 long-rank

R-CVP 37.7 CVP 13.5 p 0.0001 long-rank

p=0.029,

long-rank 53 R-CVP 80.9% vs CVP 71.1%

42 R-CVP CVP

3

3. CVP vs R-CVP 42

Kaplan-Meier k Ž ŕ

	CVP	R-CVP	Log-Rank p
	41.3	42.1	
	6.6	27.0	<0.0001
×	14.5	33.6	<0.0001
	NR	NR	0.0700
CR Cru PR *	57%	81%	<0.0001**
	13.5	37.7	<0.0001
	20.5	44.8	0.0005
	12.3	46.3	<0.0001

§
× G
*
**
CR CRu NR
Kaplan-Meier 50% PR

R-CVP CVP p=0.02 log-rank

R-CVP 3 93% CVP 85%

M39021 CVP

BNLI vs ≤ 60 > 60 0-1

vs >1 vs LDH β_2-

B < 5 vs ≥ 5

≤ 12 g/dL vs >12 g/dL IPI ≤ 1 vs > 1 FLIPI index 0-2 vs 3-5

CVP CHOP MCP -

4

4. III

	n		%	%	TTF/PFS/EFS,	%
M39021	CVP, 159 R-CVP, 162	53	57 81	10 41	TTP 14.7 33.6	

					P <0.0001	P=0.0096
FL2000	CHVP-IFN, 183 R-MCP,105	42	85 94	49 76	EFS 36 P <0.0001	42 84 91 P=0.029

TTP- , PFS- , TTF- ,OS rate-

1:1 1018

III 465 /

6 CHOP

N=231 CHOP R-CHOP N=234

334

N=167 N=167 3

375mg/m^2 BSA 2

31 R-CHOP CHOP /

5

5. CHOP R-CHOP 31

	CHOP	**R-CHOP**	**p**	[1]
[2]	74%	87%	0.0003	
[2]	16%	29%	0.0005	
[2]	58%	58%	0.9449	
			0.0508	32%
	19.4	33.2	0.0001	38%

[1]

[2] / / p<0.0001

28

PFS

p<0.0001 log-rank

PFS 42.2 14.3 Cox

61% $CI_{95\%}$ 45%-

72% 12 Kaplan- Meier PFS 78%

57% p=0.0039

log-rank 56% $CI_{95\%}$ 22%-75%

38.8 vs 20.1

p<0.0001 log-rank 50% $CI_{95\%}$ 30%-64%

CR CRu

DFS 53.7 vs 16.5 p=0.0003 log-rank

6 CR 67% $CI_{95\%}$ 39%-82%

6. vs 28

		Kaplan-Meier		
	N=167	**N=167**	log-rank **p**	
	14.3	42.2	<0.0001	61%
			0.0039	56%
	20.1	38.8	<0.0001	50%
[a]	16.5	53.7	0.0003	67%
CHOP	11.6	37.5	<0.0001	71%
R-CHOP	22.1	51.9	0.0071	46%
	14.3	52.8	0.0008	64%
	14.3	37.8	<0.0001	54%
CHOP			0.0348	55%
R-CHOP			0.0482	56%

[a]

CHOP R-CHOP CR PR

6

CHOP PFS 37.5 11.6 p<0.0001 R-CHOP PFS

51.9 22.1 p=0.0071 PFS

CHOP R-CHOP

≤60 >60

III IV WHO 0 vs >0 B

vs IPI 0-2 vs 3-5 FLIPI

0-1 vs 3-5 0-1 vs >1 <5 vs ≥5 1 vs 2

CR/PR vs [NC]/ [PD] <12g/dl vs

≥12g/dl β_2- <3mg/l vs ≥3mg/l LDH

B

399 B 60 80

CHOP 750mg/m^2 50 mg/m^2

1.4 mg/m^2 2mg 1-5 40 mg/m^2/ 3

8 375 mg/m^2 CHOP R-CHOP

CHOP=197 R-CHOP=202 31

R-CHOP p=0.0001

“ ” R-CHOP

K-M 35 CHOP 13 41% 24

R-CHOP 68.2% CHOP 57.4% p=0.0071 60

R-CHOP CHOP R-CHOP 62.4% CHOP 50.8% p=0.0071

32%

PFS DFS R-CHOP CHOP 8

R-CHOP CR 76.2% CHOP 62.4% p=0.0028 46%

51%

IPI Ann Arbor ECOG 2 LDH

B R-

CHOP vs CHOP 0.83 0.95 [IPI] R-CHOP

/

1:1

CLL 1 n=817 CLL 2 n=552

FC FC 6

1 2 3 25 mg/m2/ 250 mg/m2/

71% CLL 6 90% 3

1 30% 65 31% Binet C 45% B 99%

ECOG PS 74% 100% 2 44%

65 28% B 82% 18% 100%

67% 98%

PFS

1 2

2 7

7 1 2

	1*		2*	
	R-FC	FC	R-FC	FC
	N = 408	N = 409	N = 276	N = 276
PFS	39.8	31.5	26.7	21.7
95% CI	0.56 0.43, 0.71		0.76 0.6, 0.96	
P	< 0.01		0.02	
	86%	73%	54%	45%
95% CI	82, 89	68, 77	48, 60	37, 51

* 1996

243/676 36% 65 100 15%

70 8

8 1 2 [a]

	1			2		
		PFS	95% CI		PFS	95% CI
< 65	572	0.52	0.39, 0.70	313	0.61	0.45, 0.84
≥ 65	245	0.62	0.39, 0.99	233	0.99	0.70, 1.40
< 70	736	0.51	0.39, 0.67	438	0.67	0.51, 0.87
≥ 70	81	1.17	0.51, 2.66	108	1.22	0.73, 2.04

B

63 40-75 CD20

B 32 31

+ CHOP CHOP 6

21 1 375mg/m^2 BSA

CR29.0% PR54.9% 83.9% CR31.3% PR31.3%

62.5%

CD20 CD20

B B B CD20

B B CDC

A 0 63JETQ EMC /P <</011<40132CB41D6A>11<08660A1F>11R31.3%

75mg/kg 1 0 20 100mg/kg

20 78 76 134 132 28

B

6 B

298 CHOP NHL

CL_1 B

CL_2 V_1 0.14 L/day 0.59 L/day 2.7 L

22 6.1 52 161 375

mg/m^2 4 CD19

500mg/m^2 5 Cmax n=15 408 μ g/mL 97-764 μ g/mL

2~8°C

12

2~8°C 24

100mg/10ml 1 /

500mg/50ml 1 /

30

YBS05092020

100mg/10ml/ S20190021

500mg/50ml/ S20201002

1289

1289

200233

021-33395800

021-33681208

400--086-6800 24