

4239 2; 4;  
 423; 28 49  
 .....423; 2; 47  
 .....4242 25 38  
 .....4242 26 42  
 .....4242 28 46

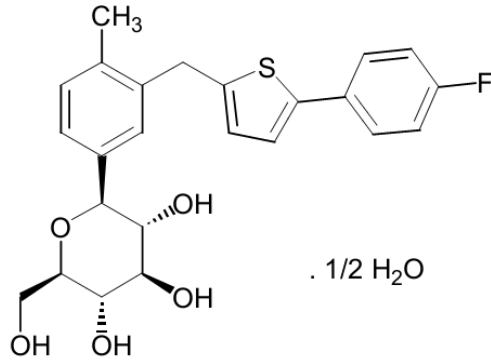
- CVD CVD 2  
 CANVAS CANVAS-R  
 (CANVAS 5.9 vs 2.8 /1000 - CANVAS-R 7.5  
 vs 4.2 /1000 -
- 
- 
- 

ì

Epcil nq| k'Vcdrgw  
 Mci grigkpi 'Rkcp

3S /3.7/ /3/E/ 5/}7/ 6/ /4/ \_ ;/6/

/F/



E<sub>46</sub>J<sub>47</sub>HQ<sub>7</sub>U•3I4"J 4Q  
67505

322o i

522o i

4

4

3

3 322o i 4 522o i

E<sub>46</sub>J<sub>47</sub>HQ<sub>7</sub>U

.....

322o i

"322o i

gI HT ×82o Nlb kpB05o<sup>4</sup>

522o i

gI HT×82o Nlb kpB05o<sup>4</sup>

gI HT×67 >82o Nlb kpB05o<sup>4</sup>

322o i "

gI HT>67o Nlb kpB05o<sup>4</sup>

gI HT 67o Nlb kpB05o<sup>4</sup>

gI HT 52o Nlb kpB05o<sup>4</sup>

4.

1 ,

1 0

W V

322o i

gI HT"×82o Nlb kpB05"o<sup>4</sup>

522o i

gI HT ×67 >82o Nlb kpB05o<sup>4</sup>

W V



---

ETGFGPEG 4 @22"o i l  
 4423 359 "  
 ETGFGPEG 4  
 408 322"o i 3405"xu"3304  
 3222 /  
 ETGFGPEG 322"o i 322 / FMC  
 2043 207' 3414 422 2025 208' 414 3;9 322 /  
 ETGFGPEG 322"o i  
 ETGFGPEG 322"o i 40' 30'  
 ECPXCU ECPXCU  
 T  
 : 8399  
 3  
 30' 322o i 404' 522o i 402'  
 208' 322o i 209' 522o i 308'  
 : 322o i 522o i  
 208' 204' 208'  
 :  
 322o i 522o i 502' 50'  
 604' 7 6 3  
 4 3

322o i                    522o i                    208'    204'    204'

EXF                    EXF                    4

ECPXCU    ECPXCU/T

ECPXCU 70 "xu"40    B222    /    ECPXCU/T 907"xu"604    B222    /

ECPXCU    ECPXCU/T                    70    408

ECPXCU    ECPXCU/T                    4    5

### 2 CANVAS

	N=1441	100mg N=1445	300mg N=1441	N=2886
<b>n %</b>	<b>22 (1.5)</b>	<b>50 (3.5)</b>	<b>45 (3.1)</b>	<b>95 (3.3)</b>
	<b>33</b>	<b>83</b>	<b>79</b>	<b>162</b>
<b>1000</b>	<b>2.8</b>	<b>6.2</b>	<b>5.5</b>	<b>5.9</b>
<b>95% CI</b>	<b>--</b>	<b>2.24 (1.36, 3.69)</b>	<b>2.01 (1.20, 3.34)</b>	<b>2.12 (1.34, 3.38)</b>

1

2

1

1

### 3 CANVAS-R

	N=2903	100mg 300mg N=2904
<b>n %</b>	<b>25 (0.9)</b>	<b>45 (1.5)</b>
	<b>36</b>	<b>59</b>
<b>1000</b>	<b>4.2</b>	<b>7.5</b>
<b>95% CI</b>	<b>--</b>	<b>1.80 (1.10, 2.93)</b>

1

2

1

1

ECPXCU

70

2087'    4B553    204;'    : 14938

8

; 2

522o i "

gI HT 52 >82o Nlo kP1305o 4

97

6

		I C	I C
		30'	40'
97	*4+	40'	60'
gI HT	82o Nlo kP1305'o 4"	40'	60'
	*4+	60'	50'

\*3+

\*4+

3

97

;

:7

322o i

522o i

30'

30'

40'

6

322o i

522o i

40'

32068'

33068'

2'

20'

6

322o i

522o i

20'

604'

50'

2' 207'

:

205'

204'

92o i lf N

7

	P ?3; 4	322o i P ?3; 7	522o i P ?3; 9
]P * ±	7*408+	9*508+	8*502+
	- *P ?3: 5+	322o i - P ?58:	522o i - *P ?589+
]P * ±	5*308+	38*605+	39*608+
]P * ± <sup>4+</sup>	2*2+	3*205+	3*205+
	- *P ?6: 4+	322o i - P ?6: 5	522o i - *P ?6: 7+
]P * ±	387*560+	49*708+	46*60 +
]P * ± <sup>4+</sup>	37*508+	4*206+	5*208+
	- P ?8;	322o i - P ?96	522o i - P ?94
]P * ±	6*70 +	5*608+	; *3407+
<b>D</b>	- *P ?378+	322o i - - P ?379	522o i - - *P ?378+
]P * ±	46*3706+	65*4906+	69*5208+
]P * ± <sup>4+</sup>	3*208+	3*208+	2
<b>D</b>	- *P ?59: +		522o i - - *P ?599+
]P * ±	376*6209+		385*6504+
]P * ± <sup>4+</sup>	35*506+		37*602+





@7'

\_\_\_\_\_

8

6

322o i 522o i : 08' ; 05' /208'  
322o i 522o i 204'

; 04' 360'

\_\_\_\_\_

6

322o i 522o i 508' 708'  
322o i

307'  
522o i 304' 702' ; 05'

NFNE /J FNE

\_\_\_\_\_

6

NFNE 322o i 522o i NFNE

606o i IfN\*607' + : 04o i IfN\*: 02' +

NFNE 326 332o i IfN

J FNE 322o i

522o i J FNE 408o i IfN\*307' +

708o i IfN\*508' + J FNE 362 369o i IfN

\_\_\_\_\_

6

/208: i IfN\*/308' + 322o i 2069i IfN\*507' + 522o i

2073i IfN\*50' + 3608i IfN

322o i 522o i

20' 602' 409'

\_\_\_\_\_

936 86 Z

DOF 4 322o i



gI HT>82o Nlo kp1305o 4

/ /  
]CTD\_

]CEG\_

/

4 UI NV4

3 4

3

472o i lfN

3

472o i lfN

3

5

UI NV4

gI HT

87

CEG

CTD PUCK

gI HT

gI HT      82o Nlo k1305o<sup>4</sup>  
67o Nlo k1305o<sup>4</sup>

gI HT      30mL/min/1.73m<sup>2</sup>

UI NV4

UI NV4

UI NV4

ECPXCU'

34

((

NFNE

NFNE

---

J dC<sub>3E</sub> 9'

8/32'

J dC<sub>3E</sub> 32'

42/47'

4/6' 37/42'

---

1 1

\_\_\_\_\_

3:

35

44; 6 87

573 97

87

522o i

97

J dC<sub>3E</sub>

87

322o i

/2083'

522o i

206'

322o i

/204'

522o i

/209'

**1 0**

UGT2B4

UGT

UGT1A9

AUC

51%

UGT

100mg

eGFR>60mL/min/1.73m<sup>2</sup>

300mg

eGFR

45

<60mL/min/1.73m<sup>2</sup>

UGT

58' 522o i CWE E\_o cz 42'

"" UI NV4 UI NV4

"" 3.7/ 3.7/CI  
UI NV4

6

4

J dC<sub>3E</sub>

DO K

J dC<sub>3E</sub>

34: 6 4222o i l 48  
3722o i l 4 77 69'

gI HT : ; o Nlo kp1305o<sup>4</sup> 4

P ? 322;

P ? 497

: 4  
322o i 522o i 322o i

322o i 522o i J dC<sub>3E</sub>  
r >2023 322o i 522o i



J dC<sub>3E</sub>

9'

HRI

RRI

8

322o i 522o i

r >2023

/706o o J i /808o o J i

	+	100mg+	300mg+
	(N=183)	N=368	N=367
<b>HbA<sub>1c</sub>(%)</b>			
	7.96	7.94	7.95
	-0.17	-0.79	-0.94
(95%CI) <sup>(2)</sup>		-0.62 <sup>(3)</sup> -0.76 - 0.48	-0.77 <sup>(3)</sup> -0.91 -0.64
<b>HbA<sub>1c</sub>&lt;7%</b>	30	46 <sup>(3)</sup>	58 <sup>(3)</sup>
<b>(mg/dL)</b>			
	164	169	173
	2	-27	-38
(95%CI) <sup>(2)</sup>		-30 <sup>(3)</sup> -36 -24	-40 <sup>(3)</sup> -46 -34
<b>2 (mg/dL)</b>			
	249	258	262
	-10	-48	-57
(95%CI) <sup>(2)</sup>		-38 <sup>(3)</sup> -49 -27	-47 <sup>(3)</sup> -58 -36
<b>kg</b>	86.7	88.7	85.4
<b>%</b>	-1.2	-3.7	-4.2
(95%CI) <sup>(2)</sup>		-2.5 <sup>(3)</sup> -3.1 -1.9	-2.9 <sup>(3)</sup> -3.5 -2.3

\*3"

\*4"

\*5"t >2023

68;

4222o i 1

3722o i 1

4

48

79 73'

gI HT : ; o Nlo kpB05o 4

P ?594

4

P ?; 9

:

4

322o i

522o i

322o i

522o i J dC<sub>3E</sub>

r >2023

322o i 522o i

J dC<sub>3E</sub>

9'

HRI

9

	D	I O	I O
	*	*	*
	: 04	: 05	: 05
	/205	/207	/308
*, 7' EK <sup>*4+</sup>		/203 <sup>*5+</sup> /202 /204	/204 <sup>*5+</sup> /303 /205
	3:	65 <sup>*5+</sup>	79 <sup>*5+</sup>
I C (			
	392	395	38:
	6	/3:	/53
*, 7' EK <sup>*4+</sup>		/44 <sup>*5+</sup> */53 /35+	/57 <sup>*5+</sup> /66 /47
m	: 20	: 50	: 50
'	/20	/40	/40
*, 7' EK <sup>*4+</sup>		/30 <sup>*5+</sup> /40 /20	/40 <sup>*5+</sup> /40 /30

\*3+

\*4+

\*5+ >2023

77 : 2

936 77/: 2 4

48

86 77'

gI HT 99o Nlo kP B05o<sup>4</sup>

3-3-3

322o i

522o i

322o i

522o i J dC<sub>3E</sub> r  
 >2023 322o i /2079' \*,7' EK/203' /2066' + 522o i /  
 202' \*,7' EK/206' /2079' +

48; 4 gl HT  
 52o Nlb lpB05o<sup>4</sup> 72o Nlb lpB05o<sup>4</sup> 48  
 8: 83'  
 gl HT 5; o Nlb lpB05o<sup>4</sup> 3-3-3 322o i

522o i  
 J dC<sub>3E</sub> 322o i 522o i  
 522o i /2062' . ;7' EK/2086' ≠2089'

2

ECPXCU ECPXCU/T 1  
 ECPXCU ECPXCU/T 52  
 88' 72 4  
 4 56'  
 ECPXCU ECPXCU/T  
 OCEG  
 4 5 3  
 ECPXCU 3-3-3 322'o i 522'o i  
 ECPXCU/T 3-3 322'o i  
 35  
 522'o i  
 32356 ECPXCU 6549 ECPXCU/T 7: 29  
 6566 79; 2 36; JECPXCU 445 \*605  
 + ECPXCU/T ;6 \*30 ± 9: ' 35' 5'

85 86'

J dC<sub>3E</sub> : 0'

350' 92' 32

53' 43' 39'

gI HT 98' b N l o k p 1305' b<sup>4</sup> 3;' : 2'

99' 72' 65'

359' b o J i 9: ' b o J i NFN ; ; ' b i l f N

J FN 68' b i l f N WCET 337' b i l i : 2'

75' 35'

58' 97' 96'

70' x u' 60' 70' x u' 60'

Eqz OCEG

305

ECP XCU ECP XCU/T OCEG

OCEG ; 7' "EK 20 8 207 209 :

; ; 0' 3 OCEG M c r n p / O g l t

**8 CANVAS CANVAS-R MACE**

\*

	N=4347 %	N=5795 %	95% C.I.) <sup>¶</sup>
t, t, s,	426 (10.4)	585 (9.2)	0.86 (0.75, 0.97)
t, s	159 (3.9)	215 (3.4)	0.85 (0.69, 1.05)
t, s	116 (2.8)	158 (2.5)	0.90 (0.71, 1.15)
t, s	185 (4.6)	268 (4.1)	0.87 (0.72, 1.06)

\*

t P =0.0158

t

s

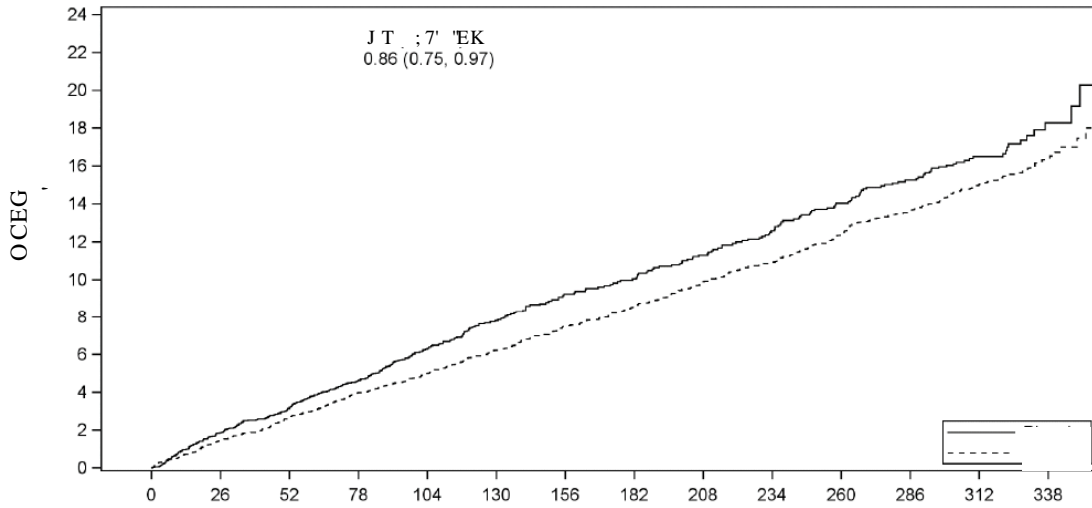
CMH

¶

Cox

1

**MACE**



4347	4239	4153	4061	2942	1626	1240	1217	1187	1156	1120	1095	789	216
5795	5672	5566	5447	4343	2984	2555	2513	2460	2419	2363	2311	1661	448

ECPXCU

ECPXCU/T

; 4

68

:

OCEG

;

ECPXCU/T

9

**CANVAS**

**CANVAS-R**

**MACE**

1

	n/N %	EVRT <sup>2</sup>	n/N %	EVRT <sup>2</sup>	HR <sup>3,5</sup> (95% CI)	P	3,5
MACE <sup>4</sup>	3/ 46 ( 6.5)	43.23	5/ 46 (10.9)	72.42	-	-	
MI	0/ 46 ( 0.0)	0.00	3/ 46 ( 6.5)	42.49	-	-	
	3/ 46 ( 6.5)	43.23	2/ 46 ( 4.3)	28.09	-	-	
	0/ 46 ( 0.0)	0.00	0/ 46 ( 0.0)	0.00	-	-	

1.

2. 1000 -

3. P 0.05

Cox

95%CI p

4. OCEG MACE

MI

5.

32

3

;7' EK r

CREDESCENCE /  
 [ (ACEi)  
 II (ARB)] 2 eGFR 30 <90 mL/min/1.73 m<sup>2</sup>  
 [ / >300 5000 mg/g]  
 CREDESCENCE  
 ESKD  
 100 mg N=2202 N=2199  
 4401 137 99.9%  
 67% 20% 9% 5%  
 32% 63 66%  
 HbA<sub>1c</sub> 8.3% / 927 mg/g eGFR 56.2  
 mL/min/1.73m<sup>2</sup> 50% CV 15% AHA  
 66% 58% 29%  
 99.9% ACEi ARB 60%  
 69%  
 CREDESCENCE ESKD eGFR<15 mL/min/1.73  
 m<sup>2</sup>  
 100 mg [HR 0.70 95% CI:  
 0.59 0.82 p<0.0001] 2 10 2 ESKD  
 100 mg  
 [HR 0.61 95% CI: 0.47 0.80 p<0.001]

**10 CREDENCE**

	N=2199 %	*	N=2202 %	*	HR <sup>†</sup> 95% CI
ESKD	340 (15.5)	6.1	245 (11.1)	4.3	0.70 (0.59, 0.82) <sup>‡</sup>
ESKD	165 (7.5)	2.9	116 (5.3)	2.0	0.68 (0.54, 0.86)
	188 (8.5)	3.4	118 (5.4)	2.1	0.60 (0.48, 0.76)
	5 (0.2)	0.1	2 (0.1)	0.0	
	140 (6.4)	2.4	110 (5.0)	1.9	0.78 (0.61, 1.00)
	253 (11.5)	4.5	179 (8.1)	3.1	0.69 (0.57, 0.83) <sup>§</sup>
	269 (12.2)	4.9	217 (9.9)	3.9	0.80 (0.67, 0.95) <sup>¶</sup>
	87 (4.0)	1.6	71 (3.2)	1.3	0.81 (0.59, 1.10)
	66 (3.0)	1.2	53 (2.4)	0.9	0.80 (0.56, 1.15)
	141 (6.4)	2.5	89 (4.0)	1.6	0.61 (0.47, 0.80) <sup>§</sup>
ESKD	224 (10.2)	4.0	153 (6.9)	2.7	0.66 (0.53, 0.81) <sup>‡</sup>

\* /100 -

† Cox eGFR 30 <45 mL/min/1.73

m<sup>2</sup> 45 <60 mL/min/1.73 m<sup>2</sup> 60 <90 mL/min/1.73 m<sup>2</sup>

95% CI p

HR

<sup>†</sup> P <0.0001

<sup>§</sup> P 0.001

<sup>¶</sup> P <0.02

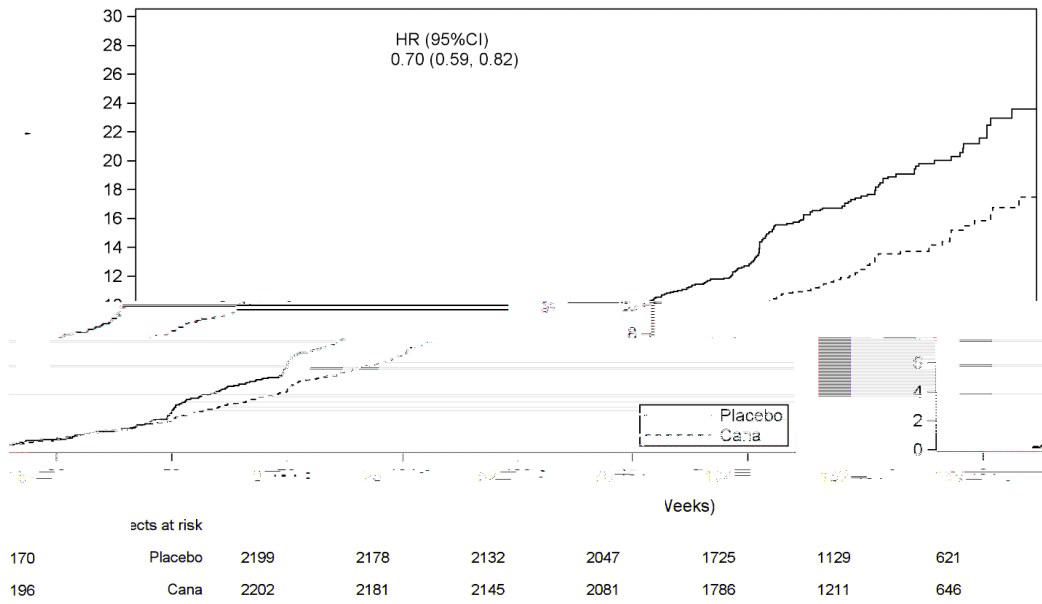
Kaplan-Meier

2

52

ESKD

## 2 CREDENCE



ETGF GPEG

34;

85

88

33

ETGF GPEG



\*

	pIP <sup>#</sup> +	GXTV <sup>4</sup>	pIP <sup>#</sup> +	GXTV <sup>4</sup>	J T]d_"; 7' 'EK-
GUMF	34 85*3; 0+	33: 03	9 188*320+	8404	206; *20; .3048+
"GUMF	32 185*370 +	; 9043	6 188*80+	57064	205*202.30; +
"	32 185*370 +	; : 063	7 188*90+	650 4	206; *205.3087+
"	2	2022	2	2022	
"	5 185*60 +	490;	3 188*30+	: 085	
	7 185*90 +	6806	6 188*80+	57047	
O CEG	: 185*340+	97068	7 188*90+	660 4	202*2042.30 6+
"	4 185*50+	3: 068	4 188*50+	39082	
"	5 185*60 +	490 ;	4 188*50+	39078	
	6 185*80+	5903	5 188*60+	48066	
GUMF	34 185*3; 0+	33: 03	8 188*; 0+	75064	2063*207.3083+
1.					
2. 1000 -					

/

UI NV4

UI NV4

UI NV4

TV<sub>i</sub>

UI NV4

Co gu

322o i ln

522o i 36 3:

/

322o i ln 1

382o i ln 1

8

43

CWE

522o i 3;

43¢; 2

6 42 87 322o i ln

CWE

522o i

207

3

1

306

EF3

UF

4

32 52 322o i ln

522o i

36

32 52 322o i ln

NJ

34

NJ

322o i ln

522o i

34

322o i ln

522o i 4

4 322o i  
 522o i 3/4 V<sub>ocz</sub> 72o i 522o i  
 E<sub>ocz</sub> CWE 322o i 522o i V<sub>34</sub> 3208  
 350 322o i 522o i 6/7  
 322o i 522o i 58'

87'

: 507N

;;'

O/

WI V3C; WI V4D6

O/

E[ R5C6

9'

] <sup>36</sup>E\_

O/

6307' 902' 504'

55'

O/

5207'

3'

322o i 522o i

3052 3077o Nlo kp

3; 4o Nlo kp

\_\_\_\_\_

OFTF/gI HT

422o i

E<sub>o.cz</sub>

P ?5 gl HT

; 2o Nb lp1305o<sup>4</sup>

P ?32

P ?;

P ?32

gl HT

82

>; 2 52 >82

37 >52o Nb lp1305o<sup>4</sup>

CWE

37'

4; ' 75'

GUMF

\*P ?; +

CWE

\_\_\_\_\_

522o i

Ej kf/Rwi j

C

E<sub>o.cz</sub>

CWEô

329'

332'

Ej kf/Rwi j

D

E<sub>o.cz</sub>

CWEô

				1	I = T
				%	%
	822o i SF :	522o i		206; 2066 2076	204 2083 20 6
	622o i	522o i SF :		3045 308; 3049	3023 20 3 3083
	2025o i 2087o i	422o i SF 8		20 3 20 : 20 6	20 4 20 6 20 ;
	47o i SF 57	522o i SF 9		3084 302: 3089	3087 3028 3047
	4222o i	522o i SF :		3082 3027 3087	3027 20 8 3088
	722o i DKF 5	522o i SF 39		3043 3088 3047	3085 302 304:

\*3+ "

\*4+ "

SF "?  
CWE<sub>1ph'</sub>  
DKF "?

CWE<sub>46j</sub>

				1	I = T
				%	%
	207o i 8 2047o i	522o i 9		3042 3084 304:	3088 3043 3075
	3222o i	522o i DKF 47		3028 <sup>*5+</sup> 20 : 3086	3022 20 4 302;
	2025o i 2087o i	422o i SF 8		3029 20 ; 3087	3044 3082 3087
	3047o i	422o i SF		3028 3022 3085	3044 3083 3087
				3024	20 5

			1 %	I = T %	
		8		20 : 309	20 7 303
			5/ / /	303 20 8 309	20 ; 20 3 30:
			6/ / /	305 20 9 30;	20 8 20 : 306
	47o i SF 57	522o i SF 9		20 ; 20 7 306	20 6 20 9 303
	4222o i	522o i SF :		3042 30: 3066	308 20 5 3042
	62o i	522o i SF 9		304 20 6 3055	30; 20 3 303
				308: 305 307	308 302 307
	52o i	522o i SF 34	*T#	303 20 8 308	305 20 6 305
			*U#	308 302 304	303 20 2 305
			R T	302 20 : 305	307 20 ; 304

\*3+

\*4+

\*5+<sup>CWE</sup><sub>2/34j</sub>

SF?

CWE<sub>iph</sub>

DE?

CWE<sub>46j</sub>

R T?

47Å

37ø52Å

\*\*\*\*\*

RXE 1

32 1 1

\*\*\*\*\*46

\*\*\*\*\*

IZ42372586

322o i J 42392597

522o i J 42392596

\*\*\*\*\*

'Lcpuugp/Ekci "Kvgtpevkpcn'P X

\*\*\*\*\*

Vwtpj qwugy gi "52.'D/4562'Dggtug."

Lcpuugp/Ekci "U0 0C0

Xlc'E0Lcpuugp.'Dqti q'Ucp'O kej grg.'26322'Ncvkpc."

"

3;

932526

622: ::; ;::

\*24; #: 4798838

j wr <ly y y 0kcp/lcpuugp0eqo 0p