

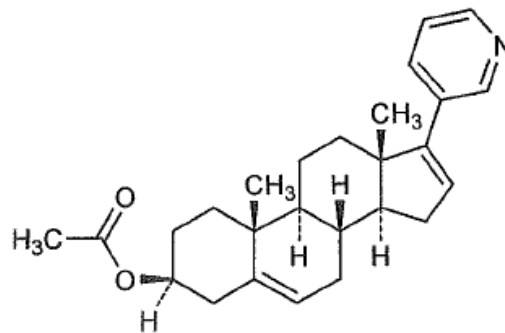
2015 05 06
2015 12 23
2016 02 09
2017 02 24
2018 01 24
2018 11 21
2019 03 06
2019 09 05
2020 06 30
2020 08 18
2020 12 03

® Zytiga®

Abiraterone Acetate Tablets

Cusuan Abitelong Pian

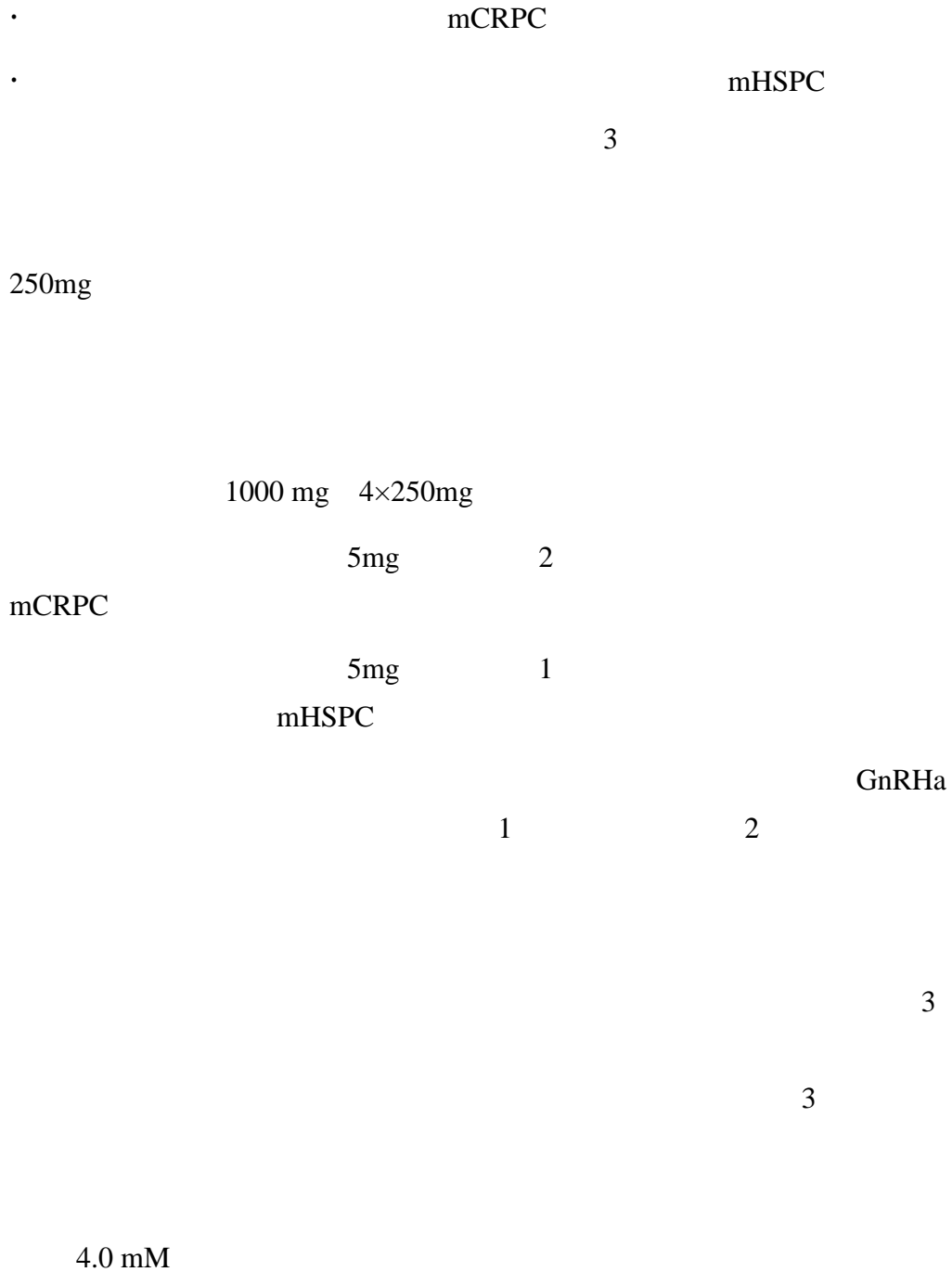
17-(3-)- -5,16- -3 -



$C_{26}H_{33}NO_2$

391.55

(K29/K32)



3 3

1

250mg		Child-Pugh B		Child-Pugh B	
		1000 mg			4
			1	2	2
		ALT		AST	
		ALT / AST		>5×	ULN
	>3×ULN				
		Child-Pugh C			8
		Child-Pugh C	8		
		AUC	7		2
				ALT / AST>5×ULN	
	>3×ULN				
		AST			
750 mg	1		2	1	
	3				
		1			
	750 mg	1			
AST					
				500 mg	1
	500 mg	1			
		ALT			ALT
3×ULN		2×ULN			

CYP3A4

		CYP3A4			
				CYP3A4	
		2	1000 mg	1	1000 mg
2		CYP3A4			

				COU-AA-301	COU-AA-
				1000mg	1
302		mCRPC		5mg	2
	5mg	2			
			212082PCR 3011		mHSPC
		1000mg	5 mg	1	
		mCRPC		2	
ABI-PRO-3001		ABI-PRO-3002	5		2230

1~4

1~4

GnRH α

11

0.1 43

7.2

0.1 43

>20%

53%

46%

3-4

14%

13%

7.5

6.6

3.3

>5

COU-AA-301

COU-AA-301

1195

AST /

AST / ALT>5 \times ULN

1

COU-AA-301

8

1 301

≥2%

		+		+	
		(N = 791)		(N = 394)	
		¹	³ ⁴	³ ⁴	
		%	%	%	%
/	²	30	4.2	23	4.1
	³	26.2	3.0	23	2.3
	⁴	27	1.9	18	0.8
		19	0.3	17	0.3
		8.5	1.3	6.9	0.3
		18	0.6	14	1.3
		6.1	0	3.3	0
		12	2.1	7.1	0.5
		5.4	0	2.5	0
		11	0	7.6	0
		7.2	0.3	5.1	0.3
		6.2	0	4.1	0
	⁵	5.9	1.4	2.3	0
	⁶	7.2	1.1	4.6	1.0
	⁷	3.8	0.5	2.8	0
	⁸	2.3	1.9	1.0	0.3

1
2
3
4
5
6
7
8

NCI CTCAE 3.0

1.3% 1.1%

2 COU-AA-301

2 COU-AA-301

	+ (N = 791)			+ (N = 394)		
	%	3	4 %	%	3	4 %
AST	63		0.4	53		0
	31		2.1	36		1.5
	28		5.3	20		1.0
ALT	24		7.2	16		5.8
	11		1.4	10		0.8
	6.6		0.1	4.6		0

COU-AA-302

COU-AA-302 1088
 AST /
 3 COU-AA-302
 13.8

3 COU-AA-302

≥5%

≥2%

		+			+		
		(N = 542)			(N = 540)		
		1	3	4		3	4
		%		%	%		%
		39		2.2	34		1.7
2		25		0.4	21		1.1
		8.7		0.6	5.9		0.2
	/ 3	30		2.0	25		2.0
		6.6		0.4	4.1		0.7
		23		0.4	19		0.6
		22		0.9	18		0.9
		11		0.0	5.0		0.2
		22		0.2	18		0.0
		22		3.9	13		3.0
		17		0.0	14		0.2
		12		2.4	9.6		0.9
		14		0.2	11		0.0
		13		0.0	9.1		0.0
		5.9		0.0	3.3		0.0
		13		0.0	8.0		0.0
		11		0.0	8.1		0.0
		10.3		1.3	5.6		0.6
		8.1		0.0	3.7		0.0

¹ NCI CTCAE 3.0

²

³

⁴ COU-AA-302 15%
>5%

4	COU-AA-302	>15%		>5%	
		+	(N = 542)	+	(N = 540)
		3	4	3	4
		%	%	%	%
		38	8.7	32	7.4
	¹	57	6.5	51	5.2
	ALT	42	6.1	29	0.7
	AST	37	3.1	29	1.1
		33	0.4	25	0.2
		17	2.8	10	1.7

¹

5		212082PCR 3011		5%		2%	
		1					
				N=597		N=602	
		2		3-4		3-4	
/		%		%		%	
		37		20		13	
		15		0.0		13	
		20		10		3.7	
ALT		16		5.5		13	
AST		15		4.4		11	
		7.0		1.0		3.7	
		6.7		0.2		4.7	
		7.5		0.3		5.0	
4		6.5		0.0		3.2	
1		GnRHa					
2		CTCAE 4.0					
3							
4							
6						5	
6		212082PCR 3011		15%			
		>5%					
6		212082PCR 3011		>15%			
				(N=597)		(N=602)	
		1-4		3-4		1-4	
		%		%		%	
		20		4		14	
		30		9.6		6.7	
ALT		46		6.4		45	
						1.3	
						1.3	

	16	0.2	6.2	0.2
--	----	-----	-----	-----

6

5

3	COU-AA-301	ABI-PRO-3001	COU-AA-302	ABI-PRO-
3002	212082PCR 3011			
	6			
NYHA	III IV	COU-AA-301	ABI-PRO-3001	II-IV
	212082PCR 3011	COU-AA-302	ABI-PRO-3002	
<50%				ADT
	GnRH α			
	2.6%vs.0.9%	1.3%	3-4	5
	4	0.2%	3-4	
2				
			1-2	1
	3	5		7
		0.3%	2	0.1%
3			3	
•				
•				
•				
•				
	< 1/100,	< 1/1000	1/10000	
	:			

QT

/

-

-

-

Child-Pugh C

CYP17

5 mg

1000 mg

4

2

3-4

2

3-4

1

3-4

212082PCR 3011

5 mg

1000 mg

10

1

3-4

	20		10		3-4						
1		3-4									
											QT
				LVEF	<50%	NYHA		III	IV		
	COU-AA-301		NYHA		II	IV				COU-AA-	
302	212082PCR3011										
	2230		1763			0.3%	0.1%				
				/							
				3/4	ALT	AST			5×ULN		
	2230		6%				3				
		ALT	AST								
2230		1.1%		ALT	AST						
				3		2	1			1	
	ALT	AST								250mg	
				1			1		2		2
				1	ALT	AST					
					AST	ALT			AST	ALT	
					AST	ALT					
									5×ULN		
3×ULN											

AST

AST

/

2

1

C_{max}

AUC₀₋

17

10

223

/

223

/

223

/

1.18mmol 27mg Lapp -

4

QT

33 mCRPC 1 2

1000mg 1 5mg 2 2

2 QTc >20ms <10ms

QTc

AUC 0.03

3

75 75 70% 65 65 27%

CYP3A4
CYP3A4 1000 mg AUC 600 mg 6
55%
CYP3A4 []

CYP3A4

CYP2D6 CYP2C8

AUC₂₄ 33% AUC CYP2D6 2.9
CYP2D6 CYP2D6
CYP2D6
1000 mg
M-III M-IV AUC 10% CYP2C8 AUC 46%
CYP2C8 CYP2C8
OATP1B1 OATP1B1
QT
QT QT
III IA
PSA

COU-

AA-301 COU-AA-302 212082PCR 3011

GnRH_a

PSA

COU-AA-301

III

				2:1	1195	
	1000 mg	1		5 mg	2	N=797
1	5 mg	2	N = 398			
	PSA	/	25%			
						69
39~95			93.3%	3.6%	1.7%	
1.6%	89%		ECOG	0	1	
	24		45%	90%	30%	
	70%		30%	PSA	70%	
		30%				
	552					
OS			7	1	775	
		97%				7
7					GnRH_a	

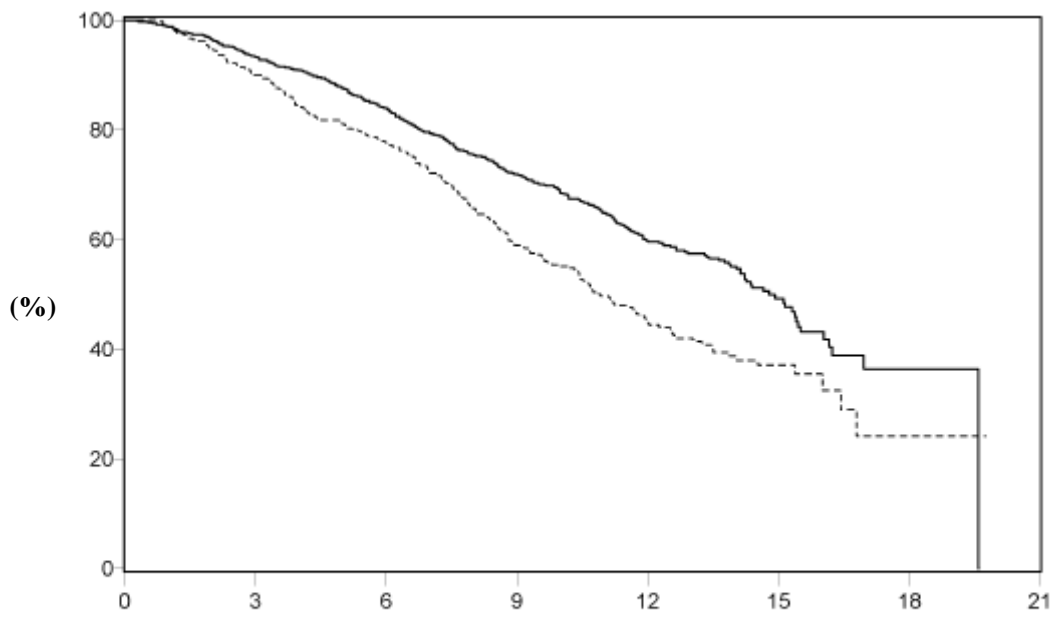
	+	+
	(N=797)	(N=398)
	333 (42%)	219 (55%)
()	14.8 (14.1, 15.4)	10.9 (10.2, 12.0)
(95%)		
P ^a	< 0.0001	
^b (95%)	0.646 (0.543, 0.768)	
	501(63%)	274(69%)
() 95%	15.8(14.8 17.0)	11.2(10.4 13.1)
^b (95%)	0.740(0.638 0.859)	

a P ECOG 0 1
 b <1

1
 1

GnRH_a

Kaplan Meier



797	736	657	520	282	68	2	0
398	355	306	210	105	30	3	0
			—			

COU-AA-302

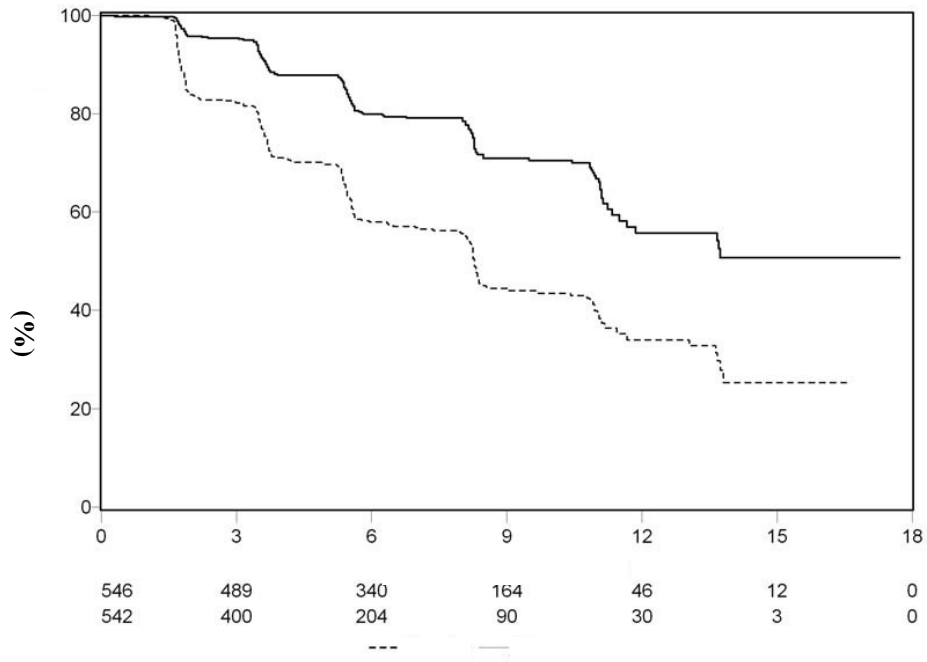
		BPI-SF	24	
0-1		2-3		
1088	1:1		1000mg	1 n=546
1	n=542		5mg	2
			ECOG	3

				71			
			70				
520	95.4%	15	2.8%	4	0.7%	6	
1.1%	76%	ECOG		0	24%		
1	50%		31%			19%	rPFS
		ECOG					
PSA		2[PCWG2]					
				RECIST 1.1		PCWG2	
						rPFS	
	rPFS	401					
	150	28%		251	46%		rPFS
	8	2					
8	COU-AA-302					GnRHα	
				+ (N=546)		+ (N=542)	
	(rPFS)						
				150(28%)		251(46%)	
	rPFS()			8.3			
	(95% CI)			(11.66 NE)		(8.12 8.54)	
	P *					<0.0001	
	** (95% CI)			0.425(0.347		0.522)	
NE=							
*P	ECOG	0	1				
**	<1						

2

GnRHα

Kaplan Meier



OS	IA	
rPFS	9	3
607		271
336		50%
62%		47%
HR=0.530	95% CI [0.451 0.623]	p<0.0001
16.5	8.3	rPFS

9: COU-AA-302:

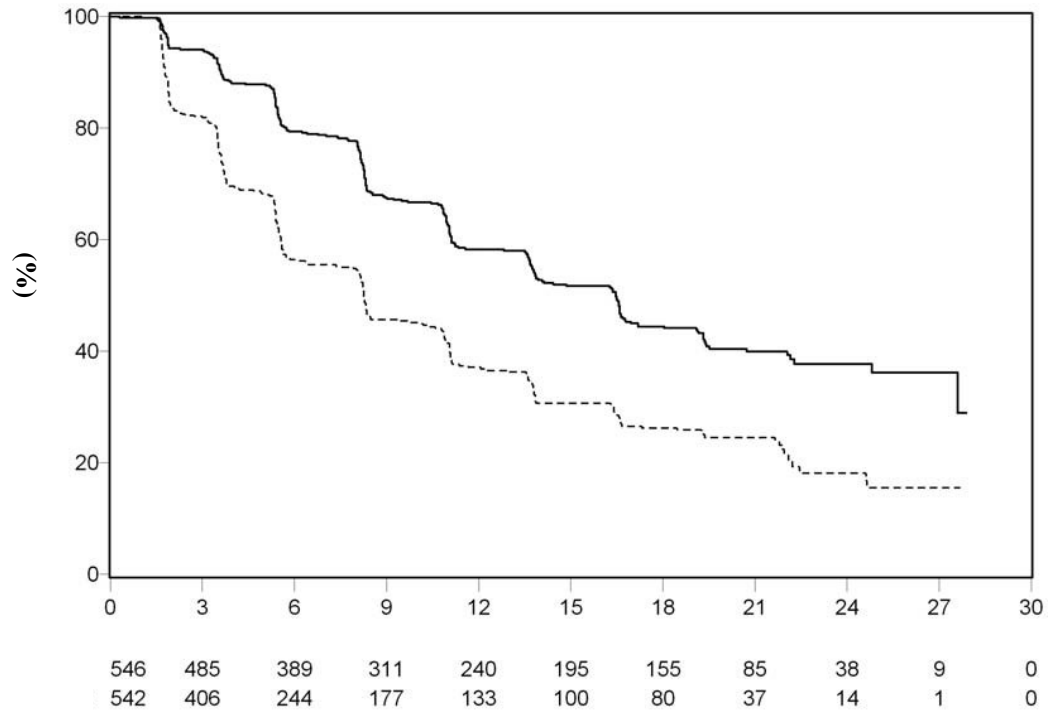
OS GnRHα -

	+	+
	(N=546)	(N=542)
(rPFS)		
rPFS()	271(50%)	336(62%)
(95% CI)	16.5 (13.80 16.79)	8.3 (8.05 9.43)
P *	<0.0001	
** (95% CI)	0.530(0.451 0.623)	

*P ECOG 0 1
 ** <1

3:

GnRHa
Kaplan Meier **OS** -



333

OS

25% HR=0.752 95% CI [0.606

0.934] p=0.0097

OS

10

IA

741

OS

49

65%

546

354

71%

542

387

19.4%

HR=0.806

95% CI [0.697

0.931] p=0.0033

OS

OS

4.4

34.7

30.3

10

4

44%

10: COU-AA-302

GnRHa

	+	+
	(N=546)	(N=542)
(%)	147(27%)	186(34%)
()		27.2
(95% CI)	(NE NE)	(25.95 NE)
P *		0.0097
** (95% CI)		0.752(0.606 0.934)
(%)	354(65%)	387(71%)
()	34.7	30.3
(95% CI)	(32.7 36.8)	(28.7 33.3)
P *		0.0033
** (95% CI)		0.806(0.697 0.931)

NE=

*P ECOG

	PCWG2	PSA		PSA
	11.1	5.6	HR=0.488	95% CI [0.420 0.568]
p<0.0001	PSA		HR=0.488	
	PSA		62% vs. 24%	p<0.0001

	33.4	23.4	HR=0.721	95% CI [0.614 0.846]
p<0.0001				

	25.2	16.8	HR=0.580	95% CI [0.487 0.691]
p<0.0001				

	ECOG			ECOG
		12.3	10.9	HR=0.821 95% CI
[0.714 0.943]	p=0.0053			

RECIST

16%	p<0.0001	36%
		18%
p=0.0490		26.7
18.4		

	FACT-P		FACT-P
	22%	p=0.0028	
FACT-P	12.7	8.3	

	212082PCR 3011		mHSPC
	212082PCR 3011	1:1	1199
	1000 mg 1	5 mg 1	mHSPC N=597
1	N=602		mHSPC
	ADT	GnRHα	3
	1	1	

Gleason

3

ECOG

3

67

	69%	2.5%	21%	8.1%	ECOG
0	76%	1	42%	2	3.5%
	24				0~1
50%	2~3		23%	28%	93.4%
		3.8%		3.8%	93.2%
	GnRHa	75.0%		12.0%	
62.1%		1.4%			

406

OS

21%

41

CRPC OS

618

52

11

5

29%

45%

CRPC

OS

11 212082PCR3011/LATITUDE

	N=597	(N=602)
1		
%	169 28%	237 39%
95% CI	NE(NE, NE)	34.7(33.1, NE)
p ²	<0.0001	
(95% CI) ³	0.621 (0.509 0.756)	
%	275 (46%)	343 (57%)
95% CI	53.3 (48.2, NE)	36.5 (33.5, 40.0)
(95% CI) ³	0.66 (0.56, 0.78)	

NE=

1

² p

³

ECOG

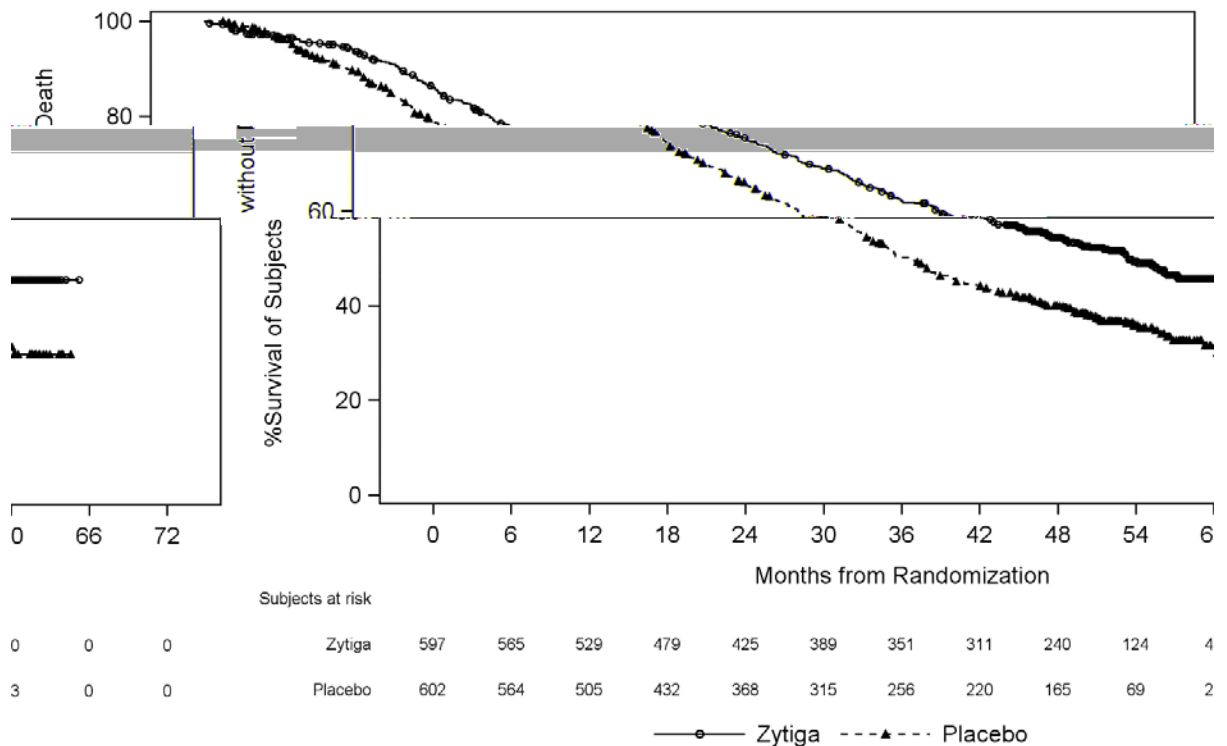
0/1 vs2

vs

1

5

**Kaplan-Meier
212082PCR3011/LATITUDE**



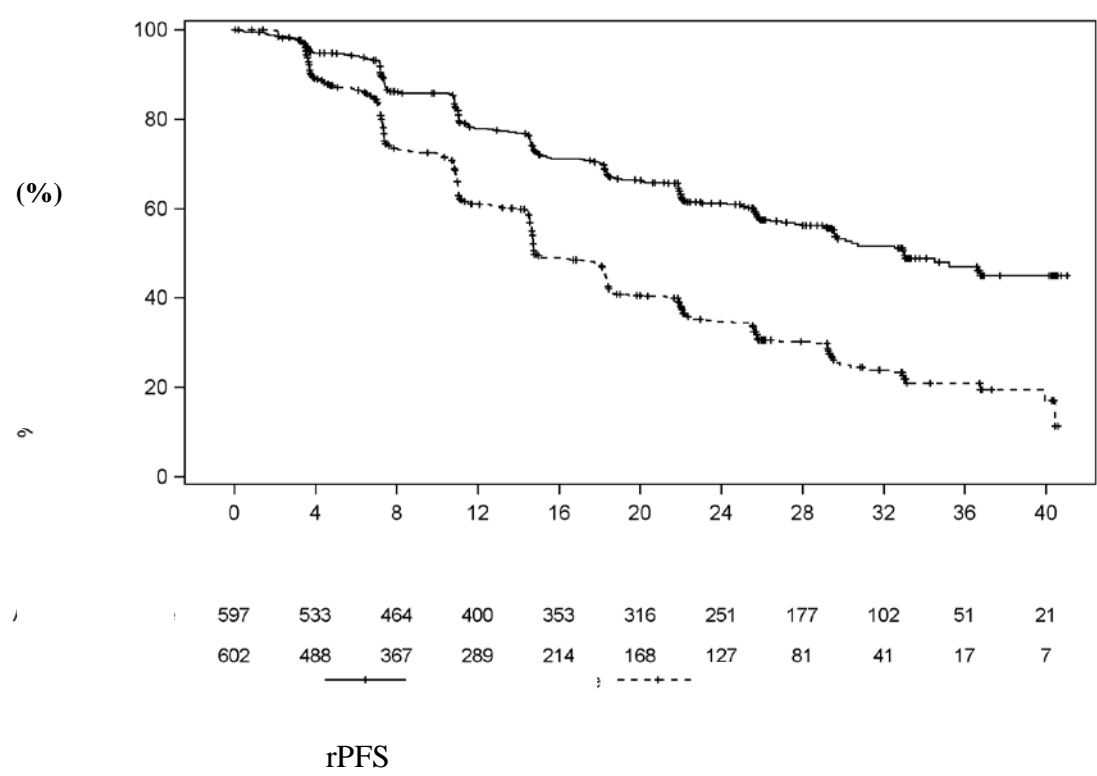
rPFS 593 239
 40.0% 354 58.8%
 rPFS 12 6
12 212082PCR 3011

	(N=597)	(N=602)
rPFS	239 40.0%	354 58.8%
95% CI	33.0	14.8
	29.57, NE	(14.69 18.27)
p ¹	<0.0001	
² (95% CI)	0.466 (0.394 0.550)	

NE=

¹ p ECOG 0/1 2
² <1 ADT

6 212082PCR 3011 Kaplan-Meier



24% HR=0.759; 95% CI:0.601, 0.960; p=0.0208
 43.0 31.3
PSA PCWG2 PSA

71

48~90

PSA

58%

HR=0.418 p<0.0001

PSA

44% HR=0.563, p=0.0173

13 ABI-PRO-3002 PSA

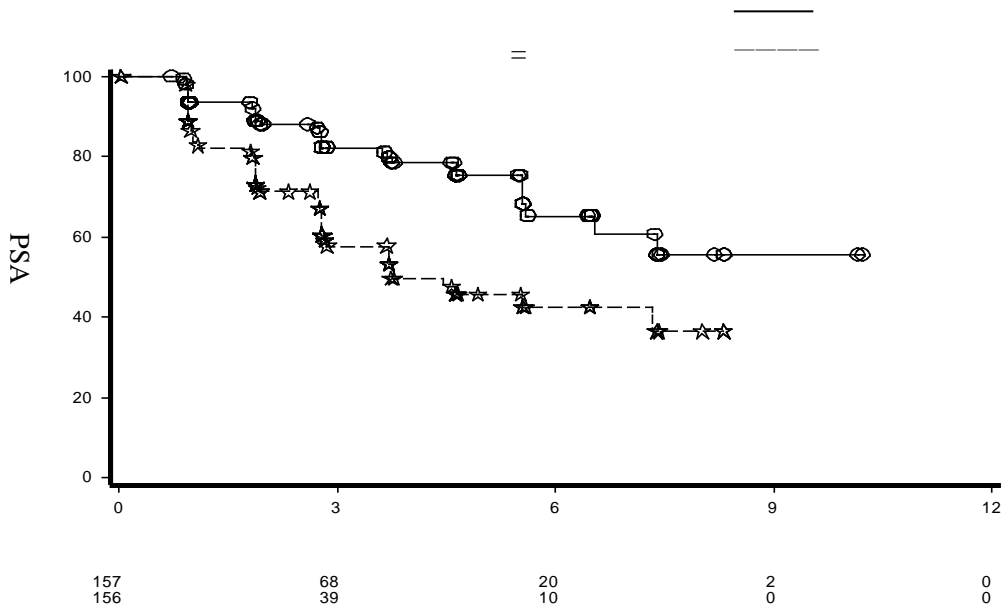
	AA		AA	
a	(N=119)	(N=119)	(N=157)	(N=156)
	119	119	157	156
	30 (25.2)	43 (36.1)	34 (21.7)	60 (38.5)
	89 (74.8)	76 (63.9)	123 (78.3)	96 (61.5)
p ^b		0.0173		<0.0001
(95% CI) ^c		0.563 (0.349; 0.909)		0.418 (0.271; 0.646)

^a Kaplan-Meier

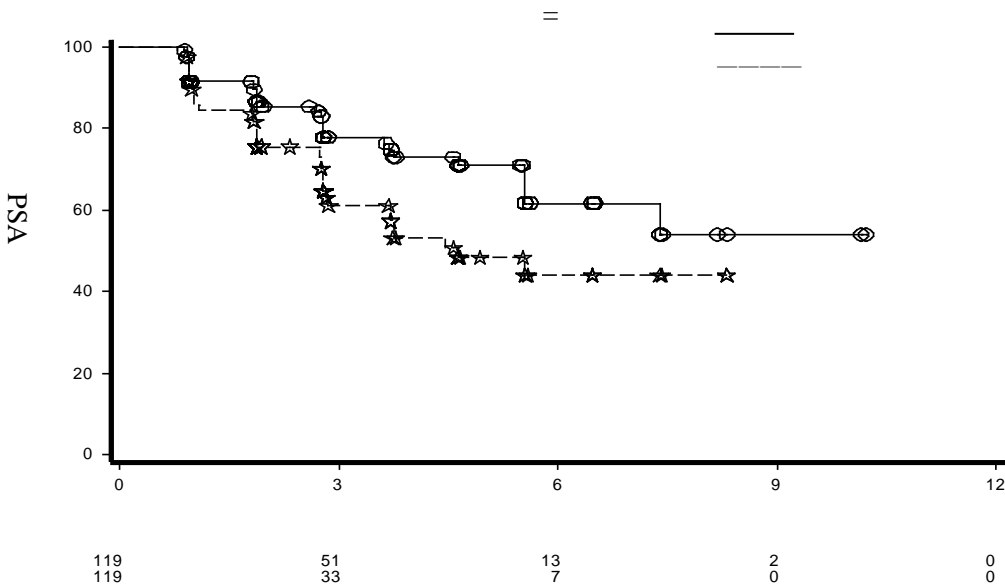
^b p () ECOG

^c <1

7 ABI-PRO-3002 PSA Kaplan-Meier ()



8: ABI-PRO-3002 PSA Kaplan-Meier ()

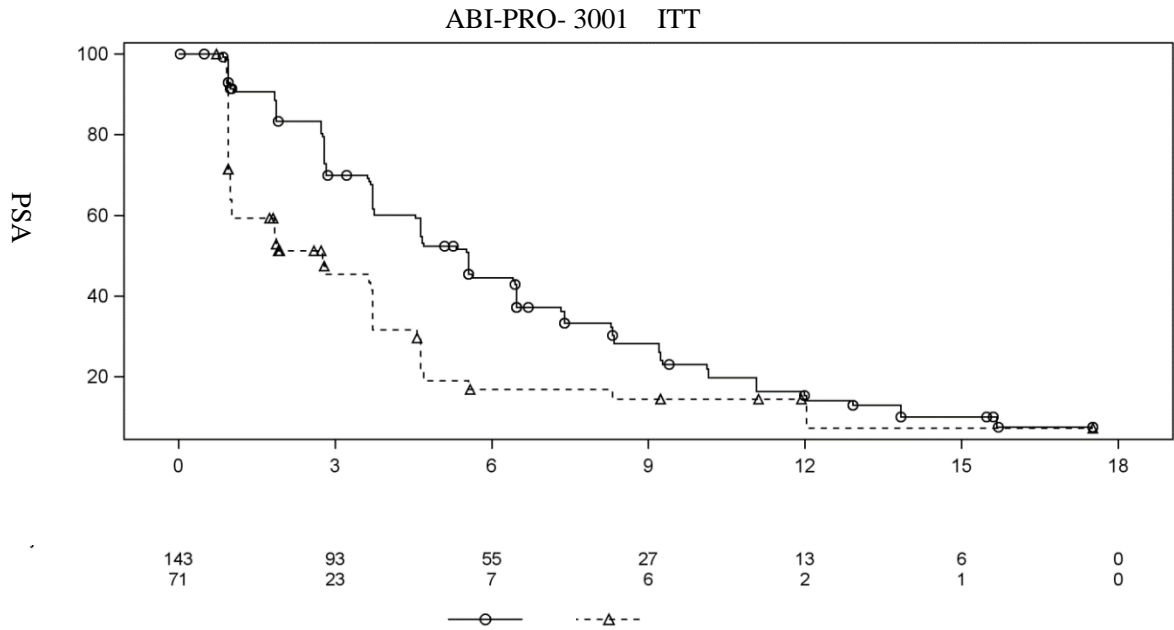


PSA 67% 31%
 $p < 0.0001$ $p < 0.0001$
 PSA 67% 37%
 CR+PR

23% 5%
 4.8 p=0.0369
 32% 0% p=0.0052
 17% 3 4
 21% 4% 7%
 3% 4% 3% 5%
 ABI-PRO-3002 mCRPC
 -
 III COU-AA-302
ABI-PRO-3001
 III
 1 1 2:1 1000 mg 4 x 250 mg
 1 1 4 1 5 mg
 28
 214 ITT
 143 71
 PSA [PSAWG]
 RECIST 1.1
 [BPI-SF]
 PSA
 PSA PSA TTPP
 PSA PSAWG
 PSA FACT-P
 BPI-SF
 BFI
 68 PSA

		95.1%	94.4%		
		72.7%	66.2%		61.7%
		54.7%		GnRHa	
			9	32.3	16.9
				5	
				16.0	4
16					
				PSA	49%
HR=0.506	p=0.0001		ECOG	2	
					TTPP
14	PSAWG		PSA		
	ABI-PRO-3001	ITT			
				AA	
				(N=143)	(N=71)
				143	71
PSA				109(76.2%)	52(73.2%)
				34(23.8%)	19(26.8%)
PSA	() ^a				
25	(95% CI)			85.00(83.00, 112.00)	29.00(29.00, 30.00)
	(95% CI)			169.00(141.00, 197.00)	84.00(31.00, 113.00)
75	(95% CI)			281.00(252.00, 337.00)	141.00(113.00, 366.00)
				(1.0+, 533.0+)	(22.0+, 533.0+)
3	(95% CI)			0.699(0.614, 0.769)	0.454(0.329, 0.572)
6	(95% CI)			0.446(0.360, 0.528)	0.169(0.082, 0.283)
12	(95% CI)			0.153(0.092, 0.230)	0.145(0.064, 0.257)
p	^b			0.0001	
	(95% CI) ^c			0.506(0.356, 0.719)	
	+ =	NE=			
^a	PSAWG	PSA		PSA	
	PSA			PSA	
		PSA			
^b	p				
^c		<1	AA		

9: PSAWG PSA Kaplan-Meier



mCRPC
TTTP HR=0.604 [0.356, 1.026]
PSA HR [0.543, 0.768]
OS HR=0.646
 14.1% =3.525 p<0.0001 37.1%
 50.7%
 50% HR=0.496 p=0.0014
 4
 23%
 32.2% 3 4
 28.2% 14.0% 19.7%
 7.0% 9.9% 6.3% 12.7%

ABI-PRO-3001

mCRPC

III COU-AA-301

212082PCR 3011

212082PCR 3011

137

69

68

80

		GnRHa							
		28	31	22	24				
	rPFS		18	26.1					38
55.9									
					66	HR = 0.341	95	CI	0.193
0.605			rPFS					rPFS	18.4
		OS		29					
14	20.3		15	22.1	OS		0.862	95	CI
0.415	1.788								
									HR = 0.433 95% CI:
0.146, 1.279									
									HR = 0.349 95% CI: 0.173, 0.707
									HR = 0.680 95% CI: 0.416, 1.111
									12.9
	PSA								PSA
									HR = 0.261 95% CI: 0.157, 0.433
									9.2
									94.2 98.5%
									37.7 20.6%
ALT	30.4	26.5	AST	27.5	22.1				24.6
20.6		24.6	14.7	10.1	20.6				3 4
			60.9	50.0					
23.2	32.4								13.0 16.2
									8.7
									1.5
									212082PCR 3011
									212082PCR 3011
									mHSPC -

17 - /C17,20- CYP17

CYP17
17 - 2 1 17 -
C17,20

CYP17

GnRH α

PSA

13 26 13 39
AUC

AUC 26

39

AUC 2

: Ames

mg/kg/ 13 26 39 /

AUC 0.6

30mg/kg/

4

30mg/kg/

16 7

30mg/kg/ 300mg/kg/

30mg/kg/ 1000mg/ 0.3

30 100mg/kg/ / 6~17 10

AUC 0.03 0.1 0.3

100mg/kg/

5 15

50 mg/kg/ 15 50 150mg/kg/ 0.8

Tg.rasH2 6

mCRPC

>99%

<0.2 ng/ml

mCRPC 2

AUC 1000 mg 2

mCRPC 1000 mg 1 C_{max} AUC ± SD

226±178 ng/ml 993±639 ng h/ml 250 1000 mg

1000mg 2000mg AUC

8%

300 C_{max} AUC₀₋ 7 5 7%

57% 825 17 10

	2		1				
				-1		>99%	
	±SD		19669±13358 L				
	P-			P-			
¹⁴ C-							
						CYP	
						N-	
		43%	CYP3A4	SULT2A1		N-	
	SULT2A1						
mCRPC						± SD	12±5
¹⁴ C-						88%	5%
						55%	22%
	n = 8		n = 8			Child-Pugh A	B
8							
			1000 mg				
1.1	3.6						
18	19						
	8			Child-Pugh C			8
					AUC	7	
					2		
				n=8			n=8
						1	
1000 mg			96				

1000 mg

15~30°C

120 /

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