2019 09 05

2020 08 12

2020 11 09

2021 05 06

2022 08 15

2023 04 20

® ERLEADA®

Apalutamide Tablets

Apata'an Pian

4-[7- 6- -5- -3- -8- -6- -5,7- [3.4] -5-]-2- -N-

$C_{21}H_{15}F_4N_5O_2S$

477.43

HPMC-AS

E172) E172

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Child-Pugh A B

TITAN SPARTAN ≥ 10%
≥ 2%

mHSPC

TITAN 1 1 mHSPC
240 mg TITAN
GnRHa
20 0 34
18 0.1 34
10 1.9%
n=3 n=2 n=1 n=1
n=1 n=1 n=1 8%
2% 23%
>1%
20% 20%
1 TITAN ≥ 10 ≥ 2
2 ≥ 15 5

1 TITAN mHSPC

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- /

1

2

SPARTAN

4% 3% TITAN

4 2 SPARTAN TITAN

6 0.5% 2 0.2%

SPARTAN 32.9 11.5

4% 1% TITAN

1.5% 1.5%

SPARTAN TITAN 2 0.2%

SPARTAN TITAN 6

SPARTAN 12%

7%

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2.7% 0.8% 3-4

314 20 953 SPARTAN

TITAN 9%

6% 3-4

1.5% 56 2 111 TITAN

SPARTAN

16 9

SPARTAN TITAN 5 0.4% 1

0.1% 159

650

SCAR

SCAR([DRESS]

- / [SJS/TEN] SCAR

SCAR

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CYP2C9

INR

QT

QT QT QT

-

45 CRPC QT

240 mg QTc QTcF

12.4 ms 90% CI 16.0 ms -QT

QTcF

3

/

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1327 19% 65 41%
65 74 40% 75

n=1073 65 39% 65-74
41% 75 49% 3-4
65 8% 65-74
10% 75 19%

CYP2C8 CYP3A4

CYP2C8 CYP3A4
N-
CYP2C8 CYP3A4

CYP3A4 CYP2C9 CYP2C19 UGT

CYP3A4 CYP2C19 CYP2C9
CYP3A4 CYP2C19 CYP2C9

UDP- UGT
UGT

P-gp BCRP OATP1B1

P- P-gp BCRP
1B1 OATP1B1 P-gp
BCRP/OATP1B1 P-gp
BCRP OATP1B1 P-gp BCRP
OATP1B1

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TITAN ***mHSPC***

TITAN 1052 mHSPC
1 1 240 mg N=525 N=527
TITAN GnRHa
Gleason
mHSPC
1 4 1

68 43-94
23% ≥ 75 68% 22% 2% 63%
37% 16%
Gleason ≥ 8 67% 68%
1
ECOG PS 0 1
OS rPFS

2 2 /

OS rPFS
OS OS
405 44 39%
TITAN 5 1 2

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5 TITAN

	(N=525)	**(N=527)**
[a]		
(%)	83 (16%)	117 (22%)
95% CI [b]	NE (NE, NE)	NE (NE, NE)
95% CI [c]	0.67 (0.51, 0.89)	
p [d]	0.0053	
(%)	170 (32%)	235 (45%)
(95% CI) [b]	NE (NE, NE)	52 (42, NE)
(95% CI) [c]	0.651 (0.534, 0.793)	
P [c]	<0.0001	
(%)	134 (26%)	231 (44%)
95% CI [b]	NE (NE, NE)	22.1 (18, 33)
95% CI [c]	0.48 (0.39, 0.60)	
p [d]	<0.0001	

[a] 50% α =0.01

[b] NE=

[c] <1

[d] Gleason ≤ 7 vs. 7 NA/EU vs.

p

rPFS vs

Gleason ≤ 7 vs.>7

OS Gleason

≤ 7 >7

HR=0.39 95%CI=0.27 0.56

p<0.0001

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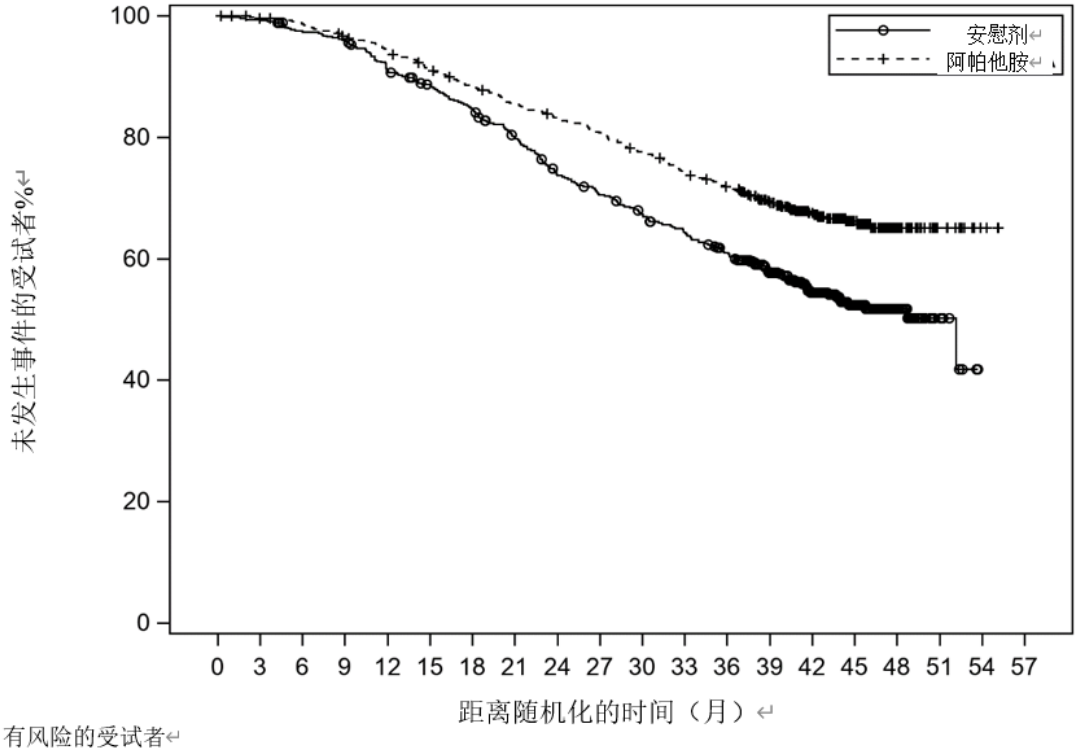
1 OS Kaplan-Meier mHSPC TITAN



有风险的受试者

安慰剂	527	524	510	503	474	458	436	408	374	357	339	322	301	248	181	102	43	10	0	0
阿帕他胺	525	519	513	500	489	469	452	438	425	412	394	376	362	321	227	139	52	15	3	0

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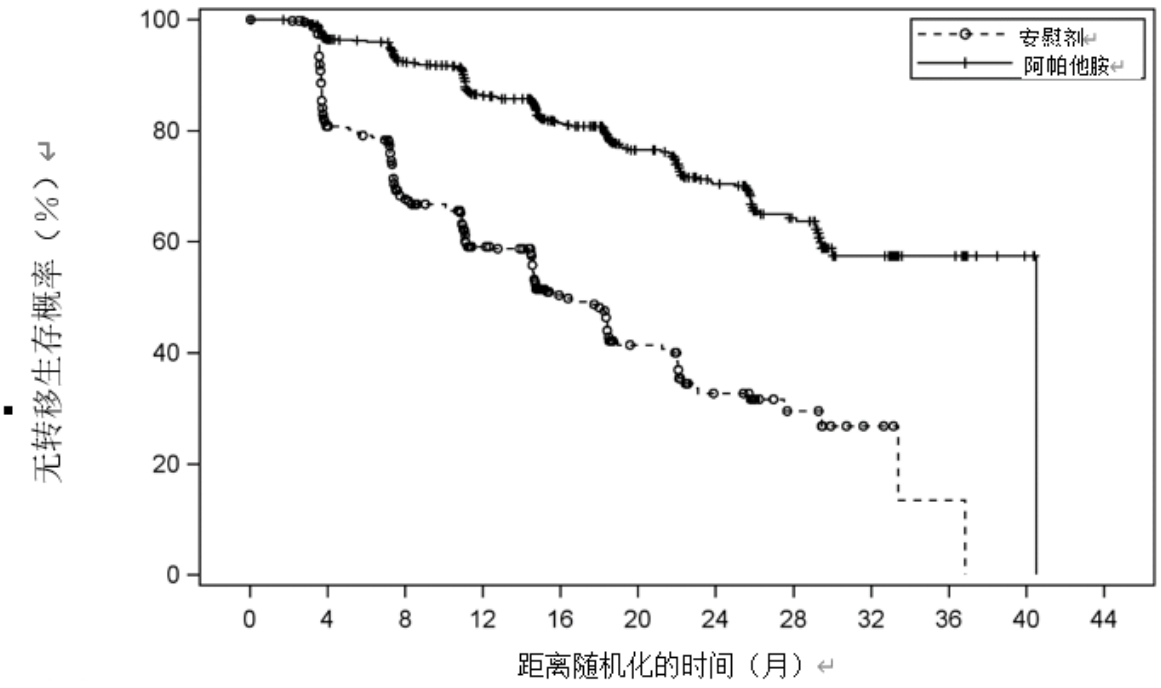
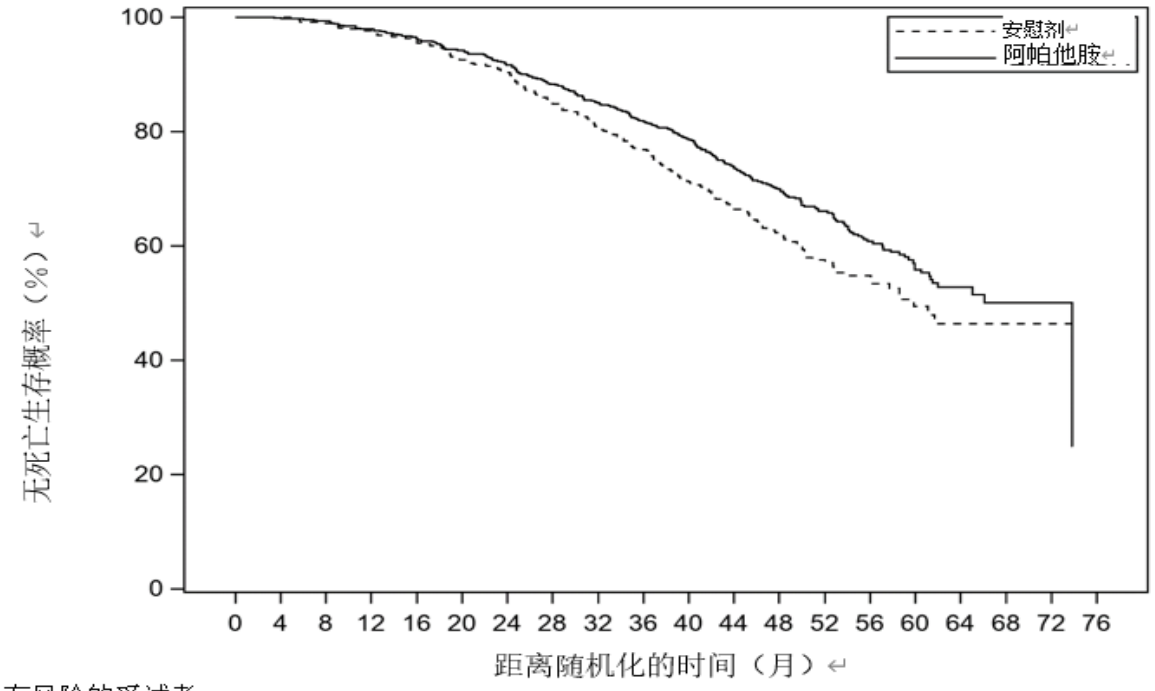
3 SPARTAN MFS Kaplan-Meier



有风险的受试者												
安慰剂	401	291	220	153	91	58	34	13	5	1	0	0
阿帕他胺	806	713	652	514	398	282	180	96	36	16	3	0

4: SPARTAN nmCRPC OS Kaplan-Meier



有风险的受试者																			
安慰剂	401	392	385	373	357	339	328	306	286	263	240	204	155	114	82	38	21	6	2	0
阿帕他胺	806	791	774	758	739	717	691	658	625	593	558	499	374	269	181	100	47	19	4	0

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AR AR

AR DNA AR N-

AR

Ames

26 39

≥25 mg/kg/ AUC 1.4 ≥2.5 mg/kg/

AUC 0.9 /

/

≥25 mg/kg/ AUC 0.8

4

150 mg/kg/ AUC

5.7 4 /

8

- 6-20

25 50 100 mg/kg/ ≥ 25 mg/kg/

/ ≥ 50 mg/kg/ / 100 mg/kg/

AUC 2 4 6

2 5 15 50 mg/kg/

≥ 5 mg/kg/ AUC 0.2

rasH2 6 30 mg/kg/

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[SD] 30 480 mg
0.125 2 C_{max}
AUC 4
5 C_{max} 6.0 µg/mL 1.7 AUC 100 µg.h/mL 32
1.63 CL/F
30 480 mg

N- C_{max} 5.9 µg/mL
1.0 AUC 124 µg.h/mL 23 N-
1.27 N- / AUC 1.3
N-

100% t_{max} 2 1 5

4 60 mg / 4
60 mg / C_{max} AUC

500 600 250
150 C_{max} AUC
t_{max} 2

276 L
N- 96% 95%

CL/F 1.3 L/h 2.0 L/h
3

CYP2C8 CYP3A4
N- CYP2C8 CYP3A4
58% 13% 40% 37%

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240 mg AUC 45% N-
44%

70 65% 1.2%
2.7% N- 24% 1.5% 2% N-

18-94 [ ]
eGFR 30-89 mL/min/1.73 m^2 [MDRD]
Child-Pugh A Child-Pugh B N-

eGFR ≤ 29 mL/min/1.73 m^2 MDRD
Child-Pugh C

CYP2C8
240 mg CYP2C8 C_{max}
21% AUC 68% C_{max} 32% AUC
44% N-
C_{max} 19% AUC 23%
CYP3A4
240 mg CYP3A4 C_{max}
22% AUC CYP3A4
AUC 24% C_{max} C_{max} 38% AUC
51% C_{max} 23% AUC 28%
CYP3A4/CYP2C8
CYP3A4 CYP2C8
C_{max} 25% AUC 34% C_{max} 15% AUC 19%

pH
H_2-

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N- P-gp BCRP OATP1B1 OATP1B3 P-gp P-gp

CYP

N- CYP3A4 CYP2B6 CYP2B6 CYP2C8 CYP2C9 CYP2C19 CYP3A4 N- CYP1A2 CYP2D6 CYP CYP3A4 AUC 92% CYP2C19 AUC 85% S- CYP2C9 AUC 46% CYP2C8

P-gp BCRP OATP1B1

P-gp AUC 30% BCRP/OATP1B1 AUC 41% C_{max}

UGT

UGT UGT

OCT2 OAT1 OAT3 MATE

N- 2 OCT2 3 OAT3 MATE 1 OAT3

30

160 ml HDPE PP 120 / /

24

JX20190110

H20190050

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HJ20200029

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