

Les antiandrogènes de 2^{ème} génération pour le cancer de prostate métastatique hormonosensible

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En 2015...

Castration + docetaxel: Standard de prise en charge des patients porteurs d'un ADK prostatique métastatique de novo

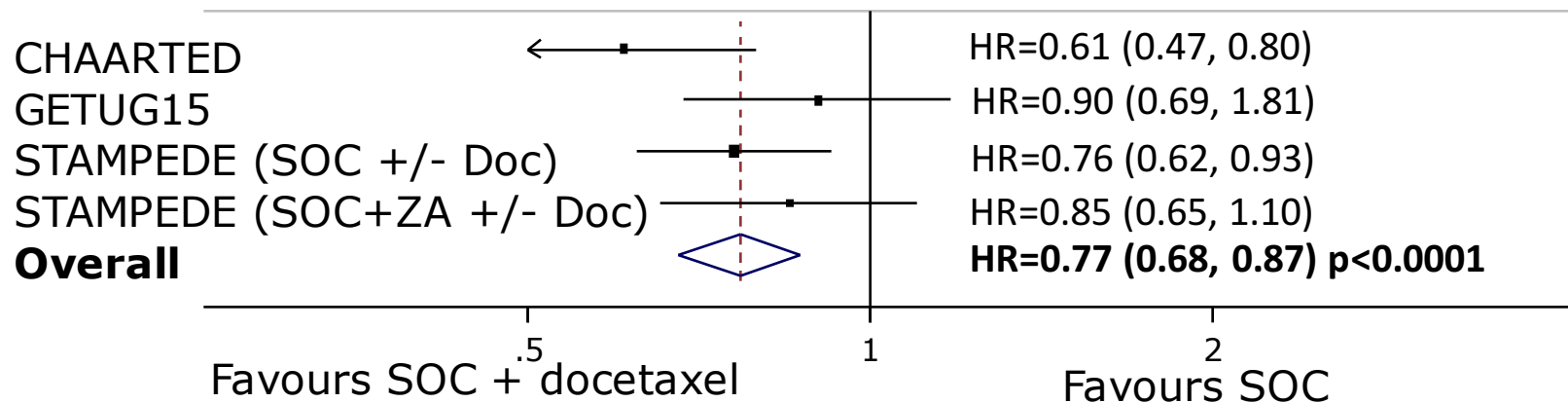
OS	ADT + DOC	ADT		
	Median (mOS)	Median (mOS)	HR (95% CI)	P Value
GETUG 15 ¹	62.1	48.6	0.88 (0.68-1.14)	0.3
CHAARTED ²	57.6	44	0.61 (0.47-0.80)	< 0.001
CHAARTED ² « high Volume »	49,2	32,2	0,60 (0,45-0,81)	0,0006
CHAARTED ² « Low Volume »	NR	NR	0,63 (0,34-1,17)	0,1398
STAMPEDE ³	60	45	0.76 (0.62-0.92)	0.005

Haut volume : ≥ 4 métastases osseuses dont une en dehors de l'axe ou métastase viscérale

mHSPC docetaxel: Survie

Results based on 2992 men / 1271 deaths

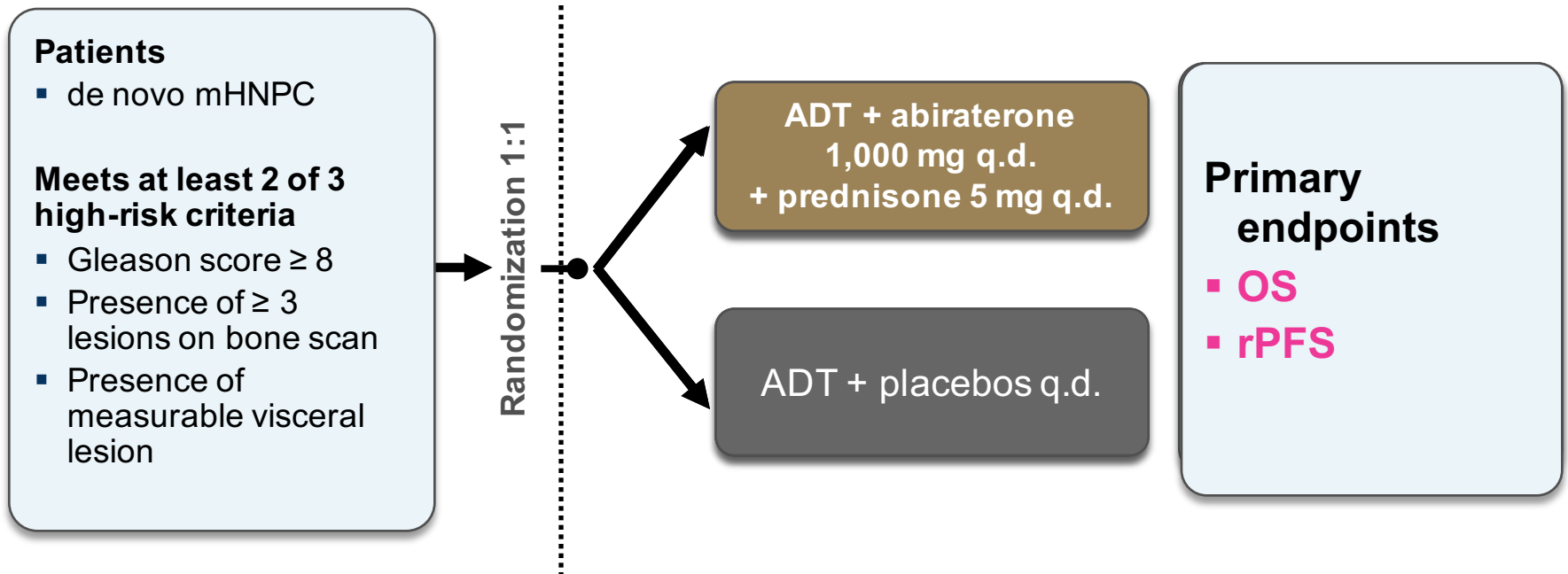
Trial name



9% absolute improvement in survival
(from 40%) at 4 years

Juin 2017... ESSAI LATITUDE

Randomized, double-blind, active-controlled, multicentre, phase 3 study



mHNPC, metastatic hormone naive prostate cancer;
q.d., once daily; rPFS, radiographic progression-free survival.

Juin 2017... STAMPEDE (Abiraterone comparaison).

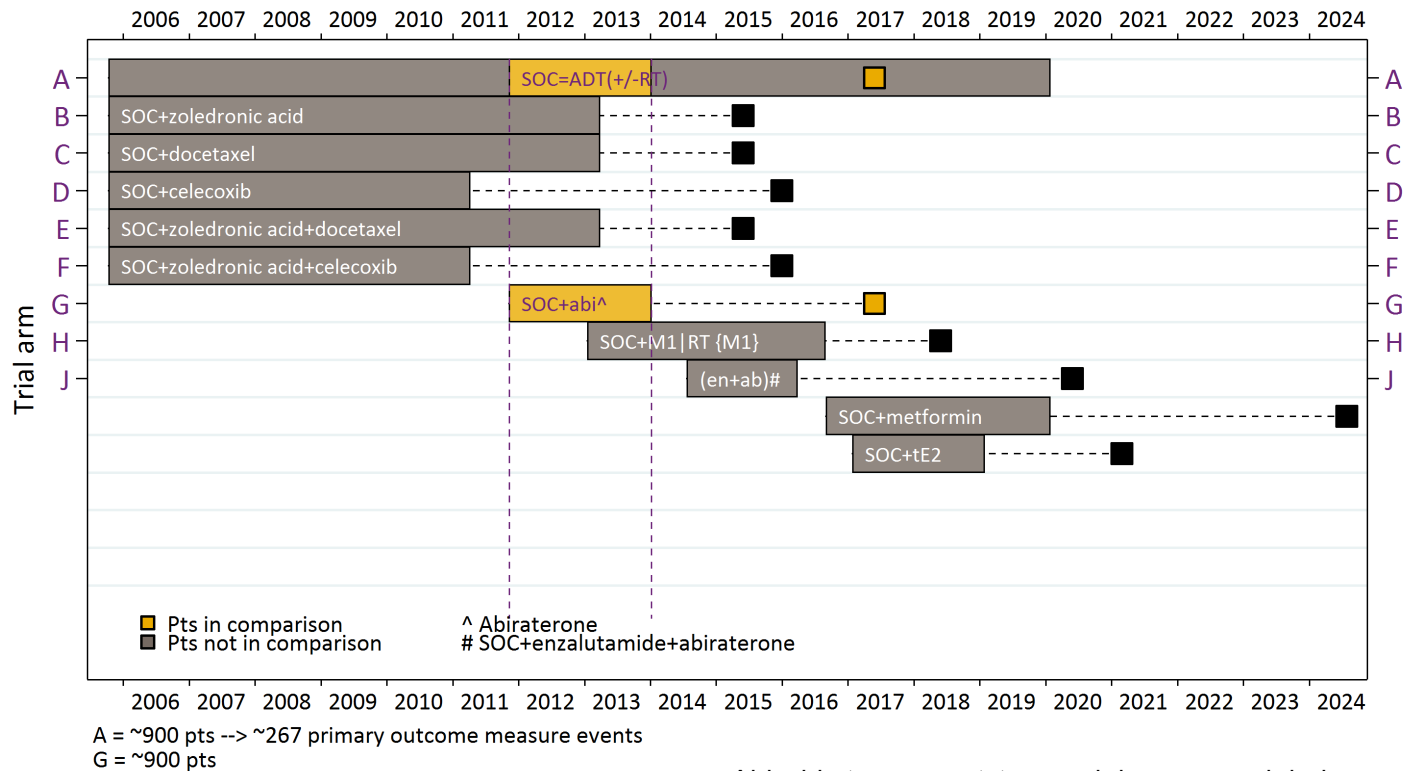
CaP nouvellement diagnostiqué avec 1 des critères suivants :

- Métastatique
- Ganglions positifs
- Plus de 2 critères (stades T3/4, PSA \geq 40 ng/ml, Score de Gleason 8-10)

CaP en rechute après prostatectomie radicale ou radiothérapie avec \geq 1 des critères suivants :

- PSA $>$ 4 ng/ml et en augmentation avec PSADT $<$ 6 mois
- PSA \geq 20 ng/ml
- Métastatique
- Ganglions positifs

STAMPEDE: Abiraterone comparisons



Abi, abiraterone acetate + prednisone or prednisolone; pts, patients; RT, radiotherapy; SOC, standard of care.

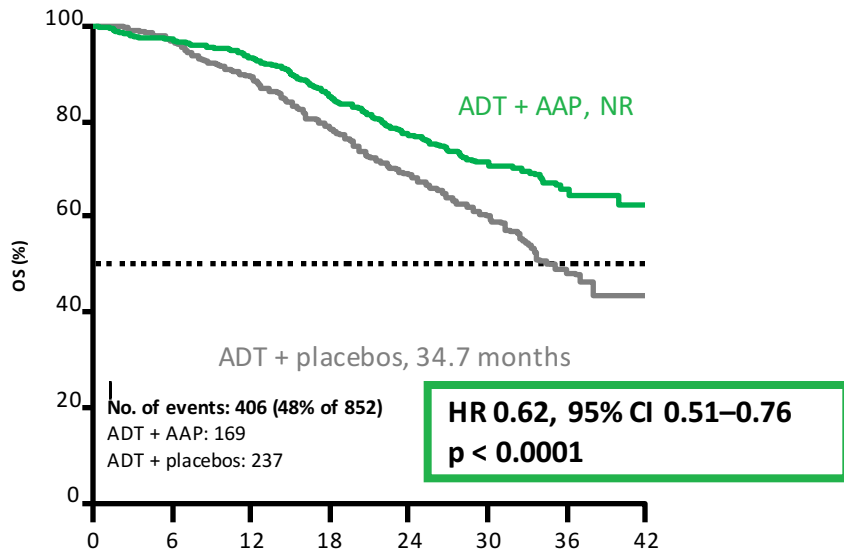
ADT + AAP dans le mHSPC

	LATITUDE ¹	STAMPEDE ²
	de novo high risk M1	M1
OS		
Experimental arm (median), months	NR	NR
Benefit, months	NR (34.7 to NR)	NR
HR for OS	0.62	0.61
Progression	rPFS	FFS
Experimental arm (median), months	33.0	NR
Benefit, months	18.2 (14.8 to 33.0)	NA
HR for progression	0.47	0.31

Not head-to-head comparison studies. NR, not reached.

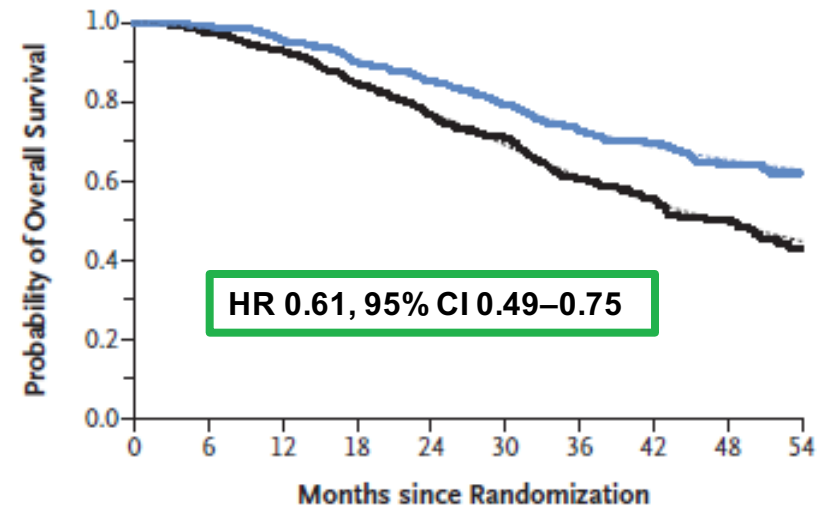
Réduction similaire du risque de décès dans les études AAP

LATITUDE 1: OS



No. at risk	Time (months)							
	0	6	12	18	24	30	36	42
ADT + AAP	597	565	529	479	388	233	93	9
ADT + placebos	602	564	504	432	332	172	57	2

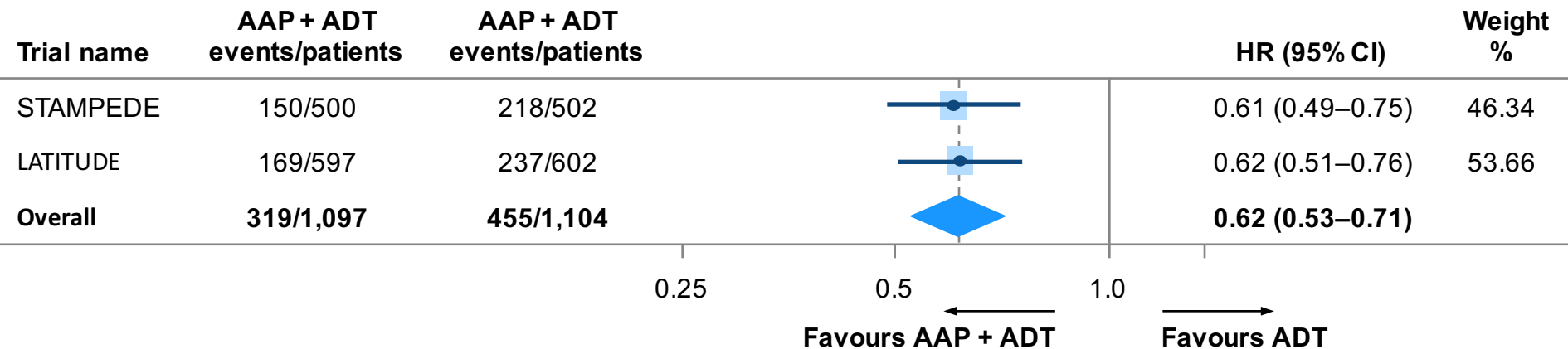
STAMPEDE 2: OS in M1 patients



No. of Patients (no. of deaths)	Months since Randomization									
	0	6	12	18	24	30	36	42	48	54
Combination therapy	500	(22)	469	(50)	415	(57)	256	(18)	81	
ADT alone	502	(35)	460	(80)	371	(73)	215	(23)	60	

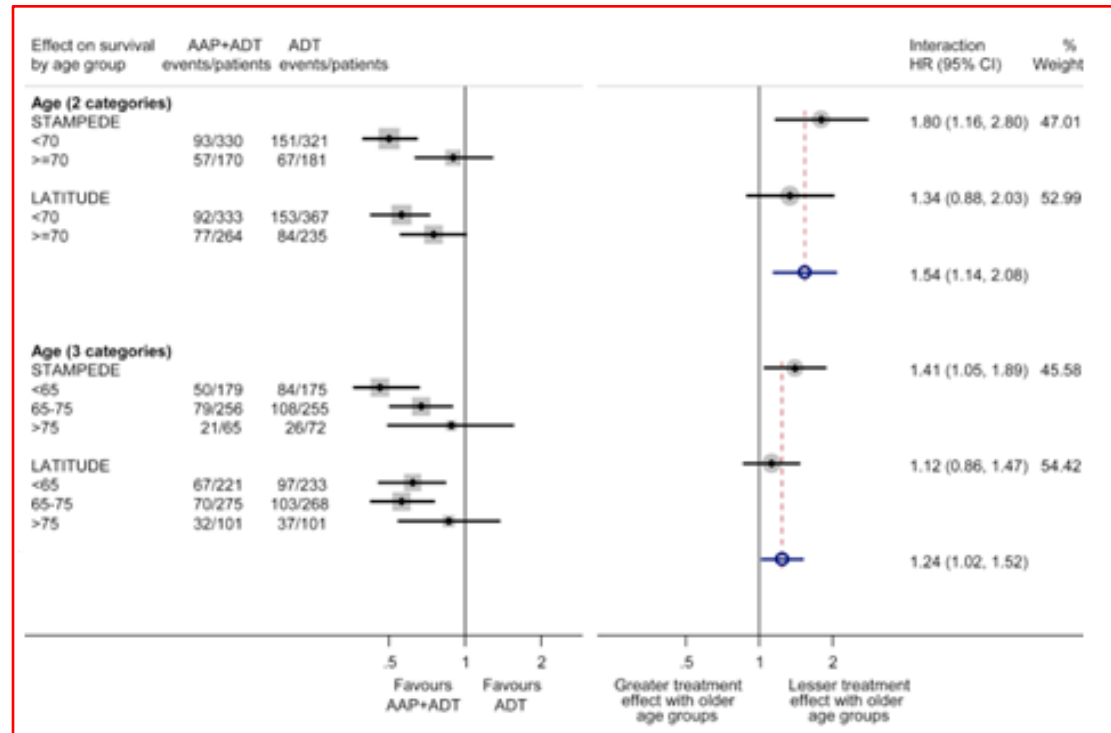
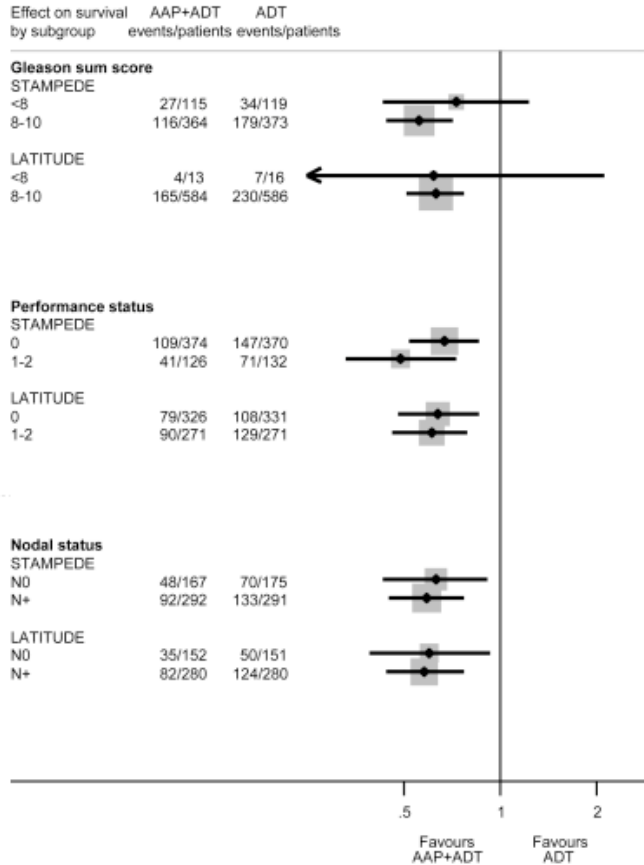
Effet AAP + ADT sur la Survie Globale des patients mHSPC

Results based on 2,201 men/774 events



14% absolute improvement in survival at 3 years

OS benefit consistently favorable across subgroups...

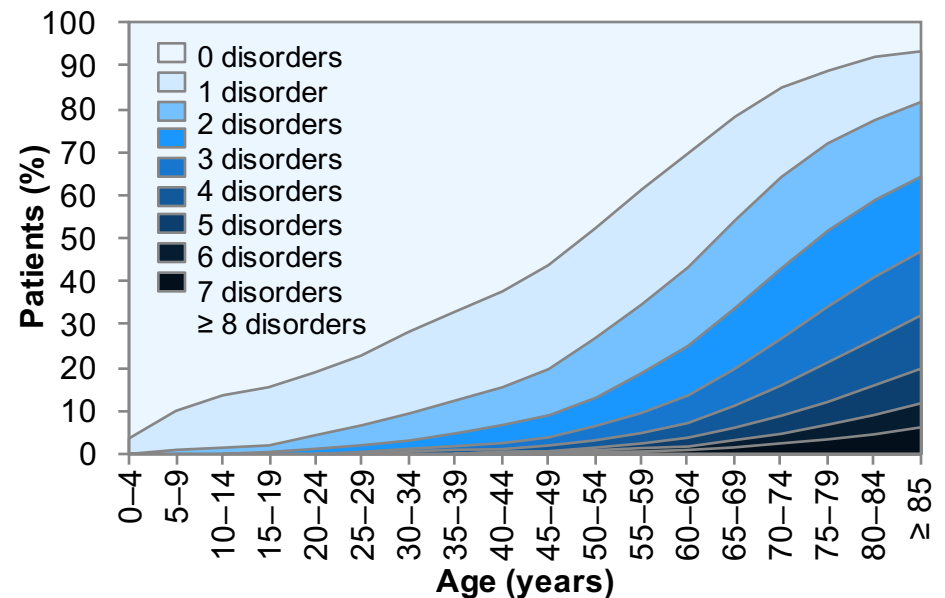


Age des patients au diagnostic de mHSPC

	Median age, years	ECOG PS 0, n (%)
GETUG-AFU15 ¹	63	181 (99)
CHAARTED ²	64	277 (69.8)
STAMPEDE, Doc arm ³	65 (includes M0 disease)	461 (79)
STAMPEDE, AAP arm ^{5,6}	67 (includes M0 disease)	745 (78)
LATITUDE, AAP arm ^{7, 8}	68	326 (55)

Age at diagnosis of metastatic prostate cancer : 74 ans ⁴

Number of chronic comorbidities by age stratum



SEER, Surveillance, Epidemiology, and End Results.

Latitude : Critères secondaires et exploratoires pré-spécifiés

	ADT+AA+P (n = 597)	ADT+placebos (n = 602)	Hazard Ratio (95% CI)	P Value*
Secondary end points				
Time to pain progression — mo	NR	16.6	0.70 (0.58–0.83)	< 0.001
Time to PSA progression — mo	33.2	7.4	0.30 (0.26–0.35)	< 0.001
Time to next symptomatic skeletal event — mo	NR	NR	0.70 (0.54–0.92)	0.009
Time to chemotherapy — mo	NR	38.9	0.44 (0.35–0.56)	< 0.001
Time to subsequent prostate cancer therapy — mo	NR	21.6	0.42 (0.35–0.50)	< 0.001
Exploratory end point				
Patients with a PSA response (decline ≥ 50% from baseline) — %	91	67	1.36 (1.28–1.45)*	< 0.001

- The superiority of ADT+AA+P over ADT+placebos was observed for all secondary end points

L'ajout d'AAP à l'ADT améliore la quantité de vie mais aussi la qualité de vie : PROs LATITUDE

	ADT plus abiraterone acetate and prednisone (n=597)	ADT plus placebos (n=602)	HR (95% CI)	p value
FACT-P total score	12.9 (9.0-16.6)	8.3 (7.4-11.1)	0.85 (0.74-0.99)	0.032
FACT-G general function subscale including physical, social and family, emotional, and functional wellbeing items	12.9 (9.3-18.4)	8.3 (7.4-11.1)	0.87 (0.75-1.01)	0.058
Trial outcome index including physical, functional, and prostate cancer-specific items	18.4 (14.4-22.6)	9.2 (7.4-11.2)	0.73 (0.63-0.85)	0.0001
Pain-related subscale including 4 pain-specific items: GP4 and P1-P3	10.2 (8.3-14.8)	6.5 (5.6-7.5)	0.76 (0.66-0.88)	0.0001
Prostate cancer-specific subscale including additional concerns section items	8.3 (6.5-11.1)	5.6 (4.6-7.3)	0.81 (0.70-0.93)	0.0025
Emotional wellbeing including items GE1-GE6	16.1 (10.2-20.7)	10.2 (8.3-14.8)	0.92 (0.79-1.08)	0.31
Functional wellbeing including items GF1-GF7	7.4 (5.6-9.2)	5.5 (3.8-6.4)	0.89 (0.78-1.03)	0.11
Physical wellbeing including items GP1-GP7	14.4 (10.2-18.2)	7.4 (6.5-9.2)	0.75 (0.65-0.87)	0.0001
Social and family wellbeing including items GS1-GS7	3.8 (2.9-4.7)	5.5 (4.6-6.4)	1.06 (0.92-1.23)	0.38

Data are median (95% CI). ADT= androgen deprivation therapy, HR=hazard ratio. FACT-P=Functional Assessment of Cancer Therapy-Prostate. FACT-G=Functional Assessment of Cancer Therapy-General.

Table 2: Median time to deterioration of functional status (months) in FACT-P total and subscale scores

Tolérance

	LATITUDE ¹		STAMPEDE ²	
	ADT + AAP (n = 597)	ADT + placebos (n = 602)	ADT + AAP (n = 960)	ADT alone (n = 957)
Any AE, n (%)	558 (93)	557 (93)	943 (99)	950 (99)
AEs grade 3 or 4	374 (63)	287 (48)	443 (47)	315 (33)
AEs grade > 3 , n (%)				
Cardiac disorder	20 (4)	6 (1)	92 (10) ^a	41 (4) ^a
Atrial fibrillation	2 (0.3)	1 (0.2)	NA	NA
Myocardial infarction	NA	NA	10 (1)	9 (1)
Cardiac dysrhythmia	NA	NA	14 (1)	2 (< 1)
Hypertension	121 (20)	60 (10)	44 (5)	13 (1)
Hypokalaemia	62 (11)	8 (1)	12 (1)	3 (< 1)
ALT increased	33 (5)	8 (1)	53 (6)	4 (< 1)
AST increased	26 (4)	9 (1)	10 (1)	2 (< 1)
Hyperglycaemia	27 (4)	18 (3)	NA	NA
Any AE leading to treatment discontinuation	73 (12)	61 (10)		
AE leading to death	28 (5)	24 (4)		

Not head-to-head comparison studies.

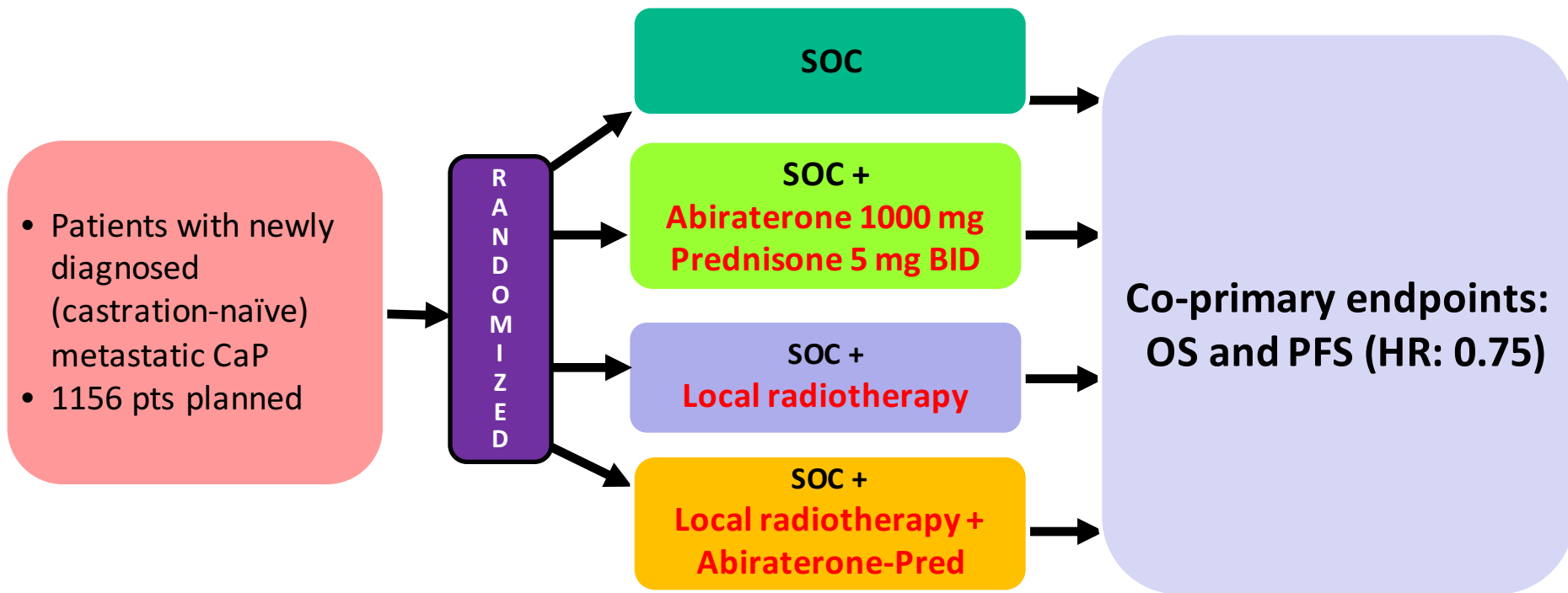
^a All cardiovascular disorders (including hypertension, myocardial infarction, cardiac dysrhythmia).

1-Fizazi K, et al. N Engl J Med. 2017;377:352-60.

2. James ND, et al. N Engl J Med. 2017;377:338-51.

Effets additifs de la combinaison Abiratérone/ Docetaxel au stade mHSPC???

Essai PEACE-1 : Inclusions temporairement suspendues



Standard of Care (SOC)= Androgen deprivation therapy (ADT) +/- docetaxel (Stratification)

Study sponsor: Unicancer

MERCI
