Incontournables en 2019

Pr Jean-Alexandre Long

Cancer de la Prostate

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 10, 2018 VOL. 378 NO. 19

MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis

V. Kasivisvanathan, A.S. Rannikko, M. Borghi, V. Panebianco, L.A. Mynderse, M.H. Vaarala, A. Briganti, L. Budäus, G. Hellawell, R.G. Hindley, M.J. Roobol, S. Eggener, M. Ghei, A. Villers, F. Bladou, G.M. Villeirs, J. Virdi, S. Boxler, G. Robert, P.B. Singh, W. Venderink, B.A. Hadaschik, A. Ruffion, J.C. Hu, D. Margolis, S. Crouzet, L. Klotz, S.S. Taneja, P. Pinto, I. Gill, C. Allen, F. Giganti, A. Freeman, S. Morris, S. Punwani, N.R. Williams, C. Brew-Graves, J. Deeks, Y. Takwoingi, M. Emberton, and C.M. Moore, for the PRECISION Study Group Collaborators*

- Essai de non infériorité
- Multicentrique, randomisé
- 1ère série de biopsie, PSA<20

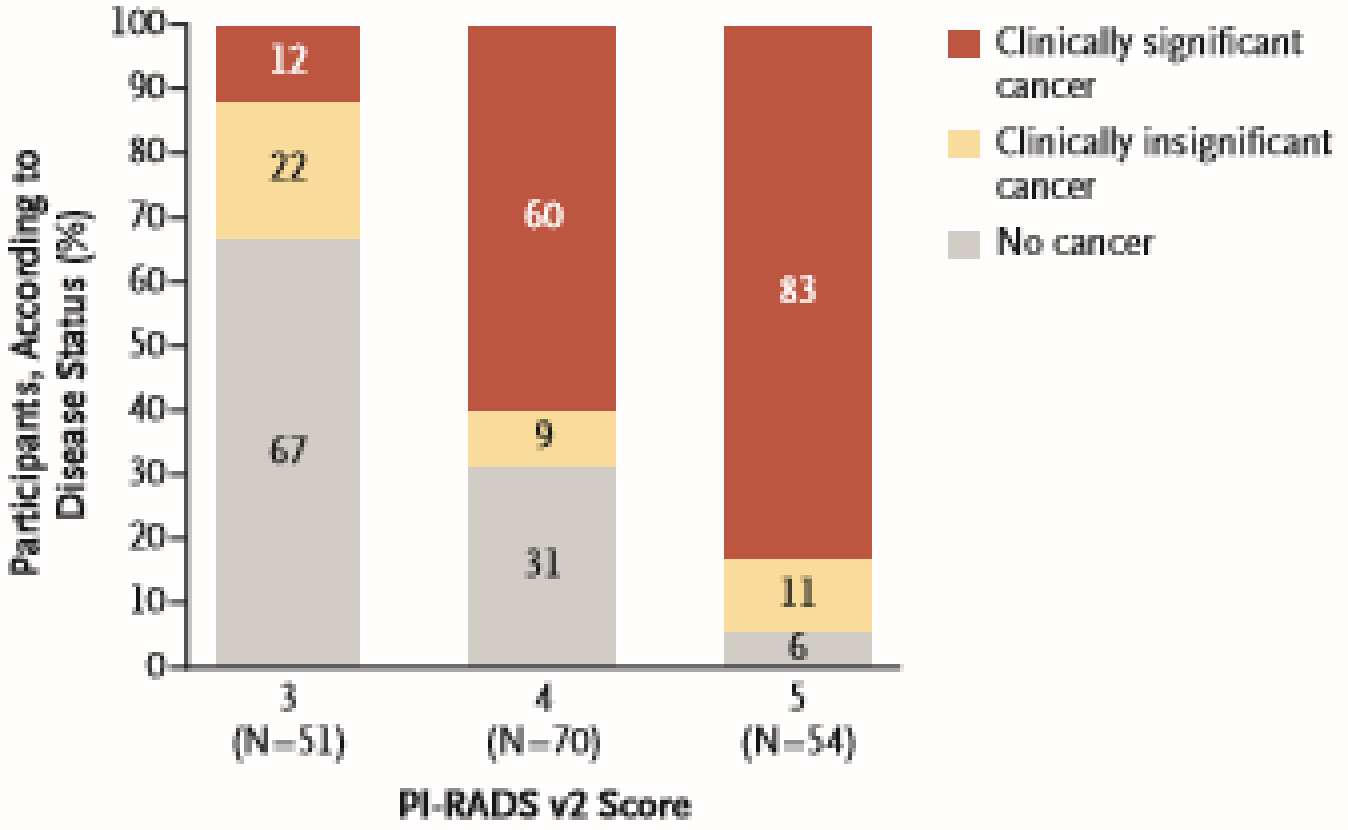
PRECISION

- 2 bras:
  - IRM + Guidage IRM
    - Si PIRADS <3 : pas de biopsie
    - Guidage mental ou assisté par ordinateur
    - Max 12 bx dans 3 cibles
  - Biopsies randomisées (10-12 bx)

PRECISION

Table 2. Comparison of Cancer Detection between Groups.*

Outcome	MRI-Targeted Biopsy Group (N=252)	Standard-Biopsy Group (N=248)	Difference†	P Value
Biopsy outcome — no. (%)			—	—
No biopsy because of negative result on MRI	71 (28)	0		
Benign tissue	52 (21)	98 (40)		
Atypical small acinar proliferation	0	5 (2)		
High-grade prostatic intraepithelial neoplasia	4 (2)	10 (4)		
Gleason score				
3+3	23 (9)	55 (22)		
3+4	52 (21)	35 (14)		
3+5	2 (1)	1 (<1)		
4+3	18 (7)	19 (8)		
4+4	13 (5)	6 (2)		
4+5	7 (3)	2 (1)		
5+5	3 (1)	1 (<1)		
No biopsy‡	4 (2)	3 (1)		
Withdrawal from trial§	3 (1)	13 (5)		
Clinically significant cancer¶				
Intention-to-treat analysis — no. (%)	95 (38)	64 (26)	12 (4 to 20)	0.005
Modified intention-to-treat analysis — no./total no. (%)	95/245 (39)	64/235 (27)	12 (3 to 20)	0.007
Per-protocol analysis — no./total no. (%)	92/235 (39)	62/227 (27)	12 (3 to 20)	0.007
Clinically insignificant cancer — no. (%)	23 (9)	55 (22)	−13 (−19 to −7)	<0.001
~~Maximum cancer core length — mm~~	~~7.8±4.1~~	~~6.5±4.5~~	~~1.0 (0.0 to 2.1)~~	~~0.053~~
Core positive for cancer — no./total no. of cores (%)	422/967 (44)	515/2788 (18)	—	—
Men who did not undergo biopsy — no. (%)‖	78 (31)	16 (6)	—	—


Participants, According to Disease Status (%)
100
90
80
70
60
50
40
30
20
10
0
12
22
67
60
9
31
83
11
6
3
(N=51)
4
(N=70)
5
(N=54)
PI-RADS v2 Score
Clinically significant cancer
Clinically insignificant cancer
No cancer

Prostatectomie radicale vs abstention

- De 1989 à 1999
- 695 patients randomisés

Juan Manuel Santos

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Radical Prostatectomy or Watchful Waiting in Prostate Cancer — 29-Year Follow-up

Anna Bill-Axelson, M.D., Ph.D., Lars Holmberg, M.D., Ph.D., Hans Garmo, Ph.D., Kimmo Taari, M.D., Ph.D., Christer Busch, M.D., Ph.D., Stig Nordling, M.D., Ph.D., Michael Häggman, M.D., Ph.D., Swen-Olof Andersson, M.D., Ph.D., Ove Andrén, M.D., Ph.D., Gunnar Steineck, M.D., Ph.D., Hans-Olov Adami, M.D., Ph.D., and Jan-Erik Johansson, M.D., Ph.D.

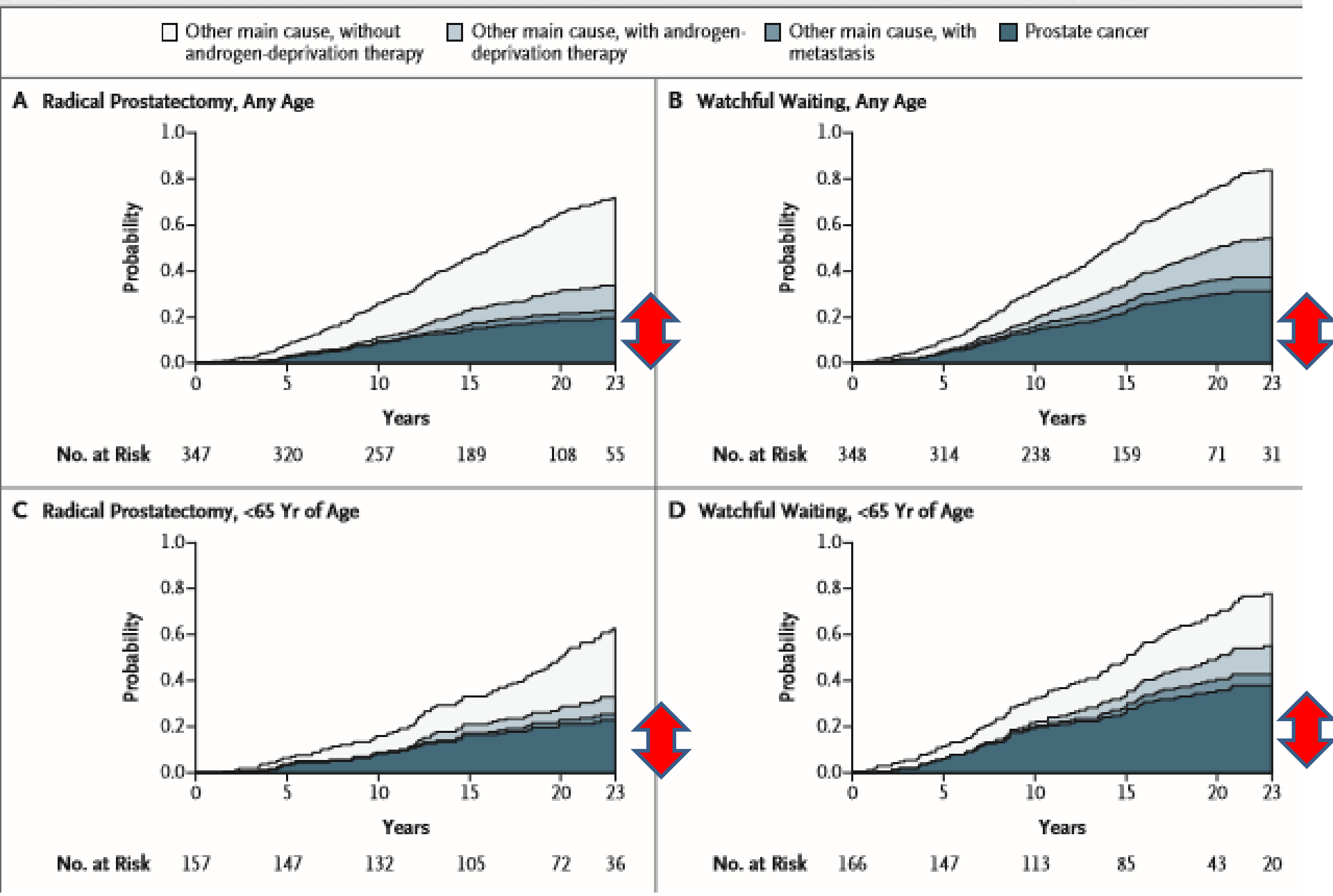
Prostatectomie radicale vs abstention

A 23 ans:

- 71% décès groupe PR
- 84% groupe abstention

- 19,6 % décès cancer prostate PR
- 31,3% avec abstention

- Gain de survie: 2.3 ans


Other main cause, without androgen-deprivation therapy
Other main cause, with androgen-deprivation therapy
Other main cause, with metastasis
Prostate cancer
A Radical Prostatectomy, Any Age
B Watchful Waiting, Any Age
C Radical Prostatectomy, <65 Yr of Age
D Watchful Waiting, <65 Yr of Age
Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
23
Years
No. at Risk
347 320 257 189 108 55
348 314 238 159 71 31
157 147 132 105 72 36
166 147 113 85 43 20

PR ouverte vs robot

Mitt Romney RARP

Lancet Oncol Aug 2018

Coughlin et al.

Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study

John W Yaxley, Geoffrey D Coughlin, Suzanne K Chambers, Stefano Occhipinti, Hema Samaratunga, Leah Zajdlewicz, Nigel Dunglison, Rob Carter, Scott Williams, Diane J Payton, Joanna Perry-Keene, Martin F Lavin, Robert A Gardiner

326 patients randomisés

A 3 mois:

Equivalence des résultats fonctionnels

Marges positives: 10 % ouvert, 15% RARP

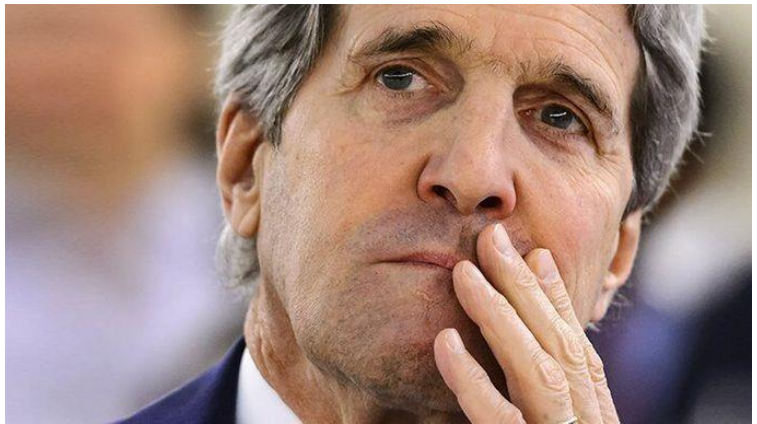
PR ouverte vs robot

A 2 ans:

- Scores urinaires identiques (EPIC, IIEF)
- Scores sexuels identiques (EPIC)

- Récidive biochimique plus fréquente en open

(9% vs 3%, supériorité RARP vs OPN, p= 0.02)

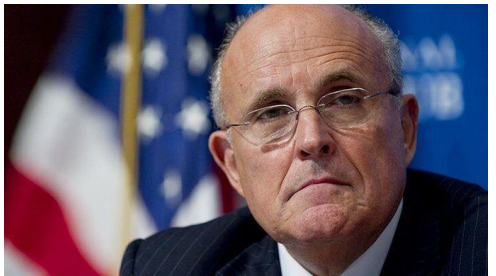


J Kerry ORP

Radiothérapie adjuvante

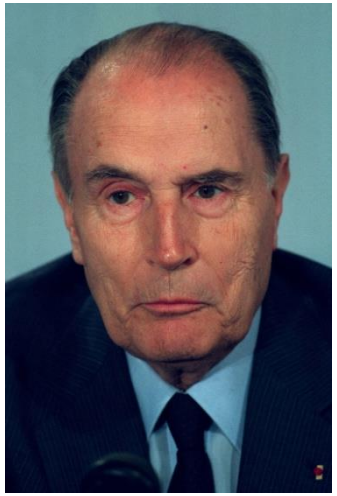
- ARTISTIC (meta-analyse de 3 essais)

  GETUF-AFU 17, RADICALS-RT, RAVES
- 1,074 RTE au rattrapage vs 1,077 men RTE adjuvante
- Pas de différence de survenue d'un évènement (HR = 1.09; 95% CI = 0.86–1.39;*P* = .47).
- Différence de probabilité de survenue d'un évènement à 5 ans <1%.



Rudy Giuliani

Hormonothérapie en phase hormono-naïve



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer

I.D. Davis, A.J. Martin, M.R. Stockler, S. Begbie, K.N. Chi, S. Chowdhury, X. Coskinas, M. Frydenberg, W.E. Hague, L.G. Horvath, A.M. Joshua, N.J. Lawrence, G. Marx, J. McCaffrey, R. McDermott, M. McJannett, S.A. North, F. Parnis, W. Parulekar, D.W. Pook, M.N. Reaume, S.K. Sandhu, A. Tan, T.H. Tan, A. Thomson, E. Tu, F. Vera-Badillo, S.G. Williams, S. Yip, A.Y. Zhang, R.R. Zielinski, and C.J. Sweeney, for the ENZAMET Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group*

The NEW ENGLAND JOURNAL of MEDICINE

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Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer

Kim N. Chi, M.D., Neeraj Agarwal, M.D., Anders Bjartell, M.D., Byung Ha Chung, M.D., Andrea J. Pereira de Santana Gomes, M.D., Robert Given, M.D., Álvaro Juárez Soto, M.D., Axel S. Merseburger, M.D., Mustafa Özgüroğlu, M.D., Hirotsugu Uemura, M.D., Dingwei Ye, M.D., Kris Deprince, M.D., Vahid Naini, Pharm.D., Jinhui Li, Ph.D., Shinta Cheng, M.D., Margaret K. Yu, M.D., Ke Zhang, Ph.D., Julie S. Larsen, Pharm.D., Sharon McCarthy, B.Pharm., and Simon Chowdhury, M.D., for the TITAN Investigators*

TITAN (Apalutamide)

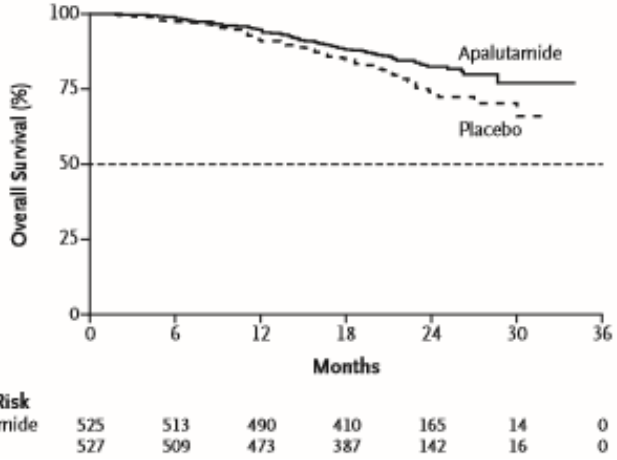
- Phase 3 randomisée double aveugle
- Apalutamide vs Placebo
- En complément d'une hormonothérapie
- +/- Docetaxel

- Au moins une lésion métastatique

- Survie sans progression radio et globale

TITAN

A Overall Survival

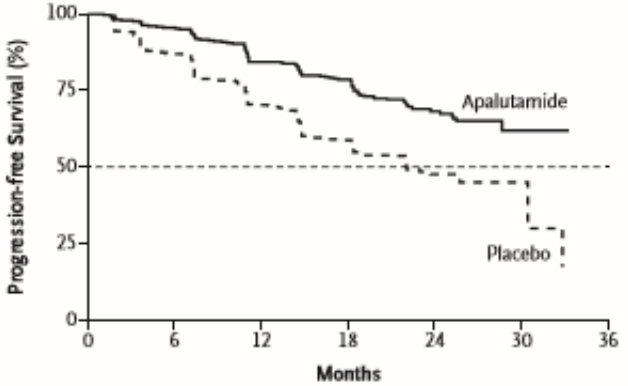


No. at Risk							
Apalutamide	525	513	490	410	165	14	0
Placebo	527	509	473	387	142	16	0

	No. of Patients	Median Overall Survival (95% CI)	Patients with Overall Survival at 24 Mo (95% CI)
		mo	%
Apalutamide	525	NE	82.4 (78.4–85.8)
Placebo	527	NE	73.5 (68.7–77.8)

Hazard ratio for death, 0.67 (95% CI, 0.51–0.89)
P=0.005

A Radiographic Progression–free Survival



No. at Risk							
Apalutamide	525	469	389	315	89	2	0
Placebo	527	437	325	229	57	3	0

	No. of Patients	Median Radiographic Progression–free Survival (95% CI)	Patients with Radiographic Progression–free Survival at 24 Mo (95% CI)
		mo	%
Apalutamide	525	NE	68.2 (62.9–72.9)
Placebo	527	22.1 (18.5–32.9)	47.5 (42.1–52.8)

Hazard ratio for radiographic progression or death, 0.48 (95% CI, 0.39–0.60)
P<0.001

TITAN

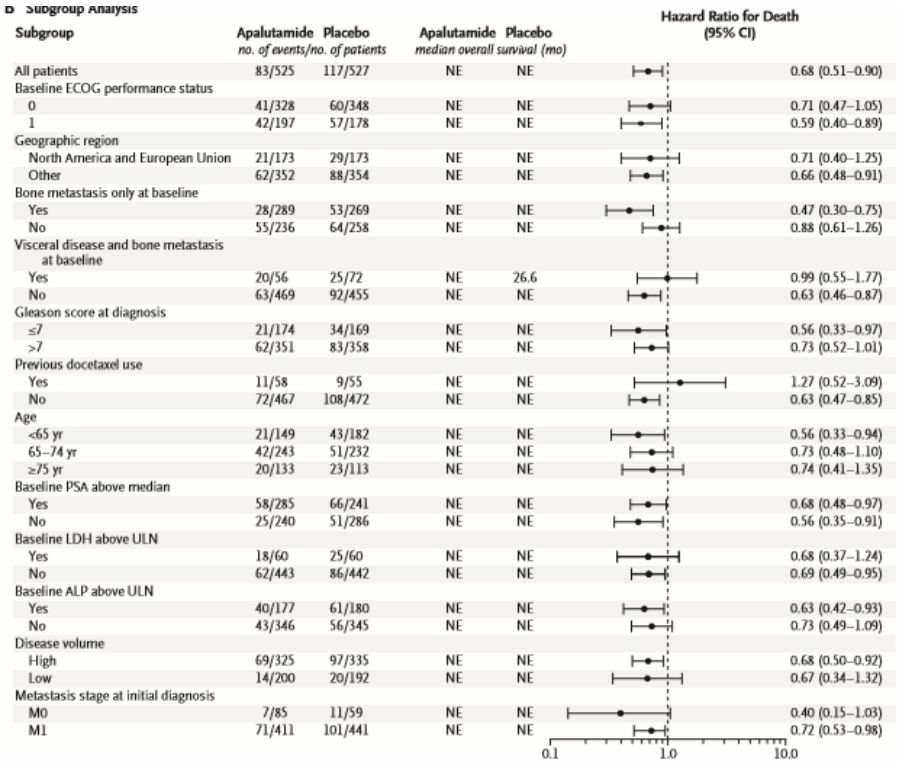
Table 3. Summary of Adverse Events.*

Event	Apalutamide (N = 524)	Placebo (N = 527)
	number of patients (percent)	
Any adverse event	507 (96.8)	509 (96.6)
Grade 3 or 4 adverse event	221 (42.2)	215 (40.8)
Any serious adverse event	104 (19.8)	107 (20.3)
Any adverse event leading to discontinuation of the trial intervention	42 (8.0)	28 (5.3)
Adverse event leading to death	10 (1.9)	16 (3.0)

* Shown are adverse events of any cause that occurred from the time of the first dose of the trial intervention through 30 days after the last dose. Adverse events were graded according to National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.3. One patient who was assigned to the apalutamide group withdrew consent before treatment.

TITAN

- Survie à 2 ans
  - 82.4% Apalutamide
  - 73.5% Placebo
- Volume métastatique



B Subgroup Analysis

Subgroup	Apalutamide (no. of events/no. of patients)	Placebo (no. of events/no. of patients)	Apalutamide (median overall survival (mo))	Placebo (median overall survival (mo))	Hazard Ratio for Death (95% CI)
All patients	83/525	117/527	NE	NE	0.68 (0.51–0.90)
Baseline ECOG performance status					
0	41/328	60/348	NE	NE	0.71 (0.47–1.05)
1	42/197	57/178	NE	NE	0.59 (0.40–0.89)
Geographic region					
North America and European Union	21/173	29/173	NE	NE	0.71 (0.40–1.25)
Other	62/352	88/354	NE	NE	0.66 (0.48–0.91)
Bone metastasis only at baseline					
Yes	28/289	53/269	NE	NE	0.47 (0.30–0.75)
No	55/236	64/258	NE	NE	0.88 (0.61–1.26)
Visceral disease and bone metastasis at baseline					
Yes	20/56	25/72	NE	26.6	0.99 (0.55–1.77)
No	63/469	92/455	NE	NE	0.63 (0.46–0.87)
Gleason score at diagnosis					
≤7	21/174	34/169	NE	NE	0.56 (0.33–0.97)
>7	62/351	83/358	NE	NE	0.73 (0.52–1.01)
Previous docetaxel use					
Yes	11/58	9/55	NE	NE	1.27 (0.52–3.09)
No	72/467	108/472	NE	NE	0.63 (0.47–0.85)
Age					
<65 yr	21/149	43/182	NE	NE	0.56 (0.33–0.94)
65–74 yr	42/243	51/232	NE	NE	0.73 (0.48–1.10)
≥75 yr	20/133	23/113	NE	NE	0.74 (0.41–1.35)
Baseline PSA above median					
Yes	58/285	66/241	NE	NE	0.68 (0.48–0.97)
No	25/240	51/286	NE	NE	0.56 (0.35–0.91)
Baseline LDH above ULN					
Yes	18/60	25/60	NE	NE	0.68 (0.37–1.24)
No	62/443	86/442	NE	NE	0.69 (0.49–0.95)
Baseline ALP above ULN					
Yes	40/177	61/180	NE	NE	0.63 (0.42–0.93)
No	43/346	56/345	NE	NE	0.73 (0.49–1.09)
Disease volume					
High	69/325	97/335	NE	NE	0.68 (0.50–0.92)
Low	14/200	20/192	NE	NE	0.67 (0.34–1.32)
Metastasis stage at initial diagnosis					
M0	7/85	11/59	NE	NE	0.40 (0.15–1.03)
M1	71/411	101/441	NE	NE	0.72 (0.53–0.98)

0.1 1.0 10.0

ENZAMET (enzalutamide)

- Phase 3, randomisé, double aveugle
- Enzalutamide vs AANS
- +/- Docetaxel

- Survie globale et survie sans progression biochimique

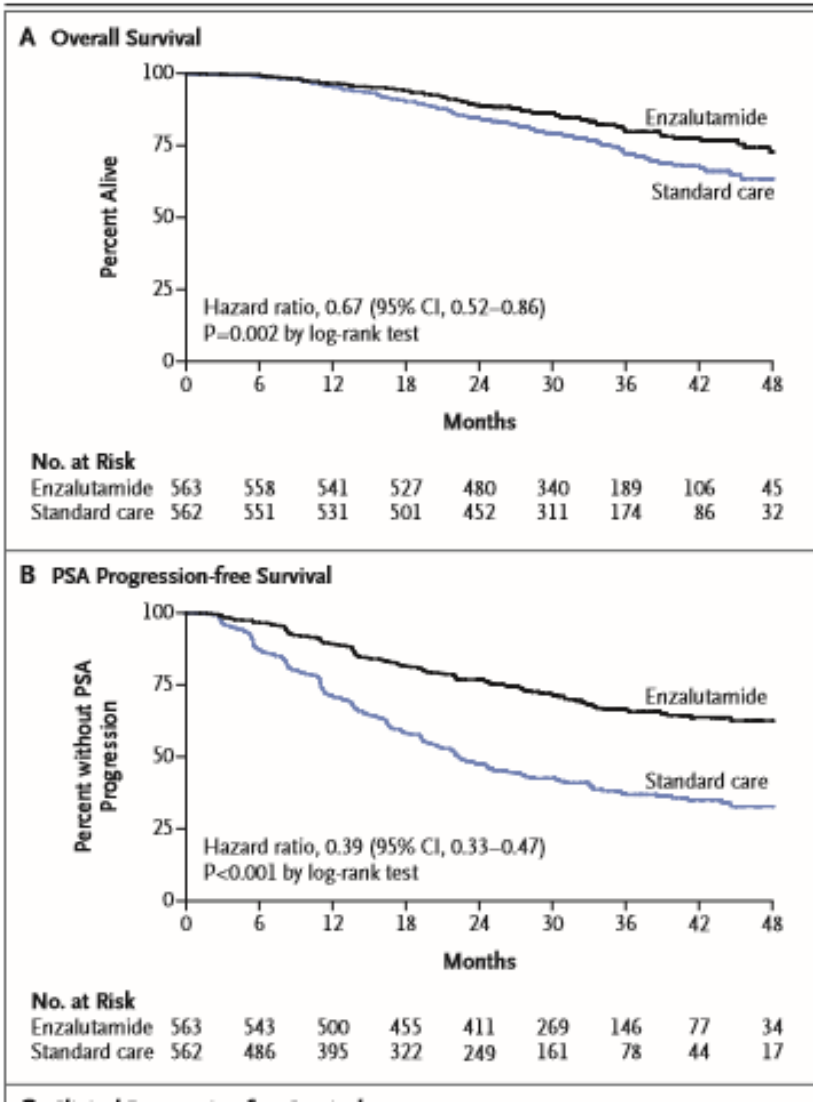
Robert Mugabe

ENZAMET

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Enzalutamide (N = 563)	Standard Care (N = 562)
Age — yr		
Mean	68.9±8.1	68.8±8.3
Median (IQR)	69.2 (63.2–74.5)	69.0 (63.6–74.5)
Region — no. (%)		
Australia	324 (58)	321 (57)
Canada	97 (17)	107 (19)
Ireland	39 (7)	43 (8)
New Zealand	20 (4)	19 (3)
United Kingdom	63 (11)	50 (9)
United States	20 (4)	22 (4)
Planned use of early docetaxel — no. (%)	254 (45)	249 (44)
Volume of disease — no. (%)		
High	291 (52)	297 (53)
Low	272 (48)	265 (47)
Visceral metastases — no. (%)	62 (11)	67 (12)
No. of months since diagnosis of metastasis		
Mean	2.9±6.9	3.1±7.2
Median (IQR)	1.9 (0.9–2.8)	1.9 (1.0–2.8)
Gleason score — no. (%)†		
≤7	152 (27)	163 (29)
8–10	335 (60)	321 (57)
Missing data	76 (13)	78 (14)

ENZAMET


A Overall Survival
Percent Alive
100
75
50
25
0
Enzalutamide
Standard care
Hazard ratio, 0.67 (95% CI, 0.52–0.86)
P=0.002 by log-rank test
0 6 12 18 24 30 36 42 48
Months
No. at Risk
Enzalutamide 563 558 541 527 480 340 189 106 45
Standard care 562 551 531 501 452 311 174 86 32
B PSA Progression-free Survival
Percent without PSA Progression
100
75
50
25
0
Enzalutamide
Standard care
Hazard ratio, 0.39 (95% CI, 0.33–0.47)
P<0.001 by log-rank test
0 6 12 18 24 30 36 42 48
Months
No. at Risk
Enzalutamide 563 543 500 455 411 269 146 77 34
Standard care 562 486 395 322 249 161 78 44 17

ENZAMET

Table 2. Adverse Events.

Adverse Event	Enzalutamide (N=563)	Standard Care (N=558)
Any adverse event — no. of patients (%)*		
Grade 1	40 (7)	77 (14)
Grade 2	202 (36)	230 (41)
Grade 3	277 (49)	194 (35)
Grade 4	38 (7)	40 (7)
Grade 5	6 (1)	7 (1)
Serious adverse event		
No. of patients (%)	235 (42)	189 (34)
No. of events	385	297
Rate during treatment exposure (95% CI) — no./yr†	0.34 (0.29–0.40)	0.33 (0.28–0.39)
Adverse event leading to treatment discontinuation at any time — no. of patients	33	14
Grade 3 to 5 adverse event — no. of patients (%)‡		
Febrile neutropenia	37 (7)	32 (6)
Hypertension	43 (8)	25 (4)
Neutrophil count decreased	31 (6)	16 (3)
Fatigue	31 (6)	4 (1)
Syncope	20 (4)	6 (1)
Surgical or medical procedure	13 (2)	10 (2)
Anemia	4 (1)	5 (1)
Fall	6 (1)	2 (<1)
Thromboembolic event	4 (1)	4 (1)
Acute coronary syndrome	3 (1)	4 (1)

Résumé de la prise en charge du CaP métastatique hormonosensible
Octobre 2019

mHSPC	NOUVELLES HORMONOTHERAPIES				CHIMIOTHERAPIE
	Acétate abiratérone	**Apalutamide**	**Enzalutamide**		**Docetaxel**
Etude pivotale	**LATITUDE publiée Analyse finale**	**TITAN Publiée**	**ARCHES 1ere Analyse ASCO GU 2019**	**ENZAMET Publiée**	**CHAARTED publiée**
Population	M1 Haut risque 100% DE NOVO	M1 78% DE NOVO	M1 70% DE NOVO	M1 58% DE NOVO	M1 Haut volume 73% DE NOVO
Traitement associé	ADT	ADT +/- Docetaxel (11%)	ADT +/- Docetaxel (18%)	ADT +/- Docetaxel (44%)	ADT
Critère Principal	Survie globale rPFS	Survie globale rPFS	rPFS	Survie globale rPFS	Survie globale
AMM		✓			
Remboursé		✓			
Recommandé*	**De novo Haut risque**				**De novo HAUT VOLUME**

Les hormonothérapies de 2nde génération dans le CPRC M0

	SPARTAN [1]	PROSPER [2]	ARAMIS [3]
Agent testé	Apalutamide	Enzalutamide	Darolutamide
Critères d'inclusion	• CPRC * cM0 cN0-1 • Tps de doublement du PSA ≤ 10 mois • Ganglions pelviens < 2 cm sous la bifurcation iliaque autorisés	• CPRC * cM0N0 • Tps de doublement du PSA ≤ 10 mois • Ganglions pelviens < 1,5 cm sous la bifurcation iliaque autorisés	• CPRC * cM0 cN0-1 • Tps de doublement du PSA ≤ 10 mois
Critère principal d'évaluation	Survie sans métastases (MFS)	Survie sans métastases (MFS)	Survie sans métastases (MFS)
Nb total de patients	1207	1401	1509
Résultats MFS	40,5 mo (APA) vs 16,2 mo (placebo) HR=0,28 ; p<0,0001	36,6 mo (ENZ) vs 14,7 mo (placebo) HR=0,29 ; p<0,0001	40,4 mo (APA) vs 18,4 mo (placebo) HR=0,41 ; p<0,0001
Résultats Survie globale	Analyse intermédiaire: Non atteinte (APA) vs 39 mo (placebo) HR=0,70 ; p=0,07 (non significatif [1])	Analyse intermédiaire: Non atteinte (ENZA) vs Non atteinte (placebo) HR=0,80 ; p= 0,1519 (non significatif [2])	Analyse intermédiaire: Non atteinte (DARO) vs Non atteinte (placebo) HR=0,71 ; p=0,0452 (non significatif [3])

1 Smith et al, N Engl J Med 2018
2 Hussain et al, N Engl J Med 2018
3 Fizazi et al, N Engl J Med 2019 : risque alpha ajusté à a=0,0005 pour l'analyse intermédiaire de la survie globale (Fizazi et al, Poster #140, congrès de l'ASCO-GU 2019)

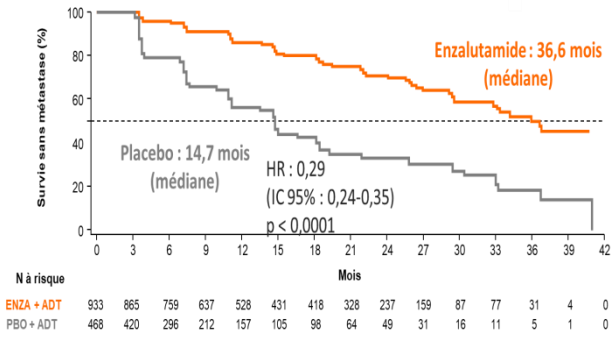
Prise en charge du CPRC M0

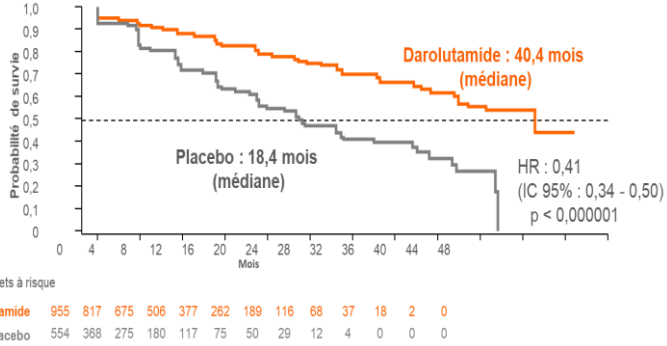
PSA_{DT} < 10 mois

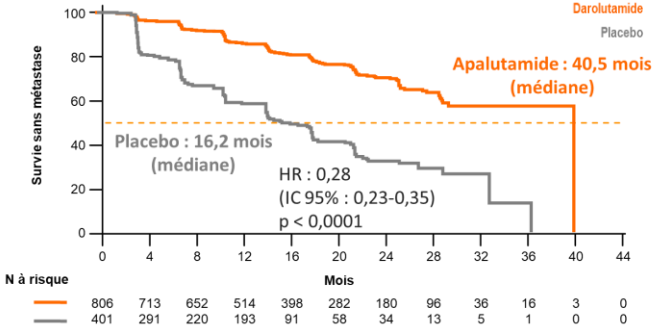
- **Enzalutamide**[1]
  - → AMM
  - → Remboursement en attente
  - → ASMR III

- **Apalutamide**[2]
  - → AMM
  - → Délivrance hospitalière jusqu'au remboursement
  - → ASMR III

- **Darolutamide**[3]
  - – Pas d'AMM







L'utilisation du Darolutamide au stade CPRC M0 est hors-AMM (cf. Art L5121-12-1 du CSP)

1. Hussain et al, N Engl J Med 2018
2. Smith et al, N Engl J Med 2018
3. Fizazi et al, N Engl J Med 2019

CPRC M0 = Cancer de la prostate Résistant à la Castration non métastatique; PSA_{DT} = Temps de doublement du PSA

HTNG et CRPC M0 : **Comparaison de la tolérance**

		HTNG		Placebo	
		All Grades	Grade ≥3	All Grades	Grade ≥3
ENZA	Any adverse event	808 (87)	292 (31)	360 (77)	109 (23)
	Any serious adverse event*	226 (24)	—	85 (18)	—
	Adverse event leading to discontinuation of trial regimen	87 (9)	—	28 (6)	—
	Adverse event leading to death	32 (3)	—	3 (1)	—
APA	Any adverse event	775 (96.5)	362 (45.1)	371 (93.2)	136 (34.2)
	Serious adverse event	199 (24.8)	—	92 (23.1)	—
	Adverse event leading to discontinuation of the trial regimen	85 (10.6)	—	28 (7.0)	—
	Adverse event associated with death	10 (1.2)	—	1 (0.3)	—
DARO	Any adverse event	794 (83.2)	236 (24.7)	426 (76.9)	108 (19.5)
	Serious adverse event	237 (24.8)	151 (15.8)	111 (20.0)	70 (12.6)
	Grade 5 adverse event	37 (3.9)	—	18 (3.2)	—
	Adverse event leading to discontinuation of the trial regimen	85 (8.9)	32 (3.4)	48 (8.7)	24 (4.3)

L'utilisation du darolutamide au stade CPRCM0 est hors-AMM cf. Art L5121-12-1 du CSP) »

D'après Hussain M et al. N Engl J Med. 2018, Smith MR et al. N Engl J Med. 2018 et Fizazi K et al. N Engl J Med. 2019

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cabazitaxel versus Abiraterone or Enzalutamide in Metastatic Prostate Cancer

R. de Wit, J. de Bono, C.N. Sternberg, K. Fizazi, B. Tombal, C. Wülfing, G. Kramer, J.-C. Eymard, A. Bamias, J. Carles, R. Iacovelli, B. Melichar, Á. Sverrisdóttir, C. Theodore, S. Feyerabend, C. Helissey, A. Ozatilgan, C. Geffriaud-Ricouard, and D. Castellano, for the CARD Investigators

CARD: STUDY DESIGN

- Multicenter, randomized, open-label study
- Enrollment: Nov 2015 – Nov 2018
- Median follow-up: 9.2 months

Patients with mCRPC who progressed ≤ 12 months on prior alternative ARTA (before or after docetaxel)

N = 255

RANDOMIZE

1:1

Cabazitaxel (25 mg/m² Q3W) + prednisone + G-CSF
n = 129

Abiraterone (1000 mg QD) + prednisone
OR
Enzalutamide (160 mg QD)
n = 126

Endpoints

Primary: rPFS

Key secondary: OS, PFS, PSA response, tumor response

Other secondary: Pain response, time to symptomatic skeletal event, safety, HRQoL, biomarkers

Stratification factors:

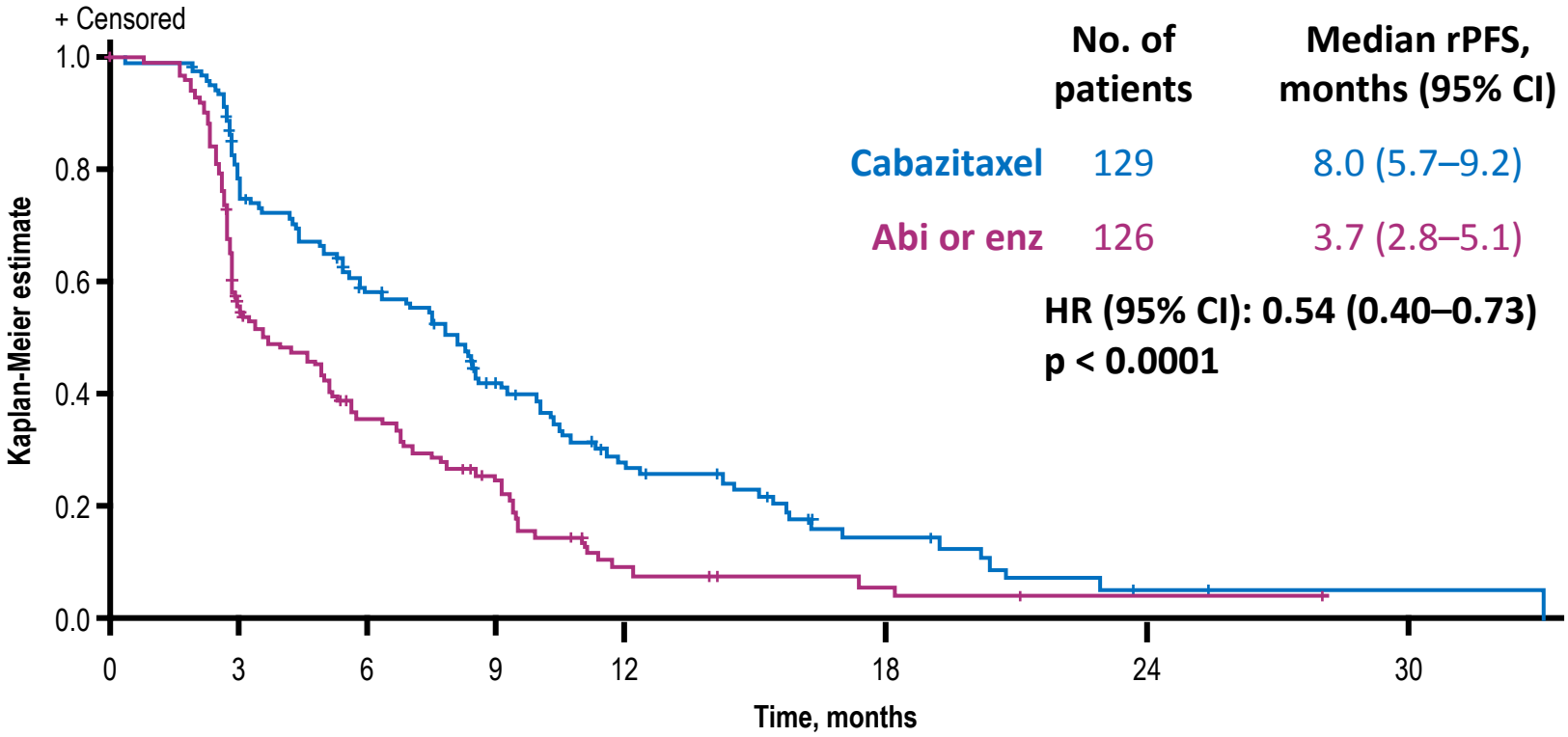
- ECOG PS (0/1 vs 2)
- Time to progression on prior alternative ARTA (0–6 vs > 6–12 months)
- Timing of ARTA (before vs after docetaxel)

ORIGINAL ARTICLE

Cabazitaxel versus Abiraterone or Enzalutamide in Metastatic Prostate Cancer

R. de Wit, J. de Bono, C.N. Sternberg, K. Fizazi, B. Tombal, C. Wülfing, G. Kramer, J.-C. Eymard, A. Bamias, J. Carles, R. Iacovelli, B. Melichar, Á. Sverrisdóttir, C. Theodore, S. Feyerabend, C. Helissey, A. Ozatilgan, C. Geffriaud-Ricouard, and D. Castellano, for the CARD Investigators

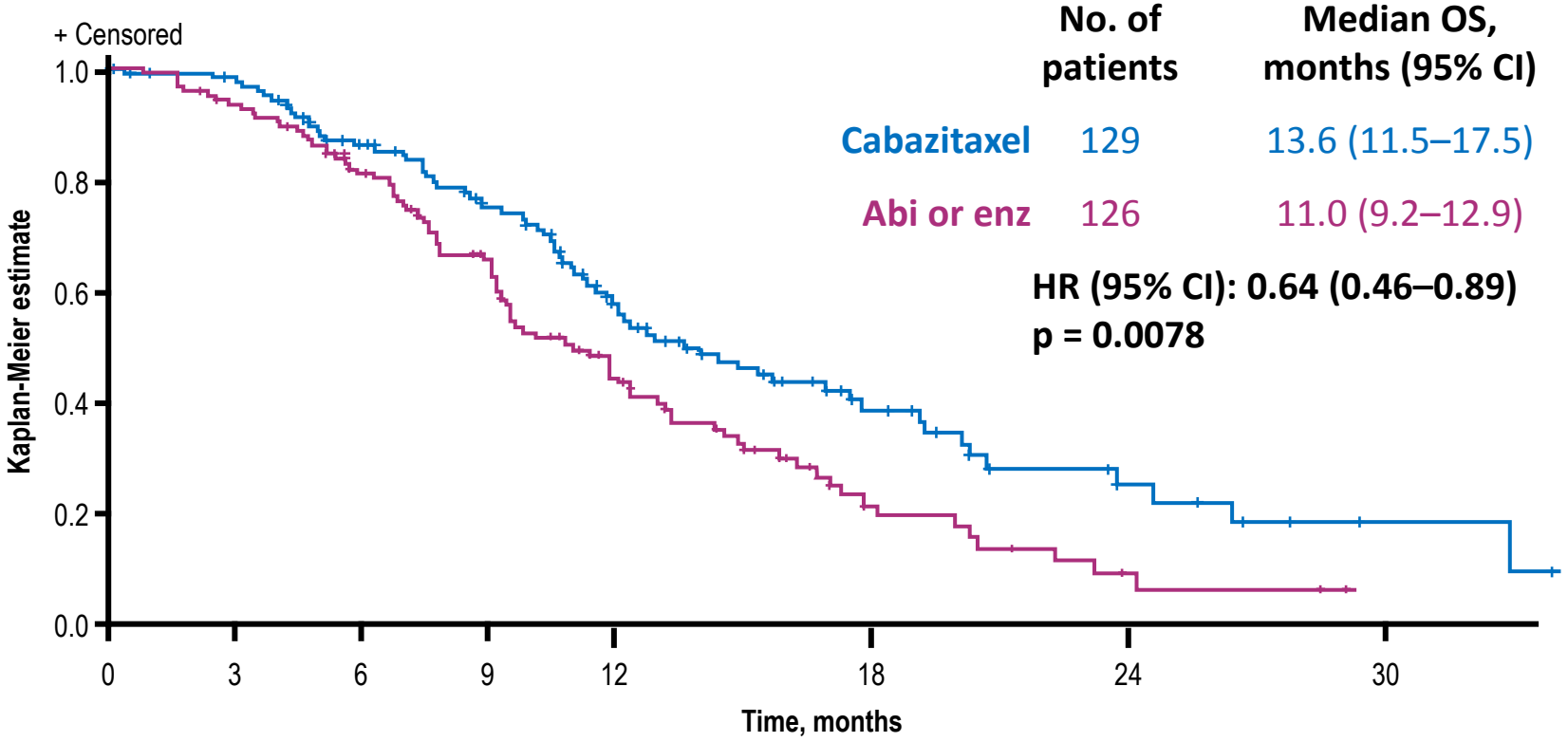
RADIOGRAPHIC PFS (PRIMARY ENDPOINT)



	No. of patients	Median rPFS, months (95% CI)
Cabazitaxel	129	8.0 (5.7–9.2)
Abi or enz	126	3.7 (2.8–5.1)

HR (95% CI): 0.54 (0.40–0.73)
p < 0.0001

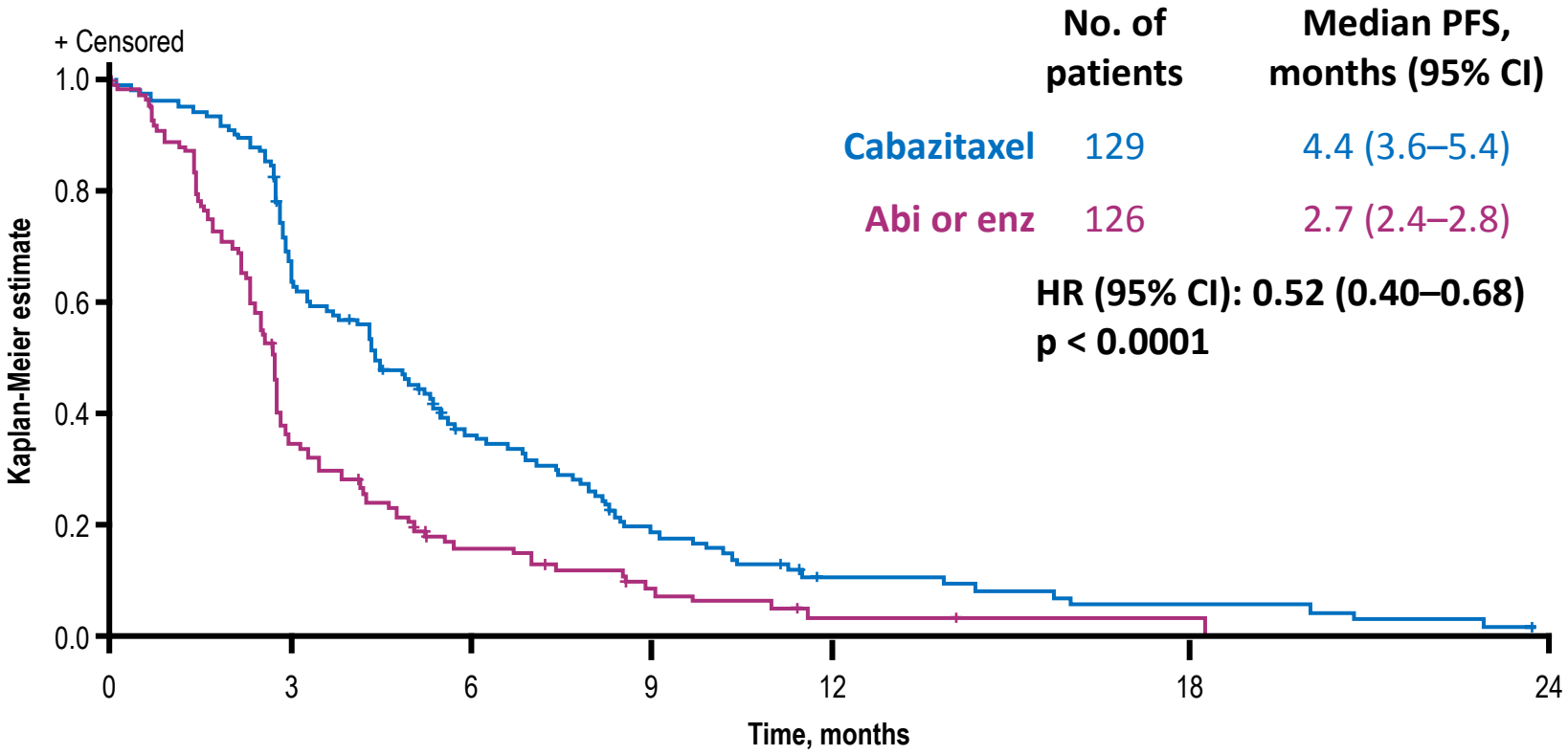
OVERALL SURVIVAL (KEY SECONDARY ENDPOINT)



	No. of patients	Median OS, months (95% CI)
Cabazitaxel	129	13.6 (11.5–17.5)
Abi or enz	126	11.0 (9.2–12.9)

HR (95% CI): 0.64 (0.46–0.89)
p = 0.0078

PROGRESSION-FREE SURVIVAL

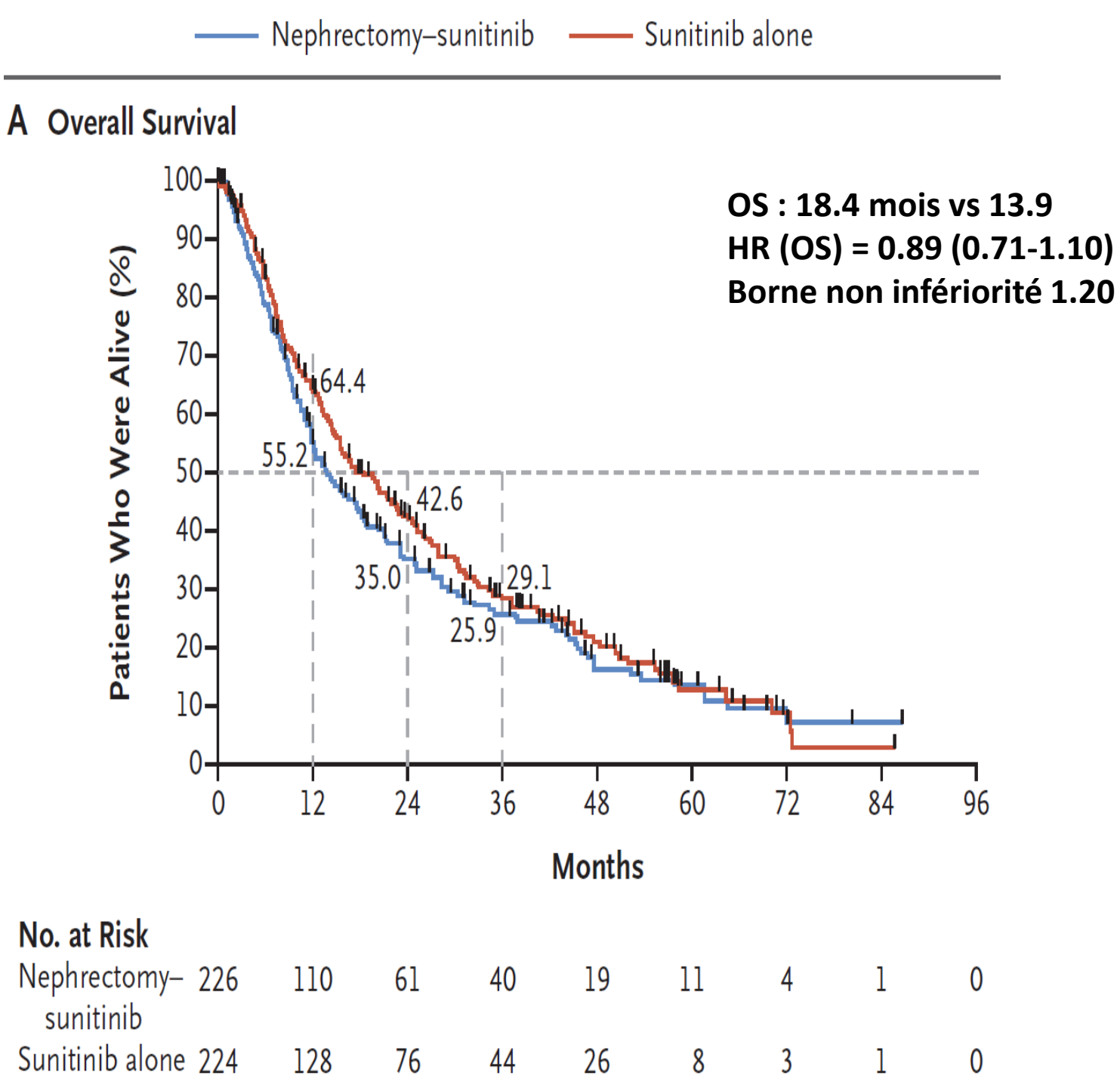


	No. of patients	Median PFS, months (95% CI)
Cabazitaxel	129	4.4 (3.6–5.4)
Abi or enz	126	2.7 (2.4–2.8)

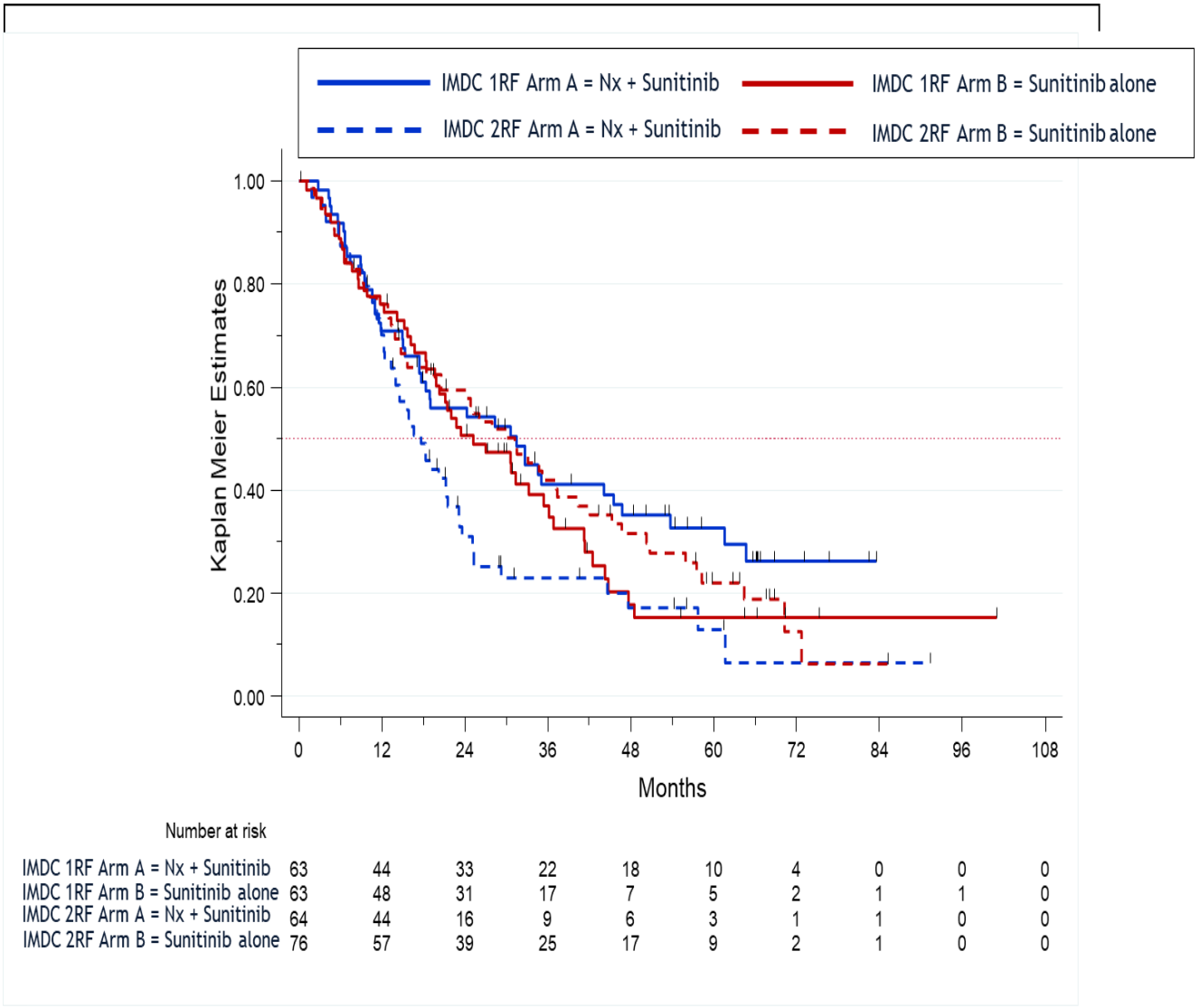
HR (95% CI): 0.52 (0.40–0.68)
p < 0.0001

Cancer du rein

Ivica Racan,
premier ministre
Croatie



OS : 18.4 mois vs 13.9
HR (OS) = 0.89 (0.71-1.10)
Borne non infériorité 1.20

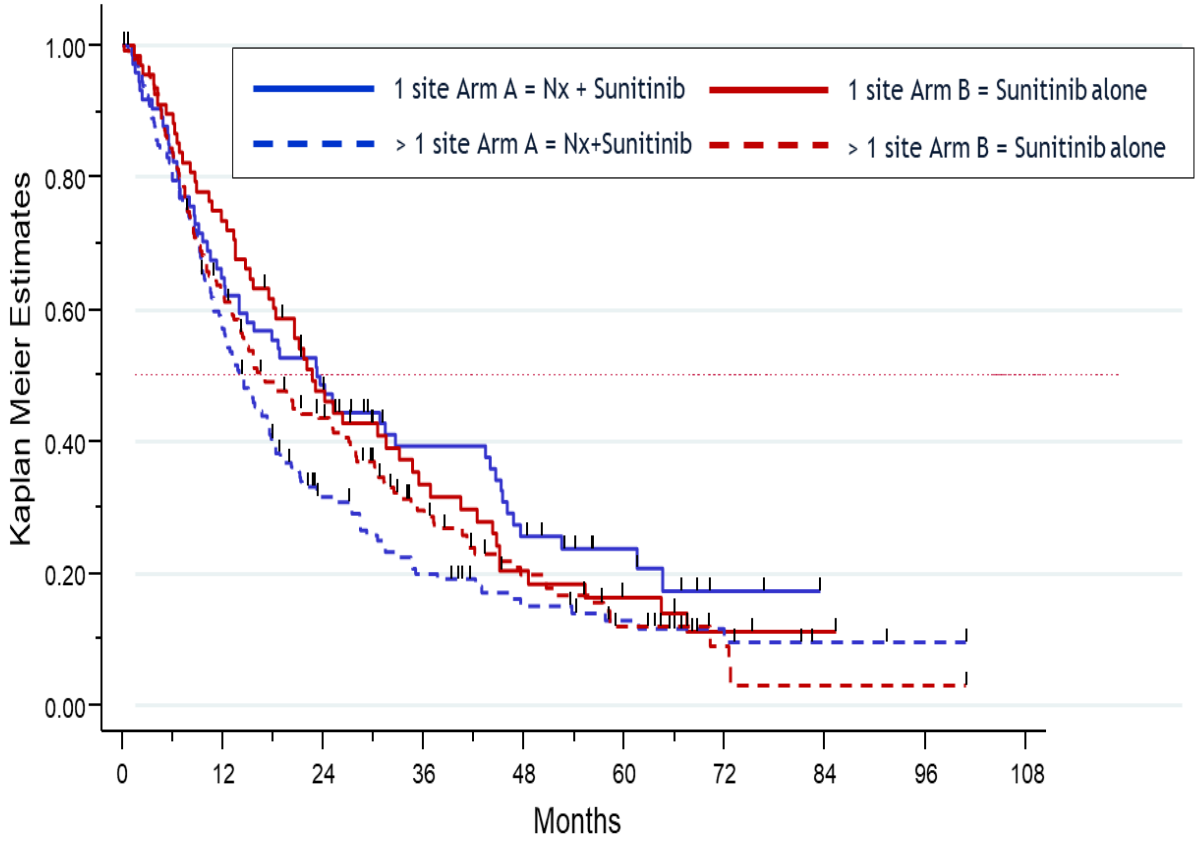


IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; Nx, nephrectomy

Median Overall Survival (ITT) Intermediate patients

Median OS, months (95% CI)	Arm A: Nephrectomy + Sunitinib (n=127)	Arm B: Sunitinib alone (n=139)	HR (95% CI)	p
IMDC 1 risk factor	(n=63) **31.4** (17.3-45.5)	(n=63) **25.2** (19.6-35.4)	**1.29 (0.85-1.98)**	0.232
IMDC 2 risk factors	(n=64) **17.6** (13.7-21.5)	(n=76) **31.2** (20.5-40.4)	0.63 (0.44-0.97)	**0.033**
HR (95% CI)	1.68 (1.10-2.57)	0.88 (0.59-1.30)		
p	**0.015**	0.515		

ITT, intent to treat; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium



Number at risk

1 site Arm A = Nx + Sunitinib	75	48	35	23	15	8	2	0	0	0
1 site Arm B = Sunitinib alone	68	50	29	18	10	7	2	1	0	0
> 1 site Arm A = Nx+Sunitinib	148	83	39	24	15	10	6	2	1	0
> 1 site Arm B = Sunitinib alone	155	94	61	33	19	9	3	1	1	0

Nx, nephrectomy

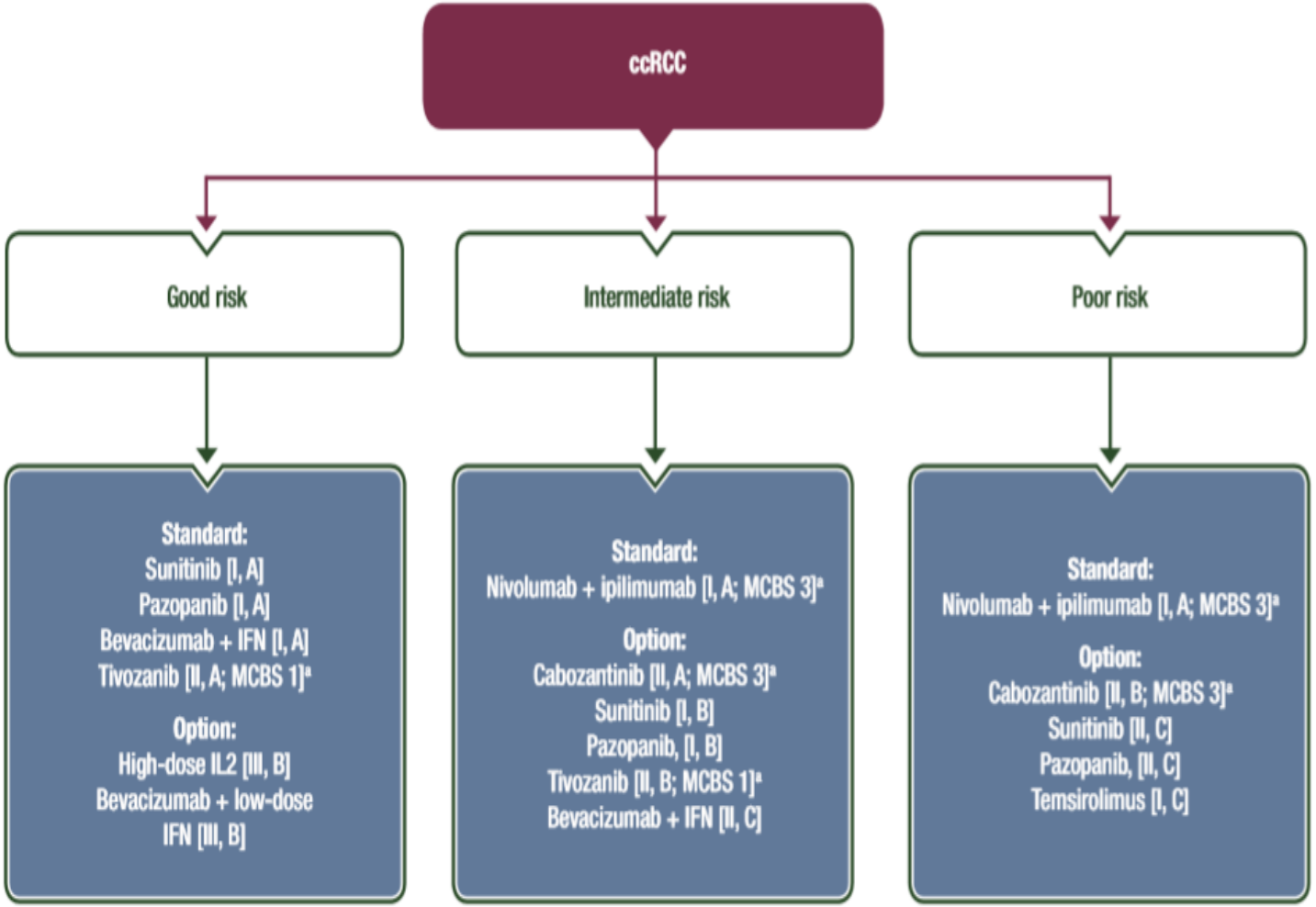
Arnaud Méjean

Median OS (ITT) patients with 1 metastatic si

Median OS, months (95% CI)	Arm A: Nephrectomy + Sunitinib (n=226)	Arm B: Sunitinib alone (n=224)	
1 site	(n=75) **23.2** (13.9–43.4)	(n=68) **22.7** (17.5–33.1)	1.09
>1 site	(n=148) **14.4** (11.8–17.6)	(n=155) **16.7** (13.8–24.8)	0.87
HR (95% CI)	1.42 (1.03–1.96)	1.19 (0.86–1.64)	(
p	0.032	0.292	

OS, overall survival; ITT, intent to treat

ESMO Guidelines



Nivolumab + Ipilimumab CheckMate 214

Phase 3, randomized, open-label trial of nivolumab combined with ipilimumab vs sunitinib monotherapy in treatment-naïve patients with advanced or metastatic clear cell RCC[1]

N=139

Key Inclusion Criteria[a]

- Advanced/metastatic clear cell RCC
- No prior systemic therapy for RCC
- Prior adjuvant/neoadjuvant therapy allowed if the agent did not target the VEGF pathway, and recurrence occurred ≥6 months after last dose
- KPS ≥70%
- Available FFPE archival or recent tumor tissue sample
- No prior treatment with VEGF pathway agents or agents targeting T-cell co-stimulation or checkpoint pathways
- No current or history of CNS metastases

R 1:1

Nivolumab
3 mg/kg IV q3w for 4 doses, then q2w

Patients receiving NIVO monotherapy could switch to NIVO 240 mg flat dosing

Ipilimumab
1 mg/kg IV q3w for 4 doses

Sunitinib
50 mg PO qd for 4 weeks (6-week cycles)

Crossover from SUN to NIVO+IPI was permitted

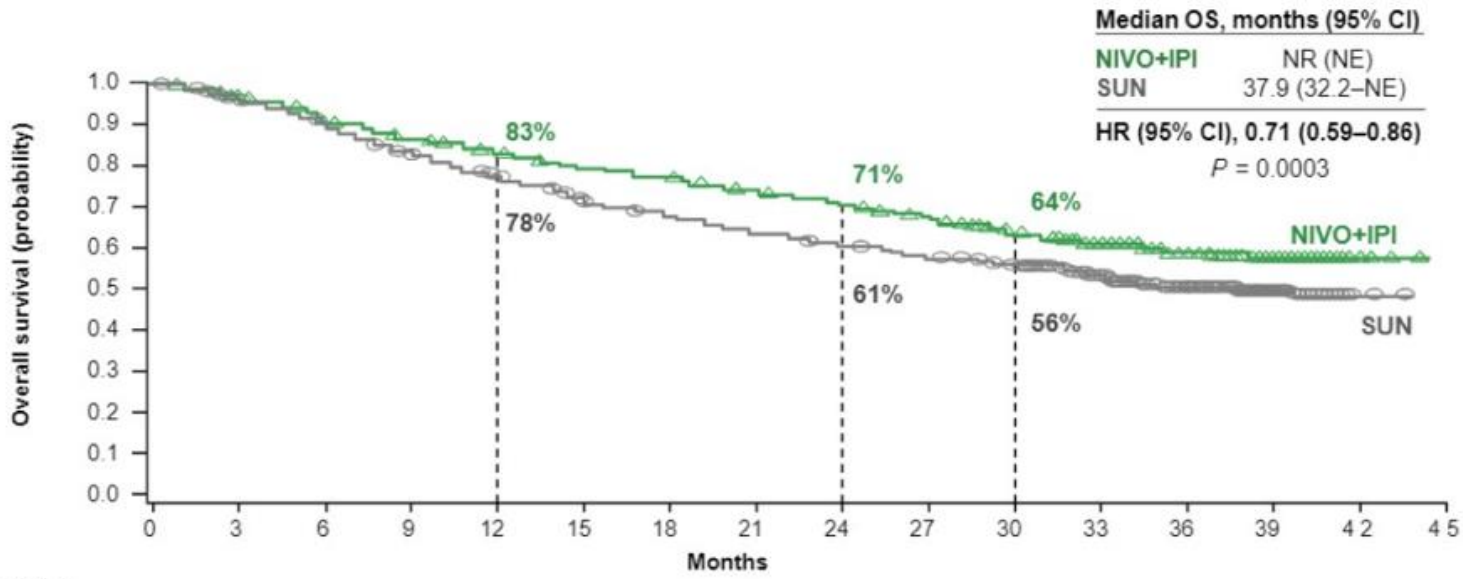
Until progression,[b] unacceptable toxicity, withdrawal of consent, or end of trial (up to 5 years)[c]

Primary Outcome Measures: PFS, OS, ORR in intermediate/poor-risk patients[2,3]

Key Secondary Outcome Measures: PFS, OS, and ORR in any-risk patients, incidence of AEs[2,3]

Select Exploratory Outcome Measures: PFS and OS in favorable-risk patients, HRQoL[2,3]

Overall Survival: ITT Patients



No. at risk

NIVO+IPI	550	523	492	464	443	425	410	389	371	351	327	271	161	58	4	0
SUN	546	507	472	435	404	367	345	325	310	295	275	232	145	55	5	0

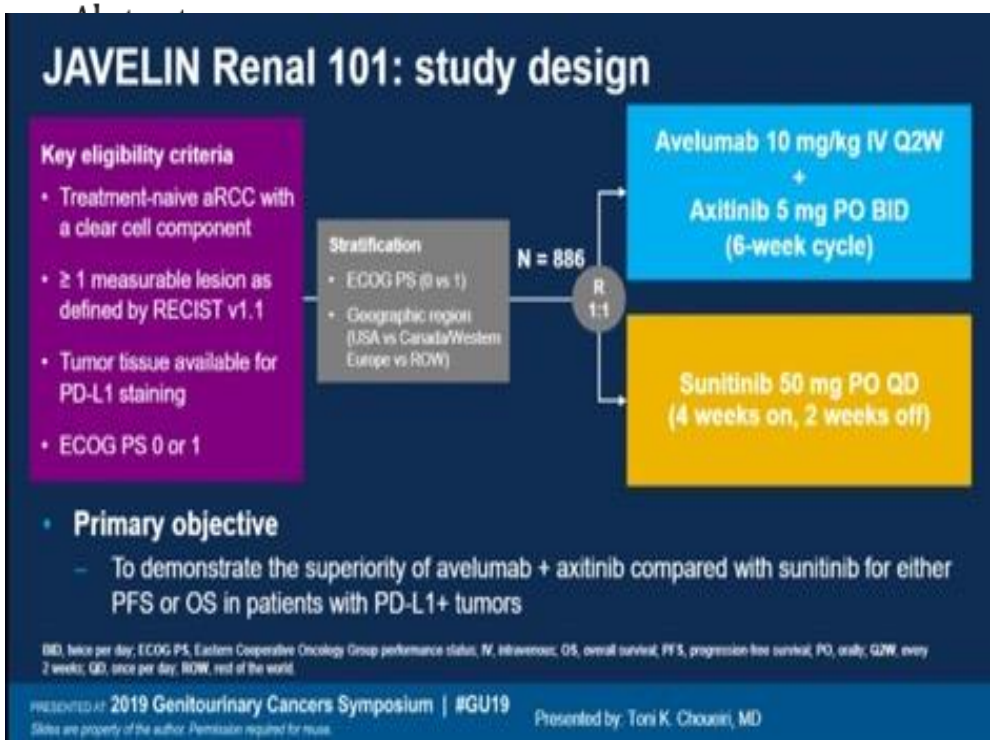
JAVELIN

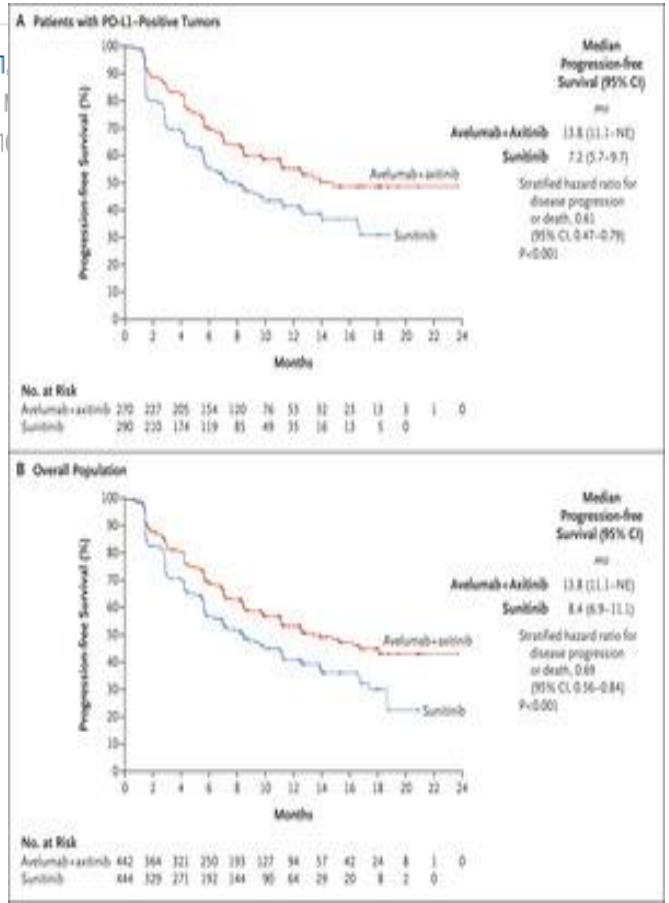
ORIGINAL ARTICLE FREE PREVIEW

Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma

Robert J. Motzer, M.D., Konstantin Penkov, M.D., Ph.D., John Haanen, Ph.D., Brian Rini, M.D., Laurence Albiges, M.D., Ph.D., Matthew T. Campbell, M.D., Balaji Venugopal, M.D., Christian Kollmannsberger, M.D., Sylvie Negrier, M.D., Ph.D., Motohide Uemura, M.D., Ph.D., Jae L. Lee, M.D., Ph.D., Aleksandr Vasiliev, M.D., et al.

March 21
N Engl J
DOI: 10.1



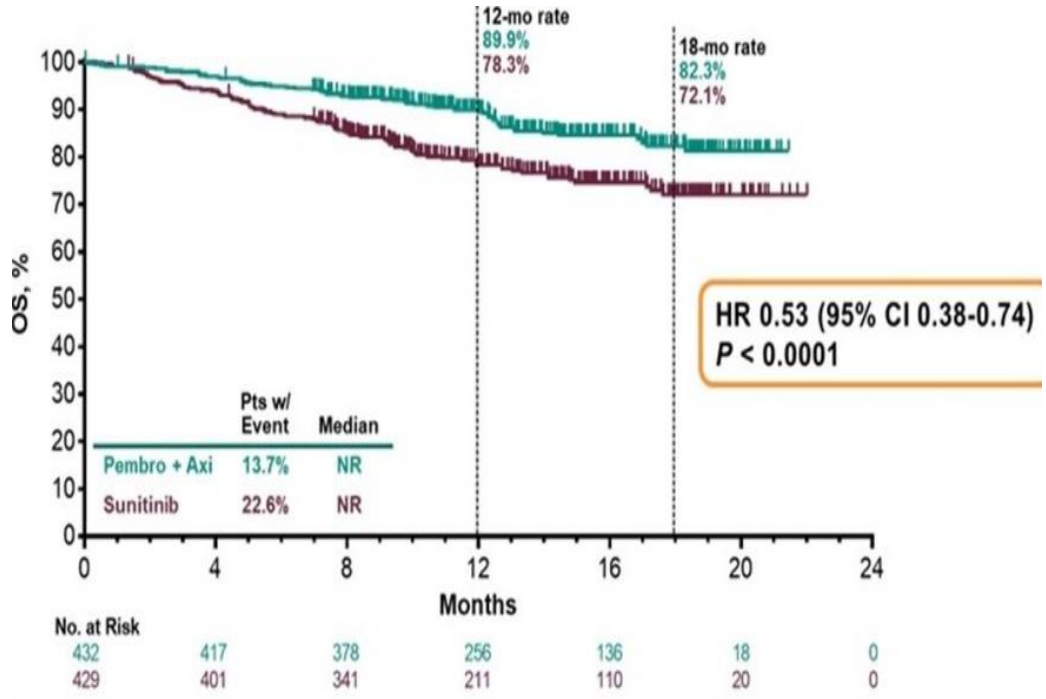


KEYNOTE 426

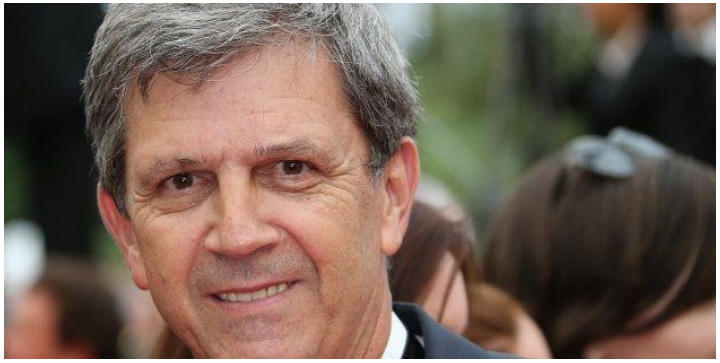
ORIGINAL ARTICLE FREE PREVIEW

Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma

Brian I. Rini, M.D., Elizabeth R. Plimack, M.D., Viktor Stus, M.D., Ph.D., Rustem Gafanov, M.D., Robert Hawkins, M.B., B.S., Ph.D., Dmitry Nosov, M.D., D.Sci., Frédéric Pouliot, M.D., Ph.D., Boris Alekseev, M.D., Denis Soulières, M.D., Bohuslav Melichar, M.D., Ph.D., Ihor Vynnychenko, M.D., Ph.D., Anna Kryzhanivska, M.D., et al., for the KEYNOTE-426 Investigators*



Cancer de la vessie



Curage étendu

EUROPEAN UROLOGY 75 (2019) 604–611

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journal homepage: www.europeanurology.com

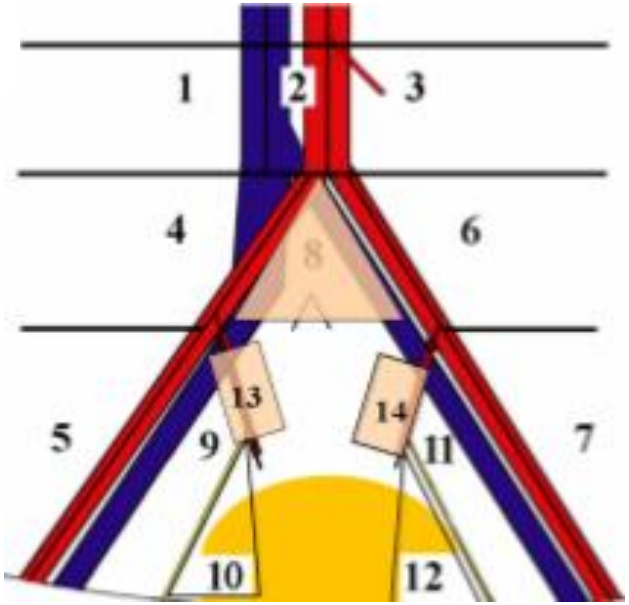
European Association of Urology

Platinum Priority – Bladder Cancer – Editor's Choice

Editorial by Seth P. Lerner and Robert S. Svatek on pp. 612–614 of this issue

Extended Versus Limited Lymph Node Dissection in Bladder Cancer Patients Undergoing Radical Cystectomy: Survival Results from a Prospective, Randomized Trial

Jürgen E. Gschwend[a,i,], Matthias M. Heck[a,i], Jan Lehmann[b], Herbert Rübben[c], Peter Albers[d], Johannes M. Wolff[e], Detlef Frohneberg[f], Patrick de Geeter[g], Axel Heidenreich[h], Tilman Kälble[i], Michael Stöckle[j], Thomas Schnöller[k], Arnulf Stenzl[l], Markus Müller[m], Michael Truss[n], Stephan Roth[o], Uwe-Bernd Liehr[p], Joachim Leißner[q], Thomas Bregenzer[b], Margitta Retz[a]*



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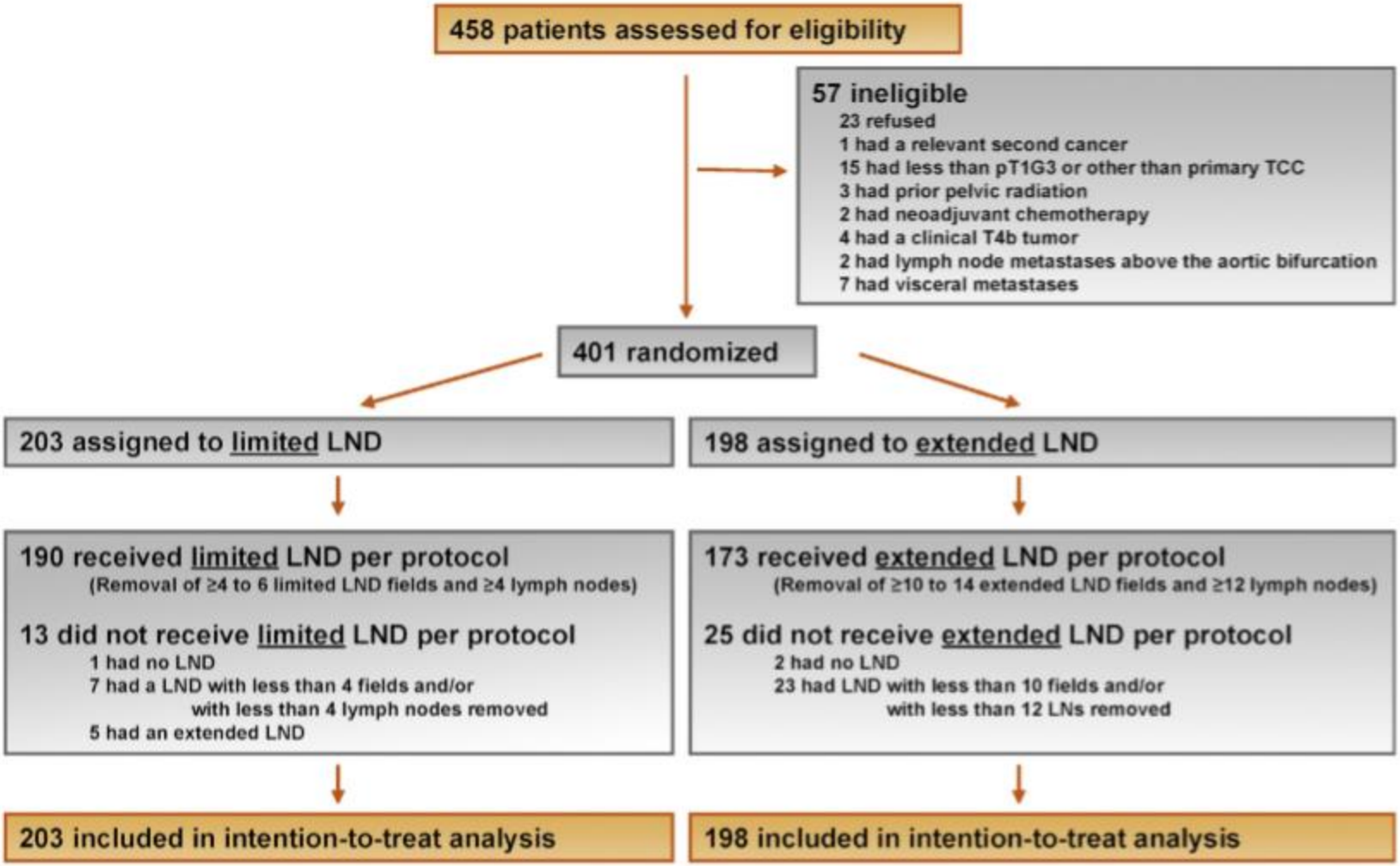
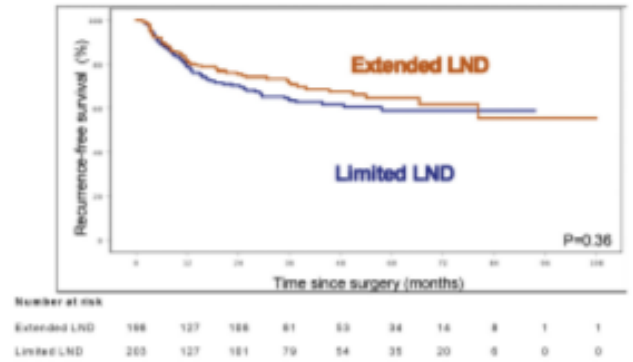
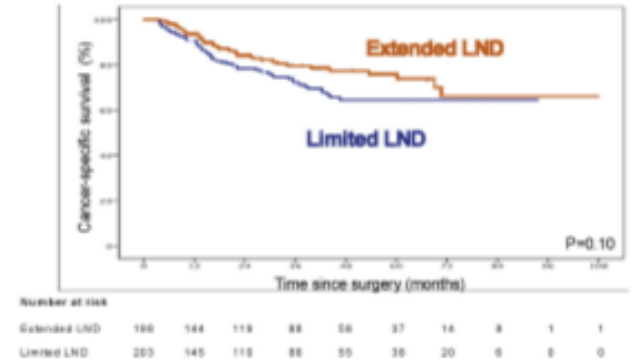


Curage étendu

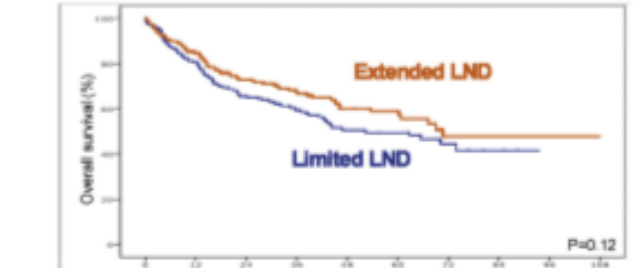
A Recurrence-free survival



B Cancer-specific survival



C Overall survival



Cystectomie robot vs open

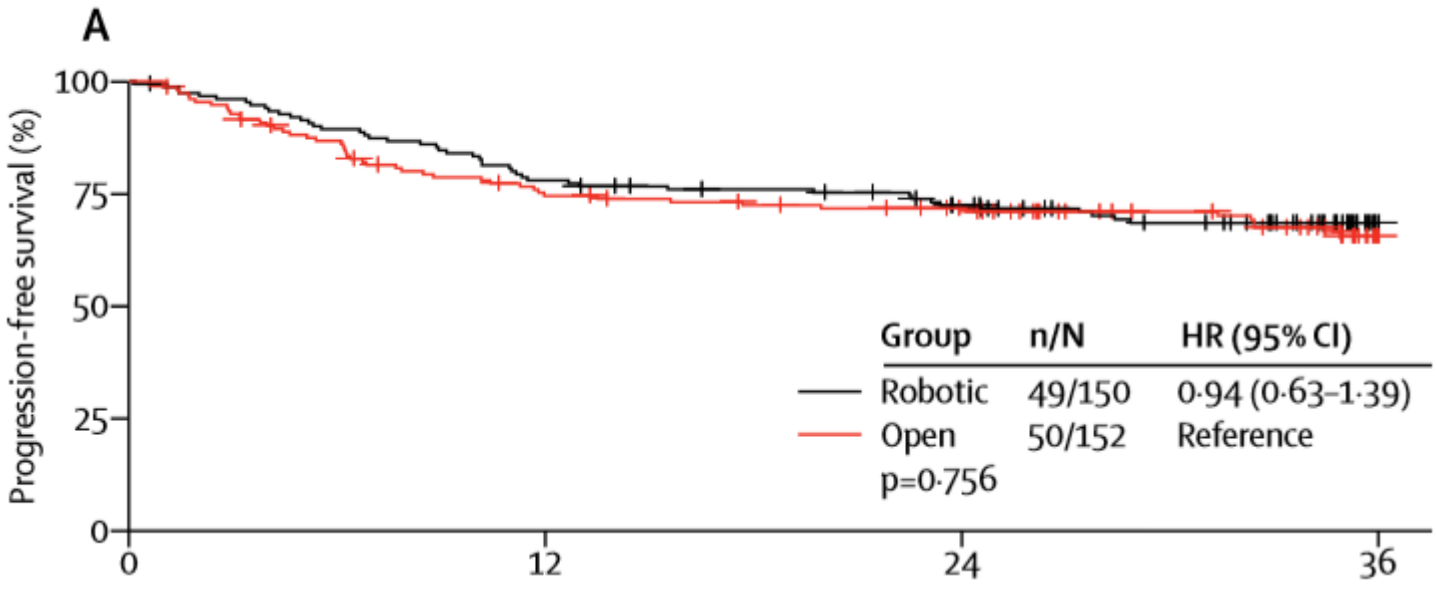
- 350 patients randomisés
- Survie sans progression
- Essai de non-infériorité

Robot-assisted radical cystectomy versus open radical cystectomy in patients with bladder cancer (RAZOR): an open-label, randomised, phase 3, non-inferiority trial

Dipen J Parekh, Isildinha M Reis, Erik P Castle, Mark L Gonzalgo, Michael E Woods, Robert S Svatek, Alon Z Weizer, Badrinath R Konety, Mathew Tollefson, Tracey L Krupski, Norm D Smith, Ahmad Shabsigh, Daniel A Barocas, Marcus L Quek, Atreya Dash, Adam S Kibel, Lynn Shemanski, Raj S Pruthi, Jeffrey Scott Montgomery, Christopher J Weight, David S Sharp, Sam S Chang, Michael S Cookson, Gopal N Gupta, Alex Gorbonos, Edward M Uchio, Eila Skinner, Vivek Venkatramani, Nachiketh Soodana-Prakash, Kerri Kendrick, Joseph A Smith Jr, Ian M Thompson

Cystectomie robot vs open

- Survie sans progression à 2 ans
  - Robot:72.3%
  - Open: 71.6%



	Robotic cystectomy (n=150)	Open cystectomy (n=152)	Difference (95% CI)	p value
Patients with blood loss data	148 (99%)	149 (98%)	..	..
Blood loss, mL	300 (200–500)	700 (500–1000)	..	<0·0001
Perioperative transfusion	35/143 (24%)	65/143 (45%)	–21·0 (–31·8 to –10·2)	0·0002
Units of blood transfused	3 (2–5)	4 (2–5)	..	0·46
Intraoperative transfusion	18/139 (13%)	46/136 (34%)	–20·8 (-30·6 to –11·2)	<0·0001
Postoperative transfusion	33/132 (25%)	54/135 (40%)	–15·0 (-26·1 to –3·9)	0·0089
Hospital stay ≤5 days	40/139 (29%)	27/146 (18%)	10·3 (0·5 to 20·1)	0·0407
Length of stay, days	6 (5–10)	7 (6–10)	..	0·0216
Operating time, min	428 (322–509)	361 (281–450)	..	0·0005
Surgical complications within 90 days*				
0	49 (33%)	47 (31%)	..	0·80
I	24 (16%)	20 (13%)	..	..
II	44 (29%)	51 (34%)	..	..
III	29 (19%)	28 (18%)	..	..
IV	0	2 (1%)	..	..
V	4 (3%)	4 (3%)	..	..
Grades I–V vs 0	101 (67%)	105 (69%)	–1·8 (–12·3 to 8·8)	0·75
Grades III–V vs 0–II	33 (22%)	34 (22%)	–0·4 (–9·0 to 9·8)	0·94
Histopathology classification				

KEYNOTE 045

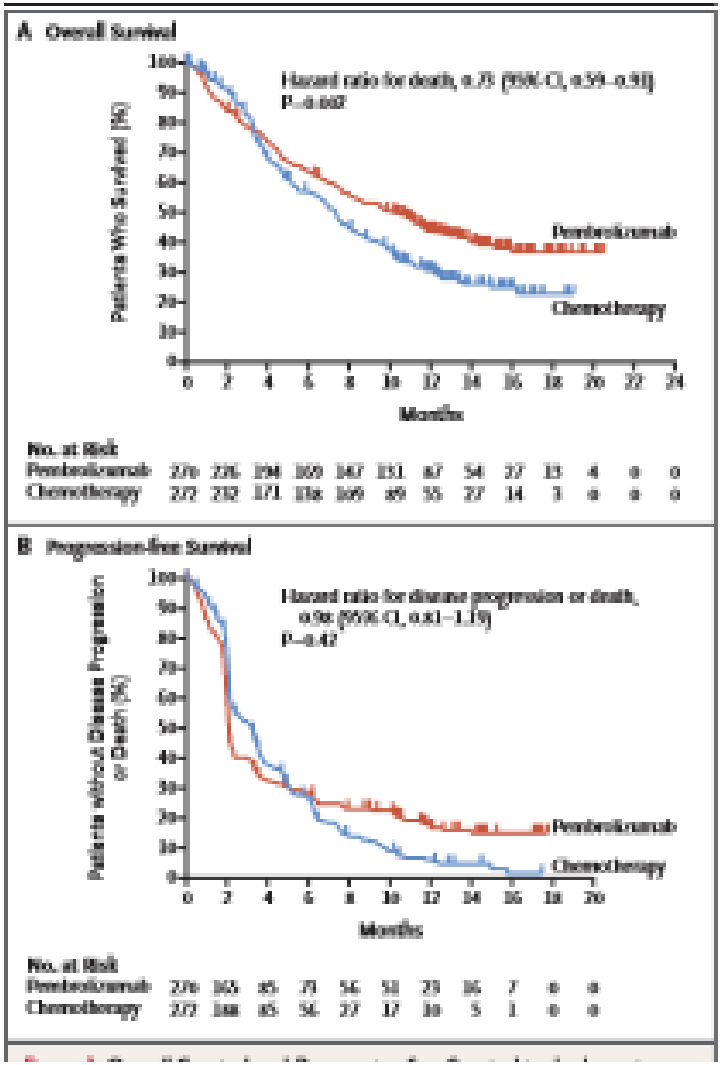
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 16, 2017 VOL. 376 NO. 11

Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma

J. Bellmunt, R. de Wit, D.J. Vaughn, Y. Fradet, J.-L. Lee, L. Fong, N.J. Vogelzang, M.A. Climent, D.P. Petrylak, T.K. Choueiri, A. Necchi, W. Gerritsen, H. Gurney, D.I. Quinn, S. Culine, C.N. Sternberg, Y. Mai, C.H. Poehlein, R.F. Perini, and D.F. Bajorin, for the KEYNOTE-045 Investigators*

2ème ligne métastatique



Conclusion

- Beaucoup de nouveautés
- Se ba
- Inclu
- L’obstination va forcément porter ses fruits