Novinky v léčbě metastatického hormonálně senzitivního karcinomu prostaty

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Prognóza pacientů s M+ karcinomem prostaty

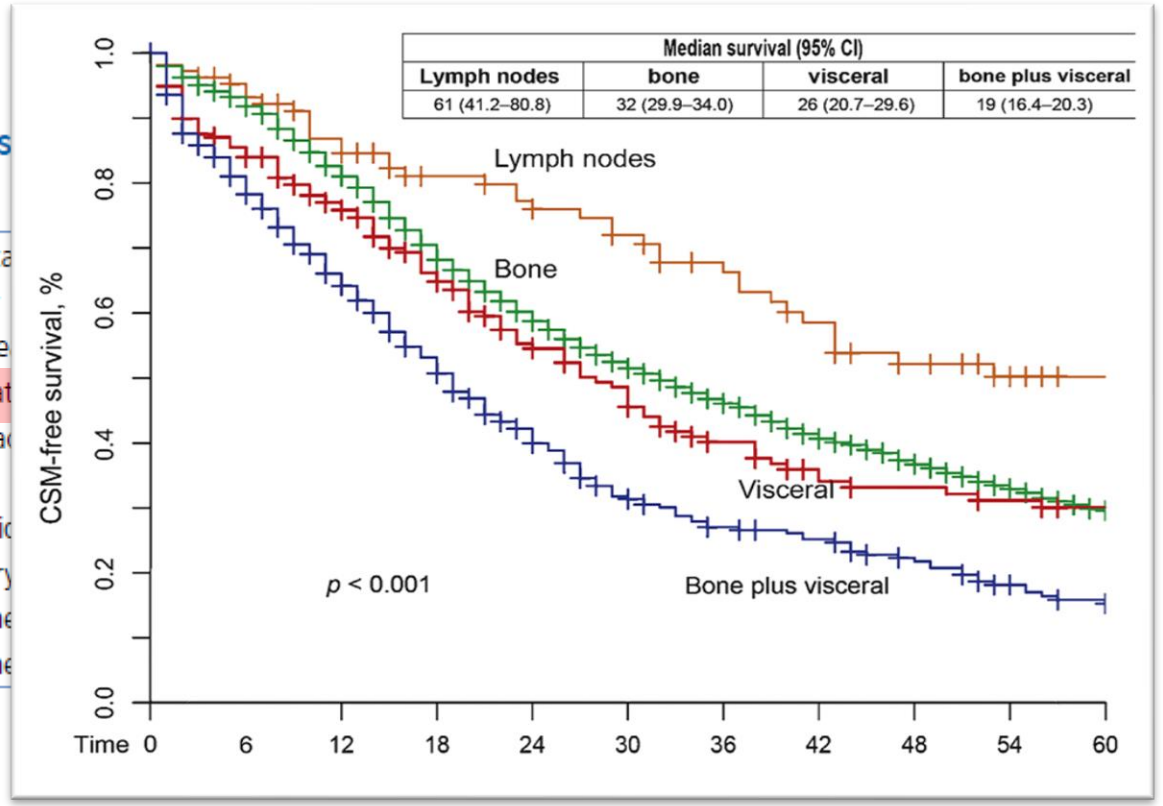
American Cancer Society

Cancer Facts & Figures
2019

Table 8. Five-year Relative Survival Rates* (%) by Stage at Diagnos

	All stages	Local	Regional	Distant
Breast (female)	90	99	85	27
Colon & rectum	65	90	71	14
Colon	64	90	71	14
Rectum	67	89	70	15
Esophagus	19	45	24	5
Kidney†	75	93	69	12
Larynx	61	78	46	34
Liver‡	18	31	11	2
Lung & bronchus	19	56	30	5
Melanoma of the skin	92	98	64	23

Oral ca	
Ovary	
Pancre	
Prostat	
Stomac	
Testis	
Thyroid	
Urinary	
Uterine	
Uterine	

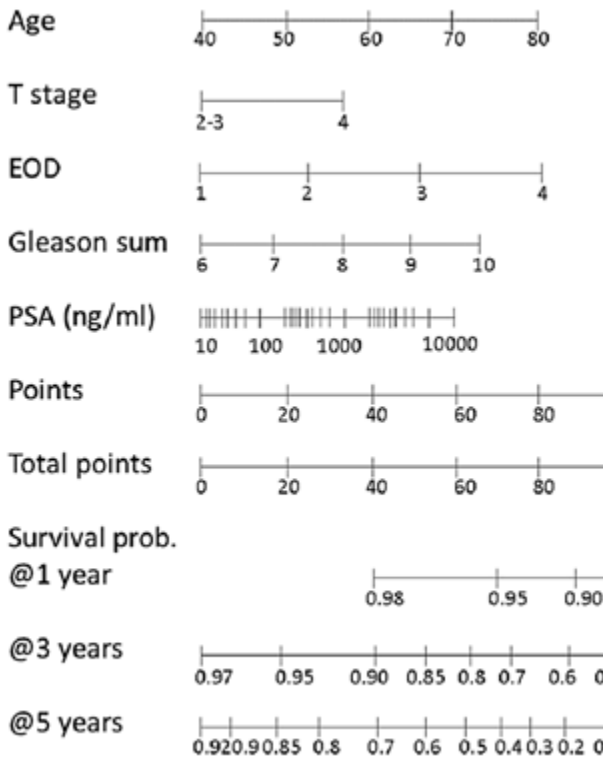


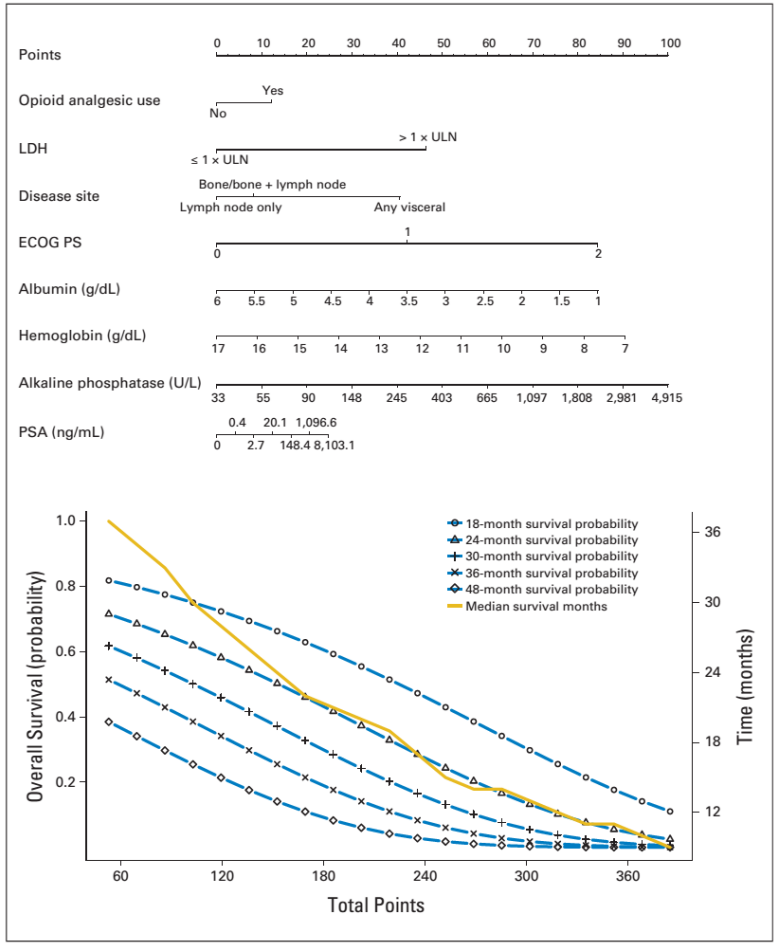
Gandaglia 2016

Prognóza pacientů s M+ karcinomem prostaty

- ECOG (PS) + věk
- Rozsah onemocnění
- Grade group (GS)
- PSA

- LDH, Hb, ALP, Alb

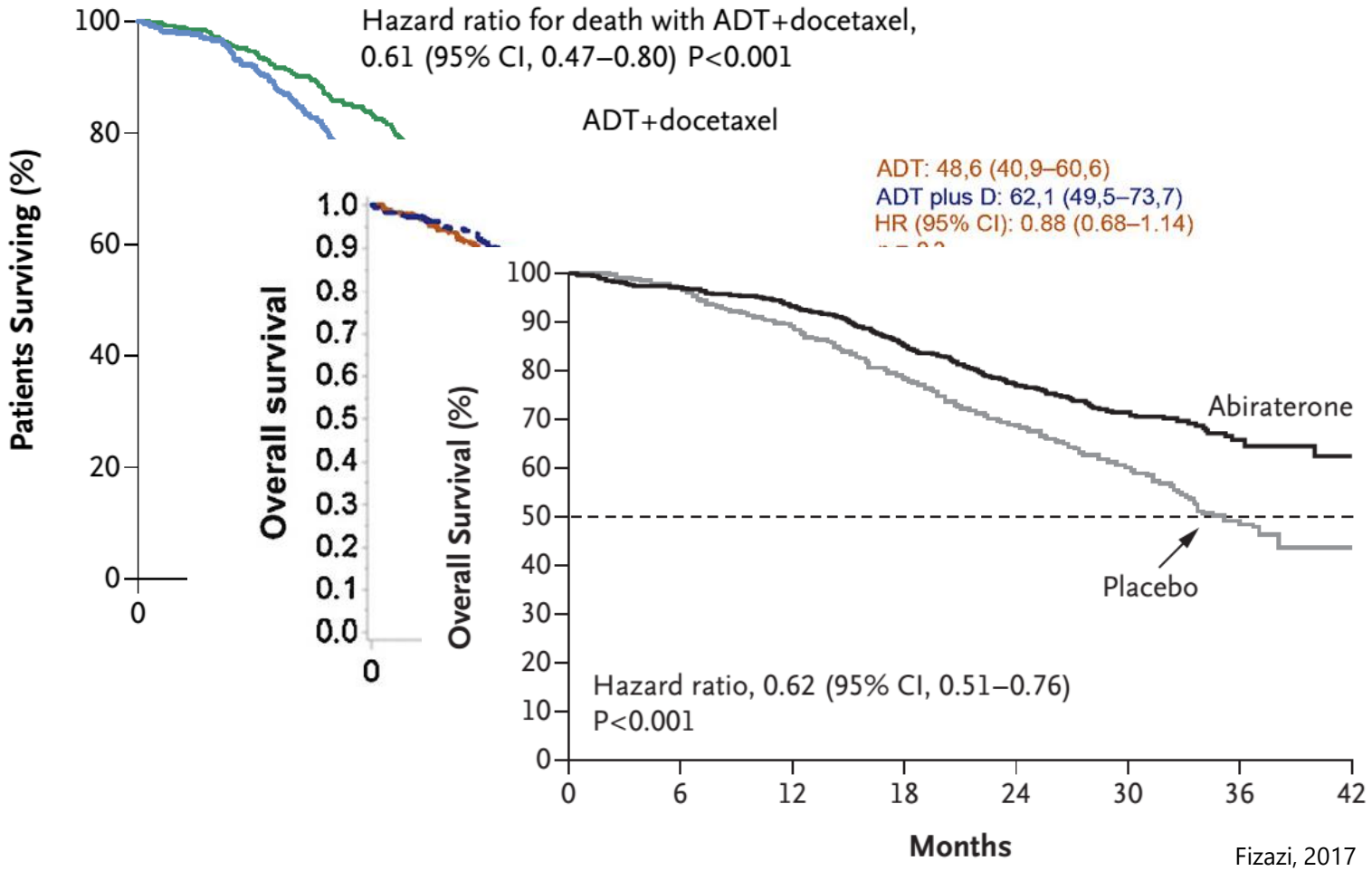




Halabi, 2015

Nové možnosti u M+ karcinomu prostaty

- Docetaxel
  - STAMPEDE,
    CHAARTED,
    GETUG-AFU15
- ARTA preparáty
  - STAMPEDE, LATITUDE
  - TITAN
  - ENZAMET, ARCHES



Fizazi, 2017

Docetaxel u M+ karcinomu prostaty - CHAARTED

- 790 pacientů
- Metastatický KP
- ECOG 0-2
- ADT + docetaxel 75 mg/m^2
  á 3 týdny - celkem 6x

  vs. pouze ADT

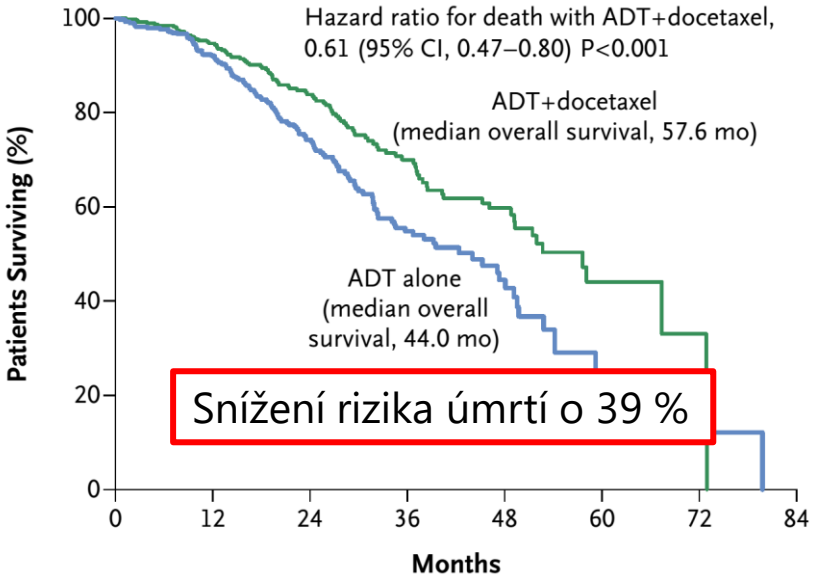
- Primární cíl: OS

Characteristic	ADT plus Docetaxel (N=397)	ADT Alone (N=393)
Age — yr		
Median	64	63
Range	36–88	39–91
Volume of metastases — no. (%)§		
Low	134 (33.8)	143 (36.4)
High	263 (66.2)	250 (63.6)
Visceral metastases — no. (%)	57 (14.4)	66 (16.8)
Gleason score — no. (%)¶		
4–6	21 (5.3)	21 (5.3)
7	96 (24.2)	83 (21.1)
8–10	241 (60.7)	243 (61.8)
PSA level at start of ADT — ng/ml		
Median	50.9	52.1
Range	0.2–8540.1	0.1–8056.0

High-volume : viscerální metastázy
nebo
≥ 4 kostní metastázy (≥ 1 mimo osový skelet)

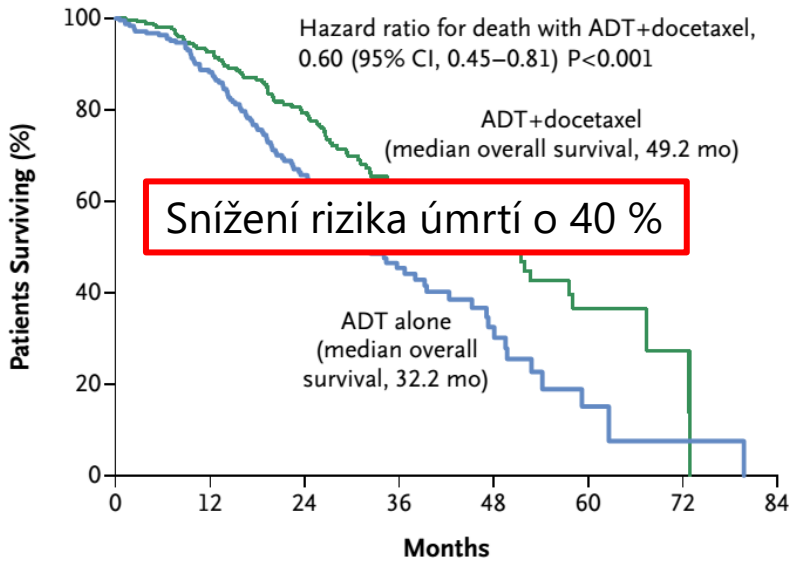
Docetaxel u M+ karcinomu prostaty - CHAARTED

Celkové přežití



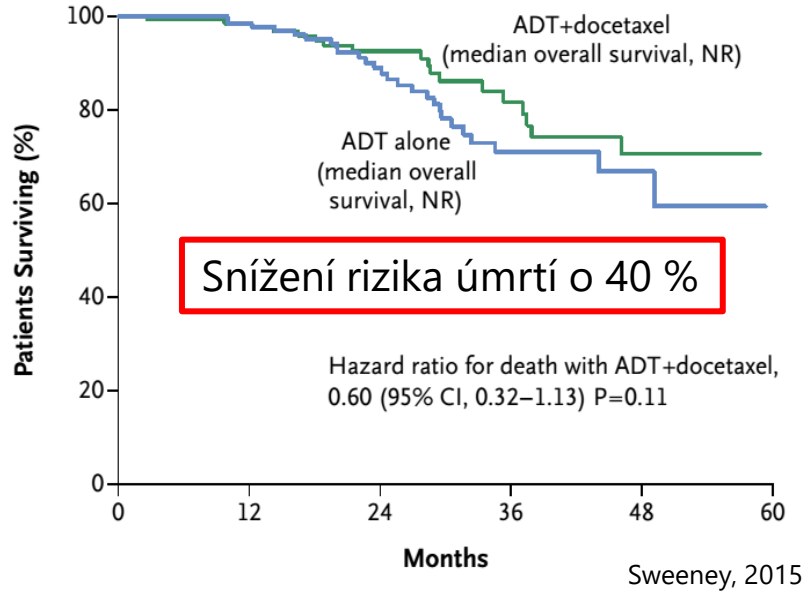
Úmrtí na KP : 85 (21,4 %) vs. 114 (29 %)

Přežití u high-volume disease



Medián přežití 49,2 vs. 32,2 měsíců

Přežití u low-volume disease



Sweeney, 2015

Medián přežití nedosažen

Abirateron u M+ karcinomu prostaty - STAMPEDE

- 1917 pacientů
- M+ KP nebo N+ nebo high-risk (T3-4; GS 8-10; PSA ≥ 40 ng(ml)
- ECOG 0-2

- ADT + abirateron 1000mg + prednison 5mg

  vs. pouze ADT (+ radioterapie!)

- Primární cíl: OS

Table 1. Characteristics of the Patients.*

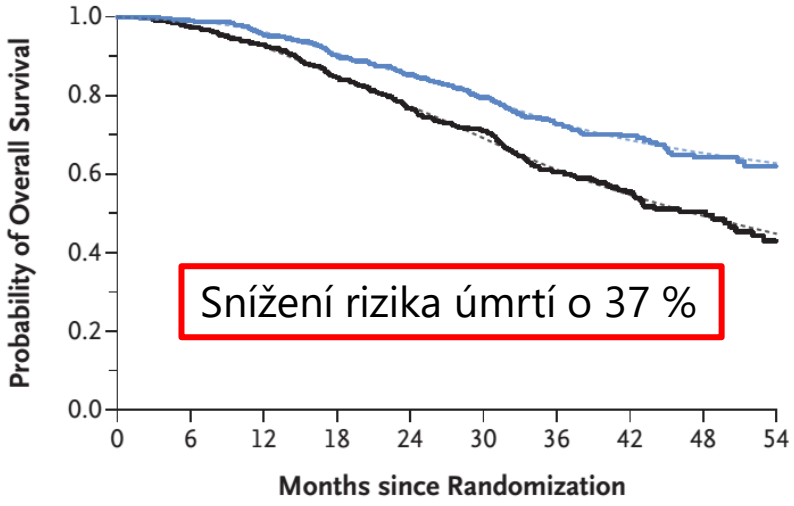
Characteristic	ADT Alone (N=957)	Combination Therapy (N=960)
Age at randomization — yr		
Median (IQR)	67 (62 to 72)	67 (63 to 72)
Range	39 to 84	42 to 85
PSA level before ADT — ng/ml		
Median (IQR)	56 (19 to 165)	51 (19 to 158)
Range	0 to 10,530	0 to 21,460
WHO performance status — no. (%)†		
0	744 (78)	745 (78)
1 or 2	213 (22)	215 (22)
Disease group — no. (%)		
Newly diagnosed node-negative, nonmetastatic disease	256 (27)	253 (26)
Newly diagnosed node-positive, nonmetastatic disease	187 (20)	182 (19)
Newly diagnosed metastatic disease	476 (50)	465 (48)
Previously treated nonmetastatic disease	12 (1)	25 (3)
Previously treated metastatic disease	26 (3)	35 (4)
Gleason score — no. (%)‡		
≤7	223 (23)	221 (23)
8 to 10	721 (75)	715 (74)
Unknown	13 (1)	24 (2)

• • •

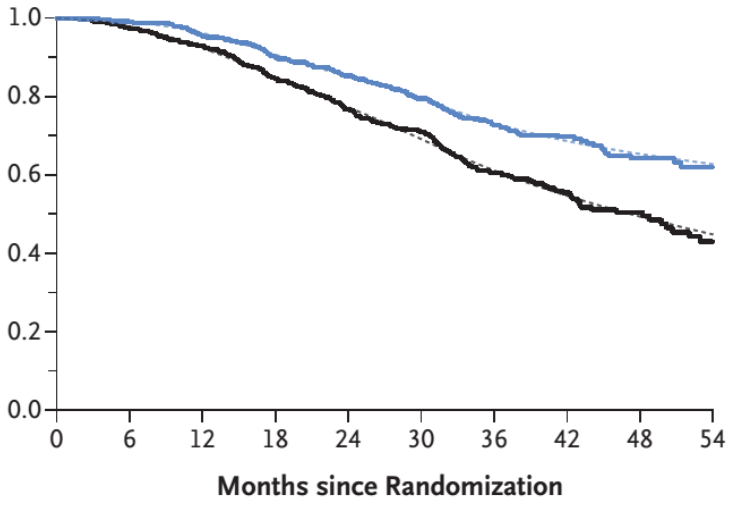
James, 2017

Abirateron u M+ karcinomu prostaty - STAMPEDE

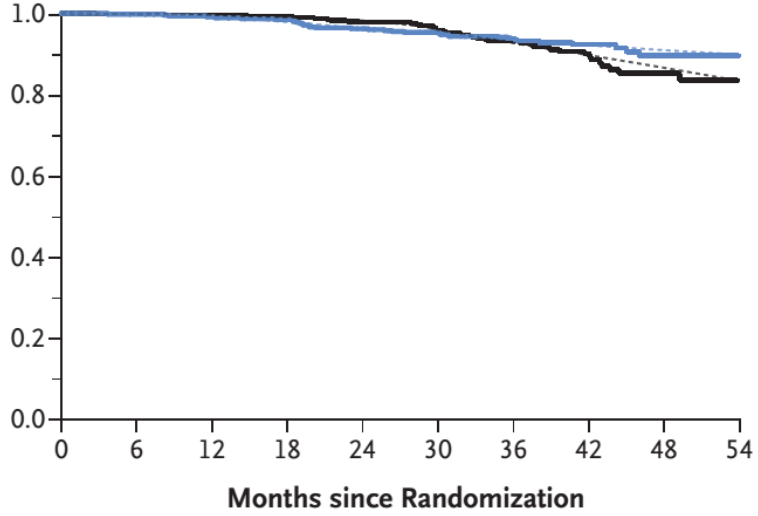
Celkové přežití



Přežití u M+ karcinomu



Přežití u M0 karcinomu

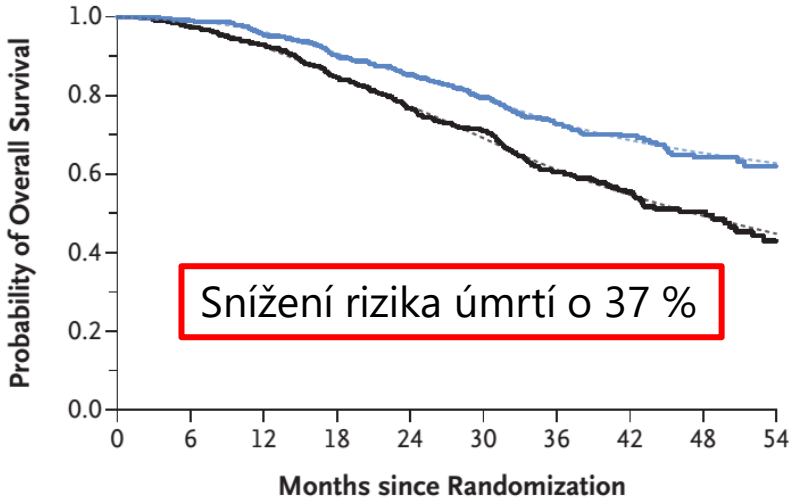


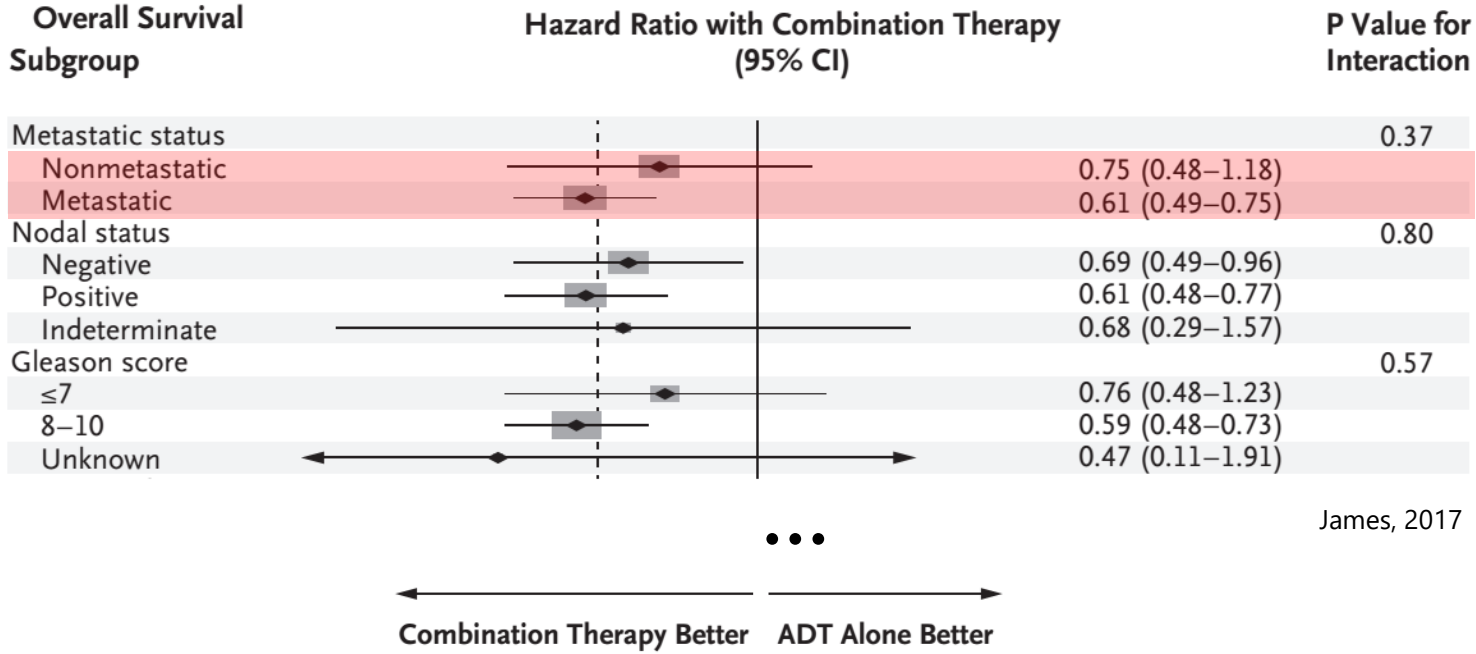
HR 0,63; 95% CI 0,52-0,76; p<0,001

OS 3 roky : 83 vs. 76 %

Abirateron u M+ karcinomu prostaty - STAMPEDE

Celkové přežití





James, 2017

HR 0,63; 95% CI 0,52-0,76; p<0,001

OS 3 roky : 83 vs. 76 %

Abirateron u M+ karcinomu prostaty - LATITUDE

- 1199 pacientů
- Metastatický KP
- ECOG 0-2

- ADT + abirateron 1000mg + prednison 5mg

  vs. pouze ADT

- Primární cíl: OS

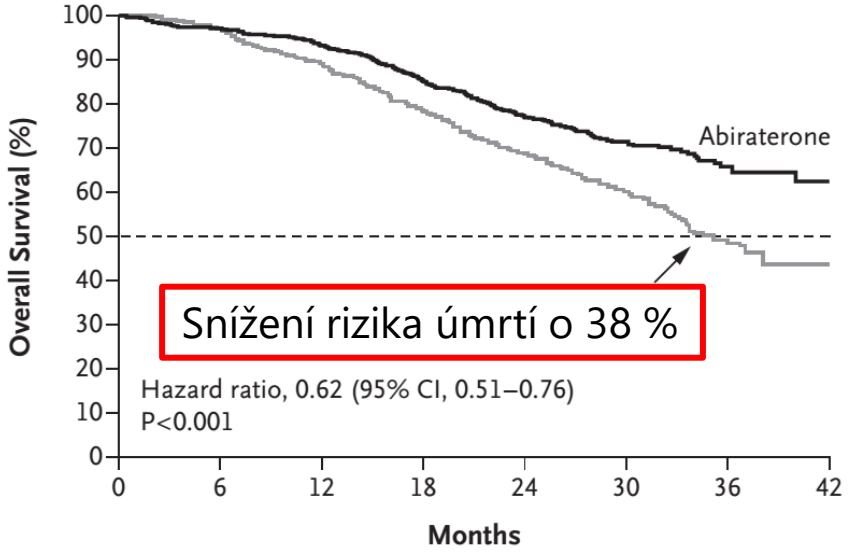
  rPFS

	Abiraterone Group (n=597)	Placebo Group (n=602)
Age (yr), n (%)		
Median	68.0	67.0
Range	38–89	33–92
Gleason score at initial diagnosis, n (%)		
<7	4 (0.7)	1 (0.2)
7	9 (2)	15 (2)
≥8	584 (98)	586 (97)
Baseline pain score (BPI-SF Item 3), n (%)		
0–1	284 (50)	288 (50)
2–3	123 (22)	137 (24)
≥4	163 (29)	154 (27)
Patients with ≥3 bone metastases at screening, n/N (%)	586/597 (98.2)	585/602 (97.2)
Patients with high risk at screening, n (%)		
Gleason score ≥8 + ≥3 bone lesions	573 (96)	569 (95)
Gleason score ≥8 + measurable visceral disease	82 (14)	87 (14)
≥3 bone lesions + measurable visceral disease	84 (14)	85 (14)
Gleason score ≥8 + ≥3 bone lesions + measurable visceral disease	71 (12)	70 (12)

High-risk (≥2/3) : GS 8-10, ≥ 3 kostní metastázy, viscerální metastázy

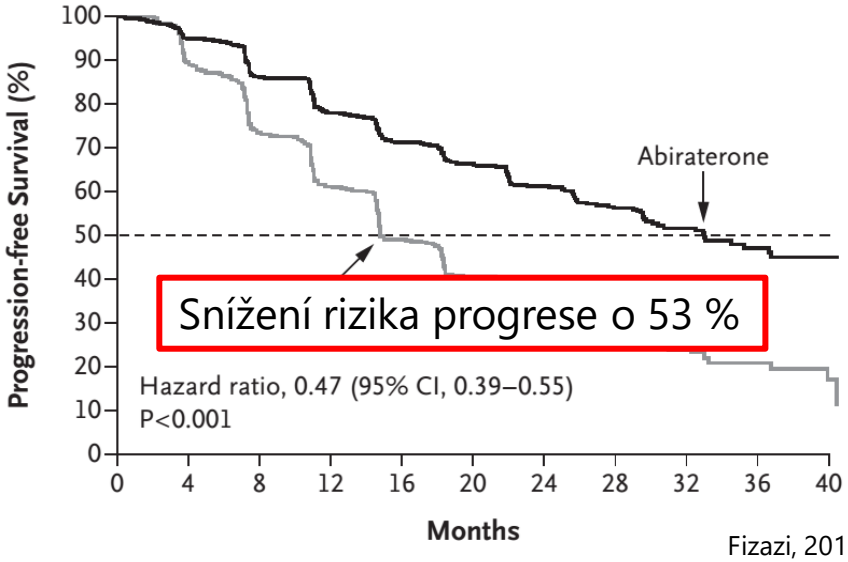
Abirateron u M+ karcinomu prostaty - LATITUDE

Celkové přežití



406 úmrtí (48%) : 169 (28%) vs. 237 (39%)

Přežití bez progrese



Fizazi, 2017

Medián do progrese 33,0 vs. 14,8 m

Enzalutamid u M+ karcinomu prostaty - ARCHES

- 1150 pacientů
- Metastatický KP
- ECOG 0-1

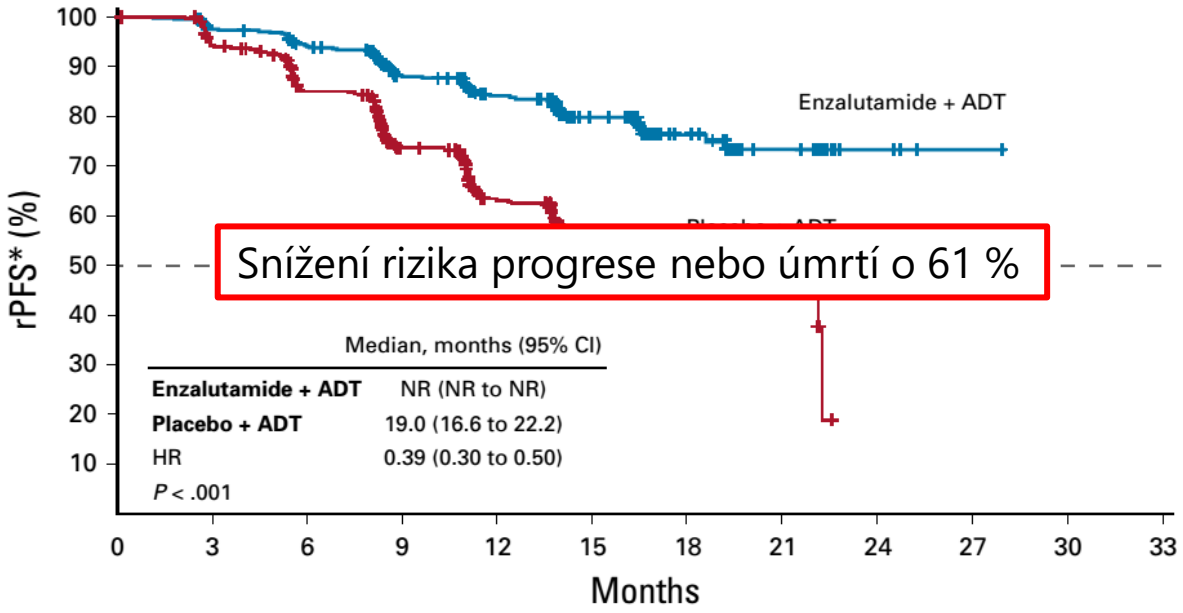
- ADT + enzalutamid 160mg

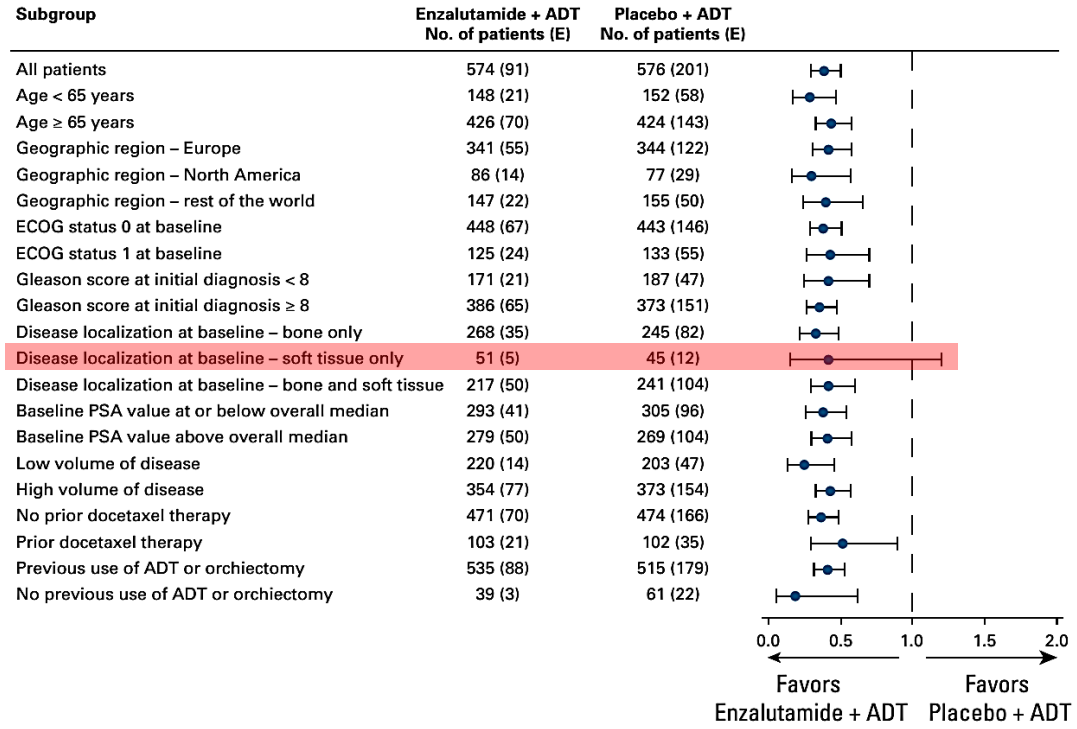
  vs. pouze ADT

- Primární cíl: rPFS

Characteristic	Enzalutamide Plus ADT (n = 574)	Placebo Plus ADT (n = 576)
Age (years)		
Median	70.0	70.0
Range	46-92	42-92
...		
ECOG performance status score on day 1		
0	448 (78.0)	443 (76.9)
1	125 (21.8)	133 (23.1)
Total Gleason score at initial diagnosis		
< 8	171 (29.8)	187 (32.5)
≥ 8	386 (67.2)	373 (64.8)
Localization of confirmed metastases at screening[b]		
Bone only	268 (46.7)	245 (42.5)
Soft tissue only	51 (8.9)	45 (7.8)
Bone and soft tissue	217 (37.8)	241 (41.8)
...		
Distant metastasis at initial diagnosis		
M1	402 (70.0)	365 (63.4)
M0	83 (14.5)	86 (14.9)
MX/unknown	88 (15.3)	125 (21.7)
Disease volume		
High[c]	354 (61.7)	373 (64.8)
Low	220 (38.3)	203 (35.2)

Enzalutamid u M+ karcinomu prostaty - ARCHES





Subgroup	Enzalutamide + ADT No. of patients (E)	Placebo + ADT No. of patients (E)
All patients	574 (91)	576 (201)
Age < 65 years	148 (21)	152 (58)
Age ≥ 65 years	426 (70)	424 (143)
Geographic region – Europe	341 (55)	344 (122)
Geographic region – North America	86 (14)	77 (29)
Geographic region – rest of the world	147 (22)	155 (50)
ECOG status 0 at baseline	448 (67)	443 (146)
ECOG status 1 at baseline	125 (24)	133 (55)
Gleason score at initial diagnosis < 8	171 (21)	187 (47)
Gleason score at initial diagnosis ≥ 8	386 (65)	373 (151)
Disease localization at baseline – bone only	268 (35)	245 (82)
Disease localization at baseline – soft tissue only	51 (5)	45 (12)
Disease localization at baseline – bone and soft tissue	217 (50)	241 (104)
Baseline PSA value at or below overall median	293 (41)	305 (96)
Baseline PSA value above overall median	279 (50)	269 (104)
Low volume of disease	220 (14)	203 (47)
High volume of disease	354 (77)	373 (154)
No prior docetaxel therapy	471 (70)	474 (166)
Prior docetaxel therapy	103 (21)	102 (35)
Previous use of ADT or orchiectomy	535 (88)	515 (179)
No previous use of ADT or orchiectomy	39 (3)	61 (22)

Progrese nebo úmrtí na KP : 91 (15,9 %) vs. 201 (34,9 %)

Armstrong, 2019

Apalutamid u M+ karcinomu prostaty - TITAN

- 1052 pacientů
- Metastatický KP
- ECOG 0-1

- ADT + apalutamid 240mg

  vs. pouze ADT

- Primární cíl: rPFS

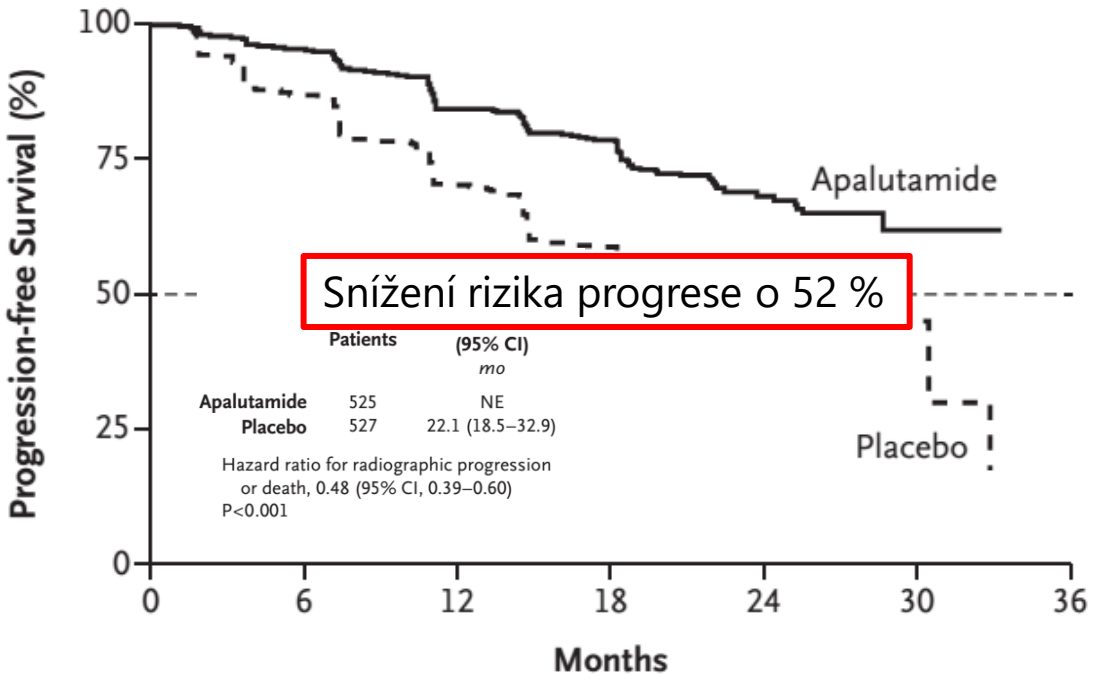
  OS

Characteristic	Apalutamide (N=525)	Placebo (N=527)
Median age (range) — yr	69 (45–94)	68 (43–90)
ECOG performance-status score — no. (%)†		
0	328 (62.5)	348 (66.0)
1	197 (37.5)	178 (33.8)
2	0	1 (0.2)
Gleason score at initial diagnosis — no. (%)‡		
<7	41 (7.8)	39 (7.4)
7	133 (25.3)	130 (24.7)
>7	351 (66.9)	358 (67.9)
Metastatic stage at initial diagnosis — no. (%)		
M0	85 (16.2)	59 (11.2)
M1	411 (78.3)	441 (83.7)
MX	29 (5.5)	27 (5.1)
Disease volume — no. (%)		
Low	200 (38.1)	192 (36.4)
High	325 (61.9)	335 (63.6)
Previous treatment with docetaxel — no. (%)§	58 (11.0)	55 (10.4)
Previous therapy for localized prostate cancer — no. (%)¶	94 (17.9)	79 (15.0)
Median prostate-specific antigen level (range) — μg/liter	5.97 (0–2682)	4.02 (0–2229)

...

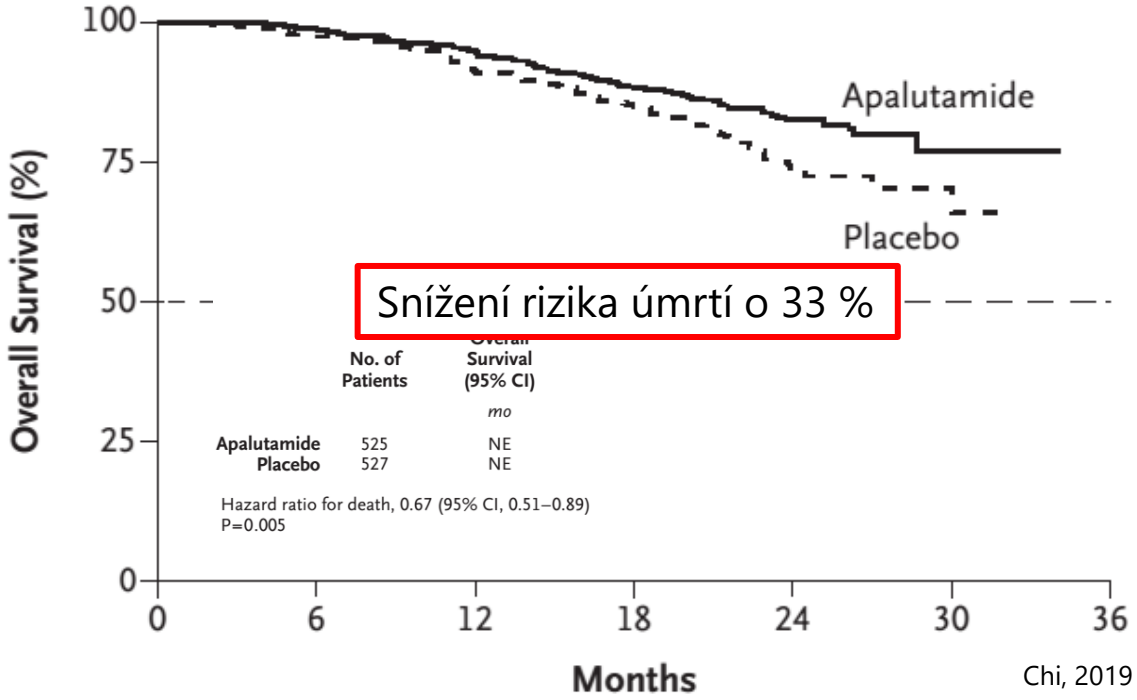
Apalutamid u M+ karcinomu prostaty - TITAN

Přežití bez progrese



Bez progrese ve dvou letech : 68,2 vs. 47,5 %

Celkové přežití

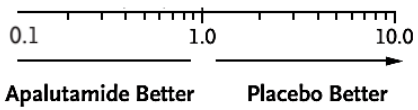


Chi, 2019

Přežití ve dvou letech : 82,4 vs. 73,5 %

Apalutamid u M+ karcinomu prostaty - TITAN

Subgroup	Apalutamide (no. of events/no. of patients)	Placebo (no. of events/no. of patients)	Hazard Ratio for Radiographic Progression or Death (95% CI)
All patients	134/525	231/527	0.49 (0.40–0.61)
Baseline ECOG performance status			
0	79/328	142/348	0.52 (0.39–0.68)
1	55/197	89/178	0.42 (0.30–0.59)
Geographic region			
North America and European Union	32/173	67/173	0.43 (0.28–0.66)
Other	102/352	164/354	0.51 (0.40–0.65)
Bone metastasis only at baseline			
Yes	49/289	102/269	0.38 (0.27–0.54)
No	85/236	129/258	0.60 (0.46–0.80)
Visceral disease and bone metastasis at baseline			
Yes	25/56	38/72	0.71 (0.43–1.18)
No	109/469	193/455	0.46 (0.37–0.59)
Gleason score at diagnosis			
≤7	41/174	65/169	0.53 (0.36–0.78)
>7	93/351	166/358	0.48 (0.37–0.61)
Previous docetaxel use			
Yes	10/58	19/55	0.47 (0.22–1.01)
No	124/467	212/472	0.49 (0.39–0.62)
Age			
<65 yr	40/149	85/182	0.45 (0.31–0.66)
65–74 yr	61/243	105/232	0.47 (0.34–0.64)
≥75 yr	33/133	41/113	0.65 (0.41–1.03)
Disease volume			
High	109/325	173/335	0.53 (0.41–0.67)
Low	25/200	58/192	0.36 (0.22–0.57)



Nežádoucí účinky:

- ukončení léčby 8,0 vs. 5,3 %
- exantém 27,1 vs. 8,5 %
- hypotyreóza 6,5 vs. 1,1 %
- ICHS 4,4 vs. 1,5 %
- pády 7,4 vs. 7,0 %
- epileptický záchvat 0,6 vs 0,4 %

První linie léčby mHSPC ?

		Docetaxel preferred	Abiraterone preferred	Enzalutamide preferred	Apalutamide preferred	ADT monotherapy preferred
Disease factors	High-volume / high-risk disease	✓	✓	✓	✓	
	Low-volume / low-risk disease	✗	✓	✓	✓	
Patient factors	Pre-existing cardiac dysfunction	✓	✗	✓	✓	✓
	Pre-existing neuropathy	✗	✓	✓	✓	
	Poorly controlled diabetes mellitus	✓	✗	✓	✓	
	Poorly controlled hypertension	✓				
	Borderline performance status	✗	✓	✓	✓	✓
	Contraindications to corticosteroids	?	✗	✓	✓	
	Unfit for cytotoxic chemotherapy	✗	✓	✓	✓	✓
	Prior seizures	✓	✓	✗		
Logistical factors	Duration of therapy	✓				✓
	Cost	✓				✓
	Patient preference for oral treatment		✓	✓	✓	

Kwan, World J Urol 2020