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# Hormonsenzitivní karcinom prostaty novinky v léčbě

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## Finanční prohlášení

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Člen odborného poradního sboru	Janssen, Astellas



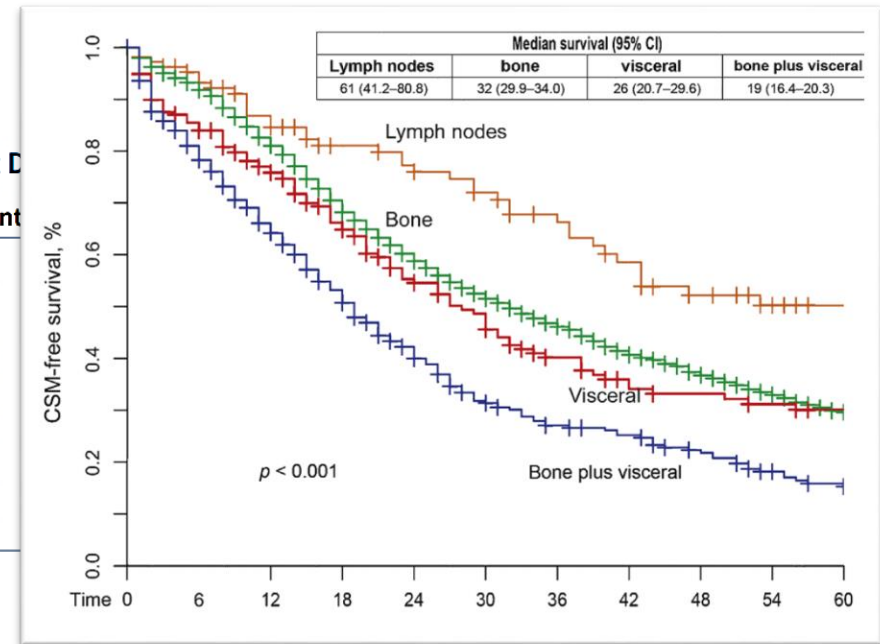
# Prognóza pacientů s M+ karcinomem prostaty



## Cancer Facts & Figures 2017

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

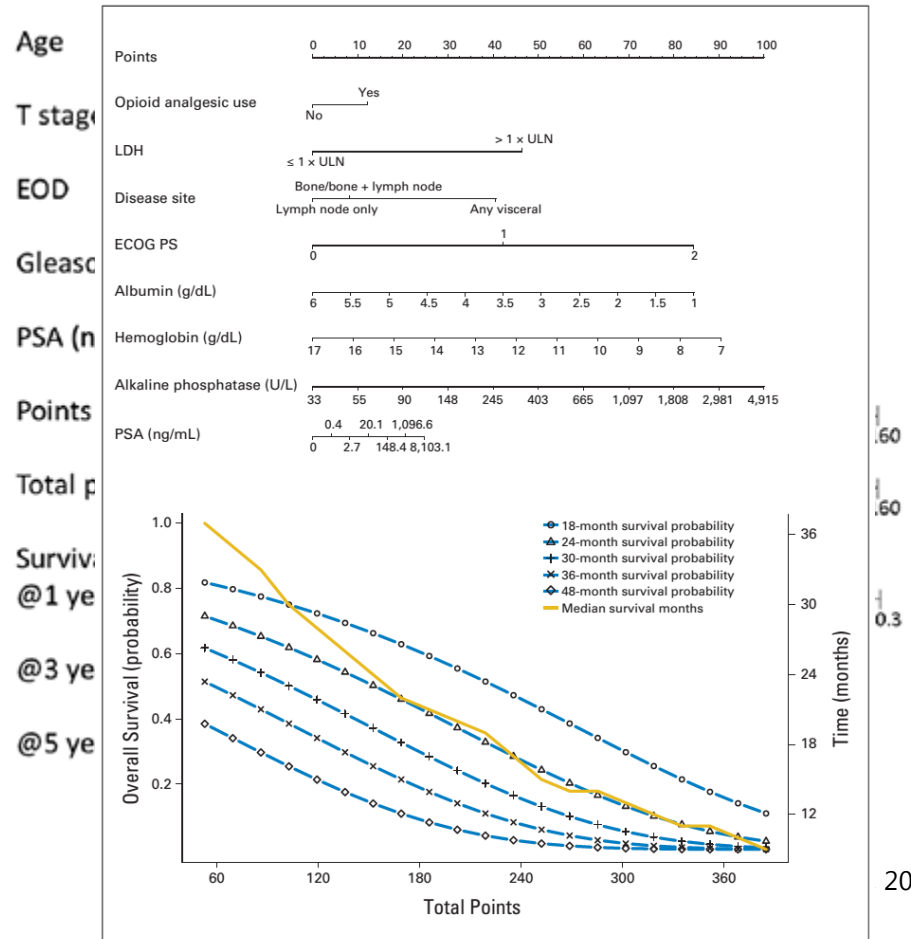
	All stages	Local	Regional	Distant
Breast (female)	90	99	85	26
Colon & rectum	65	90	71	14
Esophagus	18	41	23	5
Kidney†	74	93	66	12
Larynx	61	76	45	35
Liver†	18	31	11	3
Lung & bronchus	18	55	28	4
Melanoma of the skin	92	98	62	18
Oral cavity & pharynx	64	83	63	38





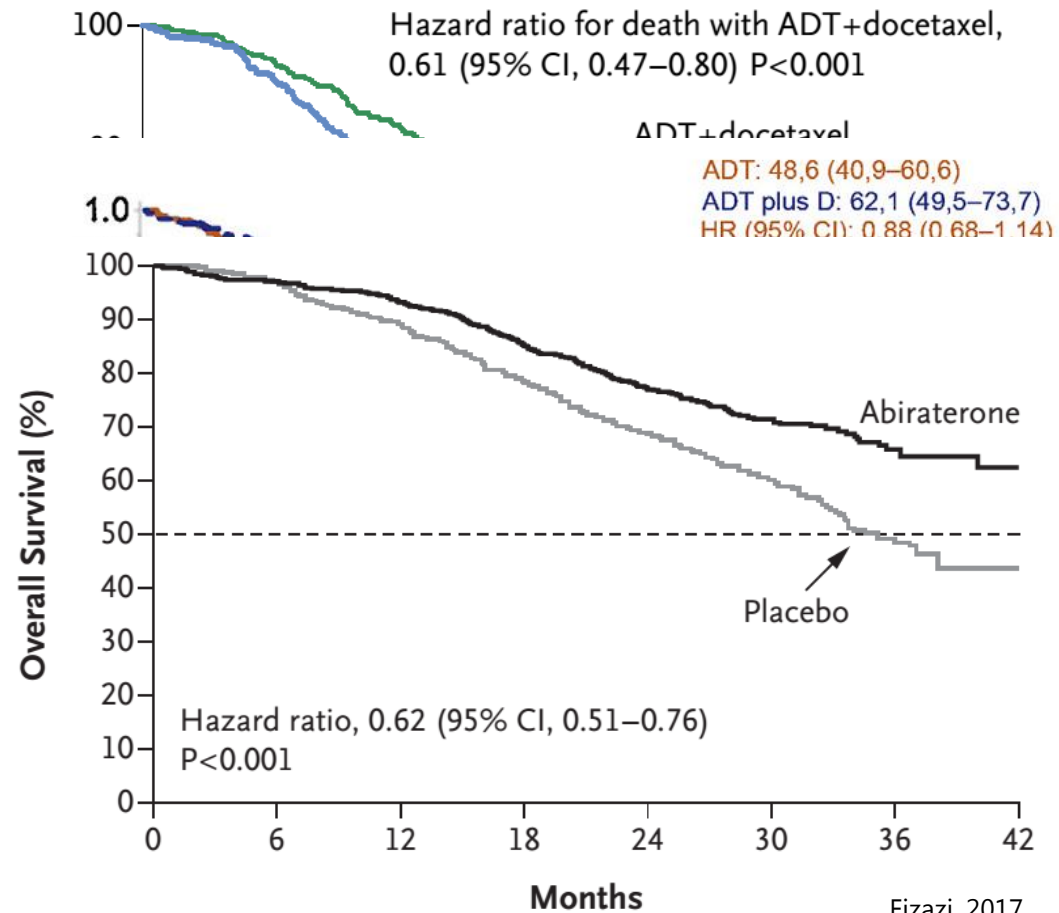
# Prognóza pacientů s M+ karcinomem prostaty

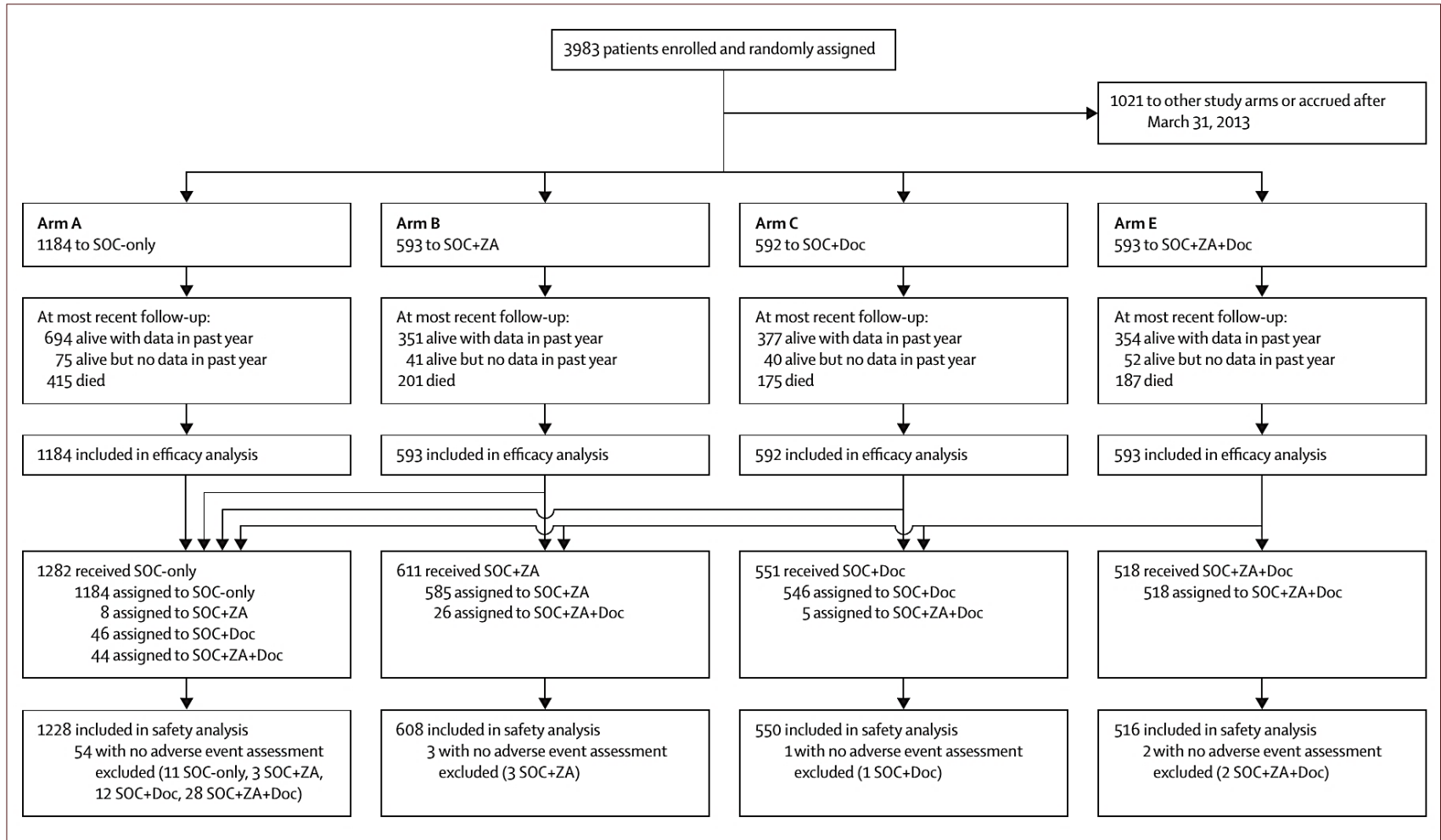
- ECOG (PS) + věk
- Rozsah onemocnění
- Grade group (GS)
- PSA
- LDH, Hb, ALP, Alb

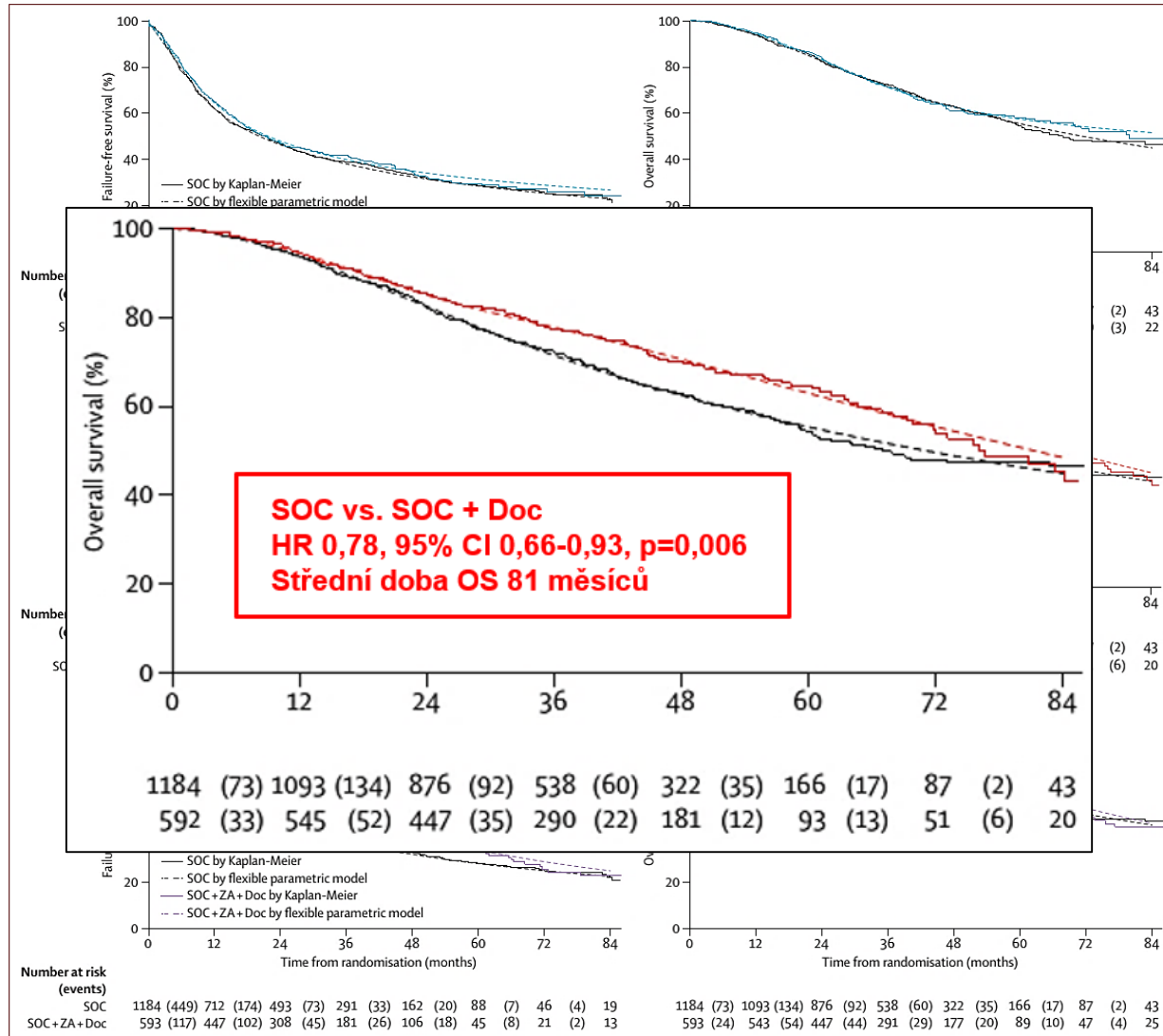


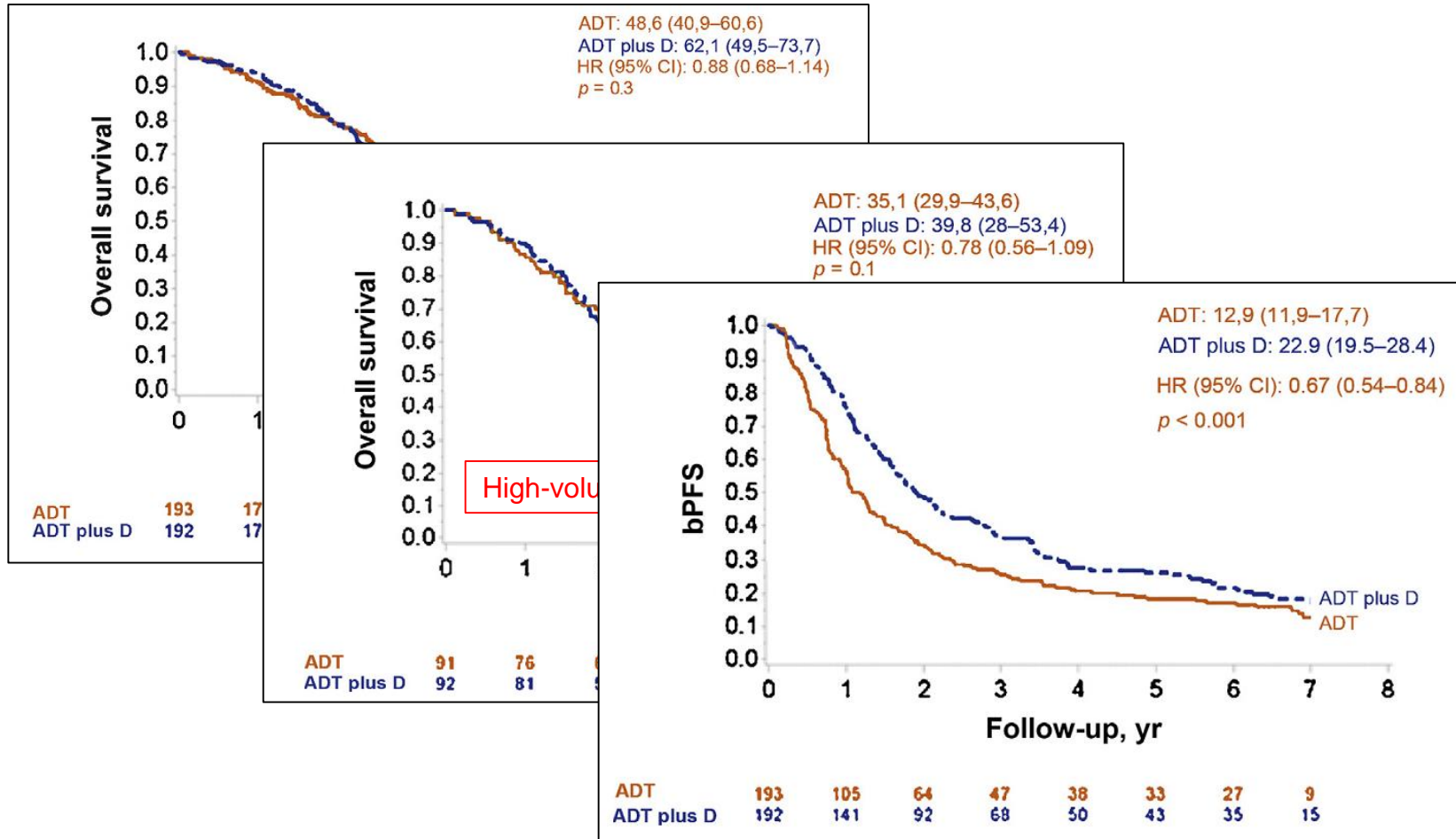
## Nové možnosti u M+ karcinomu prostaty

- Chemoterapie
  - STAMPEDE,
  - CHAARTED,
  - GETUG-AFU15
- Abirateron acetát
  - LATITUDE













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*The NEW ENGLAND JOURNAL of MEDICINE*

ORIGINAL ARTICLE

# Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

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ORIGINAL ARTICLE

# Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

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and Kim N. Chi, M.D., for the LATITUDE Investigators\*



## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

- 790 pacientů
- Metastatický KP
- ECOG 0-2
- Předchozí ADT pro M- karcinom max 24 měsíců
- Předchozí ADT pro M+ karcinom max 3 měsíce

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

- 1199 pacientů
- Metastatický KP
- ECOG 0-2
- Dg. do 3 měsíců od randomizace

- **Nejméně 2 kritéria :**

- $GS \geq 8$
- $\geq 3$  kostní léze
- viscerální léze



## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

- 1:1
  - ADT + docetaxel 75 mg/m<sup>2</sup>  
á 3 týdny - celkem 6x
- nebo
- ADT pouze

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

- 1:1
  - ADT + abirateron 1000mg +  
prednison 5mg
- nebo
- ADT + placebo + placebo



## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

- Primární cíl
  - celkové přežití
- Sekundární cíle
  - doba do klinické progresse
  - doba do progresse do CRPC
  - doba do progresse PSA
  - nežádoucí účinky, kvalita života

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

- Primární cíl
  - celkové přežití
  - přežití bez radiografické progresse
- Sekundární cíle
  - doba do SRE
  - doba do progresse PSA
  - doba do CHT
  - doba do progresse bolesti



## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

- Návštěvy á 3 týdny během CHT
- Poté á 3 měsíce
  
- Bez docetaxelu á 3 měsíce
  
- Vitální funkce, hmotnost
- Biochemie, KO, PSA
  
- CT + scinti při CRPC / rozhodnutí lékaře

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

- Návštěvy á 1 měsíc první rok
- Dále á 2 měsíce
  
- CT + scinti á 4 měsíce
  
- Vitální funkce, hmotnost
- Biochemie, KO, PSA, testosteron
  
- Dotazníky kvality života



## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

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

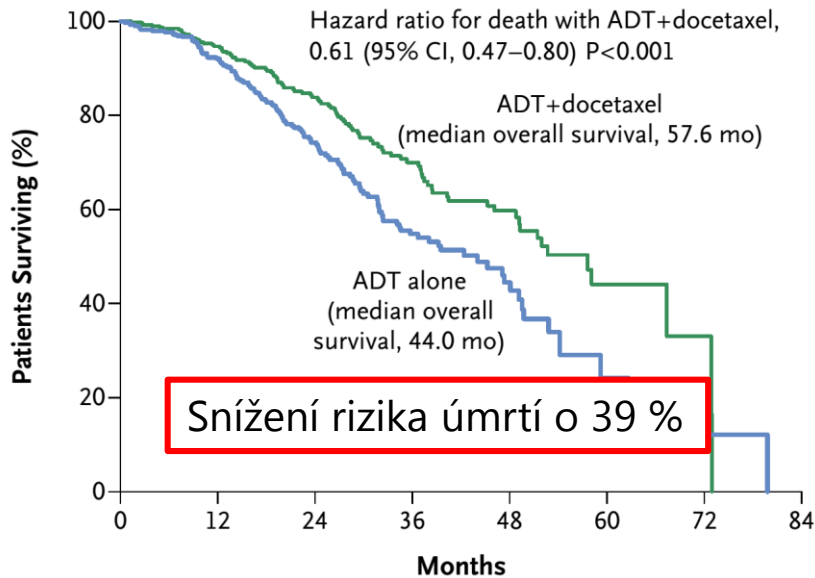
## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

	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)



## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

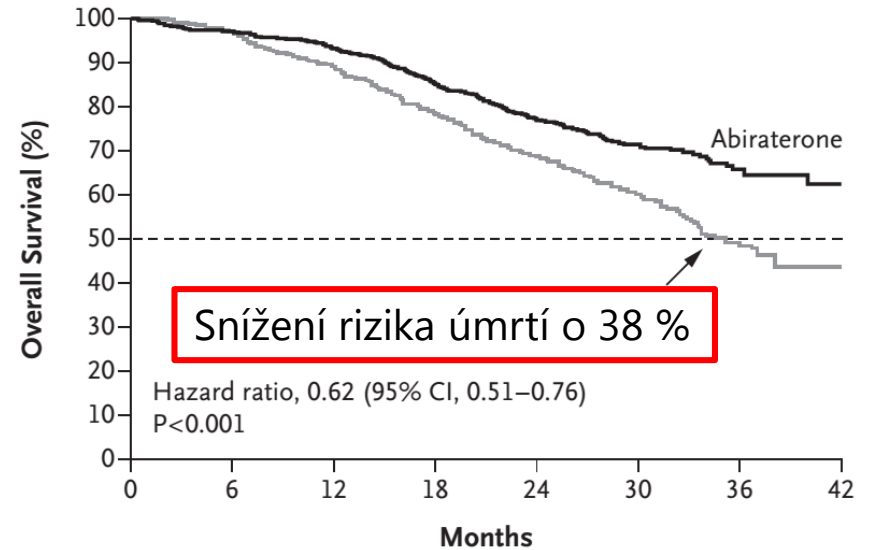
### Celkové přežití



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

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

### Celkové přežití



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

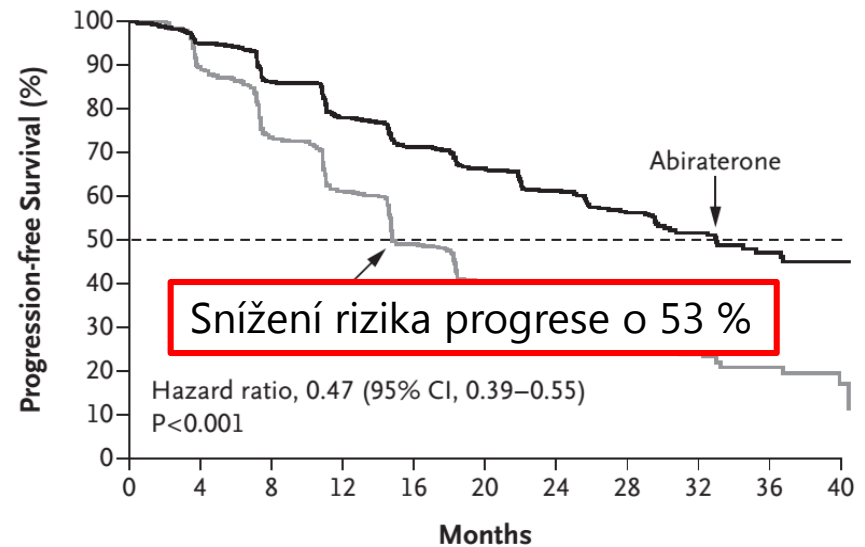




## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

### Přežití bez progrese



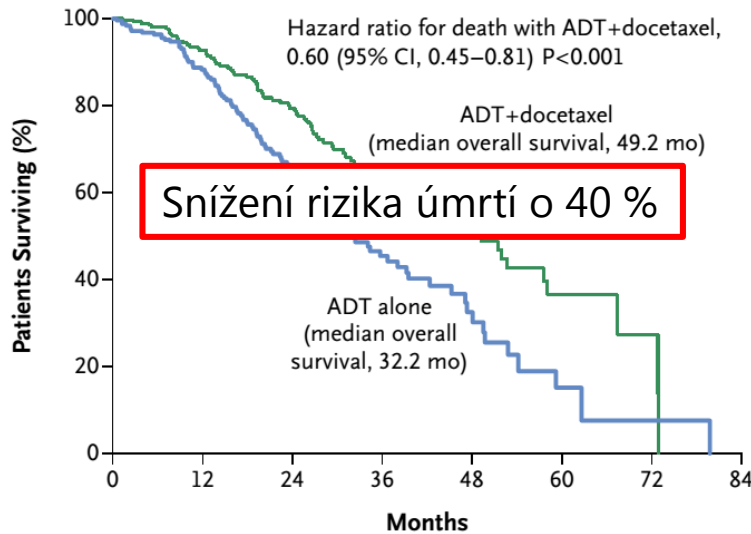
Medián do progrese 33,0 vs. 14,8 m



## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

### Přežití u HD volume disease



Medián přežití 49,2 vs. 32,2 měsíců

**Nejméně 4 kostní léze, pokud nejsou  
viscerální mts.**

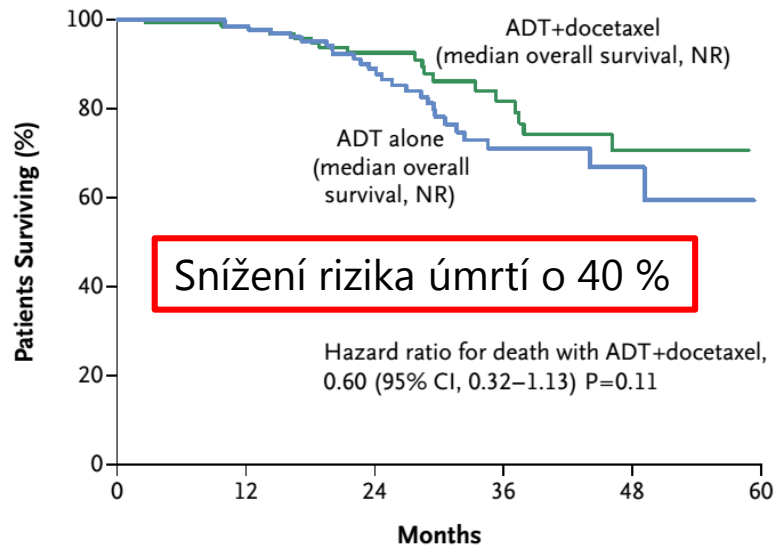
**Nejméně 1 léze mimo páteř a pánev**



## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

### Přežití u LD volume disease



Medián přežití nedosažen



## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

### Sekundární cíle studie

End Point	P Value	Hazard Ratio (95% CI)
PSA level <0.2 ng/ml at 6 mo — no. (%)	<0.001	
PSA level <0.2 ng/ml at 12 mo — no. (%)	<0.001	
Time to castration-resistant prostate cancer — mo*		
Median	<0.001	0.61 (0.51–0.72)
95% CI		
Time to clinical progression — mo†		
Median	<0.001	0.61 (0.50–0.75)
95% CI		

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

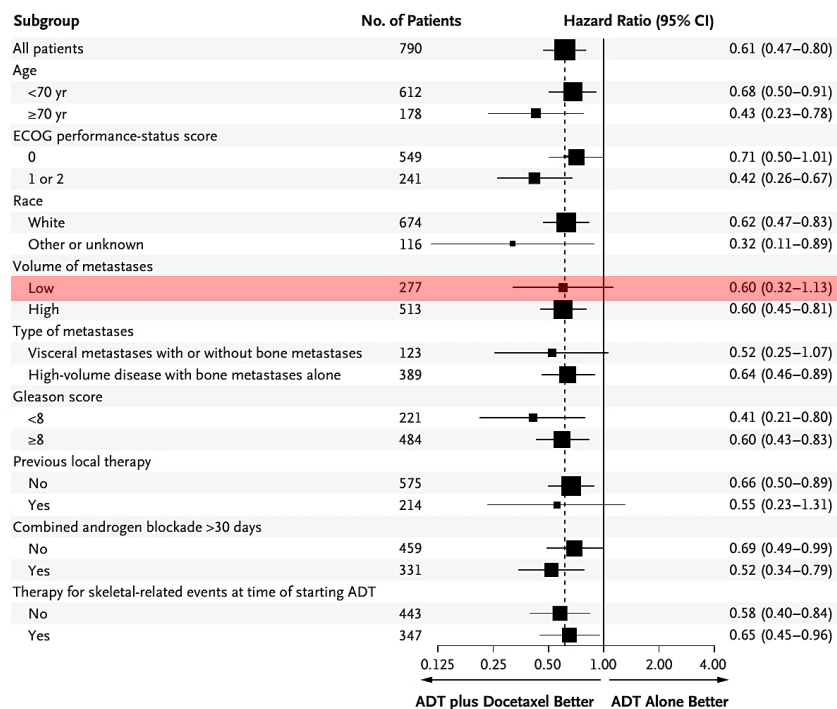
### Sekundární cíle studie

End Point	Hazard Ratio (95% CI)	P Value
<b>Secondary end points</b>		
Median time to pain progression (mo)	0.70 (0.58–0.83)	<0.001
Median time to PSA progression (mo)	0.30 (0.26–0.35)	<0.001
Median time to next symptomatic skeletal event (mo)	0.70 (0.54–0.92)	0.009
Median time to chemotherapy (mo)	0.44 (0.35–0.56)	<0.001
Median time to subsequent prostate cancer therapy (mo)	0.42 (0.35–0.50)	<0.001
<b>Exploratory end point</b>		
Patients with a PSA response (%)‡	1.36 (1.28–1.45)	<0.001



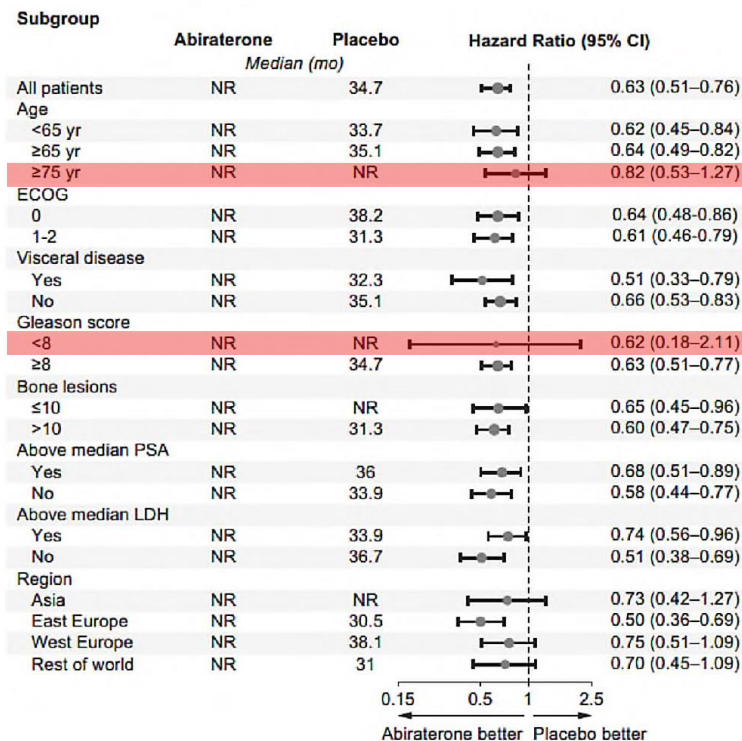
## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

### Subanalýza - celkové přežití



## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

### Subanalýza - celkové přežití





## Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

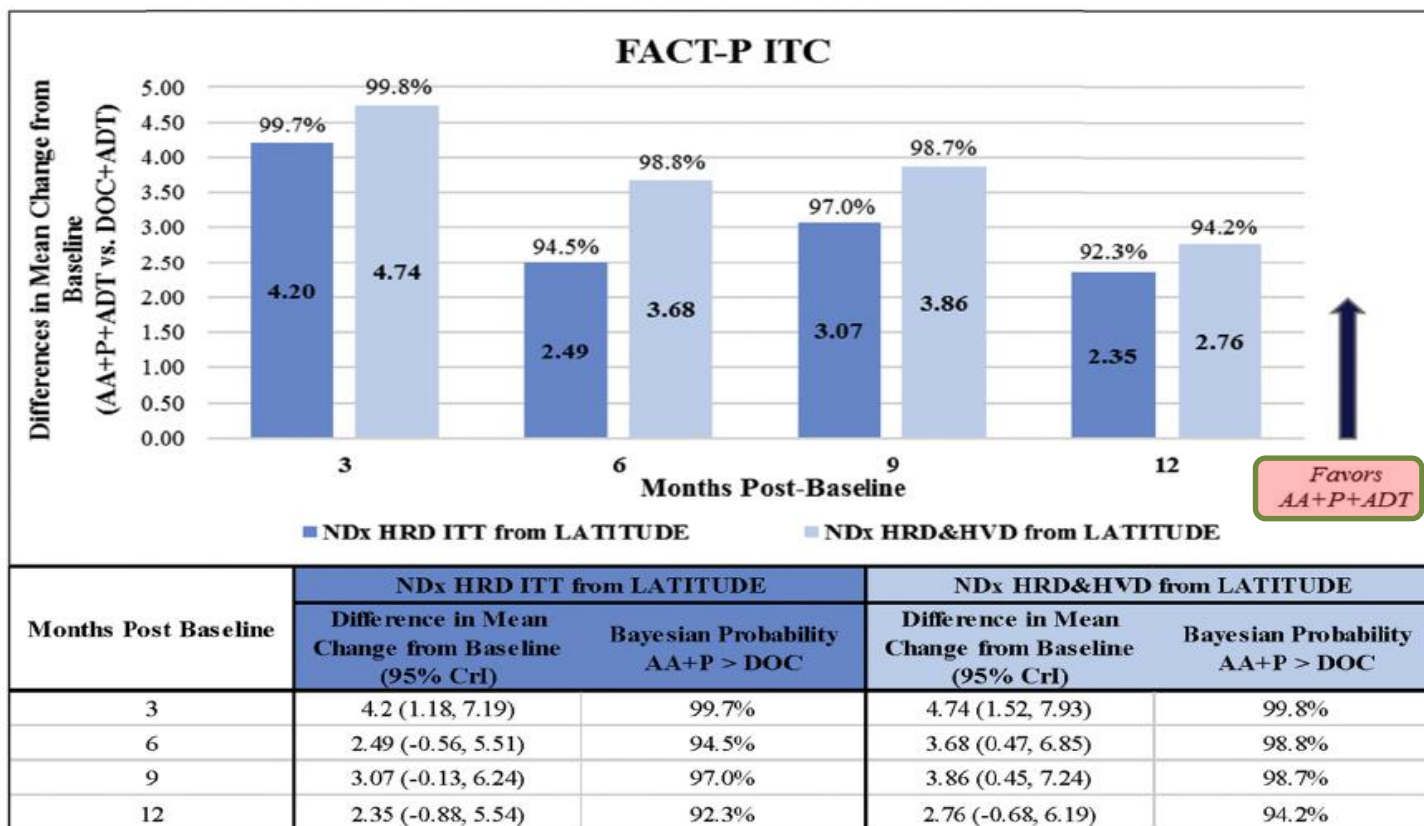
Event	Grade 3	Grade 4	Grade 5
	no. of patients (%)		
Allergic reaction	7 (1.8)	1 (0.3)	0
Fatigue	16 (4.1)	0	0
Diarrhea	4 (1.0)	0	0
Stomatitis	2 (0.5)	0	0
Neuropathy, motor	2 (0.5)	0	0
Neuropathy, sensory	2 (0.5)	0	0
Thromboembolism	1 (0.3)	2 (0.5)	0
Sudden death	0	0	1 (0.3)
Anemia	4 (1.0)	1 (0.3)	0
Thrombocytopenia	0	1 (0.3)	0
Neutropenia	12 (3.1)	35 (9.0)	0
Febrile neutropenia	15 (3.8)	9 (2.3)	0
Infection with neutropenia	5 (1.3)	4 (1.0)	0
Any event	65 (16.7)	49 (12.6)	1 (0.3)

## Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

### Nežádoucí účinky

Adverse Event	Abiraterone Group (N=597)		Placebo Group (N=602)	
	Grade 3	Grade 4	Grade 3	Grade 4
Any adverse event	558 (93)		557 (93)	
Grade 3 or 4 adverse event	374 (63)		287 (48)	
Any serious adverse event	165 (28)		146 (24)	
Any adverse event leading to treatment discontinuation	73 (12)		61 (10)	
Adverse event leading to death	28 (5)		24 (4)	
Graded adverse events†				
Hypertension	121 (20)	0	59 (10)	1 (<1)
Hypokalemia	57 (10)	5 (1)	7 (1)	1 (<1)
ALT increased	31 (5)	2 (<1)	8 (1)	0
Hyperglycemia	26 (4)	1 (<1)	18 (3)	0
AST increased	25 (4)	1 (<1)	9 (1)	0
Bone pain	20 (3)	0	17 (3)	0
Cardiac disorder				
Any	15 (3)	5 (1)	6 (1)	0
Atrial fibrillation	2 (<1)	0	1 (<1)	0
Anemia	12 (2)	3 (1)	26 (4)	1 (<1)
Back pain	14 (2)	0	19 (3)	0
Fatigue	10 (2)	0	14 (2)	0
Spinal-cord compression	12 (2)	0	7 (1)	3 (<1)

## Kvalita života (AA vs. DOC u HNMPK)



Po celou dobu léčby byla kvalita života vyšší u pacientů léčených abirateron acetátem



## Nebo začátek ?

Study	Identifier	Groups	Enrolled Pts (N)	Primary End Point	Status
LATITUDE	NCT01715285	ADT ± AA/P	1209	rPFS, OS	Ongoing
STAMPEDE (Arm G)	NCT00268476	ADT ± AA/P	1800	OS	Ongoing
PEACE-1	NCT01957436	ADT ± DOC vs. ADT + A/P ± DOC (± local RT)	916	PFS, OS	Recruiting
STAMPEDE (Arm J)	NCT00268476	ADT ± AA/P + ENZ	1800	OS	Ongoing
SWOG-1216	NCT01809691	ADT + TAK-700 vs. ADT + BIC	1304	OS	Recruiting
ENZAMET	NCT02446405	ADT + ENZ vs. ADT + antiandrogen	1100	OS	Ongoing
TITAN	NCT02489318	ADT ± APA	1000	rPFS, OS	Recruiting
ARCHES	NCT02677896	ADT ± ENZ	1100	rPFS	Recruiting
ARASENS	NCT02799602	ADT + DOC ± ODM-201	1300	OS	Recruiting