NOVINKY Z LETOŠNÍHO NEJVÝZNAMNĚJŠÍHO SETKÁNÍ ONKOLOGŮ

Shrnutí ze sekce genitourinární karcinomy

CARD: Overall survival (OS) analysis of patients with metastatic castration-resistant prostate cancer (mCRPC) receiving cabazitaxel versus abiraterone or enzalutamide
5569

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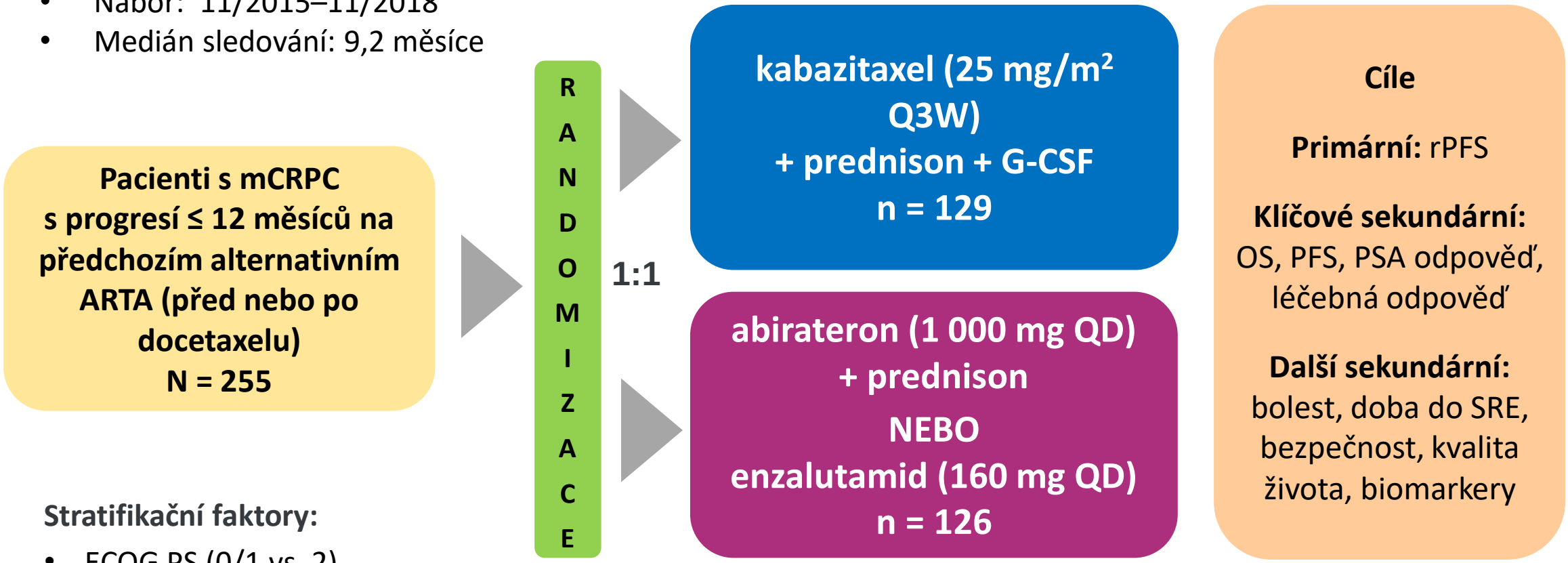
FAKULTNÍ NEMOCNICE PLZEŇ

STUDIE CARD: DESIGN

- Multicentrická, randomizovaná, otevřená studie
- Nábor: 11/2015–11/2018
- Medián sledování: 9,2 měsíce



Stratifikační faktory:

- ECOG PS (0/1 vs. 2)
- Doba do progrese na předchozím alternativním ARTA (0–6 vs. > 6–12 měsíců)
- ARTA prechemo vs. postchemo indikace

ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life;
OS, overall survival; PFS, progression-free survival; PSA, prostate-specific antigen; QD, once daily; Q3W, every 3 weeks; rPFS, radiographic progression-free survival.

Východiska

- The CARD trial (NCT02485691) compared **cabazitaxel vs. an androgen receptor targeted agent (ARTA; abiraterone/enzalutamide) in mCRPC previously treated with docetaxel and the alternative ARTA** (abiraterone/enzalutamide), in any order

- These *post hoc* analyses assessed OS from various time points and the impact of prognostic factors

Metoda

- mCRPC **previously treated with docetaxel** and **progressing ≤ 12 months on prior abiraterone/enzalutamide were randomized 1 : 1 to cabazitaxel (25 mg/m^2 IV Q3W + daily prednisone + prophylactic G-CSF) vs. abiraterone (1 000 mg PO + daily prednisone) or enzalutamide (160 mg PO)**
- OS was calculated from date of diagnosis of metastatic disease, date of mCRPC, and start of the 1st, 2nd or 3rd life-extending therapy (LET)

Výsledky CARD (N = 255)

- Median OS was longer with cabazitaxel vs. abiraterone/enzalutamide **(13.6 vs. 11.0 months; HR 0.64, 95% CI 0.46–0.89; p = 0.008)**
- **OS was numerically improved for cabazitaxel** vs. abiraterone/enzalutamide in the **1st, 2nd, 3rd line**
- In the multivariate analysis, low hemoglobin, high baseline neutrophil to lymphocyte ratio, and high PSA values at baseline were associated with worse OS
- In presence of these factors, the OS benefit observed with cabazitaxel vs. abiraterone/enzalutamide remained significant **(HR 0.63, 95% CI 0.42–0.94, p = 0.022)**

OS from time of	Median OS, months	
	Cabazitaxel n = 129	Abiraterone/enzalutamide n = 126
Metastatic disease diagnosis	54.7	42.5
mCRPC diagnosis	40.9	31.3
1st LET	36.4	30.5
2nd LET	24.2	21.9
3rd LET	13.6	11.0

Závěr

- Cabazitaxel numerically improved OS vs. abiraterone/enzalutamide in patients with mCRPC previously treated with docetaxel and the alternative ARTA (abiraterone/enzalutamide)

- The robustness of this OS benefit was confirmed by stratified multivariate analysis

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Cabazitaxel versus enzalutamide/abiraterone in CARD eligible mCRPC patients with or without germline HRR defects

55524

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Cabazitaxel and ARTA

- The CARD trial proved that in mCPRC patients (pts), previously treated with docetaxel and an androgen-receptor signaling inhibitor (ARSI), cabazitaxel (CBZ) significantly improves progression-free (PFS) and overall survival (OS) compared with the alternative ARSI

- Concurrently, the **PROFOUND** study showed the superiority of **olaparib vs. ARSI** in pts with similar prior treatment history and genetic alterations in homologous recombination DNA repair related genes (HRR)

PROREPAIR-B (NCT03075735)

- Prospective study which aimed to demonstrate the prognostic role of germline deleterious mutations in (g)HRR genes
- First therapy line (1L)
- Second therapy line (2L)
- Outcomes with 1–2L have been previously reported
- Here we evaluated radiographic (r)-PFS, clinical (c)-PFS, and OS in PROREPAIR-B pts who met CARD study eligibility criteria and who received CBZ and/or ARSI

Pacienti

- 95 out of 419 mCRPC pts included in PROREPAIR-B met CARD eligibility criteria and received CBZ (n = 60) or ARSI (n = 35)
- Including 14 gHRR carriers, 8/6 treated with CBZ/ARSI, respectively
- Visceral metastases were more frequent among pts treated with CBZ (p = 0.01)

PFS

- ECOG 2, M1 at diagnosis
- Abiraterone as the 1st ARSI and prior radiographic DP (all $p < 0.05$) were more frequent in pts than in the CARD trial

Overall, CBZ was superior to ARSI:

- rPFS (median **6.0 vs. 3.7** months (m), $p = 0.03$)
- cPFS (median **4.4 vs. 3.4** m, $p = 0.01$)
- PSA50 responses (39 % vs. 17 %, $p = 0.027$)

OS

- Differences in **OS were not observed**, approximately 60 % of patients in ARSI had crossed to CBZ at the time of the analyses
- **gHRR carriers had a significant worse prognosis** (OS HR 1.9; rPFS HR 2.4; cPFS HR 2.6) than non-carriers
- **In gHRR carriers CBZ was not superior to ARSI** in terms of rPFS (2.5 vs. 3.0 m, p = 0.8), cPFS (2.5 vs. 2.4 m, p = 0.8) and OS (4.5 vs. 3.7, p = 0.8)

Závěr

- Our results confirm the benefit of CBZ treatment over a second ARSI (either abiraterone or enzalutamide) in unselected mCRPC population
- However, the outcomes in gHRR carriers **are poor with either CBZ or ARSI supporting the need of novel therapies in this setting**