ASCO 2020

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

5569

Jindřich Fínek

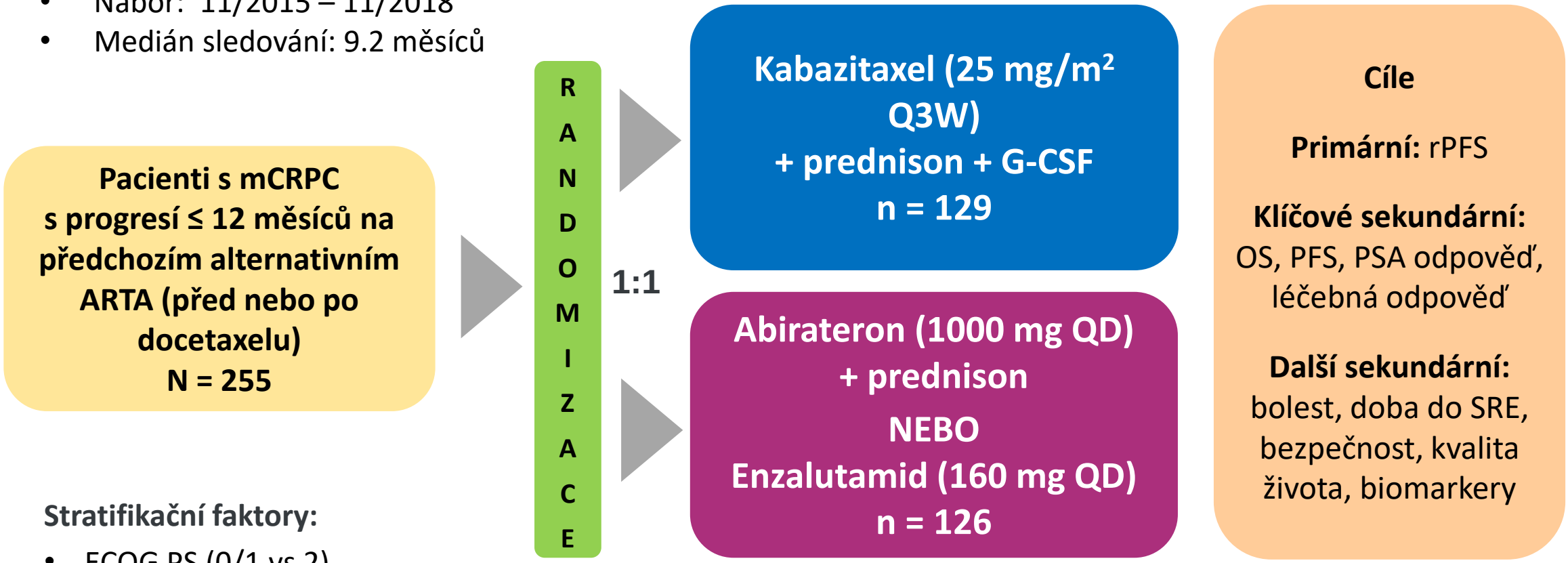
FN a LF UK

Plzeň

FAKULTNÍ NEMOCNICE PLZEŇ

STUDY CARD: DESIGN

- Multicentrická, randomizovaná, otevřená studie
- Nábor: 11/2015 – 11/2018
- Medián sledování: 9.2 měsíců



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 (ART; abiraterone/enzalutamide) in mCRPC previously treated with docetaxel and the alternative ART** (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 (1000 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 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 versus 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 ART (abiraterone/enzalutamide)

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

ASCO 2020
Cabazitaxel versus enzalutamide/abiraterone in CARD eligible mCRPC patients with or without germline HRR defects.

55524

Jindřich Fínek
FN a LF UK
Plzeň

FAKULTNÍ NEMOCNICE PLZEŇ

Cabazitaxel nad 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 Homologus 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 (1L)
- second (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 meet CARD study eligibility criteria and who received CBZ and/or ARSi.

Pacienti

- 95 out of 419 mCRPC pts included in PROREPAIR-B meet 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 1st ARSi and prior radiographic PD (all $p<0.05$) were more frequent in pts than in the CARD study.

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.
- **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.**