811P Association of grade ≥3 neutropenia (NP) with outcomes in patients with metastatic castration-resistant prostate cancer (mCRPC) receiving cabazitaxel

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Background: Subset analysis of trials investigating taxanes in patients with mCRPC suggest an association between Grade ≥3 NP and disease outcomes. In the Phase 3 PROSELICA trial (NCT01308580), NP was more common in patients receiving cabazitaxel 25 mg/m^2 (C25) vs cabazitaxel 20 mg/m^2 (C20) - 73% vs 42%, respectively. Post hoc analyses of PROSELICA examined the relationship between incidence of NP, survival and response.

Methods: PROSELICA assessed the non-inferiority of C20 (n = 598) vs C25 (n = 602) in terms of overall survival (OS) in men with mCRPC. Prophylactic granulocyte colony-stimulating factor was given to patients with Grade ≥3 NP. OS and progression-free survival (PFS) were analyzed using Kaplan-Meier (KM) estimates and Cox proportional hazard models. Nominal p values were determined by log-rank tests. Prostate-specific antigen response rate (PSArr; defined as proportion of patients with a > 50 % PSA decline from baseline) was analyzed in the eligible population using KM estimates with Chi^2 tests and odds ratios. OS, PFS and PSArr were correlated with Grade ≥3 NP occurrence and baseline neutrophilia (neutrophils ≥7000 G/l) by univariate analysis.

Results: In the intent-to-treat (ITT) population, development of Grade ≥3 NP was associated with better PSArr, PFS and OS ($p < 0.001$; Table). The positive association was observed in both treatment arms and in poor-risk patients with baseline neutrophilia.

Table: 811P

Population	Outcome	Grade ≥3 NP	No Grade ≥3 NP	Hazard ratio/Odds ratio	p value
ITT population (n = 1200)	OS, months (mo)	15.1	12.4	0.78	0.0002
	PFS, mo	3.7	2.8	0.79	0.0001
	PSArr, % n = 1079	44.1	25.5	2.3	<0.0001
C25 (n = 602)	OS, mo	15.3	12.2	0.77	0.009
	PFS, mo	3.5	3.5	0.84	0.07
	PSArr, % n = 538	46.2	34.5	1.6	0.015
C20 (n = 598)	OS, mo	14.6	12.6	0.78	0.006
	PFS, mo	4.2	2.3	0.75	0.0008
	PSArr, % n = 541	40.7	21.3	2.5	<0.0001
Neutrophilia (n = 174)	OS, mo	12.8	7.5	0.63	0.004
	PFS, mo	4.1	2.1	0.66	0.008
	PSArr, % n = 156	43.8	16.9	3.8	0.0002

Conclusions: Post hoc assessment of Grade ≥3 NP in PROSELICA was associated with improved survival and response to cabazitaxel independent of dose. These results are consistent with data obtained in the Phase 3 TAX327 (docetaxel) and TROPIC (cabazitaxel) trials. Funded by Sanofi.

Clinical trial identification: NCT01308580.

Editorial acknowledgement: Editorial assistance was provided by Danielle Lindley of Meditech Media Ltd, funded by Sanofi.

Legal entity responsible for the study: Sanofi.

Funding: Sanofi.

Disclosure: Meisel: Advisor: Astellas, Roche, Celgene, Novartis, Vifor, Sanofi, Amgen, Merck; Expert testimony: Sanofi; Research funding: Bayer (himself), Merck (institution); Expenses: Amgen, Astellas, Sanofi, Servier, Roche, Boehringer Ingelheim; Intellectual property: Merck. R. de Wit: Consultancy, Speaker fees: Sanofi. S. Oudard: Consultancy, Advisory role, Honoraria, Expense: Sanofi, Astellas, Janssen, and Ipson; Research funding: Sanofi; Speakers bureau: Sanofi, Janssen. O. Sartor: Advisor: Bellicum Pharmaceuticals, Dendreon; Advisor, Expenses: Bayer, Johnson & Johnson, Medivation, Oncogenex, Sanofi, Tokai Pharmaceuticals, AstraZeneca, Progenics; Funding (Institute): Bayer, Johnson & Johnson, Sanofi, Dendreon, Endocyte, Innocrin Pharma, Progenics. F. Stenner-Liewen: Consultancy, Advisory role, Research, expenses: Sanofi. S. Guillonneau, A. Ozatilgan: Employee: Sanofi. M. Eisenberger: Honoraria, Consultancy, Advisory role: Sanofi, Pfizer, Astellas; Research: Sanofi; Expenses: Sanofi, Pfizer. J.S. de Bono: Honoraria: Sanofi; Advisor: Sanofi, AstraZeneca, GSK, Genentech, Roche, Merck; Speakers bureau: AstraZeneca/MedImmune; Research funding (Institute): AstraZeneca/MedImmune, GSK, Sanofi, Merck Sharp & Dohme, Genmab, Genentech; Patent on abiraterone acetate with prednisone.