813P Treatment of metastatic castration-resistant prostate cancer (mCRPC); Survival by type of progression at initiation of treatment

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Background: The usual sequence of progression events in mCRPC patients treated with new hormonal agents is known: PSA progression, followed by radiological progression and finally pain progression (Ryan, NEJM 2013; Beer, NEJM 2014). Although pain was associated with poor overall survival (OS) in the TAX 327 (Berthold, Clin Cancer Res 2008) and CALGB trials (Halabi, JCO 2008), the influence of type of progression on outcomes is not well documented in phase III trials with chemotherapy. Here, we investigated the impact of type of progression on OS in mCRPC patients receiving docetaxel-based chemotherapy.

Methods: Data from the phase III study VENICE evaluating docetaxel 75mg/m^2 q3w ± aflibercept (Tannock, Lancet Oncol 2013) was used as a training dataset. At randomization, group 1 (G1) had PSA progression only (n = 231), G2 had radiological progression (± PSA) but no pain (n = 348), and G3 had pain (± PSA, ± radiological) (n = 447). The TAX327 definition for pain was used: Mean present pain intensity $\geq$ 2 and/or mean analgesic score $\geq$ 10 within 7 days prior to randomization (Tannock, NEJM 2004). The impact of type of progression on OS was evaluated in a multivariate Cox regression analysis with backward elimination (5% level), stratified for ECOG performance status (0-1 vs 2) and treatment arm.

Results: In the VENICE trial median OS was 28.6 months for G1, 26.3 months for G2 and 16.9 months for G3. Hazard ratios [95% CI] for death were 1.14 [0.92-1.41] in G2

and 2.13 [1.75 - 2.59] in G3 compared to G1. In multivariate analysis, pain at randomization was the strongest predictor of poor OS: HR 1.71, 95% CI 1.39-2.11, vs PSA progression only. Other significant prognostic factors included older age, high alkaline phosphatase, short duration of first androgen deprivation therapy, low hemoglobin level and high neutrophil-lymphocyte ratio. Docetaxel led to $\geq$ 50% decline in PSA in 67.5%, 80.5% and 77% in G1, G2 and G3 respectively.

Conclusions: The type of progression at initiation of first-line chemotherapy in mCRPC is prognostic. Patients with pain at initiation of chemotherapy had a median OS of $\sim$1 year shorter than those having PSA progression only. Validation of these results by an independent dataset (TAX 327) is ongoing. Results will be presented at ESMO.

Legal entity responsible for the study: Sanofi.

Funding: Sanofi.

Disclosure: R.J. van Soest: Honoraria: Astellas, Sanofi, Janssen. I.F. Tannock: Data monitoring reimburse: Janssen, Roche. S. Oudard: Personal fees: Sanofi, Janssen, Astellas. B. Tombal: Advisor, investigator: Sanofi-aventis; Janssen Pharmaceuticals, Inc., Takeda, Astellas, Pharma, Inc., Kyocyt. M. Eisenberger: Consultancy: Sanofi. F. Mercier: Research funding: Sanofi. R. de Wit: Consultant: Sanofi, Merck, Roche; Speaker fees: Merck. All other authors have declared no conflicts of interest.