Global Advanced Research Journal of Medicine and Medical Sciences (ISSN: 2315-5159) Vol. 2(10) pp. 207-208, October, 2013
Available online http://garj.org/garjmms/index.htm

Letter to Editor

Role of time to PSA progression as prognostic factor for overall survival in new therapeutic agents for treatment of patients with metastatic hormone-refractory prostate cancer

Giandomenico Roviello

Medical Oncology Unit, University of Siena, Policlinico Le Scotte, Viale Bracci 11, 53100 Siena, Italy.
E-mail: giandomenicoroviello@hotmail.it; Fax: +390577586139

Accepted 09 October, 2013

Metastatic castration-refractory prostate cancer (mCRPC) is a heterogenous disease, with wide variation in clinical response to hormone manipulation and chemotherapy. More recently, several therapies (Cabazitaxel (Cbz), Abiraterone Acetate (AA) and Enzalutamide (E) have been approved for the management of the mCRCP after Docetaxel failure. Although, Prostate-specific antigen (PSA) has been the most studied biomarker in prostate cancer, little studies described its trend during the administration of one of these new therapies. In order to verify the role of PSA as prognostic marker for patients exposed to Cbz, AA, E, we analyzed the data of repsonse of PSA (PSA response rate (PSA RR) and time to PSA progression (TTPP) reported in the phase III TROPIC, AFFIRM and COU-AA-301 trail. We also established Δ OS (overall survival) by subtracting the value of each OS from the respective value of time to PSA progression. All trails did not fail their primary end point. In regard of Δ OS, we noted a mayor value in the Cbz and E trail (8.7 and 10.1 months), in contrast we observed a minor value in the AA trail (5.6 months). These findings could suggest that an increase of PSA during AA therapy might predict a poor prognosis only for AA. In conclusion, although, our results can not be conclusive, a revision of PSA as prognostic marker is required for the novel agents (Cbz, E, and AA). Meanwhile, we deem that a close monitor of PSA seems particularly important for patients treated with AA and less important during E-based therapy.

Keywords: Cabazitaxel, Abiraterone Acetate, Enzalutamide, Prostate-specific antigen (PSA)

INTRODUCTION

Metastatic castration-refractory prostate cancer (mCRPC) is a heterogenous disease, with wide variation in clinical response to hormone manipulation and chemotherapy. More recently, several therapies (Cabazitaxel, Abiraterone Acetate and Enzalutamide) have been approved for the management of the mCRCP after Docetaxel failure (de Bono et al., 2010; de Bono et al., 2011; Scher et al., 2012). Cabazitaxel (Cbz) is a new semisynthetic taxane, instead, Abiraterone Acetate (AA) and Enzalutamide (E) are a new systemic hormonal therapies. This rapid increase of new effective drugs highlights the need of development of prognostic biomarkers of response.

Although, Prostate-specific antigen (PSA) has been the most studied biomarker in prostate cancer, little studies described its trend during the administration of one of

Table 1. Trials included in the Analysis.

Trial	No. of patients	Median OS (months)	PSA response rate %	Time PSA progression	Δ OS
De Bono et al, 2010 (TROPIC)					
Cbz + P	378	15.1	39.2	6.4	8.7
Mtx + P	377	12.7	17.8	3.1	
De Bono et al, 2011 (COU-AA-301)					
AA + P	797	15.8	29	10.2	5.6
PL + P	398	11.2	6	6.6	
Scher et al, 2010 (AFFIRM)					
E	800	18.4	54	8.3	10.1
PL	399	13.6	1.5	3	

these new therapies. In contrast, during Docetaxel administration, serum PSA as marker of response is also commonly used to guide treatment decisions on individual patients. Therefore, Prostate Cancer Working Group (PCWG2) recommend a baseline and regular (per cycle or monthly) assessment and reporting of PSA levels during therapy of men with mCRPC.

In order to verify the role of PSA as prognostic marker for patients exposed to CBZ, AA and E. We analyzed the data of repsonse of PSA (PSA response rate (PSA RR) and time to PSA progression (TTPP) reported in the phase III TROPIC, AFFIRM and COU-AA-301 trail (de Bono et al., 2010; de Bono et al., 2011; Scher et al., 2012) (Table 1). We also established Δ OS by subtracting the value of each OS from the respective value of time to PSA progression.

All trails did not fail their primary end point. Cbz, E and AA showed a longer OS vs control arm. In all experimental arms, PSA RR and TTPP were reported as better vs respective controls. In regard of Δ OS, we noted a mayor value in the Cbz and E trail (8.7 and 10.1 months), in contrast we observed a minor value in the AA trail (5.6 months). These findings could suggest that an increase of PSA during AA therapy might predict a poor prognosis only for AA. In fact, Δ OS represents the median time from a PSA progression (according PCWG2 criteria) to death. Particularly, in AFFIRM trail, from median TTPP to median time of death spent almost a year. Therefore, monitor of PSA not seem so relevant to predict OS in patients exposed to E.

In conclusion, although, our results can not be conclusive, a revision of PSA as prognostic marker is required for the novel agents (Cbz, E, and AA). Meanwhile, we deem that a close monitor of PSA seems particularly important for patients treated with AA and less important during E-based therapy.

REFERENCES

de Bono JS, Logothetis CJ, Molina A, Fizazi K, North S, Chu L, Chi KN, Jones RJ, et al (2011). Abiraterone and increased survival in metastatic prostate cancer. N. Engl. J. Med. 364(21):1995-2005

de Bono JS, Oudard S, Ozguroglu M, Hansen S, Machiels JP, Kocak I, Gravis G et al (2010). Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. The Lancet. 376: 1147-1154

Scher HI, Fizazi K, Saad F, Taplin ME, Sternberg CN, Miller K, de Wit R, Mulders P, Chi KN et al (2012). Increased survival with enzalutamide in prostate cancer after chemotherapy. N. Engl. J. Med. 367(13):1187-97