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PROSTATE CANCER

Validating early PSA response to enable improved treatment decisions

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A retrospective analysis in patients with metastatic castration-resistant prostate cancer (mCRPC) receiving abiraterone shows that PSA level changes at 4 weeks are associated with overall survival and could be a clinically useful response biomarker associating with treatment effectiveness and facilitating decisions on early therapy adjustments.

Novel endocrine agents, such as abiraterone, are the standard treatment for men with mCRPC. However, achieving optimal therapeutic results is hampered by a lack of markers that enable clinicians to discontinue ineffective drugs early; at present, most patients receive a drug for 12 weeks before a decision to switch treatments is made. "If patients stay on inactive drugs, although they are not responding, they can eventually become too unwell to receive an active alternative agent," points out Johann de Bono, senior author of the new study performed by a team from The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, UK.

The researchers analysed data of PSA level changes in 274 men with mCRPC who had received abiraterone before or after chemotherapy (median follow-up duration 14.6 months). At 4 weeks, median PSA level change was -21.2%; 126 patients (46%) had a reduction of ≥30% and this decline was associated with significantly extended overall survival (25.8 months versus 15.1 months, HR 0.47), regardless of chemotherapy status. Of these 126 men, 84.1% and 71.4% had confirmed 30% and 50% PSA declines at 12 weeks, respectively; however, of those who had not had a ≥30% reduction at 4 weeks, only 10.1% and 6.1% achieved these thresholds at 12 weeks. The decline of PSA levels at 4 weeks was significantly correlated with that at 12 weeks. Furthermore, men who had a ≥30% decline at 4 weeks were 11.7 times more likely to have a 50% decline at 12 weeks compared with those who did not (sensitivity 90.9%, specificity 79.4%).

By contrast, 102 patients (37.2%) had a 25% PSA rise at 4 weeks after commencing abiraterone. Patients who experienced this early increase in PSA levels had significantly shortened overall survival (15.1 months versus 23.8 months, HR 1.7). Of these men, 48% had PSA progression at 12 weeks according to Prostate Cancer Working Group consensus criteria. Furthermore, men who had a ≥25% PSA rise at 4 weeks were 5.5 times more likely to have confirmed PSA progression at 12 weeks (sensitivity 76.6%, specificity 74.8%).

"Our data show that if PSA levels don't fall by 30% in the first month of abiraterone treatment it is highly unlikely that the patient will benefit," summarizes de Bono. "A multicentre, international validation study is now being pursued to confirm these findings."

Clemens Thoma

ORIGINAL ARTICLE Rescigno, P. *et al.* Prostate-specific antigen decline after 4 weeks of treatment with abiraterone acetate and overall survival in patients with metastatic castration-resistant prostate cancer. *Eur.Urol.* http://dx.doi.org/10.1016/j.eururo.2016.02.055 (2016)