Editorial Comment

Editorial Comment to Safety and efficacy of apalutamide in Japanese patients with metastatic castration-sensitive prostate cancer receiving androgen deprivation therapy: Final report for the Japanese subpopulation analysis of the randomized, placebo-controlled, phase III TITAN study

The epidemiology, cancer genomic, and germline polymorphism characteristics of Asian men with prostate cancer (PCa) do have some differences compared to European and North American populations.[1] However, it is uncertain if treatment outcomes of Asian PCa patients differ from that of western men. An analysis of 22 293 US men with *de novo* metastatic PCa showed that Asian American men had a better median overall survival than white American men.[1] Another trans-Pacific comparative study showed that PCa-specific mortality after androgen deprivation therapy (ADT), was lower in the Japanese cohort compared to US men (48% reduction).[1] Thus, population-based analyses of PCa treatment outcomes may have some relevance.

The TITAN trial showed that Apalutamide significantly improved survival outcomes compared with ADT alone, for metastatic castration-sensitive prostate cancer (mCSPC) patients.[2] In this current study, analysis of the Japanese subgroup (TITAN trial) did show a trend in overall survival, time to chemotherapy, and time to pain progression favoring the Apalutamide group, although the *P*-values did not reach significance.[2] This was likely because the trial was not designed or powered to measure statistical significances in smaller subgroups. Perhaps, a larger proportion of Asian patients in the trial may have allowed for more meaningful efficacy analysis.

Health-related quality of life analysis from the TITAN trial suggested that Apalutamide with ADT was well-tolerated.[3] In the current study, the safety profile of Apalutamide in the Japanese subgroup was comparable to the global population, with the exception of a higher incidence of fracture and rash.[2] The Japanese appeared to have high baseline fracture incidence (13% placebo group) with the risk being higher in the Apalutamide group (28.6%), with a specific preponderance in spinal compression fractures. Factors to be considered include the unknown baseline bone mineral density or fracture risks, and that fewer Japanese men in the Apalutamide group received bone targeting agents compared to the placebo group (14.3% *vs* 26.1%) or the Apalutamide group in the overall TITAN trial population (14.3% *vs* 20.2%). Interestingly, the increased fracture risk was not observed in the SPARTAN trial or the East Asian subgroup analysis of the TITAN trial (221 patients from China, Japan, and Korea).[4,5] Hence, the increased bone-related complications may be in part related to the bone management measures of the individual patients studied. Therefore, this study suggests that the need for bone health-related monitoring and early preventive bone management in patients receiving advanced hormonal manipulation cannot be overemphasized. Another intriguing finding of the study was that Japanese men had more skin rash incidences than the overall population (53.6% *vs* 29.2%) following Apalutamide treatment. About 1/3 of skin rash were serious events requiring discontinuation or dose reduction. Uemura *et al*. performed a comprehensive review of the type, severity, and treatment of Apalutamide-related rash in the Japanese subpopulation, thus providing a good management guide for this particular adverse event.[2]

Overall, Uemura *et al*. performed a comprehensive overview of the efficacy and adverse events of Apalutamide in the Japanese subpopulation of the TITAL trial.[2] This article highlights the importance of bone health management, informs of Apalutamide-related rash management strategies, and also makes the case for including more Asian patients in international interventional trials, in patients with advanced PCa.

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Conflict of interest

None declared.

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