Prostate

[177 Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase II trial

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Lancet, 2021 Feb 27;397(10276):797-804. doi: 10.1016/S0140-6736(21)00237-3. Epub 2021 Feb 11.

BACKGROUND

Lutetium-177 [^{177}Lu]Lu-PSMA-617 is a radiolabelled small molecule that delivers β radiation to cells expressing prostate-specific membrane antigen (PSMA), with activity and safety in patients with metastatic castration-resistant prostate cancer. We aimed to compare [^{177}Lu]Lu-PSMA-617 with cabazitaxel in patients with metastatic castration-resistant prostate cancer.

METHODS

We did this multicentre, unblinded, randomised phase II trial at 11 centres in Australia. We recruited men with metastatic castration-resistant prostate cancer for whom cabazitaxel was considered the next appropriate standard treatment. Participants were required to have adequate renal, haematological, and liver function, and an Eastern Cooperative Oncology Group performance status of 0.0-2.0. Previous treatment with androgen receptor-directed therapy was allowed. Men underwent gallium-68 [^{68}Ga]Ga-PSMA-11 and 2-flourine-18[^{18}F]fluoro-2-deoxy-D-glucose (FDG) PET-CT scans. PET eligibility criteria for the trial were PSMA-positive disease, and no sites of metastatic disease with discordant FDG-positive and PSMA-negative findings. Men were randomly assigned (1:1) to [^{177}Lu]Lu-PSMA-617 (6·0-8·5 GBq intravenously every 6 weeks for up to six cycles) or cabazitaxel (20 mg/m^2 intravenously every 3 weeks for up to ten cycles). The primary endpoint was prostate-specific antigen (PSA) response defined by a reduction of at least 50% from baseline. This trial is registered with ClinicalTrials.gov, NCT03392428.

FINDINGS

Between 6 Feb 2018, and 3 Sept 2019, we screened 291 men, of whom 200 were eligible on PET imaging. Study treatment was received by 98 (99%) of 99 men randomly assigned to [^{177}Lu]Lu-PSMA-617 versus 85 (84%) of 101 randomly assigned to cabazitaxel. PSA responses were more frequent among men in the [^{177}Lu]Lu-PSMA-617 group than in the cabazitaxel group (65 vs 37 PSA responses; 66% vs 37% by intention to treat; difference 29% (95% CI 16-42; p<0·0001; and 66% vs 44% by treatment received; difference 23% [9-37]; p=0·0016). Grade 3-4 adverse events occurred in 32 (33%) of 98 men in the [^{177}Lu]Lu-PSMA-617 group versus 45 (53%) of 85 men in the cabazitaxel group. No deaths were attributed to [^{177}Lu]Lu-PSMA-617.

INTERPRETATION

[^{177}Lu]Lu-PSMA-617 compared with cabazitaxel in men with metastatic castration-resistant prostate cancer led to a higher PSA response and fewer grade 3 or 4 adverse events. [^{177}Lu]Lu-PSMA-617 is a new effective class of therapy and a potential alternative to cabazitaxel.