Effects of [^{177}Lu]Lu-PSMA-617 on overall survival in TheraP (ANZUP 1603) versus VISION randomized trials: An Exploratory Analysis

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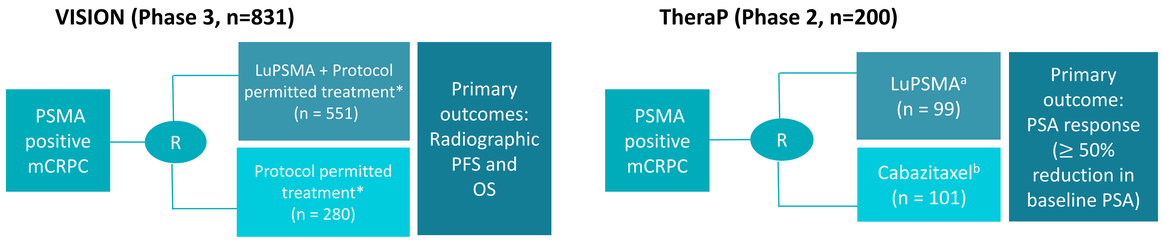
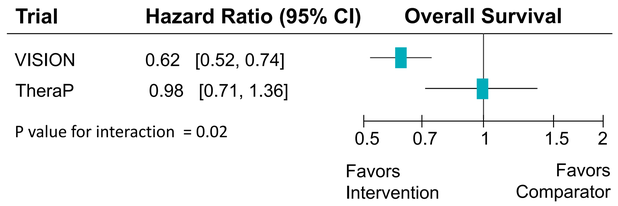
1. Background

LuPSMA in metastatic castration-resistant prostate cancer (mCRPC) was evaluated in the VISION and TheraP RCTs that reported ***remarkably different*** effects on overall survival (OS).



*Did not include cytotoxic chemotherapy, systemic radioisotopes and immunotherapy

[a]32% of participants in LuPSMA group received cabazitaxel after disease progression
[b]20% of participants in Cabazitaxel group received LuPSMA after disease progression



2. Study question

Why are the effects of LuPSMA on OS different between VISION and TheraP?

3. Methods

We evaluated possible explanations for the differing hazard ratios for overall survival.

We compared the **baseline characteristics** of participants from VISION and TheraP.

We explored LuPSMA's effect on OS **if treatment switching on progression did not occur** in TheraP.

Switching-adjusted estimates were obtained using rank-preserving structural failure time model (RPSFTM) and inverse probability censoring weighting (IPCW) approach.

Individual time-to-event data from VISION was extracted from published survival curves.

Overall survival curves from the 2 trials were re-constructed using the Kaplan Meier method and compared using the Cox Proportional Hazards model.

Hazard ratios for overall survival (OS) differed in VISION vs TheraP (0.62 vs 0.98; p = 0.02).

This difference was not explained by treatment switching on progression in TheraP.

OS across trials was similar in the experimental groups treated with LuPSMA, but different in the control groups.

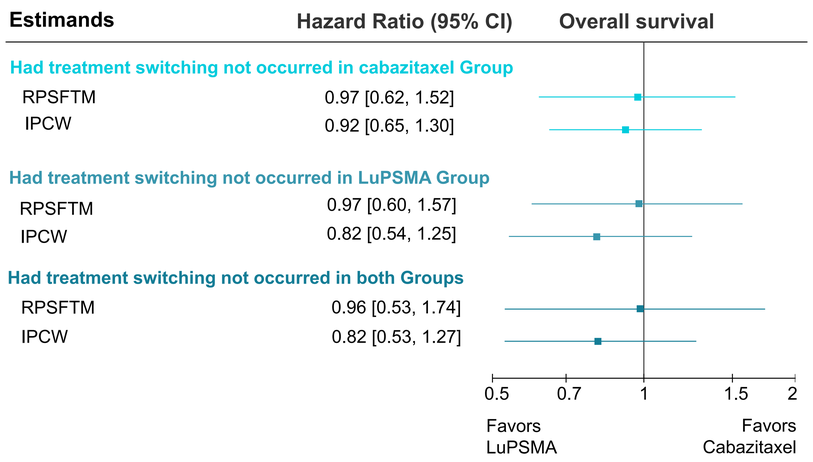
Choice of comparator treatment matters!

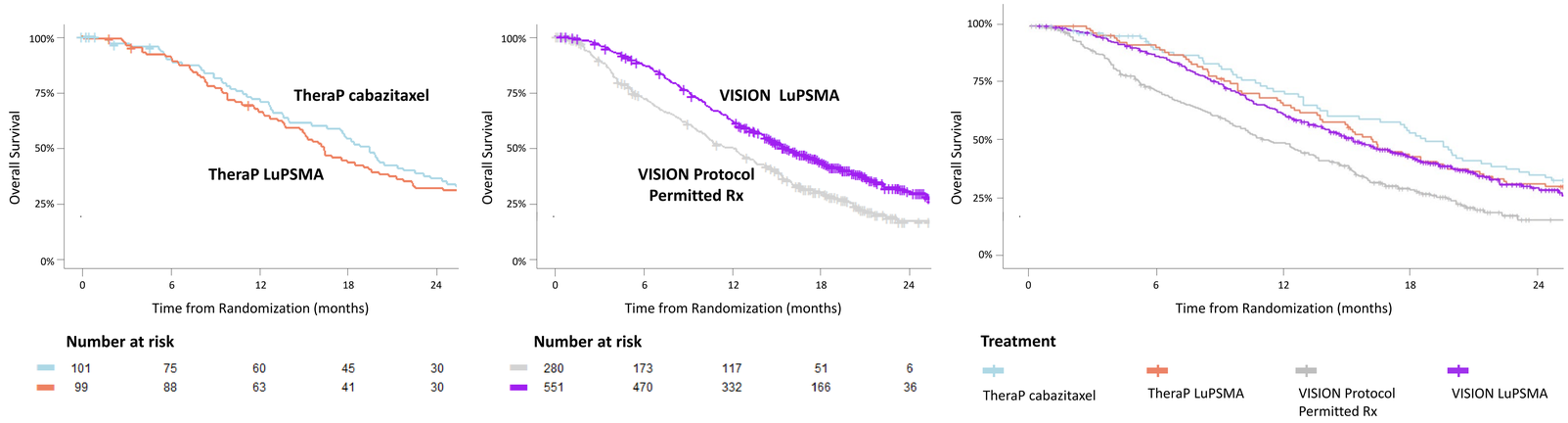
4. Results

Baseline characteristics were similar except that prior cabazitaxel was used by 38% in VISION vs 0% in TheraP.

OS similar in experimental groups of VISION and TheraP (both treated with LuPSMA)
OS shorter in control group of VISION (Protocol Permitted Rx) than TheraP (cabazitaxel)

Cross trial treatment comparisons	Unadjusted Hazard Ratio (95% CI)
TheraP LuPSMA vs VISION LuPSMA (reference)	0.92 (0.70 – 1.19)
TheraP cabazitaxel vs VISION Protocol Permitted Rx (reference)	0.57 (0.43 – 0.75)





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