2. Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs)
14. Genitourinary Tract Disorders (including Climacteric Disorders)

References

Koga N, Moriya F, Waki K, et al. Immunological efficacy of herbal medicines in prostate cancer patients treated by personalized peptide vaccine. *Cancer Science* 2017; 108: 2326-32. Pubmed ID: 28898532

1. Objectives

To evaluate the immune-enhancing efficacy and safety of Kampo medicines using hochuekkito（補中益気湯）and keishibukuryogan（桂枝茯苓丸)in combination with personalized cancer peptide vaccination (PPV) in patients with castration-resistant prostate cancer (CRPC)

2. Design

Randomized controlled trial (RCT)

3. Setting

One university hospital, Japan

4. Participants

Seventy patients with CRPC aged 20 years or older with a Performance Status score of 0 or 1 (ECOG).

Inclusion criteria: life expectancy of 12 weeks or more, HLA haplotype of A2, A24, A26, A3, A11, A31, or A33, and normal hepatorenal functions.

Exclusion criteria: acute infection, history of severe allergic reactions, cardiac or pulmonary insufficiency

5. Intervention

Arm 1: PPV (weekly 8 times) plus TSUMURA Hochuekkito（補中益気湯）Extract Granules 7.5 g/day and TSUMURA Keishibukuryogan（桂枝茯苓丸）Extract Granules 7.5 g/day (2.5 g t.i.d. administered orally before meals for 50 days) (n=31)

Arm 2: PPV alone (weekly 8 times) (n=35)

6. Main outcome measures

Primary endpoint: immune response to PPV.

Secondary endpoints: overall survival (OS), progression-free survival (PFS), and safety.

7. Main results

Four patients withdrew consent prior to treatment in Arm 1. Treatment was discontinued because of disease progression or death in 3 patients in Arm 1 and 4 patients in Arm 2. At the end of follow-up, 19 patients in Arm 1 (63%; median duration of follow-up 14.9 months) and 26 patients in Arm 2 (74%; 13.6 months) had disease progression or died. The OS and PFS did not differ significantly between the arms. The baseline and Week 8 cancer peptide-specific IgG, CTL, and regulatory T cells (Treg) did not significantly differ between the arms. Comparing before to after the treatment, the frequency of monocytic myeloid-derived suppressor cells (Mo-MDSC) (before-after: 1.91%–1.92%) and the IL-6 level (19.2 pg/mL–16.1 pg/mL) were stable in Arm 1 but significantly increased in Arm 2 (0.91%–1.49% for Mo-MDSC [P=0.012] and 9.2 pg/mL–19.4 pg/mL for IL-6[P=0.043]).

8. Conclusion

In CRPC patients, the use of herbal medicines of hochuekkito and keishibukuryogan during PPV treatment had no impact on clinical outcome but has the potential to modify the immune response to PPV.

9. From Kampo medicine perspective

None

10. Safety assessment in the article

No treatment-related deaths occurred in either arm. Adverse events such as injection site reactions did not differ between the two treatment arms. Appetite loss was less frequent in the PPV + herbal medicines arm than in the PPV alone arm.

11. Abstractor's comments

While cancer immunotherapies are entering a new phase, this pioneering study applied a novel immunotherapy with personalized cancer peptide vaccination (PPV) to patients with CRPC, and analyzed whether herbal medicines could modify the immune response to PPV. Since the RCT design was employed, the study yielded objective results, and was meaningful both basically and clinically. In Arm 1, the frequency of Mo-MDSC (%) and the IL-6 level were stable, suggesting the possibility that these herbal medications may prevent a decrease in the immune response to PPV, although clinical endpoints unfortunately failed to show significant differences. The results of this study are clinically interesting, considering that the authors previously reported significantly lower IL-6 levels in long-term survivors of prostate cancer. As the authors state that more research is needed, new results are awaited in the future.

12. Abstractor and date

Kogure T, 1 June 2020.