2. Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs)

Reference

Kono T, Hata T, Morita S, et al. Goshajinkigan oxaliplatin neurotoxicity evaluation (GONE): a phase 2, multicenter, randomized, double-blind, placebo-controlled trial of goshajinkigan to prevent oxaliplatin-induced neuropathy. *Cancer Chemotherapy and Pharmacology* 2013; 72: 1283-90. CENTRAL ID: CN-00961704, Pubmed ID: 24121454

1. Objectives

To investigate the inhibitory effect of TSUMURA Goshajinkigan (牛車腎気丸) Extract Granules(TJ-107) on oxaliplatin-induced peripheral neuropathy (OPN).

2. Design

Double-blind randomized controlled trial (DB-RCT).

3. Setting

Twenty centers including university hospitals, Japan.

4. Participants

Patients with pathologically confirmed colorectal cancer receiving a chemotherapy regimen including oxaliplatin (85 mg/m^2 oxaliplatin every two weeks in FOLFOX4 or mFOLFOX6) (n=93).

5. Intervention

Arm 1: TSUMURA Goshajinkigan (牛車腎気丸) Extract Granules (2.5 g t.i.d.) administered before meals, continued for 26 weeks after start of chemotherapy (n=47).

Arm 2: placebo administered under the same schedule as above (control group, n=46).

6. Main outcome measures

An investigating physician graded peripheral neuropathy and other adverse effects between 0 and 4 according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) ver. 3 before the start of chemotherapy, then every 2 weeks (8 times), then every 4 weeks until the 26th week. The patients also graded themselves for degree of numbness before therapy and then before each chemotherapy treatment between grade 0 and 4 according to the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity 12 items questionnaire (FACT/GOG-Ntx-12).

7. Main results

Three patients in arm 1 and one patient in arm 2 dropped out of the study. OPN appearing by the 8th anticancer drug administration and graded at least grade 2 occurred in 39% of arm 1 and in 51% of the placebo group, and of those, 7% in arm 1 and 13% in arm 2 had grade 3: arm 1 had the lower scores in both cases. TJ-107 inhibited the advance of OPN severity, with the median length of time to reach at least Gr. 2 being 5.5 months in arm 1 and 3.9 months in arm 2. The percentage of patients displaying OPN by the 26th week was 54.1% in arm 1 and 62.5% in arm 2. The degree of OPN as measured by the patients showed no significant difference between groups in the 8th and 26th weeks. There was no difference between the effects of TJ-107 for FOLFOX4 and mFOLFOX6. There was no difference between groups for other adverse effects, although there were fewer cases of vomiting in arm 1. There was no difference between groups for antitumor effects (percentages of complete response [CR] + partial response [PR] and CR+PR+ stable disease [SD]): TJ-107 had no adverse effect.

8. Conclusions

Goshajinkigan delays onset of peripheral neuropathy of Grade 2 or more induced by oxaliplatin.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There was no difference in adverse drug reaction incidence for arms 1 and 2. There was no issue with the safety of goshajinkigan.

11. Abstractor's comments

The results of chemotherapy for colorectal cancer have dramatically improved with the advent of oxaliplatin in recent years. However, overcoming OPN has been an issue as it is a dose-limiting toxicity. The authors used goshajinkigan for this study as it has previously been useful for diabetes-induced peripheral neuropathy. Starting with a retrospective trial, they conducted a multi-center RCT before this multi-center DB-RCT, which suggested the preventative effect of goshajinkigan for OPN. The authors consider that goshajinkigan's main mechanism of action lies in the analgesic action of bushi, as well as the neuroprotection, neurotransmitter modification, bloodstream improvement mediated by the production of nitric oxide, and various actions of the other crude drugs. However, as the quantity of bushi in goshajinkigan is no more than 1 g per day, increasing the quantity of bushi may increase its anti-OPN effect. Further investigation into the therapeutic effects of Kampo for OPN under a protocol including an increased quantity of powdered processed Aconite Root for ethical dispensing in the goshajinkigan is anticipated.

12. Abstractor and date

Hoshino E. 6 June 2015.