ABSTRACT: In order to evaluate the efficacy of combined immunochemotherapy with mitomycin-C, tegafur, PSK and/or OK-432 as an adjunct for curatively resected gastric cancer, a prospective randomized controlled study using the envelope method was performed, in which 266 institutions from around Japan participated. The 3 year survival rates for all cases, and for ps(+)? n(+) cases, were insignificantly higher in the immunochemotherapy groups receiving PSK and/or OK-432 than in the control group. However, because 28.2 per cent of the cases were excluded from the final statistical analyses, the results of this study may have questionable statistical credibility. Changes in the stimulation index (SI) suggest that the administration of PSK may result in an inhibition of the immunosuppressive activity of cancer patients. The high SI group showed a significantly higher 4 year survival rate than the low SI group.

KEY WORDS: gastric cancer, mitomycin-C, tegafur, PSK, OK-432

INTRODUCTION

Many kinds of non-specific immunotherapeutic agents are clinically applied in the treatment of cancer in Japan, and the different mechanisms of each drug have been reported. In Japan, PSK and OK-432 are the
non-specific immunostimulating agents most broadly used in clinical fields. It is interesting that PSK, when administered to normal mice showed no enhancing effect on immune activity, but when administered to tumor bearing mice with reduced immune activity, a recovery effect was observed. On the other hand, it has been reported that the administration of OK-432 to normal mice activated macrophages and T-lymphocytes and increased their immunoreactivity. The combined use of these two agents thus seemed reasonable and was therefore selected for investigation. Cooperative project No. 1 of the Japanese Foundation for Multidisciplinary Treatment of Cancer was established for observing the effects of the combined use of PSK and/or OK-432 as an adjuvant immunotherapy after surgery for gastric cancer. In this paper, the 3 year survival rates and changes in immunoparameters, such as the Stimulation Index (SI) and Immunosuppressive Acidic Protein (IAP) are reported.

**MATERIALS AND METHODS**

*Treatment schedule*

Two hundred and sixty six institutions participated in this co-operative study in which gastric cancer patients aged under 75 years, who had undergone no previous treatment, including surgery, radiation, chemotherapy, or immunotherapy, and whose disease complied with the following conditions, were entered.

1. Cases of Stages II or III, diagnosed macroscopically, and curative resection cases, excluding m-n classification according to the General Rules for Gastric Cancer Study.
2. Cases in which a histologically definite diagnosis of gastric cancer had been obtained.
3. Cases having no malignant cancer in any other region at the same or different times.
4. Cases having no multiple gastric cancers.

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment Regimen</th>
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<tbody>
<tr>
<td>Group A</td>
<td>Mitomycin-C 20mg (10mg) Op. 2W Tegafur 8Mo</td>
</tr>
<tr>
<td>Group B</td>
<td>Mitomycin-C 20mg (10mg) Op. 2W PSK 8Mo</td>
</tr>
<tr>
<td>Group C</td>
<td>Mitomycin-C 20mg (10mg) Op. 2W PSK OK-432 8Mo</td>
</tr>
<tr>
<td>Group D</td>
<td>Mitomycin-C 20mg (10mg) Op. 2W PSK OK-432 8Mo</td>
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</tbody>
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Fig. 1. Treatment regimen in each group.

- Tegafur: 600 mg/day, to a total 150 g (p.o.)
- PSK: 3 g/day, to a total 750 g (p.o.)
- OK-432: 0.5~5.0 KE/day, to a total 100 KE (i.c. or i.m.)

at the time of operation.

All cases were randomly allocated to one of four therapeutic groups as shown below (Fig. 1) by using the envelope method. In each group, mitomycin C (MMC) was administered intravenously on the day of operation and the following day, at dosages of 20 mg and 10 mg respectively. However, the additional 10 mg was not given in cases where the patient's body weight was less than 40 kg or if the age was 70 years or over, or in cases where surgery was accompanied by complicated resection of other organs. In Group A, 600 mg/day of Tegafur was administered orally for 8 months, commencing from 2 weeks after the operation, until a total dose of 150 g had been given. In Group B, PSK was added to the regimen of Group A at a dose of 3 g/day, administered orally, also commencing from 2 weeks after the operation and continuing for 8 months, until a total dose of 750 g of PSK had been given. In Group C, OK-432 was added to the regimen of Group A, commencing with an intradermal injection of OK-432 on the day of the operation, after which the dose was in-