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Clinical Trial

Health-related quality of life of adjuvant chemotherapy with S-1 versus gemcitabine for resected pancreatic cancer: Results from a randomised phase III trial (JASPAC 01)

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Abstract ***Background:*** Adjuvant chemotherapy with S-1 for resected pancreatic cancer demonstrated survival benefits compared with gemcitabine in the JASPAC 01 trial. We investigated the effect of these agents on health-related quality of life (HRQOL) of patients in the JASPAC 01 trial.
Methods: Patients with resected pancreatic cancer were randomly assigned to receive gemcitabine (1000 mg/m^2 weekly for three of four weeks for up to six cycles) or S-1 (40, 50, or 60 mg twice daily for four of six weeks for up to four cycles). HRQOL was assessed using the EuroQol-5D-3L (EQ-5D) questionnaire at baseline, months three and six, and every 6 months thereafter. HRQOL end-points included change in EQ-5D index from baseline, responses to five items in the EQ-5D, and quality-adjusted life months up to 24 months.
Results: Of randomised 385 patients, 354 patients were included in HRQOL analysis. Mean change in the EQ-5D index was similar in the S-1 and gemcitabine groups within 6 months from treatment initiation (difference, 0.024; $P = 0.112$), whereas corresponding mean from 12 to 24 months was better in the S-1 group than in the gemcitabine group (difference, 0.071; $P < 0.001$). Problems in mobility and pain/discomfort were also less frequent in the S-1 group than in the gemcitabine group in that period. Quality-adjusted life months were longer in the S-1 group than in the gemcitabine group ($P < 0.001$).
Conclusion: Adjuvant chemotherapy with S-1 does not improve HRQOL within 6 months from treatment initiation but does improve HRQOL thereafter and quality-adjusted life months.
Clinical trial registration number: UMIN000000655 at UMIN CTR.

1. Introduction

We previously reported the efficacy and safety of adjuvant chemotherapy with the oral fluoropyrimidine drug S-1 (TS-1; Taiho Pharmaceutical Co., Ltd., Tokyo, Japan) versus gemcitabine for resected pancreatic cancer in a randomised, open-label, non-inferiority, phase III trial: the Japan Adjuvant Study Group of Pancreatic Cancer (JASPAC) 01 trial [1]. This trial demonstrated not only non-inferior but also superior overall survival (OS) and relapse-free survival (RFS) in patients who received S-1 compared with those who received gemcitabine (hazard ratio, 0.57 and 0.60; $P < 0.001$ and $P < 0.001$, respectively). Although toxicities of both treatments were well tolerated, their profiles differed; haematologic adverse events were more common with gemcitabine, whereas gastrointestinal adverse events were more common with S-1.

In addition to survival and safety outcomes, assessment of health-related quality of life (HRQOL) is important in evaluating adjuvant chemotherapy for resected pancreatic cancer. Even with novel adjuvant chemotherapy after a potentially curative resection, patients often suffer an early relapse, resulting in a relatively short OS, as reported in recent randomised phase III trials [1,2]. Maintaining good HRQOL over a short OS is important for patients with this disease. Moreover, the effect of S-1 on HRQOL during adjuvant chemotherapy should be investigated because of differences in toxicity profiles and administration routes. Given these issues, HRQOL can provide important information for informed decision-making on treatment of resected pancreatic cancer [3]. So far, few detailed HRQOL results have been reported in randomised phase III trials of adjuvant chemotherapy for this disease [2,4–6].