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Prognostic impact of detecting viable circulating tumour cells in gastric cancer patients using a telomerase-specific viral agent: a prospective study

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Abstract

Background: The identification of circulating tumour cells (CTCs) in peripheral blood is a useful approach to estimate prognosis, monitor disease progression, and measure treatment effects in various malignancies. However, clinical relevance of CTCs is controversial. We attempted to detect viable CTCs in the peripheral blood of gastric cancer patients using a telomerase-specific viral agent.

Methods: We took a 7.5-ml blood sample from 65 treatment-negative gastric cancer patients before surgery and 10 healthy volunteers. We detected viable CTCs in the blood samples after incubating them with a telomerase-specific, replication-selective, oncolytic adenoviral agent carrying the green fluorescent protein (GFP) gene (OBP-401). GFP-positive CTCs were defined as having a diameter of at least 7.735 μm; this threshold was determined by receiver operating characteristic curve analysis. GFP-positive cells were counted under a fluorescence microscope.

Results: There was a significant difference in overall survival among the patients with 0–4 and those with ≥5 GFP-positive CTCs in the stage I–IV disease group and stage II–IV advanced disease group. The number of GFP-positive CTCs was not related to cancer stage. Among the pathological findings, the number of GFP-positive CTCs was only significantly related to venous invasion, although there were trends towards more GFP-positive CTCs with disease progression (tumour depth, lymph node metastasis, distant metastasis, lymphatic invasion, and histological type).

Conclusions: There was a significant relationship between the number of GFP-positive CTCs and overall survival in the patients with gastric cancer. The detection of CTCs using OBP-401 may be useful for prognostic evaluation.

Trial registration: University Hospital Medical Information Network in Japan, UMIN000002018.

Keywords: Circulating tumour cells, Gastric cancer, Telomerase

Background

Distant metastasis of a solid tumour is a strong prognostic factor [1-3]. The existence of circulating tumour cells (CTCs) in peripheral blood suggests that a patient is in a systemic disease phase [4]. The identification of CTCs in peripheral blood is a useful approach to estimate prognosis, monitor disease progression, and measure treatment effects in breast, prostate, skin, colon and gastrointestinal malignancies. Therefore, various methods have been developed to detect CTCs, and are occasionally used in combination. Common techniques for the enrichment and detection of CTCs are density gradient separation [5], direct enrichment by filtration [6,7], immunomagnetic separation [8], flow cytometry [9], real-time reverse transcriptase polymerase chain reaction (RT-PCR) [10,11], and microchip technology [12].

Cell enrichment by density gradient separation is performed using commercial kits such as OncoQuick®

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