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Original Research

Dynamic evaluation of circulating tumour cells in patients with advanced gastric and oesogastric junction adenocarcinoma: Prognostic value and early assessment of therapeutic effects

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Abstract ***Background:*** The identification of dynamic biomarkers in advanced gastric and oesogastric junction adenocarcinoma (GOA) could help to tailor strategies for each patient. Enumeration of circulating tumour cells (CTCs) is approved by the US Food and Drug Administration in breast, colon and prostate cancer but is not in advanced GOA. Our study aims to establish the optimal threshold and the clinical significance of CTC count in advanced GOA before and during treatment.
Methods: One hundred six patients with untreated advanced GOA were included in the ancillary study of the PRODIGE 17-ACCORD 20 trial. CTCs were detected in the peripheral blood using the CellSearch system on day 0 (D0) and day 28 (D28). The prognostic value of CTCs at D0 and D28 was analysed by testing several thresholds.
Results: At baseline, median CTC count was 1 (range, 0–415). While CTCs $\geq$1, 2 or 3 at D0 were all significantly associated with worse overall survival (OS) and progression-free survival (PFS), CTCs $\geq$2 were the optimal threshold, on D0 or D28. CTCs $\geq$2 at D28 were also predictive of disease control. Taking into account both D0 and D28 CTC count defined 3 groups (low/low, high/low and low-high/high) with significantly different PFS ($p = 0.0002$) and OS ($p = 0.003$).
Conclusion: Quantification of CTCs at baseline and during treatment may be a useful prognostic tool in advanced GOA, as it is associated with worse PFS and OS. A threshold $\geq$2 CTCs seems to have the best discriminant value. Change in CTC count between baseline and D28 could help to tailor treatment to each individual patient.

Key message

Circulating tumor cells (CTC) count at baseline and day 28 is a strong prognostic factor in patients with advanced gastric and esogastric junction adenocarcinoma. CTC count at day 28 is also predictive of disease control. Therefore, evolution of CTC count between baseline and D28 could help to early adjust treatment.

1. Introduction

Gastric and oesogastric junction adenocarcinoma (GOA) is a major health problem, with 951,000 new cases worldwide in 2012 [1]. The few prognostic factors previously reported relate mostly to the host, as Eastern Cooperative Oncology Group (ECOG) performance status (PS), age and sex. Other prognostic factors related to the tumour are still debated, such as the impact of the pathological type and the location of the tumour [2]. The identification of biomarkers before and during the treatment would be of great value, since they could help to tailor treatment regimens and strategies better for each individual patient situation. It could be interesting to assess therapeutic efficacy early, in order to switch to a second-line therapy as soon as possible in patients with disease resistant to first-line treatment. Indeed, a large proportion of patients do not receive more than one line of treatment because of their poor general condition and rapid tumour progression, despite new second-line therapy such as antiangiogenics [3,4], irinotecan [5] and taxanes [6,7] have demonstrated a survival advantage. On the other hand, some patients may benefit from aggressive approaches such as intraperitoneal treatments or even surgical removal of oligometastatic disease, but we are currently unable to identify them correctly.

Circulating tumour cells (CTCs) could reflect tumour burden and has been proposed as a prognostic factor and a follow-up tool in several cancer types [8–10]. The CellSearch system uses an immunomagnetic method to detect low numbers of cells with high sensitivity and specificity. The Food and Drug Administration (FDA) has approved this technique in metastatic breast, prostate and colorectal cancer patients as an aid to prognosis before and during the treatment [8–10]. The prognostic relevance of CTC detection in gastric cancer patients remains controversial, and there is no consensus regarding the optimal threshold.

To investigate the clinical significance of CTCs in advanced GOA, we performed an evaluation of CTCs in patients with newly diagnosed advanced GOA and treated with chemotherapy based on 5FU plus platinum in the randomised MEGA (Met or EGFR inhibition in Gastroesophageal Adenocarcinoma)/PRODIGE 17 therapeutic trial. The objectives of this translational study were to assess the prognostic value of CTCs at baseline (day 0 [D0]) and day 28 (D28), the optimal threshold and the value of CTC count evolution in assessing the therapeutic effect.