Title: Evaluation of CA 19-9, a predictive biomarker of response and survival in patients undergoing chemotherapy for metastatic pancreatic ductal adenocarcinoma

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Background
Patients with pancreatic ductal adenocarcinoma (PDAC) are subject to poor outcomes, with a median overall survival of 6-12 months in patients treated with palliative chemotherapy for metastatic disease. Appropriate patient selection for palliative chemotherapy is therefore critical to avoid detrimental outcomes. Although CA 19-9 is the only recommended biomarker for clinical use in PDAC, it is not routinely used as a predictive marker of response to chemotherapy. We hypothesised that falls in CA 19-9 > 50% at the end of chemotherapy are associated with improved survival outcomes.

Method
We conducted a retrospective review of patients treated with palliative chemotherapy for metastatic PDAC over a 9-year period, at two separate university teaching hospitals in London, UK (n = 179). Median progression free (PFS) and overall survival (OS) were correlated with patient specific factors including CA 19-9, gender, age, number of visceral sites affected, previous surgical / adjuvant therapy and palliative chemotherapy.

Results
93% of patients had an elevated CA 19-9 at diagnosis. Median PFS and OS were significantly greater when serum CA 19-9 fell > 50% from the initiation of chemotherapy to the end of treatment. Patients demonstrating a fall in CA 19-9 >50%, who received 1 line of palliative chemotherapy, had a median PFS of 5.3 months compared with 3 months for patients who did not (p= <0.001), regardless of whether they received subsequent lines of chemotherapy. Patients only receiving 1 line of chemotherapy with a fall in CA 19-9 >50% had a PFS of 4.5 months, compared with 2.9 months (p= 0.005).

In patients who received 1st line chemotherapy (n=150), median OS was 5.6 months, when associated with a fall in CA 19-9 >50%, compared with 5.3 months (p= 0.017). Similarly, those who received 2nd line chemotherapy (n=29) had an OS of 16 months versus 13.4 months (p= 0.703). Compared with the other measured variables, for 1st line treatment, this was an independent prognostic factor in multivariate analysis. We also demonstrated that the higher the level of CA 19-9, both prior to chemotherapy and at the end of treatment, the poorer the prognosis and earlier the relapse. Those with pre-treatment CA 19-9 levels between 0-100 kU/L had a median OS of 6.9 months (p= 0.034) compared with 4.6 months (p= <0.001), when greater than 1000 kU/L.

Conclusion
We demonstrate that patients receiving chemotherapy with lower baseline CA 19-9 levels and reductions > 50% at the end of treatment are associated with improved survival outcomes. Regular CA 19-9 testing should be used to aid decision making in these patients. These results should be validated with prospective data from randomised clinical trials of patients undergoing palliative chemotherapy for metastatic PDAC.
References