Pleural effusions: diagnosis and prognosis

S21 A PROSPECTIVE STUDY USING SERUM MESOTHELIN TO MONITOR MALIGNANT PLEURAL MESOTHELIOMA

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10.1136/thoraxjnl-2017-210983.27

Background Radiological monitoring of malignant pleural mesothelioma (MPM) using modified RECIST criteria is limited by low sensitivity and inter-observer variability. Serial serum mesothelin measurement has shown utility in the assessment of treatment response during chemotherapy but has never been assessed in the longer term follow up of patients.
Methods This is a single centre study of consecutive patients diagnosed with MPM who received chemotherapy or best supportive care (BSC). Serum mesothelin measurements with paired 6 monthly CT scans were performed following the completion of chemotherapy, or from baseline in the BSC group. Changes in mesothelin were correlated with radiological progression and overall survival.
Results Forty-one patients with MPM were recruited and followed up for a minimum of 12 months (range 12–21 months). The majority of patients (n=23) received chemotherapy with pemetrexed and cisplatin. Across the cohort a 10% rise in serum mesothelin could predict radiological progression with a sensitivity of 96% (IQR; 79–100) and specificity of 74% (IQR; 50–91) (figure 1). Sensitivity fell to 80% in sarcomatoid only disease. Patients with a rising mesothelin at 6 months had significantly worse overall survival (175 days) compared to stable/falling levels (448 days) (p=0.003).
Conclusions This is the first study to assess serum mesothelin's ability to detect progression of MPM following chemotherapy or during BSC. A 10% rise in serum mesothelin level showed excellent sensitivity at predicting progressive disease. Mesothelin measurement has several advantages over serial CT imaging including reducing hospital visits and cost.

S22 BAP1 EXPRESSION AND TREATMENT OUTCOMES IN MALIGNANT PLEURAL MESOTHELIOMA IN A PROSPECTIVE UK BASED CLINICAL TRIAL

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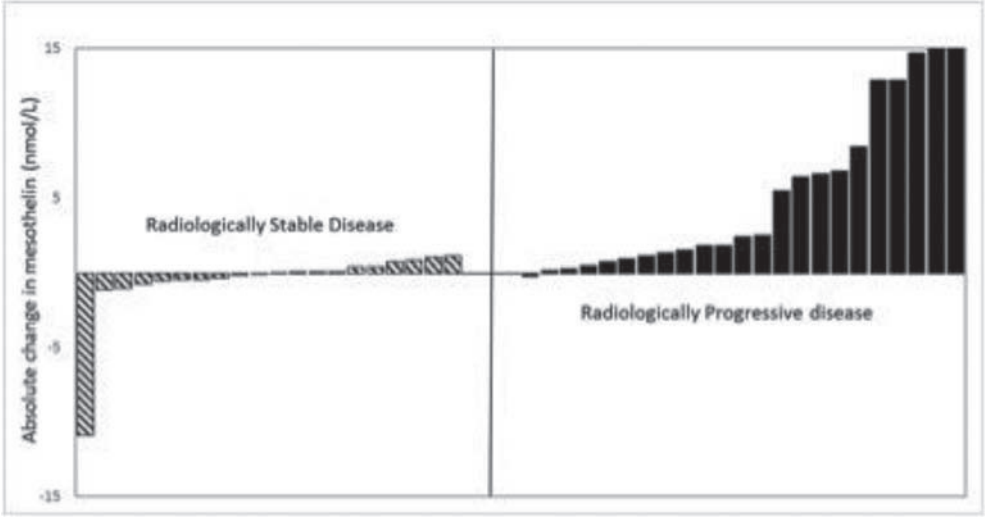
10.1136/thoraxjnl-2017-210983.28

Objectives Genomic studies of malignant pleural mesothelioma (MPM) have identified frequent mutations in the nuclear deubiquitinase BRCA Associated Protein 1 (BAP1). Previous studies have identified 100% correlation between BAP1 nuclear staining and wild type BAP1 status, pointing to immunohistochemistry (IHC) as a reliable technique to detect BAP1 molecular status. The objective of this study is to assess BAP1 expression and infer molecular status using IHC in a cohort from a prospective UK based clinical trial (MSO1). Furthermore, we aim to evaluate the effect of BAP1 status on treatment outcomes.
Methods BAP1 expression was evaluated by IHC in 79 biopsies independently by two consultant histopathologists. Cases were considered positive (wild type BAP1) if strong nuclear staining was present and negative (mutant BAP1) if absent.
Results Assessment of BAP1 expression was concordant in 77 of 79 cases (97%). BAP1 expression was negative in 66 of these 77 cases (86%). Patient characteristics and the effect of BAP1 expression on treatment outcomes are in Table 1.
Conclusions BAP1 expression was negative in 86% of MPM tumours suggesting a high frequency of BAP1 mutations in this UK cohort. No significant differences in clinical characteristics or outcomes were noted between cases with positive or negative BAP1 expression overall. When analysed by treatment subgroup, there was a trend towards a survival benefit in cases with negative BAP1 expression (BAP1 mutants) in the ASC plus vinorelbine arm, but no statistically significant difference in outcomes within any treatment arm. We plan to further validate our findings by correlating BAP1 expression directly with BAP1 molecular status in this cohort using laser capture microdissection and sequencing.



Abstract S21 Figure 1