Active symptom control (ASC) with or without chemotherapy in the treatment of patients with malignant pleural mesothelioma. The UK Medical Research Council/British Thoracic Society MS01 randomised clinical trial

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Background: Mesothelioma is invariably fatal and virtually all treatments are given with the primary aim of relieving symptoms. Although chemotherapy is now widely used it has never been compared in a randomized trial with ASC alone. Two chemotherapy regimens were chosen for investigation: MVP and vinorelbine which had both shown good palliation in phase II studies.

Methods: Patients with malignant pleural mesothelioma were randomized to (a) ASC alone, (b) ASC+MVP (4 × 3-weekly cycles of mitomycin 6 mg/m^2, vinblastine 6 mg/m^2, and cisplatin 50 mg/m^2), and (c) ASC+N (12 × weekly injections of vinorelbine 30 mg/m^2). The primary endpoint was overall survival, and secondary endpoints were response, toxicity, palliation, and quality of life (QL). QL was assessed by patients completing the EORTC QLQ-C30. Slow accrual forced a re-design from a 3-arm to a 2-arm trial by combining the 2 chemotherapy arms and aiming to accrue 420 patients, to reliably detect a 3-month improvement in median survival (76% power, 5% significance level).

Results: A total of 409 patients were randomized (136 ASC, 137 ASC+MVP, and 136 ASC+N). The median age of the patients was 65 years, 91% were male, 23% performance status (PS) 0, 63% PS 1, 73% epithelial histology, 33% stage III and 48% stage IV. The main (moderate or severe) symptoms at the time of randomization were: lethargy (54%), chest pain (51%), breathlessness (41%) and sweating (30%). In the MVP arm 61% of patients received 4 cycles and in the N arm 49% received at least 10 weekly cycles of vinorelbine. All 3 treatment groups resulted in good palliation (defined as prevention, control or improvement) at 6 months. No differences between treatments or over time were observed in 4 pre-defined QL subscales (physical functioning, dyspnoea, pain and global QL). 349 patients have died, and a small, but non-significant, survival benefit was seen for ASC+CT (HR 0.89, 95% CI 0.72, 1.12, p = 0.32). The median and 1-year survival for the ASC arm was 7.6 months and 30%, and applying the HR to this, gave 8.5 months and 34% for the ASC+CT arm. Exploratory analyses suggested a survival advantage for vinorelbine compared with ASC (HR 0.81, 95% CI 0.63, 1.05).

Conclusions: The MRC/BTS MS01 trial is the 2nd largest ever randomized trial in mesothelioma and although overall the addition of chemotherapy to ASC did not result in a statistically significant survival benefit, there was a suggestion that vinorelbine should be investigated further.