



Mesothelin and osteopontin

To the Editor:

The review by PANTAZOPOULOS *et al.* [1] on mesothelin and osteopontin was timely and well written. However, I would like to comment on some of the statements that were made. Firstly, it states that “patients with early-stage disease can survive for more than 5 years if the tumour is promptly resected”. This implies that resection would benefit the patient, which is far from proven; there is no randomised study showing this, except for the much criticised the Mesothelioma and Radical Surgery (MARS) study [2] in England, which showed that resection considerably shortened survival. The good survival seen by SUGARBAKER *et al.* [3] and in other studies can be explained by very strict selection and these patients are likely to survive at least as long without resection, as seen from studies where “operable” patients were treated conservatively. Furthermore, the authors claim that “early diagnosis offers the best hope for a favourable prognosis”, which is an interesting but unproven hypothesis. There is of course a lead time bias, the earlier the diagnosis the longer the survival, but unfortunately we do not know whether early intervention will in fact prolong survival. Thus, screening for mesothelioma in risk groups is not indicated at present, screening should only be performed in diseases where the prognosis has been shown to be improved by early discovery.

I fully agree with the other main conclusions in the review, namely that mesothelin, in serum or pleura, can be a useful aid in the diagnostic setup and also used for monitoring patients for recurrence.



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Early stage mesothelioma and surgery: where do we stand?

<http://ow.ly/kRTJ2>

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- 2 Treasure T, Lang-Lazdunski L, Waller D, *et al.* Extra-pleural pneumonectomy *versus* no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study. *Lancet Oncol* 2011; 12: 763–772.
- 3 Sugarbaker DJ, Flores RM, Jaklitsch MT, *et al.* Resection margins, extrapleural nodal status, and cell type determine postoperative long-term survival in trimodality therapy of malignant pleural mesothelioma: results in 183 patients. *J Thorac Cardiovasc Surg* 1999; 117: 54–63.

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From the authors:

We would like to thank G. Hillerdal for his interest in our article [1] and for giving us the opportunity to make some comments regarding multimodality therapy and early stage disease.

SUGARBAKER *et al.* [2] reported a groundbreaking result in 1999: patients with early stage malignant pleural mesothelioma (MPM) had a 5-year survival rate after trimodality therapy that exceeded 40%. Since then, there have been a number of subsequent prospective and retrospective series, which have all demonstrated a median survival of 16.8–25.5 months [3–8]. Moreover, on September 11, 2012, in Boston (MA, USA) when the International Mesothelioma Interest Group met to discuss the role of surgery in the treatment of MPM, Valerie Rusch (New York, NY, USA) presented a preliminary analysis of the International Association for the Study of Lung Cancer (IASLC) staging project [9, 10]. In the IASLC worldwide registry of patients with all stages of epithelial MPM, the analysis showed a 19-month median survival among 1359 patients

undergoing surgical resection. Moreover, patients undergoing extrapleural pneumonectomy for early-stage disease demonstrated survival superior to that of all other subgroups, a median of 40 months [9].

This finding, that early disease may be effectively treated, emphasises the importance of identifying a tumour marker that is practical for screening and can allow physicians to make an early diagnosis. In our review we clearly state that mesothelin family proteins and osteopontin have limited sensitivity for identifying early stage disease, and this might limit their use in screening. Furthermore, in the near future, their application in clinical practice is most probably in monitoring response to therapy, rather than in risk assessment for asbestos-exposed populations.

We fully agree that the Mesothelioma and Radical Surgery (MARS) I trial, which concluded that extrapleural pneumonectomy offers no benefit, was characterised by strong biases which make drawing any conclusion impossible [11]. On the basis of the current literature and the IASLC report we believe that “there is life after MARS”. International Mesothelioma Interest Group members also concluded that surgery should be performed in the multimodality treatment of MPM [9].

Mesothelioma is a heterogeneous disease and some long-term survivors clearly benefit from surgery. Future studies must explore new markers that will predict for resection only those patients most likely to achieve long-term survival. Well-designed randomised studies are needed, accompanied by a careful interpretation of the results, to avoid movement of clinical research for mesothelioma in the wrong direction.



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Early stage mesothelioma and surgery: where do we stand?

<http://ow.ly/kTms5>

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