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## Commentary: Go small or go home

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At the start of 2020, it will have been nearly 1 decade shy of a century since malignant pleural mesothelioma (MPM) was recognized as its own disease.<sup>1</sup> Its first appearance in the *Journal* was in 1959, and even then it appears that the entity that later would become known as MPM remained incompletely accepted universally.<sup>2</sup> The inadequate efficacy of radiation therapy and chemotherapy at that time resulted in the conclusion that radical surgical extirpation was the only way to “salvage” patients. In many ways since then, as the saying goes, the more things have changed the more they have stayed the same. Although radical resection in the form of pleural pneumonectomy is still necessary at times, cytoreductive surgery with pleurectomy and decortication is becoming more widely accepted and the preferred approach. Surgical intervention, although not performed in isolation, remains an important part of the multimodal approach to this complex disease. Exactly what modalities should comprise multimodal therapy in MPM is the subject of intense investigation, such as by Chu and colleagues<sup>3</sup> in this issue of the *Journal*.

In a murine model in which cell lines of mesothelioma were injected into the pleural space, Chu and colleagues<sup>3</sup> evaluated the efficacy of paclitaxel-loaded pH-responsive expansile nanoparticles in treating early and late stages of MPM. In their early stage model, the pure therapeutic efficacy of these paclitaxel-loaded pH-responsive expansile nanoparticles was shown clearly through a doubling of the overall survival. In an effort to mimic treating the more typical clinical presentation of MPM, their late stage model was associated with a greater tumor burden and used surgery as a part of a multimodal approach.

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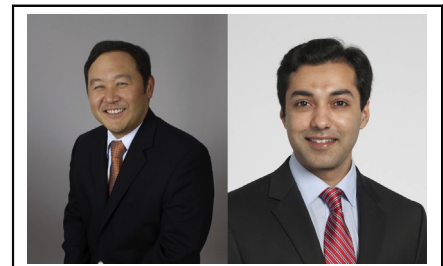
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### CENTRAL MESSAGE

The benefits of nanoparticle therapy observed in the murine model of malignant pleural mesothelioma are both pioneering and foundational.

The median overall survival of those mice undergoing paclitaxel-loaded pH-responsive expansile nanoparticle therapy followed by surgery was greater than for those mice receiving chemotherapy alone by an astounding 126%. If even a fraction of this effect observed in mice were to be replicated in humans, it would represent a paradigm shift. The median survival for patients with MPM undergoing trimodality therapy has ranged from 15 to 18 months.<sup>4,5</sup> A 126% improvement would translate into median overall survivals of 34 to 41 months, which would place the outcomes associated with MPM in the same realm as those of other malignancies associated with pleural involvement. In fact, this type of intervention could also open the possibility of treating even secondary pleural-based malignancies with this novel therapeutic strategy, possibly changing the landscape of how we manage all thoracic malignancies with pleural involvement.

The work of Chu and colleagues<sup>3</sup> in the Colson Laboratory with nanoparticles in the treatment of MPM is both pioneering and foundational. It will be exciting to see how their work meshes with the evolving field of immunotherapy, including other adoptive cellular therapies such as chimeric antigen receptor T-cell therapy and tumor-infiltrating lymphocyte therapy. As

surgeons who are deeply invested in moving the proverbial needle, we eagerly await more scientific data describing this interplay from their laboratory. In the course of time and through the work of our colleagues, “going big” in the efforts to modernize MPM therapy may actually mean going small or smaller—nanoparticle smaller!

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