Author’s response to reviews

Title: Gallbladder Cancer: Review of a Rare Orphan Gastrointestinal Cancer with a Focus on Populations of New Mexico

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Author’s response to reviews:

Dear Drs Tan and Lefor,

My co-authors and I thank you for the review and the comments associated with our review paper.

In particular, the review comments regarding the need for an incidence graph are very well taken. Following up on Dr Tan's suggestion to include GBC incidence data, we reviewed the latest available data from the SEER database for current GBC incidence trends in the state of New Mexico among the three major ethnicities (Caucasians, Hispanics and Native Americans). Dr. Nir's earlier paper in the American Journal of Surgery reviewed the data from 1981-2008. In this paper we have reviewed the latest SEER data for the years 2000 through 2014. This data has been plotted in the form of a comparison graph for women and men of New Mexico separately, stratified by ethnicity (Figure 1). Indeed, as previously noted, the rates of gallbladder cancer among Native Americans (men and women) continues to be exceedingly high compared to Hispanics and Caucasians of New Mexico (over six times higher). The figure along with corresponding changed text (marked in red) has been included within the main body of the paper.

Beyond the incidence graph, motivated by Dr Tan's comments, we also sought to examine a separate, but related issue. We asked the question, what is the geospatial and county-level
preponderance of GBC incidence in the state of New Mexico? To our knowledge, this has not been looked before. This has resulted in the figure 2. We show that the incidence of GBC is highest in the North-West corner of the state where the Navajo reservation exists with the highest density of Native American population. Incidentally, this is also the location of the largest concentration of abandoned mines in the state as well. This data reinforces our current working hypothesis for a role of heavy metals in driving elevated GBC incidence among Native Americans of the state. A hypothesis, which we are currently pursuing in my own research lab. Our current review seeks to shine a light on this issue to enable greater focused research attention to our underlying hypothesis.

Once again, we thank the reviewers for their time and consideration. I would be delighted to answer any other questions in detail as necessary.

Warm regards

Rama Gullapalli, MD, PhD