



FACT SHEET

Mesothelioma: IASLC Highlights Promising Advances

Malignant mesothelioma (MM) is a tumor of the lining of the lung and chest cavity (pleura) or lining(s) of the abdomen (peritoneum) that is very often related to exposure to carcinogenic mineral fibers such as asbestos and erionite.

There are about 400 mineral fibers in nature. With the exception of palygorskyte, which was recently proven not to be carcinogenic, all mineral fibers are potentially carcinogenic for humans. Six of them, antophyllite, actinolite, crocidolite, amosite, tremolite and chrysotile were used commercially, thus millions of people were exposed to them. The use of mineral fibers other than those called “asbestos’ is not regulated yet, in spite of the fact that some of them, such as erionite, are proven human carcinogens.

Recently, exposure to non-regulated mineral fibers has increased as rural zones containing these minerals are being developed.

According to the Surveillance, Epidemiology, and End Results (SEER) Program data, the incidence of mesothelioma in the U.S. is estimated to be between 1-2/million in states with minimal exposure to mineral fibers and 10-15/million in states where large amounts of asbestos were used.

Despite regulatory actions and decline in asbestos use, the annual number of malignant mesothelioma deaths remains substantial. Contrary to past projections, the number of malignant mesothelioma deaths has been increasing. The continuing occurrence of mesothelioma deaths, particularly among younger populations, underscores the need for maintaining efforts to prevent exposure and for ongoing surveillance to monitor temporal trends. (CDC-- <https://bit.ly/2WeHw50>)

Over 20 million people in the U.S. are at risk of developing mesothelioma due to asbestos exposure, and more due to exposure to other mineral fibers. Mortality rates for mesothelioma are estimated to increase by 5-10 percent per year in most industrialized countries until about 2020 due to past exposure.

Exposure to asbestos, erionite and other carcinogenic mineral fibers may be occupational or environmental. Environmental exposure to carcinogenic fibrous minerals includes indoor and outdoor contamination caused by both asbestos-containing commercial materials and from naturally occurring asbestos and other fibers.

The latency period, which is the interval between first exposure and the development of mesothelioma, ranges from about 25 to >60 years.



Occasional exposure to asbestos or other mineral fibers is not associated with a high risk of mesothelioma, but prolonged exposure is associated with an increased risk of mesothelioma. For example, no mesotheliomas were recorded in South African crocidolite asbestos miners who worked continuously with asbestos for less than three months; most mesotheliomas occurred in miners with >10 years of continuous exposure.

Asbestos and other mineral fibers induce mesothelioma because they are deposited in the pleura and peritoneum where they cause a chronic inflammatory process that is driven by the chronic release of HMGB1 and TNF – and over the years may cause malignancy.

Radiation exposure has also been linked to mesothelioma, especially in individuals treated with radiation therapy for lymphoma and other malignancies.

The IASLC/IMIG (International Mesothelioma Interest Group) staging system for pleural mesothelioma has been revised recently to include patients who did or did not have surgery.

MM patients diagnosed and treated in Stage 1 experience a survival-rate of three or more years. However, the majority of patients are diagnosed at a later stage, when the median survival-rate is approximately 12-15 months with first line chemotherapy.

RESEARCH AND PROMISING DEVELOPMENTS:

In May 2019, the Food and Drug Administration approved NoveTTF-100L System with pemetrexed and platinum-based chemotherapy as a first-line treatment for patients with locally advanced or metastatic malignant pleural mesothelioma. This was the first therapy approved by the FDA to treat mesothelioma in 15 years.

Several biomarkers to identify individuals exposed to asbestos and/or for early mesothelioma detection have been proposed and are currently being tested for validation: osteopontin, fibulin and HMGB1. Mesothelin, the first mesothelioma biomarker identified, is used to monitor recurrence following therapy, but it is not useful in identifying asbestos exposed individuals or for early detection of mesothelioma.

A number of novel treatments for non-resectable MM are in clinical trials. These include several drugs targeting mesothelin such as immunotoxins (SS1P, RG7787), a chimeric monoclonal antibody (Amatuximab)129, an antibody drug conjugate (Anetumab Ravtansine) and a tumor vaccine (CRS-207). The role of checkpoint immunotherapies (PD1 inhibitor, CTLA4 inhibitor) is under active investigation.

The value of surgery to treat patients with mesothelioma continues to be controversial. The use of extrapleural pneumonectomy has decreased in favor of performing a maximal cytoreduction through a



parietal and visceral pleurectomy, along with pericardial and diaphragmatic resection as necessary. Further concordance among mesothelioma surgeons regarding the extent of the resection is necessary, along with novel prospective window of opportunity trials in order to define the utility of new agents for the disease.

BAP1 is the first and, to date, only gene that has been linked to familial mesothelioma. All individuals that are born with inherited germline BAP1 mutations have developed one or more malignancies in their lifetime, especially mesotheliomas and eye melanomas.

Many of these issues are reviewed in: Carbone M, et al. Consensus Report of the 2015 Weinman International Conference on Mesothelioma. *J Thorac Oncol*, 11:1246-1262, 2016.

About the IASLC:

The International Association for the Study of Lung Cancer (IASLC) is the only global organization dedicated solely to the study of lung cancer and other thoracic malignancies. Founded in 1974, the association's membership includes more than 6,500 lung cancer specialists across all disciplines in over 100 countries, forming a global network working together to conquer lung and thoracic cancers worldwide. The association also publishes the *Journal of Thoracic Oncology*, the primary educational and informational publication for topics relevant to the prevention, detection, diagnosis and treatment of all thoracic malignancies. Visit www.iaslc.org for more information.