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REVIEW

Mesothelioma treatment: Are we on target? A review

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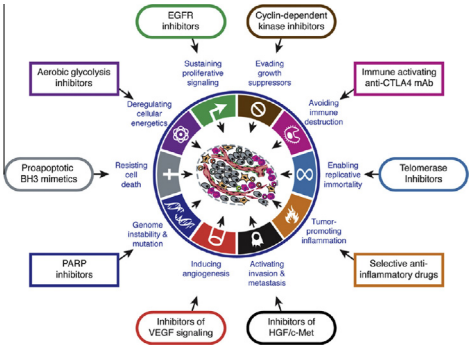
GRAPHICAL ABSTRACT



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ABSTRACT

Targeted treatment is a therapy directed at a specific molecular target close to a hallmark of cancer. The target should be measurable with a biomarker and measurement of the target should correlate with clinical outcome when targeted treatment is administered. Current clinical guidelines do not recommend targeted or biological therapy in MPM. However, since these recommendations came out, new agents have been investigated in MPM. This review updates the use of targeted and biological treatment in patients with mesothelioma.

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Christian Rolfo, MD PhD MBAH (Cordoba, Argentina) is board certified oncologist by University of Milan, Italy, and completed his PhD in Clinical and Experimental Oncology with a thesis on EGFR in NSCLC. He worked in the Spanish Group for Lung Cancer, under the direction of Prof. Rafael Rosell, actively involved in studies of molecular biology and clinical research in lung cancer. He completed his training in the Phase I program at MD Anderson, Texas, USA, with Prof. David Hong. In 2011, he has been appointed 'visiting professor' in Medical Oncology by the Molecular and Clinical Genetic Oncology Unit at the Interdepartmental Centre of Research in Clinical Oncology, School of Medicine, University of Palermo (Italy). Since 2012 he is Associate Professor in Oncology and Senior Staff Member, in the Department of Oncology at the University Hospital Antwerp (Belgium). Currently he is head of Phase I – Early Clinical Trials Unit Director of Clinical Trials Management Program in Oncology and Director of 'Investigational Cancer Therapeutics Fellowship and Drug Development: Clinical and Experimental' at Antwerp University Hospital in Belgium. His scientific interests are drug development and resistance, liquid biopsies in lung cancer, more specifically in exosomes isolation and circulating tumour DNA. Since 2013 he has a membership in the Board of IALSC (International Association for the Study of Lung Cancer) and is member of societies including AACR, BACR, EACR, ESMO and ASCO.

Jan P. van Meerbeeck, MD PhD was appointed as director of the Thoracic Oncology Program in the Multidisciplinary Oncological Center of Antwerp University Hospital (MOCA), Belgium, as of March 1, 2013. After obtaining his medical degree *magna cum laude* from the University of Antwerp in 1980, he completed training to become a board certified specialist in internal medicine and pulmonology. He is a skilled interventional pulmonologist and completed his PhD in 1997 with a dissertation on the presentation of lung cancer in Flanders, Belgium. He is professor of Thoracic Oncology at both Ghent and Antwerp University and practiced as thoracic oncologist from 1986 to 1996 at Antwerp University Hospital, Belgium, and from 1996 to 2003 at Erasmus MC-Daniel den Hoed Kliniek, Rotterdam, the Netherlands. From 2003 to 2013 he was Chair of the Thoracic Oncology Program at Ghent University Hospital, where he became also Divisional Head and CMO. His translational scientific interests include the molecular diagnosis of mesothelioma and lung cancer and the evaluation of biomarkers of asbestos exposure and mesothelioma. He is or has been the study coordinator or Principal Investigator for numerous international phases II and III studies in thoracic oncology and respiratory medicine. He is promoter of several master thesis students and research fellows, of which 5 successfully completed their PhD. Professor van Meerbeeck has served the Lung Cancer Group of the European Organisation for Research and Treatment of Cancer (EORTC) as secretary, chairman and currently as board member. He is a full member of the European Society of Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO) and the International Association for the Study of Lung Cancer (IASLC), currently as part of its Staging and Ethical Committees and previously as a member of its Scientific Advisory Committee. He is external expert at the Belgian Knowledge Center KCE, where he coordinates the working party on the organisation of care of mesothelioma. Professor van Meerbeeck has an extensive presentation and publication track, with more than 200 peer-reviewed articles in oncology and pulmonology journals and textbooks. He also serves in the review and editorial boards of several international journals, and has organised several national and international meetings.

Introduction

Malignant pleural mesothelioma (MPM) is a rare and aggressive neoplasm deriving from the pleural blades. More than 80% of cases are related to previous professional asbestos exposure and its worldwide incidence is expected to further increase [1]. Although the epidemic of asbestos-related disease is plateauing in most of the industrialised world, little is known about the epidemic in developing countries, where professional and environmental exposure is increasing [2]. With a natural history of 7–9 months if untreated and less than 5 per cent 5-year survivors, there is room for therapeutic improvement [2]. Disease extent and performance status at diagnosis are the clinical prognostic factors, besides epithelioid histological subtype that confers a better outcome than the less common sarcomatoid one.

The European Respiratory Society (ERS), the European Society of Thoracic Surgery (ESTS) and the European Society of Medical Oncology (ESMO) have issued recommendations regarding the management of MPM [3,4]. The only treatment with level one evidence of improvement in outcome is the administration of palliative chemotherapy consisting of 4–6 cycles of a platinum doublet with an antifolate, either pemetrexed or raltitrexed [5,6]. With this combination, good performance patients have a median overall survival (OS) of approximately 1 year and a median progression free survival (PFS) of less than 6 months. There is no standard second line treatment and targeted or biological treatment has no indication in these guidelines. This review updates the use of targeted and biological treatment in patients with advanced MPM.

Hallmarks of cancer and targeted treatment

Development of human cancers is a complex and multistep process. Organising the factors involved in the arise and growth of cancer is an important part of developing new treatment modalities. Hallmarks of cancer include biological capabilities and modulating factors to create an environment in which cancer cells can thrive [7] (Table 1). Eight biological capabilities allow cancer cells to survive, proliferate and