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PL-4-09 Bruce Robinson (Abstract and presentation)

New Treatments and Early Detection of Mesothelioma Using Blood Tests

Bruce Robinson
University Department of Medicine, University of Western Australia, Perth, Australia

[See also: **Blood Tests, Vaccination and other Research Approaches for Mesothelioma Patients]**

Slide presentation

Abstract

Until recently there has been an absence of effective therapies for malignant mesothelioma (MM). Two new chemotherapy regimes, gemcitabine-cisplatinum and pemetrexed-cisplatinum have both shown response rates of over 30%. We are using advanced molecular and cellular approaches to determine how these therapies can be combined with surgery and immunotherapy to enhance survival.

Mesothelioma represents one of the few animal models of cancer in which the mouse tumour is similar to the human tumour, so preclinical studies are valuable. Allo MHC class I transfectants were rejected and B7-1-transfection markedly delayed MM outgrowth, although eventually tumours formed, contemporaneous with reduction in anti-tumour cytotoxic activity. The data suggest that cytokine gene therapy of mesothelioma will be most effective when combined with a surgical debulking.

Based upon successful tumor reduction in animals, a Phase I clinical trial in pleural mesothelioma patients was carried out, using a recombinant vaccinia virus (VV) expressing the human IL-2 gene. VV-IL-2 mRNA was detected in serial tumor biopsies for 3-6 days after injection, but uniformly declined to low levels by day 8. Anti-VV IgG antibody titers were induced but did not have any bearing on VV-IL-2 mRNA expression. Autologous tumor lysates injected with GMCSF induce changes in DTH and Western blot reactivity in around 25% of mesothelioma patients.

Real improvement will require a method of early diagnosis. Soluble members of the mesothelin-family proteins (SMRP) are elevated in the serum of over 80% of mesothelioma patients. Importantly, significant elevations of SMRP can be detected several years prior to presentation with MM. Thus determination of SMRP in serum may be useful in the diagnosis of MM, may be an early marker of disease and may prove useful in screening at-risk individuals.

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