Review paper

WHAT'S NEW IN MALIGNANT MELANOMA - TREATMENT

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ABSTRACT

The authors discuss biological markers which could make us better understand the function of biological response modifiers (BRMs) and their efficacy in the advanced melanoma treatment. The demonstration, that BRMs, in vitro, inhibit the growth of melanoma cell lines and that they modulate the expression of melanoma associated antigens (MAA) justify their therapeutic application. While the results obtained with chemotherapeuthical substances - alone or in combination - are substantially not very different from the past ones, but interesting progressions are coming from the active immunotherapy. The so called "adoptive immunotherapy" made of a combination of intratumoral T lymphocytes and interleukin 2, is feasible only for a fraction of patients.

KEY WORDS

melanoma, biologic response modifiers, chemotherapy, immunotherapy

Let us examine what's new in treatment and, in particular, how the recent advances in biology may improve our strategies.

Systemic chemotherapy remains unsatisfactory for treatment of disseminated (stage IV) disease. Dacarbazin (DTIC) remains the most active simple agent, with a response rate of about 20% (37). Patients with skin, subcutaneous tissue and lymphonode involvement respond more frequently. Lung metastases are also responsive - the median duration of responses is 5 to 6 months. In the widest case control study of 580 patients treated with DTIC 5% had a complete remission, but only 1-2% presented no relapses after 6 years follow-up (1). The Nitrosoureas are a second group of agents with defined activity against metastatic melanoma. Hematologic toxicity can be more severe than with DTIC. Carmustine and Lomustine are the best studied of this class, with a response rate of 10 to 20% (1). Fotoemustine is a new drug of this class. Its activity against disseminated melanoma has been demonstrated in a large - phase two-trial including 153 evaluable patients, with 37% responses (2).

Among the Alkylating Agents, Cyclophosphamide has a higher toxicity and is less effective than DTIC. Melphalan was used in high concentrations to induce bone marrow aplasia and therefore its administration was followed by autologous bone marrow transplantation. The response rate was 50-60%, but morbidity and mortality rates were too high in relation to efficacy. There has been considerable interest in the past few years in the dose-