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Meeting Abstract

Development of cancer vaccines with the MAGE-3 protein

Vincent Brichard

GSK Biologicals, Rixensart, Belgium

GSK Biologicals' approach is based upon immunizing cancer patients with a vaccine composed of a recombinant MAGE-3-derived protein combined with an immunological adjuvant. Phase I/II clinical trials have been, and are being, performed in various indications, with emphasis upon cutaneous metastatic melanoma and NSCLC. Trials have been conducted to optimize the immune response to the MAGE-3 antigen, as follows:

(a) In a study evaluating the recombinant MAGE-3 protein alone (administered i.d. and s.c. without immunological adjuvant), a few patients responded to the treatment.

(b) Another study employed MAGE-3 combined with the GSK proprietary adjuvant AS02B. This was administered to 49 metastatic melanoma patients. Some responses among patients without visceral disease were observed and will be detailed; no patient with visceral disease responded to treatment. This accords with other observations that active immunotherapy is more effective in early-stage patients. In the same study, a bladder-cancer patient showed partial response.

(c) The MAGE-3 protein, either in solution combined with AS02B or pulsed onto dendritic cells, was administered to 19 patients.

(d) The MAGE-3 protein was administered in combination with the immunostimulatory oligodeoxyribonucleotide CpG 7909 to a total of 16 patients in two different dosages.

(e) A new adjuvant (AS15) containing CpG 7909 has been developed and tested in pre-clinical studies, in which it was found to stimulate mostly type 1 T-cell response, achieving a more robust CD8 response and better immunoprotection in a tumor challenge model. This adjuvant is now being tested in a randomized Phase II study conducted in collaboration with the EORTC melanoma group (MAGE-3 protein with AS02B or AS15; stage III/IVa early metastatic cutaneous melanoma without visceral disease). The trial design includes in particular an objective assessment of response based upon criteria adapted from the RECIST criteria for assessing solid tumors. The modified RECIST criteria are applicable to lesions below 2 mm in size and to skin lesions. Because response to active immunotherapy is slow, and because patients with mixed response have been found to proceed to complete or partial response after several series of vaccinations, this study is designed to identify patients who respond after long-term vaccinations.

Following early results of the above studies, a placebo-controlled, randomized double-blind study of the MAGE-3 antigen plus AS02B in NSCLC was initiated. The planned 182 patients have been recruited; initial data suggest that the treatment is being well tolerated.

Altogether, these results show that the MAGE-3 protein antigen combined with an immunological adjuvant is active in metastatic melanoma. Current trials are aimed at evaluating the efficacy of this treatment in order to achieve development of an effective vaccine.

Major collaborators in the studies described above have been: The EORTC Melanoma Group (Brussels); Prof. Wim Kruit (Erasmus MC, Rotterdam); Profs. Thierry Boon and Marie Marchand (Ludwig Institute for Cancer Research, Brussels); Prof. Thierry Velu (Hôpital Erasme, Brussels).