

CSF-470 vaccine plus BCG plus rhGM-CSF show superiority vs. IFN- α 2b in high risk cutaneous melanoma patients stages IIB, IIC and III: Interim results of the phase II part of phase II/III CASVAC0401 study

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Adjuvant treatment of high-risk cutaneous melanoma (CM) patients is still an unsolved issue. The CSF-470 therapeutic vaccine, a mixture of lethally irradiated allogeneic CM cell lines, combined with BCG and rhGM-CSF as adjuvants is currently tested in post-surgical adjuvancy against medium-dose IFN- α 2b in stage IIB-III CM patients (CASVAC-0401 phase II-III study). Here we present the results of the phase II part of the study. Patients in the vaccine arm (n=20) received 1.6×10^7 CSF-470 melanoma irradiated cells i.d. plus 10^6 cfu BCG and 400 μ g rhGM-CSF fractionated in 4 consecutive days were i.d. injected at the vaccination site, during 2 years (13 vaccinations in total). IFN- α 2b patients (n=11) received 10 MU/day/5 days a week for 4 weeks; then 5 MU/day thrice weekly for 23 months (m). CSF-470 was well tolerated. The main toxicity was grade 2 reaction at the vaccination site (20/20); 3/20 patients presented grade 3 allergic reactions, easily handled with anti-histamines and corticosteroids; the rest of the AE were grade 1. IFN- α 2b patients presented grade 2-3 hematologic (7/11), hepatic (2/11) and cardiac (1/11) toxicity, 9/11 patients developed AE that forced treatment discontinuation. QOL was significantly superior in CSF-470 arm vs. IFN- α 2b arm. With a maximum follow-up of 72 m (Mean: 28 m) a significant benefit in the distant metastasis-free (DMF) survival for CSF-470 was observed (p=0.028). No significant differences in OS were yet observed. DTH reaction after the 7th vaccine was higher in distant metastasis-free patients than in progressing patients. Immune monitoring at 6 months showed an increase in NK cells (p=0.009) and a slight decrease in Tregs (p=0.021) in vaccinated patients; conversely IFN- α 2b patients showed a significant decrease in total CD3+, CD4+ and CD8+T cells; serum Abs reactive with vaccine CM cells increased in all vaccinated patients (p<0.0001), but not in IFN- α 2b patients. CSF-470 vaccine +BCG +GM-CSF superiority vs. IFN- α 2b for adjuvant treatment of high-risk CM observed so far encourage continuation of the phase III part of CASVAC0401 study.

Biography

Maria Marcela Barrio was graduated in 1991 as a Biologist at the University of Buenos Aires and obtained her PhD working on monoclonal antibodies at the Fundación Instituto Leloir. She became a Member of The National Scientific and Technical Research Council (CONICET) in 2007. She has been working in the cancer immunology as part of Dr. Mordoh's team since 1984. Presently she is Sub-Director of the Centro de Investigaciones Oncológicas Fundación Cáncer. She has published more than 40 scientific papers about her specialty and she is working in translational research for the development of therapeutic vaccines for cutaneous melanoma.

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