New dissertation on the treatment of malignant melanoma

6 December 2017

Malignant melanoma is one of the most common causes of cancer deaths among young adults. Although treatment for melanoma has improved in recent years, most patients do not benefit from the treatment, which also often causes side effects. In a new dissertation from Uppsala University, Aglaia Schiza has examined new ways of treating the disease.

If malignant melanoma has spread, the prognosis is not good. That is why it is imperative to develop better treatment strategies. One new treatment strategy for cancer is to use the body's own immune system. Melanoma is considered a promising form of cancer for immunostimulatory gene therapy, which means that the immune system is activated to kill the cancer. CD40L is an immunostimulatory molecule that can, with the help of the virus, be introduced into the tumour, where it can stimulate the immune defences against the cancer cells.

Aglaia Schiza and her colleagues conducted a study in which patients with disseminated melanoma who had received established treatment were treated with injections in metastases of a virus-carrying gene for CD40L (AdCD40L). The goal was for the immunostimulatory molecule to not only work locally, but to also have a vaccinating effect and thereby affect metastases in the rest of the body. The majority of the patients also received low-dose cyclophosphamide along with the injections. In this low dose, the cytotoxic agent has no effect on the cancer, but can strengthen the effect of immunological treatment.

The treatment led to mild transient side effects. The patients who received both cyclophosphamide and AdCD40L immunotherapy had a better survival rate than those who only received AdCD40L.

"With the aid of radiography, we saw that, in addition to the injected metastasis, the treatment also affected others," says Aglaia Schiza, PhD student at the Department of Immunology, Genetics and Pathology at Uppsala University. "We also showed that the treatment gave desirable immune effects by stimulating good immune cells and inhibiting cells that counteract immune response. Using diffusion-weighted MRI, we could identify at an earlier stage which patients had a better chance of benefiting from AdCD40L treatment."

The dissertation also describes two cases of patients with disseminated melanoma who were treated with the BRAF-inhibitor vemurafenib outside indication (i.e. in situations in which vemurafenib is not approved due to as-yet insufficient findings). Half of all patients with melanoma have a mutation in their tumour in a gene that codes for the BRAF protein that is part of an important signal chain in the cancer cell. These patients can be treated with BRAF-inhibiting drugs. Schiza and her colleagues studied rare cases of disseminated BRAF-mutated melanoma in individual patients because the extremely low prevalence does not allow for any clinical trials. For the first time ever, a case of a pregnant woman treated with BRAF-inhibitors was reported. The treatment enabled a longer gestation and thereby less risk of immaturity-related complications. The dissertation also contains the first-ever report of successful treatment with vemurafenib by a patient with disseminated ocular melanoma.

More information: Experimental treatment of patients with disseminated malignant melanoma. uu.diva-portal.org/smash/record.jsf?aq2=%5B%5B%5D%5D&c=2&af=%5B%5D&searchType=SIMPLE&sortOrder2=title_sort_asc&query=Aglaia+Schiza+&language=sv&pid=diva2%3A1149354&aq=%5B%5B%5D%5D&sf=all&aqe=%5B%5D&sortOrder=author_sort_asc&onlyFullText=false&noOfRows=50&dswid=-2989

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