COMBINATION THERAPY CAN LESS REALLY BE MORE IN MELANOMA?

The incidence of melanoma is increasing worldwide, and the treatment options for patients have been rapidly expanding. However, 5–8% of patients develop metastases between the primary tumor and the draining lymph nodes—known as in-transit metastases, or IT-mets. A long-established protocol for treating patients that develop IT-mets has been refined, but a recent assessment by a team from Rotterdam has indicated that the treatment doses might need to be re-evaluated.

Treatment of IT-mets using melphalan applied by isolated limb perfusion—the standard therapy for these patients—results in a higher concentration of chemotherapy in the limb than when using systemic therapy. The addition of TNF to the therapy improved response rates in patients with large tumors. Although the concentration of melphalan has been standardized for the past four decades, the optimal concentration of TNF is still unclear.

The researchers used their experience of treating patients over the past 20 years to investigate whether a low dose of TNF is as effective as a high dose. They can use their retrospective data to answer this question because between 1991 and 2004 they performed 99 TNF perfusions using a high dose (3–4 mg for the leg, 3 mg for the arm) and between 2004 and 2009 they performed 68 low-dose TNF perfusions (2 mg for the leg, 1 mg for the arm). The change in dose in 2004 was based on data indicating that the lower dose was equally efficacious for the treatment of patients with sarcoma.

The overall response rate for all the patients treated with a TNF perfusion was 89%, with a complete response rate of 61%. Interestingly, the patients who received the high-dose therapy had an improved complete response rate compared with patients who received the low-dose treatment (70% versus 49%). No difference was observed when comparing the overall survival of the two groups.

As the goal of this therapy is local control, and not survival, it seems that high-dose TNF should be recommended for the treatment of patients with unresectable IT-mets in the future.

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Original article Deroose, J. P. *et al.* 20 years experience of TNF-based isolated limb perfusion for in-transit melanoma metastases: TNF dose matters. *Ann. Surg. Oncol.* doi:10.1245/s10434-011-2030-7