



Local recurrence of melanoma treated with electrochemotherapy during immunotherapy: case series of Central Tuscany Melanoma & Skin Cancer Unit and literature comparison.

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BACKGROUND

Electrochemotherapy (ECT) is a tumor ablation modality introduced in oncology for local control of cutaneous and subcutaneous nodules of melanoma or other primary and metastatic tumors. It is based on the use of electroporation to permeabilize the cell membrane and improve the delivery of chemotherapy into cells thus increasing the cytotoxic effect of bleomycin several hundred fold [1]. This study reports the clinical case series of patients with local recurrence of advanced melanoma treated with ECT during immunotherapy.

CASE SERIES

We have treated 15 patients in non resectable stage IIIc and IV with metastasis in transit of melanoma followed at the Central Tuscany Melanoma & Skin Cancer Unit (S. Maria Annunziata Hospital of Florence). These patients have performed ECT during immunotherapy: seven patients treated with Nivolumab, six with Pembrolizumab, one with Nivolumab plus Ipilimumab and one with Ipilimumab. A median follow-up time of 3 years, from 2019 to date. Twelve of 15 patients experienced remission: nine complete and three which lasted at least eight months. Stabilization was observed in two patients (lasting at least six months) and in only one progression.

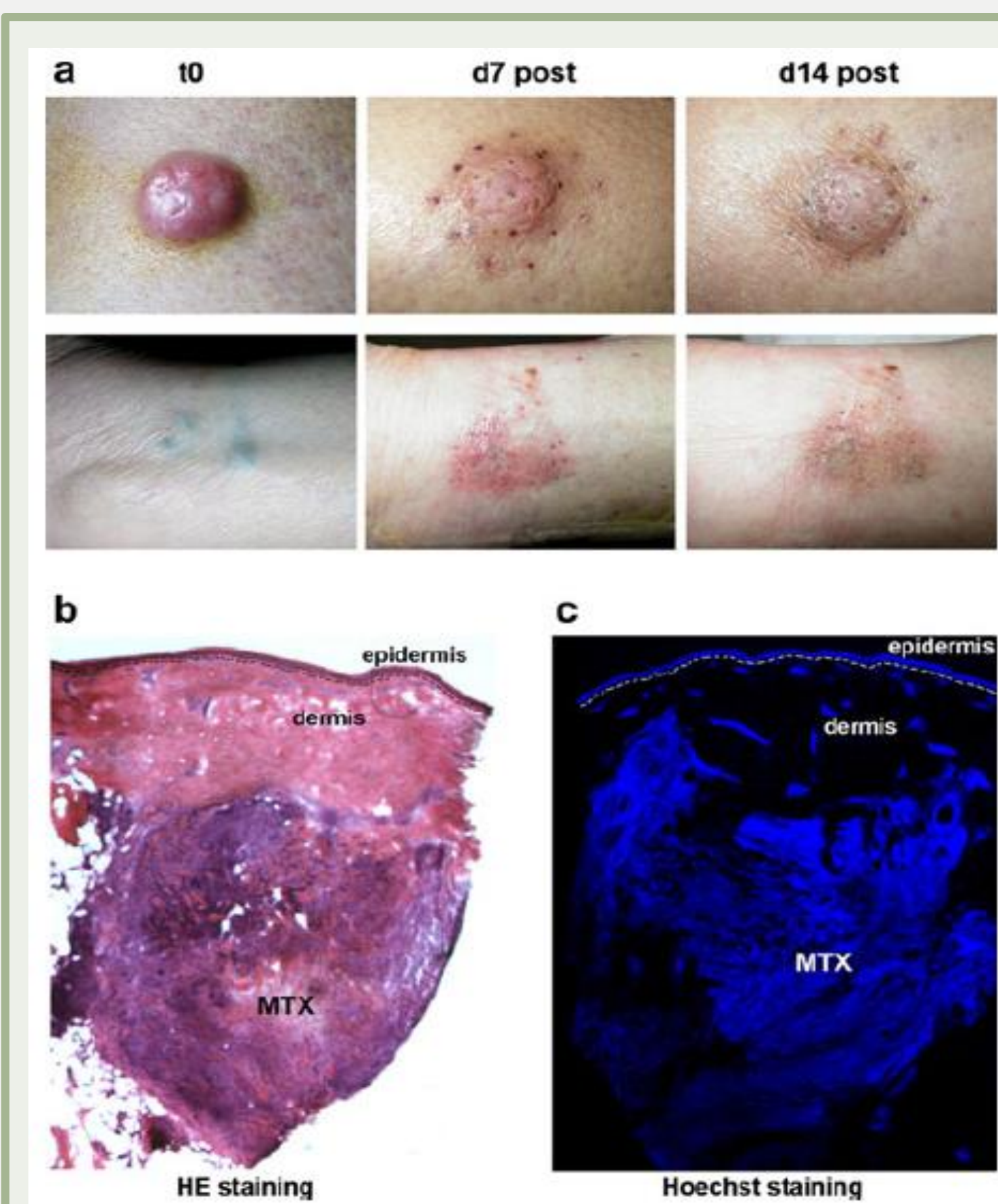


Fig. 1: Melanoma metastasis before and after ECT

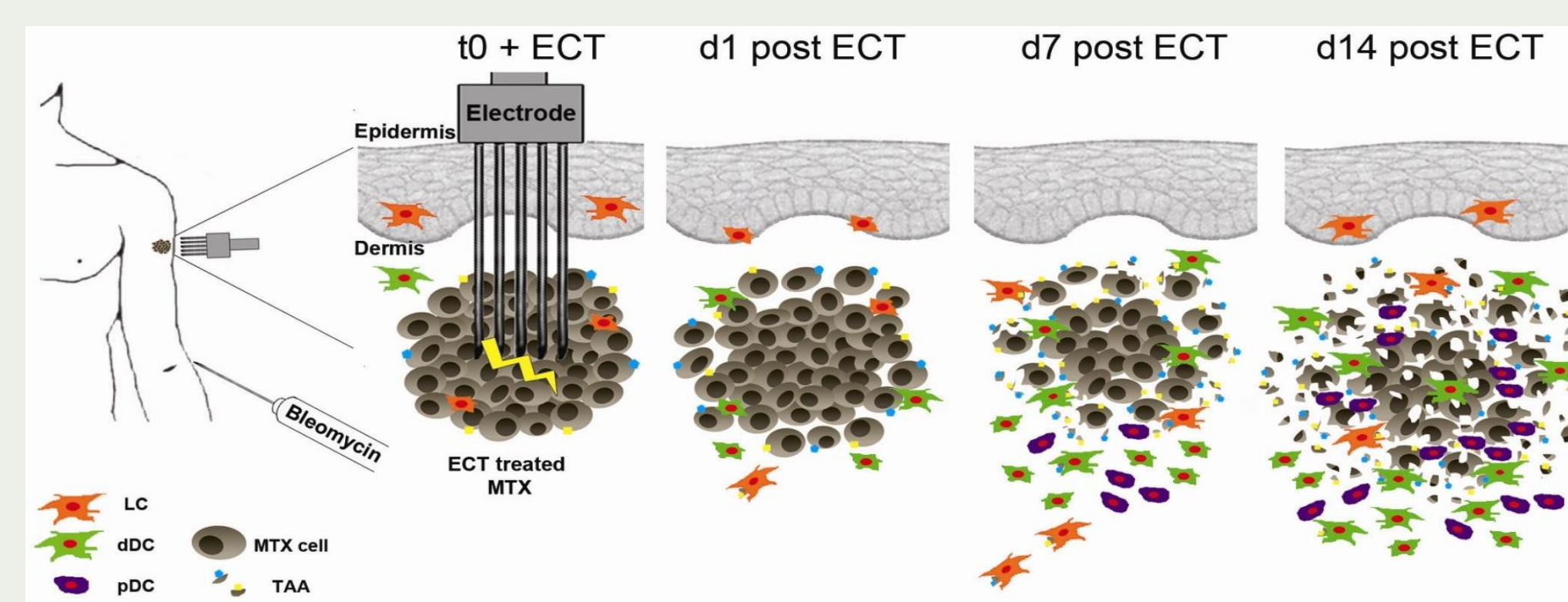


Fig. 2: Gerlini G, Sestini S, Di Gennaro P, Urso C, Pimpinelli N, Borgognoni L. Dendritic cells recruitment in melanoma metastasis treated by electrochemotherapy. *Clin Exp Metastasis*. 2013 Jan;30(1):37-45. doi: 10.1007/s10585-012-9505-1. Epub 2012 Jun 27. PMID: 22735940.

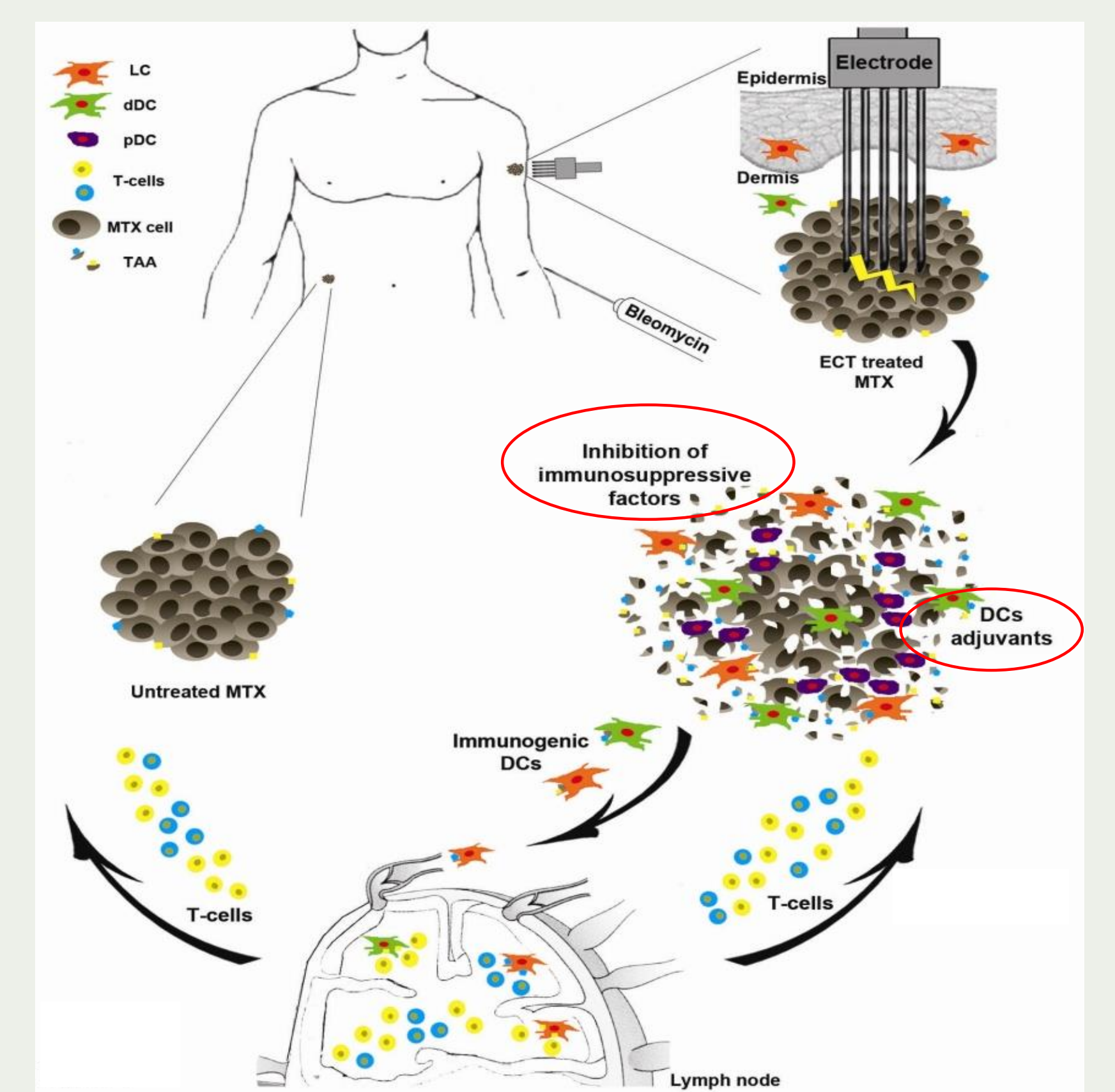


Fig. 3: Gerlini G, Di Gennaro P, Borgognoni L. Enhancing anti-melanoma immunity by electrochemotherapy and in vivo dendritic-cell activation. *Oncoimmunology*. 2012 Dec 1;1(9):1655-1657. doi: 10.4161/onci.21991. PMID: 23264927; PMCID: PMC3525636.

DISCUSSION

The availability of immunotherapy treatments and target therapies with BRAF and MEK inhibitors has greatly improved life expectancy of patients with metastatic melanoma.

Approximately 8-10% of patients with stage IIIc and IV disease develop skin metastases in the form of either in-transit or distant metastases [2].

Unlike target therapy, which also works on cutaneous and subcutaneous recurrences, immunotherapy has limited action supplemental loco-regional therapy may be necessary. Supplemental loco-regional therapies include: surgical intervention, radiotherapy, cryotherapy, laser therapy, RFA ablation, local chemotherapy, local immunotherapy with BCG, isolated limb perfusion and electrochemotherapy [3]. In the past decade, ECT has taken an increasing role in the management of local melanoma recurrences [4].

Thanks to the progressive accumulation of a solid evidence basis on its efficacy and tolerability, it has been included in the current ESMO melanoma guidelines [5].

ECT has shown to induce an immunogenic cell death and increase immune cells infiltration in the tumor environment. Therefore, ECT could render tumors more responsive to immunotherapy, thus improving both local and systemic response. Studies indicate that ECT improves the local progression-free survival and overall survival of patients receiving systemic therapies [6].

CONCLUSION

In the era of immuno-therapy, electrochemotherapy play a great role for the management local recurrences of metastatic melanoma with no toxicity concerns.

Immunotherapy combined with ECT was feasible, tolerable and showed an increased response and overall survival for the treatment of malignant [1,6].

In fact, growing evidence suggests that concurrent loco-regional and systemic treatment may lead to synergistic anti-tumor effects in advanced melanoma. By determining cytotoxicity, it reduces tumor burden, therefore, increasing the efficacy of immunotherapy.

ECT has, therefore, not only a palliative purpose in stopping bleeding, reducing pain, and improving "aesthetic" aspect for patients but, at the same time, improves the efficacy of immunotherapy.

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