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Original Research

More than 5000 patients with metastatic melanoma in Europe per year do not have access to recommended first-line innovative treatments

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Abstract ***Background:*** Despite the efficacy of innovative treatments for metastatic melanoma, their high costs has led to disparities in cancer care among different European countries. We analysed the availability of these innovative therapies in Europe and estimated the number of patients without access to first-line recommended treatment per current guidelines of professional entities such as the European Society for Medical Oncology (ESMO), the European Organisation for Research and Treatment of Cancer (EORTC), the European Association of Dermato-Oncology (EADO), and European Dermatology Forum (EDF).
Materials and methods: Web-based online survey was conducted in 30 European countries with questions about the treatment schedules from 1st May 2015 to 1st May 2016: number of metastatic melanoma patients, registration and reimbursement of innovative medicines (updated data, as of 1st October 2016), percentage of patients treated and availability of clinical studies and compassionate-use programmes.
Results: The recommended BRAF inhibitor (BRAFi) + MEK inhibitor (MEKi) combination was both registered and fully reimbursed in 9/30 (30%) countries, and in 13/30 (43%) (all from Eastern Europe) not reimbursed. First-line immunotherapy with anti-PD1 antibodies was registered and fully reimbursed in 14/30 (47%) countries, while in 13/30 (43%) (all from Eastern Europe) not reimbursed. It was estimated that in Europe 19,600 patients with metastatic melanoma are treated, and 5238 (27%) do not have access to recommended first-line therapy. Significant correlation was found between human development index (HDI, UNDP report 2015), ($r = 0.662$; $p < 0.001$), health expenditure per capita ($r = 0.695$; $p < 0.001$) and the Mackenbach score of health policy performance ($r = 0.765$; $p < 0.001$) with the percentage of patients treated with innovative medicines and a number of reimbursed medicines.
Conclusions: Great discrepancy exists in metastatic melanoma treatment across Europe. It is crucial to increase the awareness of national and European policymakers, oncological societies, melanoma patients' associations and pharma industry.

1. Introduction

A tremendous breakthrough in the treatment of metastatic melanoma occurred in recent years with the targeted inhibition of RAF-MEK-ERK (i.e. the MAP kinase) pathway with the use of MAP kinase inhibitors on the one hand and immunotherapy using immune checkpoint inhibitors on the other that have an impressive effect on overall survival. Two-year survival rates have reached 50% with either anti-PD1 immunotherapy (immune checkpoint inhibitor) or the BRAF/MEK inhibitor combination (e.g. BRAF inhibitors, such as vemurafenib or dabrafenib and MEK inhibitors, such as cobimetinib or trametenib) compared to <10% with chemotherapy [1–4]. Early clinical trials showed a dramatic improvement of 34% in 5-year survival rate for nivolumab as the first PD1-antibody tested in melanoma [2–4]. To date, the longest follow-up suggests a 3-year survival rate as high as 44% with both immunotherapy and combined targeted therapies. If patients have normal values of lactate dehydrogenase (LDH), a 3-year survival of up to 60% appears to be realistic [2–4].

These agents have become first-line recommended treatments by major international melanoma guidelines including those by the European Society of Medical Oncology (ESMO), the European Dermatology Forum