Nature Reviews Clinical Oncology **11**, 301 (2014); published online 20 May 2014; doi:10.1038/nrclinonc.2014.85

MELANOMA

You can have your cake and eat it!

One of the most aggressive forms of skin cancer is cutaneous melanoma. In the BREAK-3 study, a randomized phase III trial, the targeted agent dabrafenib had demonstrated an impressive 70% decrease in the risk of disease progression or death in patients with mutated *BRAF*, compared with dacarbazine. No drug, however, is without adverse events, and previous clinical trials of dabrafenib had shown that this agent was also associated with arthralgia, rash, photosensitivity, increased development of squamous-cell carcinomas and keratocanthomas, which could negatively impact quality of life (QoL). Therefore, assessing how the efficacy of this agent, coupled with its adverse events, correlates with real benefit from a patient perspective is paramount. So, can you have your cake and eat it? According to the latest results of a study by Jean-Jacques Grob and coauthors, apparently you can!

The premise of this study was to assess how end points that are clinically meaningful to patients (for example, QoL and symptoms) are equally important as standard end points such as progression-free survival (PFS), in terms of healthcare decisions. With the use of the EORTC QLQ-C30 questionnaire, the impact of treatment with either dabrafenib or dacarbazine was assessed relative to baseline functional dimensions in patients with advanced-stage unresectable or metastatic *BRAF*-mutant melanoma. Patients who were randomly assigned to receive dacarbazine treatment, were allowed to crossover to receive dabrafenib after initial signs of disease progression.

At baseline, the functional and symptom-related QoL scores were comparable between the two arms. In patients treated with dabrafenib, there was a stable or improved mean functional score at week 6 of treatment, with only a slight worsening of three dimensions (physical functioning, role, and cognitive functioning) at 12 weeks following treatment. In particular, loss of appetite, insomnia, nausea and vomiting, and pain showed the most improvements in mean functional scores with dabrafenib. By contrast, patients receiving dacarbazine had mean scores from baseline that were either unchanged or worsened at weeks 6 and 12 for all functional dimensions analysed. The researchers also focused on the QoL in patients randomly assigned to receive dacarbazine who then crossed over to receive dabrafenib. Meaningful improvements in most QoL dimensions were also noted in those patients who crossed over. This study shows that PFS improvement with dabrafenib equates with real QoL advantages for patients, and illustrates the importance of continued assessment of such measures in future clinical studies.

Photodisc/Getty

The researchers conclude that "this paper presents the first reported QoL analysis of a BRAF inhibitor in metastatic melanoma. High tumour response rates and PFS advantage obtained with dafrafenib compared with dacarbazine translate into rapid functional and symptomatic benefits, which are crucial to patients."

Lisa Hutchinson

Original article Grob, J.-J. *et al*. Patient perception of the benefit of a BRAF inhibitor in metastatic melanoma: quality of life analyses of the BREAK-3 study comparing dabrafenib with DTIC. *Ann. Oncol*. doi:10.1093/annonc/mdu154