Our patient received oral dosage of 150 mg vismodegib daily for 10 months. This resulted in shrinkage of the tumor by more than 80% of the externally visible lesion. Adverse events occurred in the form of alopecia, muscle cramps and dysgeusia, all known side effects of vismodegib therapy [6]. One of the goals of surgery was to get the patient off the drug that apparently cured him from the BCC, but caused side effects and did not spare him of daily dressing changes of the oozing scar. Surgery was indicated because of the patient's complaints, clinical appearance, and presumption that cancer activity could still be present. We excised the area including the irradiated volume for the best chance of a relapse-free outcome, for best healing potential and also because in this case there were no functional consequences in doing that. Interestingly, the pathology report indicated no signs of BCC. Vismodegib treatment in this locally advanced BCC therefore had complete response, as seen in the 21% from the phase 2 trial.

During the total six years the patient was followed, his mental illness stabilized allowing treatment with vismodegib. Vismodegib not only stopped the progression of the BCC, but cured the patient of his cancer. Patient involvement and the regression of the ulcer facilitated trust between patient and his physician leading to surgery. This case highlights the role of vismodegib treatment not only as efficient drug, but also as opening for treating an otherwise reluctant patient. The effect of vismodegib treatment should be further examined, especially its role as a neoadjuvant drug and its long-term risk of tumor recurrence.

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LETTER TO THE EDITOR

Patient-reported outcomes: nothing without engagement

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To the Editor,

The new European Medicines Agency (EMA) guidance on the use of patient-reported outcomes (PROs) in cancer studies is a further step toward recognition of the importance of patient perception of a disease and treatment benefits and harms [1]. This guidance is likely to stimulate wider inclusion of PROs in drug development plans and in the evidence accompanying marketing authorization applications in Europe.

Decision making processes informed also by PROs are welcome. However, the situation must be monitored and rules provided, besides acknowledging and minimizing caveats in the definition, measurement and interpretation of these outcomes. A potential benefit on a given PRO, demonstrated in trials, could support a claim of superiority over other therapeutic options, making the patient-centered approach a potential marketing tool for (new) products. As stated in the guidance, careful planning is needed when PROs have to be included among the trial endpoints. This implies transparent

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choices on what to measure, how, and the threshold for a clinically meaningful difference. Instruments should be reliable, valid, and responsive, developed using robust and reproducible methods [2] and taking account of the patients' perspective [3].

EMA's role in backing these requirements is necessary to assess the therapeutic added value related to a better PRO (which is also important for patients).

However, this may not be enough if investigators do not fully understand how a given PRO could confirm well formulated hypotheses and are not appropriately trained on the use of instruments to collect them. To ensure correct data collection throughout a trial, time and efforts must be invested to make study participants aware of the value of the information they provide with questionnaires on the definition of the overall benefit-harm profile of a new treatment. Clinical sites should be monitored and corrective measures taken to reduce missing or invalid data, which limit the robustness of the results. Even when all these specified measures are adopted, the question of data interpretation remains. To what extent a given difference is meaningful for patients depends on several factors: setting, line of therapy, patients' values and culture. This needs to be defined and agreed by all the stakeholders [4].

PROs can contribute greatly to decision making, but only if investigators and patients' representatives are fully engaged in the discussion about their importance at the same table.

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LETTER TO THE EDITOR

Acetyl-L-carnitine undervalued in the treatment of chemotherapy-induced peripheral neuropathy?

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To the Editor,

Chemotherapy-induced peripheral neuropathy (CIPN) is one of the most common side effects of anti-cancer therapy with a reported incidence of approximately 40%, occurring mainly in patients treated with platinum compounds, taxanes and vinca alkaloids. CIPN commonly presents with paresthesias and dysesthesias located in the fingers and toes affecting arms and legs symmetrically ('gloves and stockings'). Currently, there is no gold standard for assessment of CIPN severity. However, the consensus is that the gold standard should incorporate assessment of both objective neurological deficits and symptoms from patient perspective, as it is known that clinician-based outcomes tend to underestimate the significance of symptoms [1]. As cancer survival rates are improving, more and more people are living with long-term side effects of chemotherapy (e.g. CIPN), which are reported to have a negative effect on patient's quality of life (QoL) [2,3]. Notwithstanding the high burden of CIPN, available evidence supporting agents used for prevention and treatment of CIPN is limited. Currently, there are no established agents recommended for the prevention of CIPN in patients

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