

Do new anticancer drugs really work?

A serious concern

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Commentary on

Wise PH, 2016, Cancer Drugs, Survival, Ethics, *BMJ*, vol. 355, pag. 1-3.

Godlee F., 2016, Too much chemotherapy, *BMJ*, vol. 355 (Editorial).

Life expectancy of cancer patients has steadily increased during the last 40 years by nearly 20%. However, this is largely due to early diagnosis and improved surgical and radiation-based treatment, than on cytotoxic chemotherapy. As already reported by many studies (Morgan, 2004), a recent survey by P.H. Wise (Wise, 2016) points out that despite many patients' expectation of a cure, they are, in fact, deceived by inappropriate and unrealistic claims about what chemotherapy can really do. The potential drug benefit is indeed overestimated by both industry and oncologists. Consequently, as evidenced by a multicenter study (Weeks, 2012), almost 75% of 1200 metastatic colon and lung cancer patients believed to be 'cured' by chemotherapy, while "a cure in these situations is virtually unknown", as PH Wise points out: "In reality they (patients) will gain on average only a few months of extra life". Moreover, "Spending a six figure sum to prolong a life by a few weeks or months is already unaffordable" but it is also "inappropriate" for the many cancer patients who "will almost inevitably die from solid tumor metastases". Indeed, a review of 48 new cancer drugs approved by the FDA between 2002 and 2014 demonstrated that

these drugs extend survival by only few months reporting that the median overall survival benefit averaged only 2.1 months. Additionally, to reach such a modest result, patients must endure the exhausting therapy sessions in hospital and pay a price in terms of both cost and side effects. Indeed, side effects are frequently life threatening, while many of the new drugs that offer a few months of extra survival are hugely expensive, with costs of more than \$100,000 per year for the drug alone. Overall, these arguments reinforce an already documented evidence: new-targeted therapies seem to give little benefit, if any, in cancer control. Indeed, "targeted therapies are generally not curative or even enduringly effective" (Hanahan, 2014) and therefore, the "promise of molecularly targeted therapies remains elusive" (Kamb, 2010). Despite some limited progress that has been noticed in the case of a few specific cancers, changes in cancer mortality rates reflect declined incidence (mostly due to reduced tobacco smoking), early detection or improved surgical/radiotherapy interventions, whereas drug innovation is likely to have dropped cancer mortality rate by only 4 % (Lichtenberg, 2010).

These results raise several ethical, medical and scientific concerns. From an ethical point of view, “opting for supportive rather than active treatment—often called “refusal”—is an option and may give [the patients] longer as well as better quality of life than chemotherapy”. Are we sure that patients are adequately informed about chemotherapy? From a clinical point of view, for several types of cancer (lung, stomach, and brain) chemotherapy should be limited to specific sub-sets of patients (based on sensitive, new markers, still to be unveiled). Indeed, even in these cases, the clinical benefit may be very limited. As outlined in a report published in *Nature*, “When patients with diverse, relapsed cancers are given drugs based on biological markers, only around 30% respond at all, and the median progression-free survival is just 5.7 months (Schwaederle, 2016). Multiplying the percentage of patients receiving targeted therapies by this response rate [it is estimated] that precision oncology will benefit around 1.5% of patients with relapsed and refractory solid tumors” (Prasad, 2016).

Finally, from a scientific point of view, the failure of chemotherapy-based treatment of cancer highlights the inadequacy of the current carcinogenesis model – the Somatic Mutation Theory – on which those treatments are based. Single or few enzymatic and genetic targets cannot any longer be considered as “drivers” of cancer development and consequently their blockade could hardly provide any significant benefit (Bizzarri & Cucina, 2016).

Thereby, “Ethical cancer care demands empowerment of patients [...] with accurate, impartial information followed by genuinely informed consent. Funds and attention should shift towards prevention, early detection, prompt and radical treatment of localized and regional disease, and early provision of supportive care. Only then will cancer care serve patients rather than governments and industry” (Godlee, 2016).

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