# Targeted therapy in cancer care – A critical snapshot

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*"To be sure of hitting the target, shoot first, and call whatever you hit the target." Ashleigh Brilliant (English author and cartoonist, b. 1933).*

Invariably, each story of success in cancer therapy has taught us an important lesson that cuts across all therapeutic anticancer modalities. This lesson is the sombre fact that each anticancer breakthrough has its share of side effects and toxicities. In simple terms, anticancer therapies act not only on cancer cells but on normal tissue cells as well.

In the context of medical oncology, the search for having an agent which kills only the tumour cells and spares the normal tissues has therefore been on the cards for a long time. In the present day, no oncology conference or seminar is complete without special sessions on targeted therapy. The term "targeted therapy" got a buoyant headstart by the fairytale successes met in treating chronic myeloid leukaemia (CML) and gastrointestinal stromal tumour (GIST) by Imatinib [1]. The dramatic responses with these magic bullets were inspiring indeed. But it was soon realised that these breakthroughs were "case reports" in the broader perspective of overall cancer care. Millions of dollars have since been spent in pursuit of other targets and finding agents to attack these targets, with miniscule success. Invited speakers in meetings, reputed researchers in reviews and even the lay media talk about the success achieved so far and the way forward [2]. But simple queries as to why a sizeable percentage of patients receiving these drugs still relapse (or those not receiving the drugs remain disease free) have no clear answers. Despite the promise of the new generation of molecularly targeted drugs, intrinsic and acquired resistance is proving to be as problematic as with cytotoxic drugs [3]. Oncologists talk about the lessons learnt and the way to find an "enriched" population that shall benefit from these agents. The focus seems to be on finding the subgroups that shall benefit most with the targeted therapy agents. Clearly, the mandate has moved from making a therapeutic molecule for an existing target to using the available agent for fitting some indication in some subgroup.

It is hard not to compare the present state of targeted therapy to a nearly equivalent scenario in radiation oncology. Radiation oncology has become ever more sophisticated and technologically advanced in recent years. The traditional low energy orthovoltage machines have become a curiosity. Cobalt machines which replaced the othovoltage machines have themselves bowed out to elegant and sophisticated linear accelerators (LA). LA's in turn have undergone radical (and almost biannual!) metamorphosis from machines capable of shaping out simple square or rectangular 4 MV/6 MV beams to the current versions which boast of Multileaf collimators, arc treatment, asymmetric jaws, dynamic motion and image guidance capabilities. All this, again, comes at a price [4].

Two core issues still remain. One, radiotherapy, akin to chemotherapy (and targeted therapy) is far away from a stage where radiation would affect only the tumour cells, completely and immaculately sparing normal cells. Secondly, while newer imaging modalities in radiology have improved Gross Tumour Volume (GTV) imaging, serious issues regarding contouring of microscopic disease Clinical Target Volume (CTV) and the final Planning Target Volume (PTV)

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remain [5]. In patients with an intact GTV a "suitable margin" is given by the radiation oncologist to account for microscopic spread of disease (or the CTV). Literature for the extent of this margin (derived from pathological series, imaging data, wisdom earned from pattern of recurrences) is limited for most sites [6]. In brief, the gun of radiation delivery is reasonably precise, but the issue of target definition remains ever controversial.

To conclude, the biology, behaviour and even the correct radiology interpretation of cancer is far from understood. Defining targets and treating them, both in the context of medical as well as radiation oncology is challenging. The oncology community has made some preliminary progress towards the goal of real targeted therapy. But as readily evident, it is not the time to celebrate but to introspect. If needed, we should redefine our priorities and concepts, even if it means beginning afresh in some areas. We are yet so far from understanding cancer and its mystic ways. And real targeted therapy is not even on the anvil yet.

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## References

[1] Quintás-Cardama A, Kantarjian H, Cortes J. Imatinib and beyond – exploring the full potential of targeted therapy for CML. Nat Rev Clin Oncol 2009;6:535–43.

[2] Nygren P, Sørbye H, Osterlund P, Pfeiffer P. Targeted drugs in metastatic colorectal cancer with special emphasis on guidelines for the use of bevacizumab and cetuximab: An Acta Oncologica expert report. Acta Oncol 2005;44:203–17.

[3] Ellis LM, Reardon DA. Is there really a yin and yang to VEGF-targeted therapies? Lancet Oncol 2010;11:809–11.

[4] Zietman A, Goitein M, Tepper JE. Technology evolution: Is it survival of the fittest? J Clin Oncol 2010;28:4275–9.

[5] Munshi A, Agarwal JP. Evolution of radiation oncology: Sharp gun, but a blurred target. J Cancer Res Ther 2010;6:3–4.

[6] Pena PC, Kirova YM, Campana F, Dendale R, Bollet MA, Fournier-Bidoz N, et al. Anatomical, clinical and radiological delineation of target volumes in breast cancer radiotherapy planning: Individual variability, questions and answers. Br J Radiol 2009;82:595–9.