

## Lung cancer patients live longer if they use beta-blockers while receiving radiotherapy

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Patients with non-small-cell lung cancer survive longer if they are taking beta-blockers while receiving radiotherapy, according to a study of 722 patients published in the cancer journal *Annals of Oncology* today.

Researchers at the University of Texas MD Anderson Cancer Center (Houston, USA) reviewed the progress and outcomes of <u>patients</u> who had received radiotherapy as their main or first line of treatment for cancer (known as "definitive radiotherapy" i.e. radiotherapy that is delivered at doses of 60 Gy or more, with the intention of curing the disease).

They found that 155 patients who were on beta-blockers for other conditions, such as high blood pressure and heart disease, survived for an average of 23.7 months compared to the 567 patients who were not on beta-blockers, who survived for an average of 18.6 months – an improvement in survival of 22% after adjusting for other factors such as age, stage of the disease, whether or not chemotherapy was given at the same time, chronic obstructive pulmonary disease and the use of aspirin.

Beta-blocker use was also associated with improvements in survival without the disease spreading to other parts of the body (distant metastasis-free survival) and survival without the disease recurring (disease-free survival). Beta-blockers made no difference in the length of time a patient survived without the disease progressing in the part of the lungs where it had first occurred (locoregional progression-free survival).



Assistant Professor Dr Daniel Gomez, at the Department of Radiation Oncology at the MD Anderson Cancer Center, said: "Despite recent improvements in radiotherapy and chemotherapy for non-small-cell-lung cancer, the prognosis of this disease is poor, with less than 15% of patients surviving for five years after diagnosis. A major cause of death is the process of metastasis, when <u>cancer cells</u> travel from the original tumour to other parts of the body. Therefore, we urgently need to find new ways of blocking the development of metastases in these patients.

"Our results suggest that the use of beta-blockers during radiotherapy may help to prevent the formation of metastases, and could lead directly or indirectly to improved care for patients with non-small-cell lung cancer. As far as we are aware, our study is the first analysis to show a survival benefit associated with the use of beta-blockers during definitive radiotherapy in patients with NSCLC. However, prospective studies are needed to investigate these findings further and to discover whether improved survival is affected by when and for how long patients need to take beta-blockers. We are excited about using our study as a starting point for further investigations."

The mechanism underlying the development of metastases is complex, but may involve chronic stress conditions and prolonged exposure to stress hormones. One of these hormones, norepinephrine, has been shown to stimulate the migration of tumour cells to other parts of the body. Receptors on the surface of cells, which beta-blockers are designed to inhibit, are involved in this process.

Professor Zhongxing Liao, from the Department of Radiation Oncology at the MD Anderson Cancer Center, said: "Our findings agree with results from previous studies suggesting that beta-blockers have a specific effect on the cascade of events that lead to metastases. The fact that their use did not affect locoregional progression-free survival suggests that the drugs affect this metastatic cascade rather than the



primary tumour."

Patients in the study had been treated with definitive radiotherapy from 1998 to 2010 at the MD Anderson Center. The 155 patients on beta-blockers were taking a range of different types of the drug and at a range of doses depending on the medication and their need. The researchers said there were not enough patients in the study to discover whether the choice of beta-blocker might be important, but that most of the study patients who did well were on a selective beta-blocker. "This finding requires further investigation," said Prof Liao.

She added: "Due to practical limitations, we were unable to assess whether any other medications that patients were taking while receiving radiotherapy may have influenced the results. This should be the subject of future analyses, ideally in clinical trials."

Dr Gomez said the researchers were discussing the possibility of a clinical trial to investigate the efficacy of new treatments, such as beta-blockers, for <u>lung cancer</u>, but that this would require external funding. "Another future direction would be to examine further the molecular characteristics that lead to this apparent clinical improvement in survival. For instance, what cellular pathways are involved in patients that experience a benefit with beta-blockers, and can these mechanisms be altered in another way to achieve the same benefit?"

**More information:** "Improved survival outcomes with the incidental use of beta-blockers among patients with non-small-cell lung cancer treated with definitive radiation therapy", by H.M. Wang, Z.X. Liao, R. Komaki, J.W. Welsh, M.S. O'Reilly, J.Y. Chang, Y. Zhuang, L.B. Levy, C. Lu and D.R. Gomez. *Annals of Oncology*. doi:10.1093/annonc/mds616



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