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Researchers develop non-invasive technique for predicting patients' response to chemotherapy

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Researchers have developed a non-invasive way of predicting how much of a cancer-killing drug is absorbed by a tumour. The preliminary study, which will be reported at the 24th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Dublin, Ireland, today (Thursday), was conducted in lung cancer patients and it also revealed that less than one per cent of the drug, docetaxel, is absorbed by the tumours.

Dr Astrid van der Veldt (MD, PhD), from the VU University Medical Center in Amsterdam, The Netherlands, told the Symposium: "This finding underscores the fact that only a small amount of drug accumulates in tumours and indicates that there is an urgent need for strategies that selectively enhance drug delivery to tumours. For that purpose, the direct effects of other, anti-cancer drugs on metabolism as well as drug delivery to tumours need to be investigated, as other drugs may also affect metabolism and drug delivery to tumours."

Until now, there has been no accurate way of assessing how much of an anti-cancer drug is absorbed by a tumour and, therefore, what effect the drug is having on the tumour, without invasive surgery to extract samples.

Dr van der Veldt and her colleagues used an imaging technique called positron emission tomography (PET) to track very small tracer doses of

the anti-cancer drug docetaxel, which had been radiolabeled with the positron emitting radionuclide carbon-11, in the patient. The PET scan was able to follow this tiny [11C]docetaxel dose in the body non-invasively and provide information on how much reached the tumour, the amount absorbed by the tumour and its effect on the tumour (the pharmacokinetics and pharmacodynamics of the drug). By using a microdose of docetaxel in this way, the patients were protected from any docetaxel-induced toxic side-effects that could occur if the docetaxel was administered at therapeutic doses.

Dr van der Veldt said: "A potential problem with this is the fact that the behaviour of [11C]docetaxel in the tumour at tracer doses may be different from its behaviour at therapeutic doses. Therefore, we investigated whether a PET study using tracer doses of [11C]docetaxel could predict tumour uptake of docetaxel at therapeutic doses."

Six lung cancer patients who had not been treated previously with docetaxel underwent two PET scans, one with the tracer dose of docetaxel, and another during a combined infusion of a tracer dose and a therapeutic dose (75mg/m2) of docetaxel. The researchers compared the tumour uptake of both the tracer and therapeutic doses of docetaxel and found that the tracer dose correctly predicted the tumour uptake of the therapeutic dose.

"This study showed that microdosing data from PET scans of [11C]docetaxel could be used to reliably predict tumour uptake of docetaxel during chemotherapy, which was also associated with tumour response to docetaxel therapy. This is important information for us to have when we are treating patients, as it helps us to predict how well the drug is working and whether it might be better to switch to some other, potentially more effective treatment. The findings of this study warrant larger clinical studies investigating the predictive value of initial [11C]docetaxel uptake for tumour response to docetaxel therapy," said

Dr van der Veldt. "In addition, the present study provides a framework for investigating the PET microdosing concept for other radiolabeled anti-cancer drugs in patients with other cancers.

"To the best of our knowledge, the present study is the first in which absolute tumour uptake of chemotherapy is measured non-invasively in patients."

Additional analyses revealed that less than one per cent of the therapeutic dose of docetaxel that was infused in the patients was finally taken up by the tumour tissue. This uptake might also be affected by other drugs that are being delivered at the same time. "For example, in a recent study, we have shown that the drug bevacizumab, which inhibits the creation of new blood vessels supplying the tumour, induces a rapid and significant reduction in delivery of [11C]docetaxel to tumours in non-small cell lung cancer patients," said Dr van der Veldt.

She concluded: "Although, at present, [11C]docetaxel PET cannot be used on a large scale because of its complexity and high costs, it is a promising technique for several investigations. [11C]docetaxel PET may be useful to predict response to docetaxel therapy and select patients for docetaxel-containing treatment strategies, thereby contributing to more personalised treatment planning in individual cancer patients. In addition, [11C]docetaxel PET may help to define the optimal design of large clinical trials to investigate the effects of drug scheduling on efficacy in cancer patients."

Professor Stefan Sleijfer, the scientific chair of the EORTC-NCI-AACR Symposium, from Erasmus University Medical Centre (The Netherlands), commented: "This study is interesting because it provides more insight into the amount of drug that reaches the place where it should go: the tumour cell. Because of technical limitations, this is a relatively unexplored field of research, which is of great importance.

Eventually, this may lead to better prediction of outcome and novel combinations augmenting the penetration of active anti-tumour agents into the tumours."

More information: Abstract no: 245. Proffered papers, plenary session 6, 15.00 hrs, Thursday 8 November.

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