Imaging techniques in oncology

Andreas Gutzeit

Cantonal Hospital Winterthur, Switzerland/ University of Salzburg, Austria

Correspondence to:

Andreas Gutzeit,
Cantonal Hospital Winterthur,
Winterthur, Switzerland
andreas.gutzeit@ksw.ch

Identifying and diagnosing cancerous diseases is currently one of the main tasks of today's radiologist. Every year cancer is diagnosed worldwide in over 12 million people. Within a single year, 7 million people die from cancer worldwide.

The most commonly diagnosed cancers are lung, breast, and colorectal cancers. The most common causes of cancer death are lung, stomach, and liver cancers.

Besides identifying primary tumours, it is also very important that radiology identifies possible metastases in other organs such as the liver, bones, brain, etc. at an early stage. Today all this information is gained using imaging techniques. The radiologist thus plays an important part in the treatment of people suffering from cancer.

A further important task of the radiologist using imaging techniques is judging whether oncological treatment of the tumour's course has to be initiated. In this way, the radiologist is able to make a statement as to whether the targeted oncological therapy has achieved its goal or whether in the absence of a response it has to be further adjusted.

The total medical care costs for people with cancer are approximately 20% higher than those for heart or vascular diseases, which are the second leading causes of global health costs. These high costs, however, arise as the result of many different factors such as costs of medication and the various therapy options, nursing care, and a lesser proportion also due to the application of radiological techniques.

The radiologist has many different techniques at his disposal to identify neoplasias within the body.

In principle, there are techniques using or not using X-rays.

Ultrasound

Ultrasound involves emitting sound waves of different wavelengths via a special transducer and a piezoelectric crystal into the body, which are then able to be converted to images. This method is free of X-rays and can be supplemented by special well-tolerated contrast media. The procedure is relatively inexpensive but heavily dependent on how well trained the physician is in using this technique.

X-rays

This is one of the oldest imaging techniques and is based on the use of small doses of X-rays. These penetrate the body and can render images of individual structures of the body's interior. The procedure is relatively inexpensive but, depending on application, of varying sensitivity. In mammography in particular, breast cancers can be discovered relatively well.

Computer tomography

Cross-sections of the body can be used with this method, which show a very high resolution. In addition, the images can be 'reconstructed' using various techniques, which may be very useful in identifying tumours. The procedure is extremely fast and imaging of the human body from head to foot can be completed within a few seconds. These procedures are used extremely often in the diagnosis of oncological diseases. Disadvantages of the procedure are the relatively high costs and a certain degree of exposure to radiation for the patients. Using new radiation-saving techniques, it will, however, be possible to reduce exposure to radiation in the future dramatically.

Magnetic resonance tomography

This procedure is based on hydrogen atoms of the human body being excited electromagnetically with the help of a strong magnet resulting in the generation of a signal. The procedure is very versatile and in addition to medical care of cancer patients is used in practically all areas of medical care (orthopaedics, neurology, paediatrics, etc.). The advantage of this technique is extremely good contrast of soft tissues, with whose help tumours can be imaged and diagnosed very well. Clinical observations of a tumour's course are also perfectly possible using this procedure. No harmful effect of this procedure is known, this being the reason why even unborn

© The European Medical Writers Association 2012
DOI: 10.1179/204748112X13305147722934

children in the womb can be examined. The disadvantage, however, is the relatively high cost involved.

Nuclear medicine procedures

In nuclear medicine procedures, among other things, radioactive substances can be injected into the body, which can then accumulate specifically in certain diseased regions. In addition to the diagnosis of various oncological diseases, the procedures can partly be used therapeutically (e.g. in the thyroid). In the meanwhile, nuclear medicine procedures can also be combined with other radiological techniques (e.g. PET/CT).

Summarizing, there are a variety of radiological techniques for the medical care of cancer patients. Without these techniques, oncological medicine would no longer be conceivable today.

Clinical pharmacology series
Does pharmacokinetics have a role in anti-cancer drug development?

It has been estimated by the International Agency for Research on Cancer that the instances of newly diagnosed cancer will more than double from 12 million in 2008 to 27 million in 2030.[1] Furthermore, almost 13% of deaths worldwide are cancer related. Unsurprisingly the pharmaceutical industry is keen to develop novel treatments in this important disease area. In the fiscal year ending 30 September 2011, the FDA approved 35 new medicines, of these 7 provided major advances in cancer chemotherapy.[2] In a similar time period, marketing authorization approval was granted by the European Medicines Authority (EMA) for Zytiga (Abiraterone) and Yervoy (ipilimumab), respectively, indicated for the treatment of metastatic advanced prostate cancer and advanced melanoma.

Abiraterone is a small molecule administered orally as an immediate release tablet. Ipilimumab is a fully human monoclonal antibody (MoAb), given via an intravenous infusion. Nevertheless, examination of the respective EMA assessment reports for this small molecule and biologic indicated that an understanding of pharmacokinetics (PK) was an important consideration in the posology for both drugs.[3,4]

Abiraterone has a mechanism of action that is non-cytotoxic (it is anti-androgenic); hence it was safe to initially investigate the PK of the compound in healthy volunteers. A critical finding from these studies was the influence of food on the systemic exposure of the compound, up to a 10-fold increase in area under the curve was observed with a high fat meal. The summary of Medical Product Characteristics contained the consequent dosing recommendation that abiraterone should be taken at least two hours after eating and no food should be eaten for at least one hour after taking the drug.

The pharmacology of ipilimumab was such that it was not possible to study the PK in healthy volunteers. PK data were generated from patients with advanced melanoma either through extensive sampling in Phase I-type single and multiple dose studies or the use of sparse sampling and population PK methodology in efficacy studies. Population PK data, gathered from 498 patients across four Phase II studies, were instrumental in evaluating the influence of physiologic and demographic factors on ipilimumab concentration–effect relationships. These investigations found that no specific dose adjustment was necessary in patients with mild-to-moderate renal dysfunction; information that was transferred to the final product label.

For both abiraterone and ipilimumab the dose proportionality and systemic drug exposure were assessed in addition to the predictability of multiple dose PK from the single-dose data. Overall, the EMA concluded that the PK of both novel drugs had been adequately studied.

The investigation of the PK properties of anti-cancer medication during development is concurrent with the EMA 'Guideline On The Evaluation Of Anticancer Medicinal Products In Man' (2005).[5] The document outlines the need to investigate PK in vulnerable populations and those with organ impairment. For MoAbs it suggests that understanding the PK provides some guidance for dose-finding as clearance may be related to target saturation.

The development programmes for abiraterone and ipilimumab illustrate two important principles. In cancer, like other disease areas, it is important to understand the factors that can contribute to variability in PK and subsequently pharmacodynamics, as this potentially influences the dose selected. Secondly it is incumbent on the drug developer to investigate such variability, irrespective of whether the anti-cancer agent is a small molecule or a biologic.

References

1. Wilking N, Jönsson B. Cancer and economics: with a special focus on cancer drugs. Oncol News 2011;6:17–9.
2. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm278383.htm.
3. EMA, Committee for Medicinal Products for Human Use (CHMP). Assessment report Zytiga (abiraterone). 21 July 2011. Procedure No.: EMEA/H/C/002321.
4. EMA, Committee for Medicinal Products for Human Use (CHMP). Assessment report Yervoy (ipilimumab). 19 May 2011. Procedure No.: EMEA/H/C/002213.
5. EMA, CHMP, Guideline on the Evaluation of Anticancer Medicinal Products in Man. London: EMA. December 2005.

Graham Blakey
GBPK Consulting Ltd
graham@gbpkconsulting.co.uk
www.gbpkconsulting.co.uk