

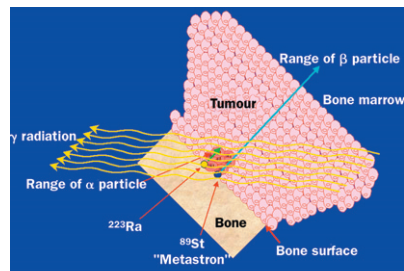
## <sup>223</sup>Ra targets skeletal metastases and spares normal tissue

A new form of internal radioisotope therapy using radium-223 may be effective for treating skeletal metastases, according to research presented at the 18th UICC Congress in Oslo, Norway, June 30–July 5, 2002.

"<sup>223</sup>Ra is incorporated in bone during synthesis of bone mineral and since skeletal metastases are often distinguished by elevated bone synthesis this approach could provide a way of targeting bone metastases," says Roy Larsen (Anticancer Therapeutic Inventions, Oslo, Norway).

Once incorporated into the bone, <sup>223</sup>Ra decays, emitting radioactive  $\alpha$ -particles which damage the surrounding tissue of the lesion. <sup>223</sup>Ra is thought to have fewer side-effects than  $\beta$ -particle emitters such as samarium-153 and strontium-89, which have also been used in this way, because  $\alpha$ -particles travel much shorter distances and are therefore less damaging to normal tissue.

As part of a phase I clinical trial to establish the safety of this approach, Larsen and co-workers gave 10 patients either 37 kBq/kg or 74 kBq/kg <sup>223</sup>Ra in a single intravenous injection. Blood <sup>223</sup>Ra activity diminished rapidly (down to 0.5% after 1 day) and scintigraphic



$\alpha$ -emitting radioisotopes like <sup>223</sup>Ra are less harmful to surrounding tissue than  $\beta$ -emitting isotopes.

analysis showed that the isotope had accumulated in known skeletal lesions. Encouragingly, patients in the study were able to reduce their dose of painkillers.

Larsen is hopeful that <sup>223</sup>Ra will prove more effective than other treatments. "We have done some comparisons using a rat skeletal-metastases model. <sup>223</sup>Ra seemed to be better than cisplatin, doxorubicin, pamidronate, and a  $\beta$ -particle emitting radioisotope." So far, however, there have been no similar studies in humans.

An independent observer commented that  $\alpha$ -emitters, such as <sup>223</sup>Ra, are a very powerful means of killing cells at close proximity. In addition, a short half life makes <sup>223</sup>Ra a far more attractive treatment option than <sup>89</sup>Sr and it is less likely to cause long-term cytopenia. He also noted that <sup>223</sup>Ra is more powerful than <sup>153</sup>Sm-EDTMP despite having less penetration of skeletal tissue.

"The results so far have been very encouraging," Larsen added, "we are in the process of planning a phase II study to evaluate the therapeutic effects of <sup>223</sup>Ra."

**Cathel Kerr**

## An infectious origin for some types of breast cancer?

The etiology of some breast cancers may be unrelated to diet or genetics and instead acquired horizontally through viral transmission, according to a recent presentation at the International Union Against Cancer's 4-yearly Congress (June 30–July 5, 2002, Oslo, Norway).

James Holland and colleagues (Mount Sinai School of Medicine, NY, USA) made a case for the viral transmission of breast cancer by presenting results from their own research and that of others carried out in recent years.

An initial study found that 38.5% of breast cancer samples from American women contained a 660 base pair sequence of the envelope (*env*) gene from the mouse mammary tumour virus (MMTV), which has limited homology to any other human or viral genes (*Cancer Res* 1995; 55: 5173–79).

Further studies have shown the geographical distribution of breast cancers positive for *env* vary (eg, USA 38%, Italy 37%, Argentina 31%, Brazil 27%, and Mexico 33%), and that these differences correlate with differences in

the geodistribution of mouse species with high copy numbers of genomic MMTV (*Brit J Cancer* 2000; 82: 446–51).

Supporting this idea, Holland points out that only about 10–12% of breast cancers from Japanese and Chinese women are positive for *env*—consistent with the prevalence of the *mus musculus* population of mice in these countries which have low MMTV infection.

"We have not proven that the gene comes from mice," says Holland. "But since mice coexist with humans, opportunities for contamination of food, air, water, and arthropod vectors are all possibilities, and we are [currently] pursuing these leads."

More recently, PCR analyses conducted by Holland and co-workers in two *env*-positive human breast carcinomas found a 9.9 kB provirus that was 95% homologous to MMTV. Furthermore, the *gag* and *pol* domains of the so-called human mammary tumour virus (HMTV) showed only 57% homology to the human

endogenous retrovirus (HERV) called K10 (*Cancer Res* 2001; 81: 1754–59).

Bernard Poiesz (Upstate Medical University, NY, USA), who is independently investigating HTMV as a cause of breast cancer, has confirmed these findings: "We have validated the essential observation that they had, although we found the sequence at a rate of only about 10–30%." Poiesz adds that different PCR methods between the two groups may account for the difference.

Poiesz emphasises that the sequences he and his colleagues have found are likely to be exogenous and not the sequences of any of the six strains of endogenous MMTVs already known to exist in all humans.

"So far, our data support the hypothesis that this sequence is exogenous," Poiesz says. "But to prove that this is an exogenous infectious agent of humans, it will have to be isolated from a patient with breast cancer and passed in vitro from one cell to another."

**Emma Hitt**