# First Phase III trial of an alpha-pharmaceutical

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Until recently, options for patients with bone metastases from advanced prostate cancer have been very limited. But now the first Phase III study of an alpha-pharmaceutical in these patients has shown that it can prolong survival significantly, according to research reported today (Saturday) at the 2011 European Multidisciplinary Cancer Congress.

Dr. Chris Parker, Consultant Clinical Oncologist at the Royal Marsden Hospital, London, UK, told the congress that the ALSYMPCA international Phase III study of the drug Radium-223 Chloride (Alpharadin TM) in 922 prostate cancer patients who were resistant to hormone treatment and had bone metastases, had been stopped early once an interim analysis by the Independent Data Monitoring Committee (IDMC) in June 2011 had revealed that patients receiving the best standard treatment plus radium-223 were living longer than those who were receiving the same standard treatment plus placebo. The hazard ratio was 0.695, (p = 0.00185), meaning that patients taking radium-223 had a 30% lower rate of death compared to patients taking placebo. Median overall survival for patients taking radium-223 was found to be 14 months, compared with 11.2 months in the placebo group. "It would have been unethical not to offer the active treatment to those taking placebo," Dr. Parker said.

Alpha-pharmaceuticals work by delivering minute, highly charged and targeted doses of damaging radiation to a secondary tumour (metastasis) in the bone. Radium is similar to calcium in that it sticks to bone, and particularly to where new bone is being formed, so it is a highly effective way of delivering radiation to a target. "It takes only a single alpha particle to kill a cell," Dr. Parker explained, "and collateral damage is minimised because the particles have such a tiny range - a few millionths of a metre (micrometres). So we can be sure that the damage is being done where it should be, to the metastasis, and very limited elsewhere."

The researchers chose to study the drug in patients with prostate cancer because of its high tendency to metastasise to bone. Around 90% of all men with prostate cancer will develop bone metastases in the advanced stage, and in many cases there are not detectable metastases elsewhere in the body. The safety profile of radium-223 was found to be highly favourable, the researchers say.

"Compared to chemotherapy, which affects all the tissues of the body, radium-223 is highly targeted to the bone metastases, and it has a completely different safety profile," said Dr Parker.

Side effects with radium-223 are minor. It can cause nausea, and occasional loose bowel movements, and there is a very small effect on the bone marrow. "Although it has never been rigorously compared with chemotherapy, from observing patients in the clinic it is clear that patients tolerate it much better than they do chemotherapy," Dr. Parker said.

The researchers now intend to submit the data for regulatory approval. "I would hope that the authorities will approve radium-223 as a treatment for bone metastases in advanced prostate cancer soon," said Dr. Parker. "This is a common cancer - the second commonest cancer killer in men in the UK - and so it's a big disease burden. We urgently need effective treatment for it.

"I have no doubt that there will be further trials looking at a combination of radium-223 with other drugs that are currently used in prostate cancer, and that there will also be studies using radium earlier in the disease. In particular, our research was restricted to those men who were not going to receive chemotherapy for prostate cancer. It would be interesting to use radium-223 chloride before chemotherapy, since it might be even more effective in that setting.

"Additionally, the drug could be used in many other types of cancers which metastasise to bone, regardless of the primary site. We believe that our trial may have paved the way for improvements in survival for very many cancer patients," he concluded.

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