Alpha Particle therapy (using actinium (Ac)-225 and its daughter product bismuth (Bi)-213 is a new and promising treatment for many forms of cancer. Clinical trials for acute myeloid leukemia have been promising, with about 25% of terminal patients going into remission. Researchers throughout the world are examining approaches for prostate cancer, bladder cancer, ovarian cancer, pancreatic cancer, melanoma and non-Hodgkin’s lymphoma. Unfortunately, there is not enough supply of the medical isotope actinium (Ac)-225 to support current world research needs much less therapeutic use.

The National Institutes of Health (NIH) conservatively projects world demand for actinium Ac-225 at 7,500 mCi per year by 2009 yet current world production is less than 600 mCi per year. Without additional supplies, further progress on clinical and preclinical research is at serious risk.

Solving Supply Issues

Medical Actinium for Therapeutic Treatment (MATT), technology was developed at the U.S. Department of Energy (DOE’s) Idaho National Laboratory (INL), to resolve this critical supply problem. Currently, there are only three sources in the world that largely “milk” these isotopes from a shrinking supply of less than 2 grams of the parent source material – Thorium (Th)-229.

MATT will significantly increase isotope production rates of Ac-225 and its daughter product Bi-213 – tripling the worldwide supply of Ac-225 within the first year of pilot-scale production and increasing supplies by 100-150 times at full production levels.

Increasing the supply of Ac-225 enables clinical cancer treatment trials to proceed. Once at full production, the process can supply sufficient isotope for treating tens to hundreds of thousands of patients each year.

MATT technology will also significantly reduce the price of production, opening the door for expanded research and therapeutic use.
Mining “Aged” Nuclear Materials for Medical Value

Through the MATT process, nuclear materials at the INL that would otherwise be destined for disposal become a valuable source of medical isotope for cancer treatment trials and therapy.

MATT separates Ac-225 from aged uranium (U)-233 in material left from DOE’s ’70s-era Light Water Breeder Reactor program at the INL, currently located in storage or in drums otherwise destined for disposal.

The only reason this stored nuclear material contains significant amounts of Ac-225 is its age. Over 40-years, a tiny fraction of the U-233 (with a half-life of 159,000 years) undergoes natural radioactive decay to form Th-229 (with a half-life of 7,340 years). The current separation technology uses this Th-229 as a “cow” source that can be periodically “milked” for the medical isotope Ac-225 (with a half-life of 10-days). It is estimated that 50g of parent Th-229 are contained in roughly 13 metric tons of unused fuel and 250 barrels slated for disposal. At least 50g more are contained in stored, irradiated nuclear fuel and another 40g is located at Oak Ridge National Laboratory.

The innovation of MATT technology is its ability to separate a tiny amount of actinium (Ac)-225, an astonishing 1 part per 165 billion, from metric tons of original source material.

Alpha-immunotherapy

At the heart of alpha-immunotherapy is a combination of alpha-emitting radionuclides carried by targeting agents. These targeting agents seek out and selectively attach to cancer cells, carrying the desired radionuclide with them. Radiation delivered by this cancer “smart bomb” kills the cancer cells.

The advantage of alpha particle therapy over other forms of radiation treatment and chemotherapies is its highly selective nature. This targeted energy of alpha particles is much more effective at killing tumor cells while nearly eliminating collateral damage to nearby healthy cells.

The isotopes Ac-225 and its daughter product, Bi-213 are ideal for alpha-immunotherapy. Ac-225 is itself an alpha-emitter requiring minimal shielding. Its half-life of 10 days is long enough to facilitate economic transport and delivery timelines, yet short enough to avoid the hassles of long-term management at medical facilities. Once there, it is “milked” for Bi-213. With a half-life of only 46 minutes, Bi-213 can be administered on an out patient basis.

Most importantly, its final non-radioactive end-product is stable bismuth (the same bismuth found in Pepto-Bismol™).

Because of the short half-life and nature of alpha radiation, alpha-immunotherapy using Ac-225/Bi-213 is especially well suited for targeting micrometastatic disease (cancers that spread) and blood-borne cancers such as leukemia. Treatment is done on an out-patient basis with no measured side effects and almost no secondary radiation exposure to family members or medical personnel.

Figure 1 Illustrates the effects of alpha-immunotherapy during and after treatment. Cancer cells are selectively destroyed with minimal collateral damage to healthy cells. This effect makes the treatment ideal for small tumors and blood-borne cancers.