Targeted alpha-ray therapy for refractory thyroid cancer

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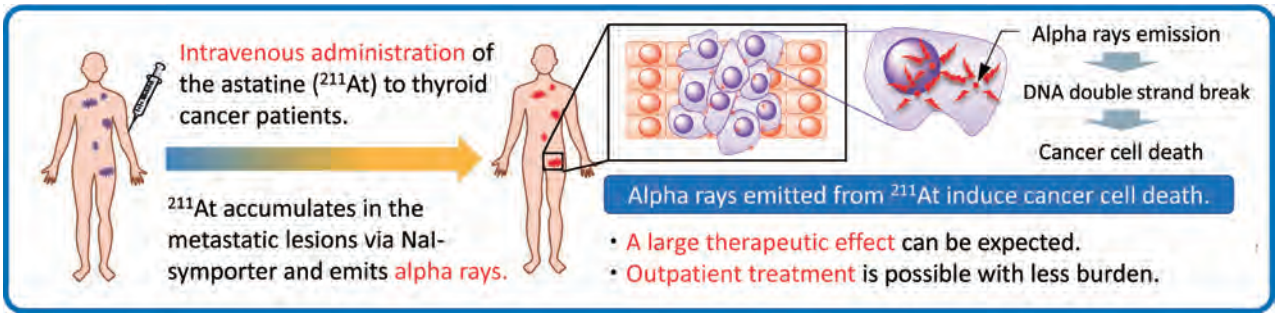
Project Outline

Cancer treatment using alpha rays has garnered attention, with excellent therapeutic effects reported in the treatment of advanced cancers. In the treatment of differentiated thyroid cancer, beta-ray therapy involving radioactive iodine (^{131}I) is commonly employed, but the therapeutic effect may prove insufficient. In addition, it needs isolated hospitalization in dedicated rooms due to regulation. Conversely, alpha rays emit a substantial amount of energy within a short range and have minimal radiation impact on their surroundings, making them suitable for outpatient treatment. Astatine (^{211}At) is an alpha-emitting nuclide that exhibits properties similar to iodine and accumulates in thyroid cancer cells. In preclinical studies, we have confirmed the efficacy and safety of [^{211}At]NaAt and have successfully established stable production as an investigational drug at Osaka University Hospital. Furthermore, we have completed an investigator-initiated clinical trial using astatine (^{211}At) in patients with refractory thyroid cancer and confirmed its tolerability and efficacy.



Outline of Investigator-Initiated Clinical Trial

A phase I investigator-initiated clinical trial (Alpha-T1 study) was conducted as a first-in-human study to evaluate the safety, pharmacokinetics, and preliminary efficacy of [^{211}At]NaAt in patients with differentiated thyroid cancer refractory to radioactive iodine (^{131}I). The study started with a low dose of 1.25 MBq/kg, followed by stepwise dose escalation to 2.5 MBq/kg and 3.5 MBq/kg. A total of 11 patients received a single administration.

Among patients in the mid- and high-dose groups (2.5 or 3.5 MBq/kg; n = 9), three patients achieved a ≥50% reduction in the tumor marker thyroglobulin compared with baseline. In addition, three patients showed disappearance of ^{131}I uptake in metastatic lesions on ^{131}I imaging (complete disappearance in one patient and near disappearance in two patients) . These results demonstrate the therapeutic potential of targeted alpha-particle therapy using astatine, even in patients refractory to conventional treatments.

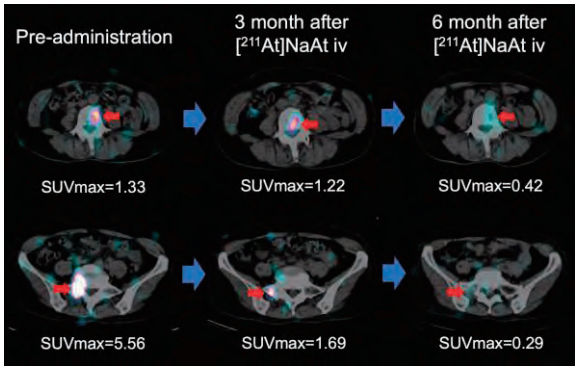


Figure 1. ^{131}I-SPECT image after administration of astatine (^{211}At): The lesions have almost completely disappeared (arrow).

- Astatine, a novel cancer therapeutic that emits alpha particles in the body, is being administered to patients with refractory thyroid cancer. Even in cases where standard treatment with radioactive iodine (^{131}I) is ineffective, alpha particles—characterized by high energy and a very short tissue range—can selectively target cancer cells and show higher therapeutic efficacy.
- As astatine can be produced using accelerator , a domestic supply network can be established and it can expand the development of targeted alpha-ray therapies for a wide range of cancers in the future.