Innovative alpha therapy targeting PSMA for refractory prostate cancer

Principal Investigator

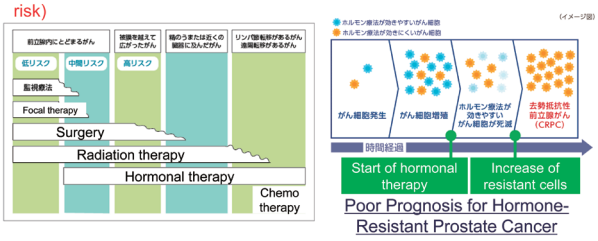
Department of Nuclear Medicine and Tracer Kinetics, Graduate School of Medicine, Osaka University

Assistant Professor Tadashi WATABE

Project Outline

Unmet needs in prostate cancer

- Patient data (2018, Japan)
  - Number of new patients: 92,021/year (1st in male)
  - Number of deaths: 12,544/year
- Castration-resistant prostate cancer
  - Five-year survival rate: 42% (low risk), 24% (intermediate risk), 5% (high risk)

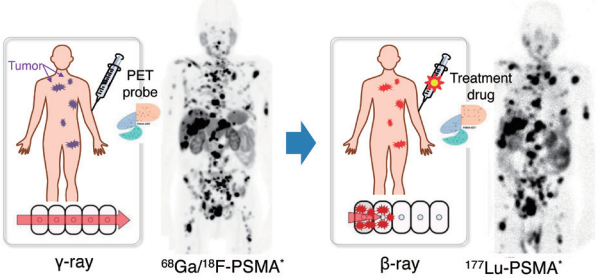


(National Cancer Center Cancer Information Service https://betterl.bayer.jp/ , Armstrong AJ, et al. Eur Urol. 2020.)

PSMA theranostics

(Prostate specific membrane antigen)

- Membrane protein highly expressed on the membrane surface of prostate cancer cells
- Expressed in most of prostate cancers, including castration-resistant prostate cancer

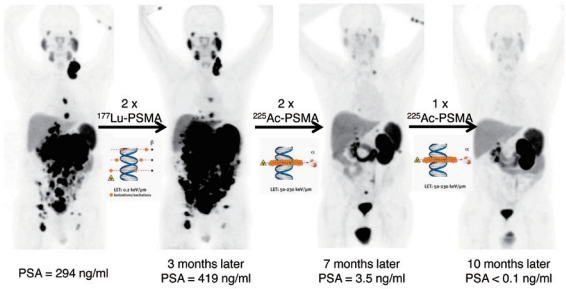


(F. Giesel et al. EJNMMI. 2016)

(* Approved by FDA and EMA)

Alpha-ray therapy with actinium(^{225}Ac)-PSMA

Advanced prostate cancer with multiple metastases

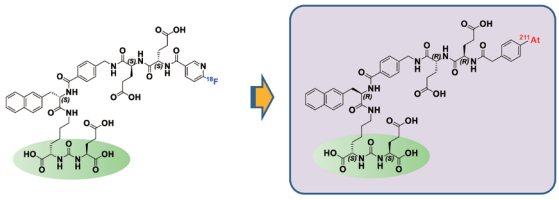


α-therapy (^{225}Ac) is remarkably effective in refractory cases in β-therapy (^{177}Lu).

(C.Kratochwil et al. J Nucl Med. 2016)

^{211}At-PSMA5: new alpha therapy

Green area: Specific binding site to PSMA (Ureido structure)



[^{18}F]PSMA-1007 PET

(Clinical research in Osaka University)

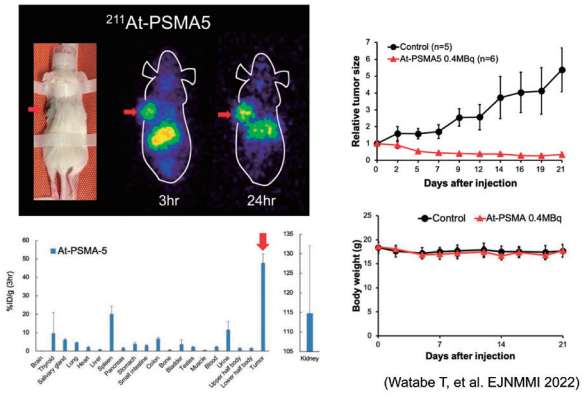
^{211}At-PSMA5 therapy

(Patent filed)

In Osaka University, we developed a new drug ^{211}At-PSMA5 by replacing the radionuclide with ^{211}At. ^{211}At is an alpha-emitting nuclide that can be produced in an accelerator, which can be used on an outpatient basis and manufactured domestically.

(Watabe T, et al. EJNMMI 2022)

^{211}At-PSMA5: new alpha therapy



(Watabe T, et al. EJNMMI 2022)

Comparison (^{177}Lu, ^{225}Ac, and ^{211}At)

	^{177}Lu-PSMA	^{225}Ac-PSMA	^{211}At-PSMA5
Radiation	β	α	α
Half-life	7 days	10 days	7.2 hrs
Therapeutic effect	△～○	◎	◎
Exposure to surroundings	Relatively high	very low	Very low
Isolation	Required	Not required	Not required
Outpatient treatment	×	○	○
Domestic production	× (Reactor)	△	◎
Cyclotron manufacturing	×	△	◎
Imaging	○	×	○
Approval status	FDA approved	No	No

Target disease: prostate cancer

Patent information: Application number: JP 2021-125774)

Technology features: An anticancer drug that emits alpha rays for advanced cancer with multiple metastases

Future plans: Under AMED translational research (seeds F) in 2022-2026, and Phase I clinical trials are scheduled to start in 2024.