Innovative alpha therapy targeting PSMA for refractory prostate cancer

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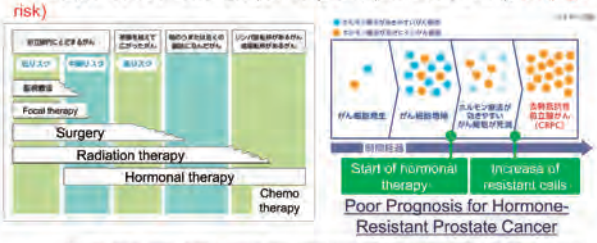
Project Outline

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://bettert.bayer.jp/ , Armstrong AJ, et al. Eur Urol. 2020.)

PSMA theranostics

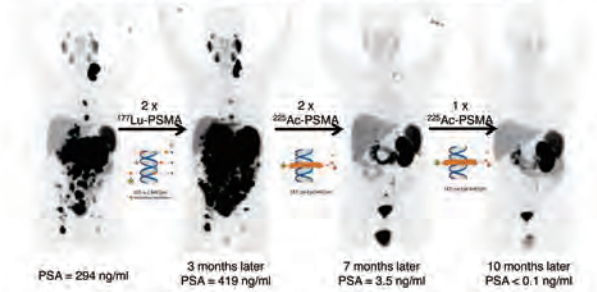
(Prostate specific membrane antigen)

- 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

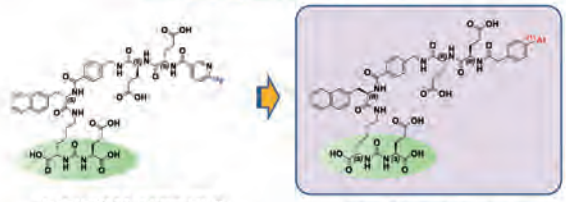


α-therapy (^{225}Ac) is remarkably effective in refractory cases in β-therapy (^{177}Lu).

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

^{211}At-PSMA5: new alpha therapy

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



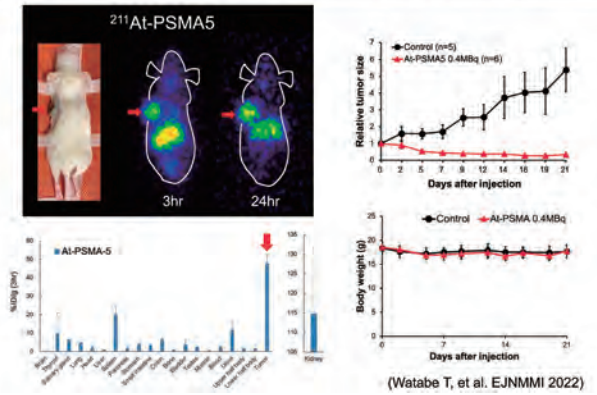
[^{18}F]PSMA-1007 PET
(Clinical research in Osaka University)

^{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

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

A first-in-human phase 1 investigator-initiated clinical trial targeting patients with castration-resistant prostate cancer began in FY2024

https://resou.osaka-u.ac.jp/ja/research/2024/20240527_1

AMED Translational Research (Seeds F) Selected Project (FY2022-2026) Patent Application Number: JP 2021-125774