targeted alpha-particle radiation therapy for LMGC in a preclinical mouse model.

Material and methods Astatine-211 (At-211), an alpha-particle emitter radionuclide, was produced by irradiation of alpha-particles to bismuth-209 using an AVF accelerator at our institute. An anti-HER2 antibody trastuzumab was conjugated with At-211 to produce alpha-emitting antibodies targeting HER2 ([At-211]-trastuzumab). To generate a mouse model of LMGC, we injected luciferase-labelled HER2-positive human metastatic NCI-N87 GC cells into splenic vein of severe combined immunodeficiency mouse. Tissue and tumour distribution of [At-211]-trastuzumab was examined in the LMGC mouse model. Therapeutic efficacy and toxicities of [At-211]-trastuzumab were evaluated in the animal model. All animal experiments conducted in this study were approved by the Animal Care and Use Committee of our institute and were undertaken in compliance with the institutional guidelines regarding animal care and handling.

Results and discussions Biodistribution studies showed that the maximum uptake of [At-211]trastuzumab in the liver metastatic tumours was approximately 12% of injected dose per tissue gram at 24 hours after injection.A systemic injection of [At-211]trastuzumab (1 MBq) significantly reduced a tumour burden in the liver and extended the survival of model mouse. Transient leukocytopenia was observed in mice received 1 MBq of [At-211]trastuzumab at 5–7 days after injection. No body weight loss was so far found in the mice treated with [At-211]trastuzumab.

Conclusion Our preclinical study provides the evidence that targeted alpha-therapy using [At-211]-trastuzumab is effective for LMGC.

PO-111 NON-CONTACT ELECTRIC FIELDS INHIBIT THE GROWTH OF BREAST CANCER CELLS IN ANIMAL MODELS AND INDUCE LOCAL IMMUNE REACTION

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Introduction Non-contact electric fields namely Electro-capacitive Cancer Therapy (ECCT) exposure with low intensity and intermediate frequency (100 KHz) exerted between two capacitive electrodes increased the percentage of cell death of MCF-7 (39.45%). In addition, a pilot study of the safety and efficacy of ECCT performed in 9 C3H mice revealed significant tumour shrinkage of more than 67% in size. Histopathological analysis of the mammary glands showed macrophages and other immune cells infiltrate through the blood vessel in the area of breast tumour. We continued our study by using bigger sample size to observe the safety and efficacy of ECCT and local immune reaction after exposure.

Material and methods All procedures involving animals were performed following approval by the Research Ethics Committee of Gadjah Mada University. Sprague Dawley rats were divided into three groups, each consisted of 9 rats. Two groups were DMBA-induced mammary tumours, and the other was placebo. One group of mammary tumour rats and the placebo ones were exposed to ECCT individually for 10 hours per day for 3 weeks. Tumour size was measured using a calliper. Blood sample were collected from rat orbital sinus for Complete Blood Count and blood chemistry tests. Finally, the rats were euthanized by using ketamine overdose for breast, kidney and liver histopathological analysis.

Results and discussions After 3 weeks of exposure to ECCT, the growth rate of DMBA-induced mammary tumour was lower (0.01 cm^2/day) than the non-therapy one (0.121 cm^2/day) with statistical significance. The development of nodules of the therapy group was fluctuated indicating fluid intake in the nodules. After necropsy, the nodules were hollow which filled with fluid. Lymphocytes were seen in the area of breast cancer. Furthermore, cancer wounds have shrunk and dried up under exposure. No significant changes were observed in the complete blood count of the therapy groups. The activity of alanine transaminase and the level of bilirubin were not affected by the exposure, but not for creatinine level. However, no significant abnormality was found in the kidney structure, and the liver as well.

Conclusion The results suggest that 100 kHz of non-contact electric fields at low intensity inhibit the growth of breast cancer in rat, and the ECCT was well tolerated by the animal. In addition, the exposure to ECCT also induces body immune system in the animal models to work against the tumour.

Radiation-activated Signalling Pathways

PO-112 THE SENESCENCE ASSOCIATED SECRETORY PHENOTYPE (SASP)-FACTOR CCL2 FOSTERS VASCULAR DYSFUNCTION AND ENDOTHELIAL CELL LOSS IN RADIATION-INDUCED LUNG DISEASE

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Introduction Blood vessels are critical targets of the radiation response. Acute vascular damage and dysfunction upon irradiation as well as delayed endothelial cell loss are particularly prominent in the radiation response of normal tissues. However, the mechanisms underlying radiation-induced adverse effects in the vascular compartment remain elusive and no causative radioprotective treatment is available to date.

Material and methods Here we investigated the therapeutic potential of Ccl2 signalling inhibition to specifically protect endothelial cells (EC) from injury of radiation-induced acute and late toxicity in lungs after whole thorax irradiation (WTI) using a mouse model of radiation-induced pneumopathy as well as *ex vivo* cultured human lung tissue.

Results and discussions RT-induced vascular dysfunction and associated adverse effects can be efficiently antagonised by inhibition of Ccl2 signalling using either the selective Ccl2 inhibitor bindarit (BIN) or mice deficient for the main Ccl2 receptor CCR2 (KO). BIN-treatment efficiently counteracted