

Study to overcome malignant skin tumors

/ Extramammary Paget's disease

Extramammary Paget's disease is not only very difficult to treat once metastasized, its treatment is not covered by insurance. In addition, there is no single drug treatment covered by insurance. Currently, existing anti-cancer drugs are being used, and therefore, patients must rely on older drugs such as docetaxel and cisplatin. Based on the report by Dr. Hirai, who focused on advanced-stage cases of extramammary Paget's disease and analyzed HER2, approximately 30% of cases were determined to be HER2 positive. It is therefore promising to apply HER2 inhibitors and evaluate its efficacy and safety.

Keio University Hospital conducted the world's first clinical trial (advanced medicine) using HER2 inhibitors. The clinical trial was completed in May 2021, and the results will be announced after the analysis.

In addition, Keio University Hospital is conducting a second clinical trial using the HER2 inhibitor, trastuzumab emtansine, which was scheduled to start in 2020. In addition, "Phase II clinical trial of trastuzumab emtansine treatment for HER2-positive advanced extramammary Paget's disease" was selected by AMED for FY2021 for investigator-initiated clinical trials aiming to develop and approve innovative cancer drugs (medicines) by expanding indications, etc. The study has been adopted and has received support.

In addition, "Phase II clinical trial of anti-androgen therapy for androgen receptor-positive advanced extramammary Paget's disease" has been adopted for FY2021 by the AMED Clinical Research and Clinical Trial Promotion Research Project for the preparation of protocols for clinical research and investigator-initiated clinical trials aiming at drug development [Preparation (Step 1)], and is receiving support.

/ Malignant Melanoma (Melanoma)

Malignant melanoma (melanoma) has a high probability of metastasizing to the lymph nodes or the whole body, even if detected and treated at the early stage. Once metastasized, it is very difficult to treat. The standard treatment based on staging is usually surgical resection of the primary tumor, lymph node dissection, and chemotherapy, but its efficacy in advanced malignant melanoma with lymph node or systemic metastasis is limited. Although novel agents, such as anti-PD-1 antibody, anti-CTLA-4 antibody, and BRAF/MEK inhibitor have been used in clinical practice, the percentage of patients who are successfully treated by these drugs is low, and the development of new effective treatment methods is warranted.

Keio University Hospital is conducting an advanced clinical trial for malignant melanoma with KIT mutations, for which a KIT inhibitor is recommended after a cancer gene panel test and expert panel meeting. This clinical trial was selected and supported as a project for 2021 by the AMED Clinical Research and Clinical Trial Promotion Project to promote clinical research and investigator-initiated clinical trials on drugs based on protocols (or protocol framework) that have already been prepared [Implementation (Step 2)].

Immunotherapy has been reported to be effective for malignant melanoma in many cases, and various immunotherapy strategies have been developed. In particular, immunotherapy using T lymphocytes infiltrating metastases cultured in vitro and combined with total-body irradiation, anticancer agents, and biological agents (interleukin-2) has already been clinically tested at NCI in the U.S. and has shown anti-tumor effects. Keio University Hospital conducted the study, titled "Feasibility study of short-term cultured antitumor autologous lymphocyte infusion combined with bone marrow non-destructive pretreatment and low-dose IL-2 for advanced stage malignant melanoma." We are analyzing the data obtained through clinical trials to establish more effective and efficient immunotherapies suitable for Japanese patients.