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To all members of the press

A clinical trial of Tazemetostat for pediatric and AYA patients with malignant tumors which have no standard treatment or which is refractory to standard treatment using Patient-Proposed Healthcare Service (NCCH2214/ TURTLE trial) to improve drug access for pediatric and AYA patients with refractory tumors.

3 April 2023.

National Cancer Center.

Highlights

- Physician-initiated clinical trials under the Patient-Proposed Healthcare Service will start for patients with refractory solid tumors for whom the efficacy of EZH2 inhibitors in the pediatric and AYA generation* has been judged to be promising for rhabdoid tumors, epithelioid tumors, synovial sarcomas, chordomas, etc.
- The project aims to improve drug access for childhood and AYA cancers, where treatment strategy is underdeveloped and there is a drug lag with other countries.

Summary

The National Cancer Center (President: Hitoshi Nakagama, Chuo-ku, Tokyo) and the National Cancer Center Hospital (Hospital Director: Kazuaki Shimada) has announced that the National Cancer Center will start a physician-initiated clinical study of EZH2 inhibitors in pediatric and AYA solid tumor patients who have no standard treatment or are refractory to treatment and for whom the efficacy of EZH2 inhibitors has been judged to be promising. Physician-initiated clinical trials using the patient-proposed Healthcare Service will commence in April 2023.

EZH2 inhibitors are approved in Japan in June 2021 for 'relapsed or refractory EZH2 mutation-positive follicular lymphoma (limited to cases that are refractory to standard treatment)', but are not approved for solid tumors. However, although it is approved in the US for adults or those aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection, and a physician-initiated clinical trial for adult patients with epithelioid sarcoma has been initiated at our hospital, there has been no way for pediatric and AYA patients to reach EZH2 inhibitors under current insurance cover.

This study aims to collect information on the efficacy and safety of the EZH2 inhibitor tazemetostat (Eisai Inc., Epizyme Inc., an Ipsen company) in pediatric and AYA patients with refractory solid tumors, and to improve drug access to EZH2 inhibitors in those patients.

National Cancer Center Hospital is launching the Consortium for the Development of Pediatric Oncology Treatment (hereinafter referred to as the "Consortium") with the aim of improving drug access for pediatric oncology patients. This clinical trial was conceived based on a proposal from

pediatric patients attending our hospital, and the Consortium Office has been preparing to start the trial at the earliest time possible. This is the first patient-proposed treatment in which pediatric patients who have difficulty swallowing pills at our hospital are also eligible to participate.

Background

In Japan, about 1,000 new cases of solid tumors occur annually in people aged 19 years and younger, and about 2,700 in young adults aged 20 to 29 years. Initial treatment options for malignant solid tumors in pediatric and AYAs vary according to the type of cancer, and some treatments have been established. However, the annual number of patients with refractory solid tumors that have no standard treatment or are refractory to treatment is extremely small, around 400 patients. For this reason, large-scale clinical studies have never been conducted and treatment has not been established. At the time of recurrence, treatment options have been limited, with the same treatment being given regardless of the type of cancer, or palliative treatment being recommended.

About the Patient-Proposed Healthcare Service

Patient-Proposed Healthcare Service is a system that enables patients with difficult illnesses to receive unapproved drugs and off-label drugs at medical institutions as close as possible, while confirming their safety and efficacy, based on the patient's request, in order to respond to the patient's desire to use unapproved drugs promptly as uninsured combined care.
Ministry of Health, Labour and Welfare, Patient-Proposed Healthcare Service:
https://www.mhlw.go.jp/moushideryouyou/

About EZH2 inhibitors (tazemetostat)

EZH2 inhibitors (tazemetostat) are small-molecule compounds with inhibitory effects on the enzymatic activity of EZH (enhancer of zeste homolog) 2, a methyltransferase of histones and other substances. By inhibiting the methylation activity of wild-type or mutant EZH2 (e.g. Y646F), tazemetostat is thought to inhibit methylation of the 27th lysine residue of histone H3 and other residues, resulting in cell cycle arrest and apoptosis induction, thereby inhibiting tumor growth.

It is indicated in Japan for the treatment of relapsed or refractory EZH2 mutation-positive follicular lymphoma in adults (limited to cases that are refractory to standard treatment). In the US, it is currently indicated for adults with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least two prior systemic therapies, and for adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options, as well as for adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.

Overview of this study

- Title of the study

  A clinical trial of Tazemetostat for pediatric and AYA patients with malignant tumors which have no standard of care or which is refractory to standard of care using Patients-Proposed Healthcare Service (NCCH2214 trial/TURTLE trial)
- Objective.

  Evaluate the efficacy and safety of tazemetostat in pediatric and AYAs with malignant solid tumors in the absence or refractory to standard treatment, where EZH2 inhibitors are expected to be effective.
- Participants.

  Treatment-refractory pediatric and AYA malignant solid tumor patients aged between 6 months and 29 years who are not on standard treatment and meet one of the following criteria

  1. EZH2 inhibitors recommended by expert panel of cancer gene panel tests.
  2. Immunostaining of pathological tissue shows reduced expression or loss of the cancer-suppressor genes INI1 or SMARCA4.
  3. Diagnosis is rhabdoid tumor (AT/RT, MRT, RTK), epithelioid sarcoma, synovial sarcoma, chordoma
- Study period

  From 27 March 2023, until the planned number of participants is reached.
- Expected number of patients enrolled in this study

  Max. 10 patients.
- Hospital where it is carried out

  National Cancer Center Hospital
- Drugs used

  Tazemetostat hydrobromide.
- Drug supply

  Eisai Co.

Prospects

This study aims to collect information on the efficacy and safety of the EZH2 inhibitor Tazemetostat (Eisai Co., Ltd., Epizyme Inc., an Ipsen company) as a treatment for malignant solid tumors and to improve drug access.

Glossary

(*) AYA (Adolescent & Young Adult): Patients between the ages of 15 and 39 are considered eligible, but this study targets patients up to the age of 29.

Contact information (for enquiries) (e.g. corporate phone number)

- Contact details for patient enquiries.

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