KURZPROTOKOLL
Eisai 213

Öffentlicher Titel	Phase I/II Studie zu Eribulin und Irinotecan bei refraktären oder rezidivierenden soliden Tumoren
Wissenschaftl. Titel	A phase 1/2 single-arm study evaluating the safety and efficacy of eribuline mesilate in combination with irinotecan in children with refractory or recurrent solid tumors
Kurztitel	Eisai 213
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig, Pharma-Studie
Studienphase	Phase I
Erkrankung	Kinder: andere Tumorerkrankungen: sonstige Studien
Einschlusskriterien	- Age: =>12 months to <18 years old at the time of consent. - Diagnosis: Phase 1: Histologically confirmed extra-cranial solid tumor, which is relapsed or refractory, and for which there are no currently available therapies; Phase 2: Histologically confirmed RMS or NRSTS which is relapsed or refractory having received at least 1 prior systemic therapy, including primary treatment. - Disease status: Phase 1: Subjects must have either measurable or evaluable disease as per RECIST 1.1.; Phase 2: Subjects must have measurable disease as per RECIST 1.1. Measurable disease is defined as meeting the following criteria: a) At least 1 lesion of >=1.0 cm in the longest diameter for a non-lymph node or >=1.5 cm in the short-axis diameter for a lymph node that is serially measurable according to RECIST 1.1 using computerized tomography/magnetic resonance imaging (CT/MRI); b) Lesions that have had radiotherapy must show subsequent radiographic evidence of increase in size by at least 20% to be deemed a target lesion. - Therapeutic options: Subject’s current disease state must be one for which there is no known curative therapy. - Performance level: Performance score >=50% Karnofsky (for subjects >16 years of age) or Lansky (for subjects <=16 years of age). - Subjects must have fully recovered from the acute toxic effects of all prior anticancer treatments prior to study drug administration: a) Myelosuppressive chemotherapy: Must not have received within 21 days prior to study drug administration (42 days if prior nitrosourea); b) Hematopoietic growth factors: Must not have received a long-acting growth factor (eg, Neulasta) within 14 days, or a short-acting growth factor within 7 days. For agents that have known AEs occurring beyond 7 days after administration, this period must be extended beyond the time during which AEs are known to occur. The duration of this interval must be discussed with the sponsor; c) Targeted therapy (antineoplastic agent eg, tyrosine kinase inhibitor): Must not have received an antineoplastic targeted therapy within 14 days. For agents that have known AEs occurring beyond 14 days after administration, this period must be extended beyond the time during which AEs are known to occur. The duration of this interval must be discussed with the sponsor; d) Immunotherapy: Must not have received immunotherapy, eg, tumor vaccines, within 42 days; e) Monoclonal antibodies: Must not have received within at least 3 half-lives of the antibody after the last dose of a monoclonal antibody; f) Radiotherapy (XRT): Must not have received within 14 days prior to study drug administration (small field) or 42 days for craniospinal XRT, or if >=50% radiation of pelvis; g) Autologous Stem cell infusion: At least 84 days must have elapsed after stem cell infusion prior to study drug administration; h) Allogeneic bone marrow transplant, including mini-transplant: No evidence of active Graft vs. Host disease and at least 100 days must have elapsed after transplant or stem cell infusion prior to study drug administration

- 7. Adequate bone marrow function, defined as: a) Peripheral absolute neutrophil count (ANC) >=1.0 × 109/L; b) Platelet count >=100 × 109/L (transfusion independent, defined as not receiving platelet transfusions within a 7-day period prior to study drug administration); c) Hemoglobin (Hb) at least 8.0 g/dL at baseline (blood transfusions are allowed during the screening period to correct Hb values less than 8.0 g/dL). As blood transfusions are permitted to meet the hemoglobin criteria, subjects requiring transfusion must not be known to be refractory to red blood cell or platelet transfusions.
- Adequate renal function, defined as: a) A serum creatinine based on age/gender, derived from the Schwartz formula for estimating GFR (Schwartz and Gauthier, 1985), See table below; b) Or serum creatinine clearance or radioisotope GFR 50ml/min/1.73m2, based on a 12 or 24h urine creatinine collection.Age Maximum Serum Creatinine (mg/dL)
- Table: Male Female 6 months to < 1 year 0.5 0.5; 1 to < 2 years 0.6 0.6; 2 to < 6 years 0.8 0.8; 6 to < 10 years 1 1; 10 to < 13 years 1.2 1.2; 13 to < 16 years 1.5 1.4; >= 16 years 1.7 1.4; The threshold creatinine values in this table were derived from the Schwartz formula for estimating GFR (Schwartz et al. J. Peds, 106:522, 1985) utilizing child length and stature data published by the CDC.
- Adequate liver function, defined as: a) Bilirubin (sum of conjugated + unconjugated) <=1.5 times the ULN for age; b) Alkaline phosphatase, alanine aminotransferase (ALT) and aspartate aminotransferase (AST); c) <=3 × ULN (in the case of liver metastases <=5 × ULN), unless there are bone metastases, in which case liver-specific alkaline phosphatase must be separated from the total and used to assess the liver function instead of the total alkaline phosphatase; d) Serum albumin >=2 g/dL.
- Informed consent: All subjects and/or their parents or guardians must sign a written informed consent. Assent, when appropriate, will be obtained according to institutional guidelines. Subjects must be willing to comply with all aspects of the protocol.

Ausschlusskriterien

- Females who are breastfeeding or pregnant at Screening or Baseline (as documented by a positive beta-human chorionic [-hCG] or human chorionic gonadotropin [hCG] test with a minimum sensitivity of 25 IU/L or equivalent units of beta-hCG [or hCG]). A separate baseline assessment is required if a negative screening pregnancy test was obtained more than 72 hours before the first dose of study drug.
- Females of childbearing potential* who do not agree to use a highly effective method of contraception for the entire study period and for 6 months after study drug discontinuation, ie: a) Total abstinence (if it is their preferred and usual lifestyle); b) An intrauterine device (IUD) or intrauterine system (IUS); c) A contraceptive implant; an oral contraceptive** OR Do not have a vasectomized partner with confirmed azoospermia. For sites outside of the EU, it is permissible that if a highly effective method of contraception is not appropriate or acceptable to the subject, then the subject must agree to use a medically acceptable method of contraception, ie, double barrier methods of contraception such as condoms plus diaphragm or cervical/vault cap with spermicide.
- *All post pubertal females will be considered to be of childbearing potential unless they have early menopause [amenorrheic for at least 12 consecutive months, in the appropriate age group, and without other known or suspected cause] or have been sterilized surgically [ie, bilateral tubal ligation, total hysterectomy, or bilateral oophorectomy, all with surgery at least 1 month before dosing]. **Must be on a stable dose of the same oral hormonal contraceptive product for at least 4 weeks before dosing with study drug and for the duration of the study and for 6 months after study drug discontinuation.

- Males who have not had a successful vasectomy (confirmed azoospermia) or they and their female partners do not meet the criteria above (ie, not of childbearing potential or practicing highly effective contraception throughout the study period or for 28 days after study drug discontinuation). No sperm donation is allowed during the study period or for 28 days after study drug discontinuation.
- Concomitant Medications: a) Corticosteroids: Subjects receiving corticosteroids who have not been on a stable dose for at least 7 days prior to study drug administration; b) Anticancer agents: Subjects who are currently receiving other anticancer agents; c) Anti-GVHD agents post-transplant: Subjects who are receiving cyclosporine, tacrolimus or other agents to prevent graft-versus-host disease post bone marrow transplant.
- Phase 1: Received prior therapies with eribulin mesilate or irinotecan hydrochloride within 6 months prior to study drug administration.
- Phase 2: Received prior therapies with eribulin mesilate or irinotecan
- Any malignancy that required treatment (except non-melanoma skin cancer, or histologically confirmed complete excision of carcinoma in situ), within 2 years prior to study drug administration.
- Has hypersensitivity to either study drug or any of the excipients.
- Has a known prior history* of viral hepatitis (B or C) as demonstrated by positive serology (presence of antigens) or have an uncontrolled infection requiring treatment (* Subjects with a known prior history of hepatitis B or C may be eligible pending agreement with the sponsor).
- Has > Grade 1 peripheral sensory neuropathy or > Grade 1 peripheral motor neuropathy graded according to the Modified (“Balis”) Pediatric Scale of Peripheral Neuropathies.
- Has cardiac pathology, defined as: Subjects with known congestive heart failure, symptomatic or LV ejection fraction <50% or shortening fraction <27% and subjects with congenital long QT syndrome, bradyarrhythmias, or QTc >480 msec on at least 2 separate ECGs.
- Has CNS disease: Subjects with brain or subdural metastases are not eligible unless the metastases are asymptomatic and do not require treatment or have been adequately treated by local therapy (eg, surgery or radiotherapy) and have discontinued the use of corticosteroids for this indication for at least 28 days prior to study drug administration. Subjects must be clinically stable. It is not the intention of this protocol to treat subjects with active brain metastases. Note: Screening CNS imaging for subjects without a known history of CNS disease is required.
- Have had or are planning to have the following invasive procedures: a) Major surgical procedure or significant traumatic injury within 28 days prior to study drug administration; b) Laparoscopic procedure or open biopsy within 7 days prior to study drug administrationCentral line placement or subcutaneous port placement is not considered major surgery but must be placed at least 2 days prior to study drug administration; c) Core biopsy, including bone marrow biopsy within 2 days prior to study drug administration; d) Fine needle aspirate within 3 days prior to study drug administration.
- Subjects with known human immunodeficiency virus (HIV); due to lack of available safety data for eribulin therapy in HIV infected patients.
- Has any serious concomitant illness that in the opinion of the investigator(s) could affect the subject’s safety or interfere with the study assessments.

Alter 1 - 17 Jahre

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Sponsor	Eisai
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03245450 EudraCT 2016-003352-67