Kwo761 trial

Fase II studie: anti-CCR4 (chemokine) antilichaam studie bij patiënten met recidief / refractair T-cel lymfoom.

Patiënten kunnen voor deelname worden door verwezen naar VUmc, EMC of UMCG

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Signed Written Informed Consent

1) Voluntarily signed and dated Ethics Committee (EC) approved informed consent form in accordance with regulatory and institutional guidelines. Written informed consent must be obtained prior to performing any study-related procedure;

Age and Sex

2) Males and female subjects ≥ 18 years of age at the time of enrollment;

Target Population

3) Histologically confirmed diagnosis of PTCL according to World Health Organization (2008) classification as specified below;[64]
   a. PTCL-NOS;
   b. Angioimmunoblastic T-cell lymphoma;
   c. Anaplastic large cell lymphoma, ALK-positive;
   d. Anaplastic large cell lymphoma, ALK-negative;
   e. Transformed mycosis fungoides.
4) Failed or intolerant of at least one prior systemic anticancer therapy;
5) Eastern Cooperative Oncology Group (ECOG) performance status score[65] of ≤ 2 at study entry;
6) At least one site of disease measurable in two dimensions by computed tomography (CT). Both nodal and extranodal disease will be considered (lymph nodes must have long axis of 1.5 cm regardless of short axis or long axis 1.1 to 1.5 cm and short axis >1.0 cm).
7) Subjects who are positive for CCR4 by immunohistochemistry.
8) The subject has resolution of all clinically significant toxic effects of prior cancer therapy to grade ≤1 by the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0 (NCI-CTCAE, v.4.0) excluding the specifications required in 9, 10, and 11 below;
9) Adequate hematological function:
   a. absolute neutrophil count (ANC) ≥ 1,500/mm^3;
   b. platelets ≥ 100,000 / mm^3 or ≥75,000 in the presence of known bone marrow involvement.

   Note: Retesting for values out of criteria will be permitted;
10) Adequate hepatic function:
   a. bilirubin ≤ 1.5 times the specific institutional upper limit of normal (ULN);
   b. aspartate transaminase (AST) and alanine transaminase (ALT) each ≤ 2.5 x ULN or ≤ 5.0 x ULN in the presence of known hepatic malignancy.

   Note: Retesting for values out of criteria will be permitted;
11) Adequate renal function as evidenced by serum creatinine of ≤ 1.5 x the ULN or a calculated creatinine clearance of ≥ 60 ml based on the Cockroft-Gault algorithm.

   Note: Retesting for values out of criteria will be permitted;

12) Women of childbearing potential (WOCBP) must have a negative pregnancy test within 7 days of receiving study medication;
13) WOCBP must agree to use effective contraception, defined as oral contraceptives, double barrier method (condom plus spermicide or diaphragm plus spermicide) or practice true abstinence from sexual intercourse (periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception) during the study and for 3 months after the last dose. WOCBP includes any female who has experienced menarche and who has not undergone successful surgical sterilization or is not postmenopausal (defined as amenorrhea $\geq$ 12 consecutive months);
14) Male subjects and their female partners of child bearing potential must be willing to use an appropriate method of contraception (defined as oral contraceptives, double barrier method (condom plus spermicide or diaphragm plus spermicide) or practice true abstinence from sexual intercourse (periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception) during the study and for 3 months after the last dose.

3.3 Exclusion Criteria

Subjects with any of the following will be excluded from the study:

Medical History and Concurrent Diseases

1) Subject with the following PTCL diagnoses are excluded;
   a. Precursor T/NK neoplasms;
   b. Adult T-cell leukemia-lymphoma;
   c. T-cell prolymphocytic leukemia;
   d. T-cell large granular lymphocytic leukemia;
   e. Aggressive NK-cell leukemia ;
   f. Systemic EBV-positive T-cell lymphoproliferative disorder of childhood;
   g. Hydroa vacciniforme-like lymphoma ;
   h. Mycosis fungoides, other than transformed mycosis fungoides;
   i. Sezary Syndrome;
   j. Primary cutaneous CD30+ disorders: Anaplastic large cell lymphoma and lymphatoid papulosis;
   k. Primary cutaneous CD8+ aggressive epidermotropic cytoxic T-cell lymphoma;
   l. Primary cutaneous CD4+ small/medium T-cell lymphoma;
   m. Primary cutaneous gamma-delta T-cell lymphoma;
   n. Extranodal NK /TT-cell lymphoma-nasal type;
   o. Enteropathy-associated T-cell lymphoma;
   p. Hepatosplenic T- cell lymphoma;

q. Subcutaneous panniculitis -likeT-cell lymphoma;
r. Chronic lymphoproliferative disorder of NK cells.

2) Have had an invasive solid tumor malignancy in the past five years except non-melanoma skin cancers, melanoma in situ, cervical carcinoma in situ, ductal/lobular carcinoma in situ of the breast, or localized prostate cancer with a current PSA of $\leq$ 0.1 ng/ml who is currently without evidence of disease.
3) Relapsed less than 75 days of autologous stem cell transplant.
4) History of allogeneic stem cell transplant.
5) Evidence of central nervous system (CNS) metastasis.
6) Psychiatric illness, disability or social situation that would compromise the subject's safety or ability to provide consent, or limit compliance with study requirements.
7) Subjects with a history of moderate or severe psoriasis (covering >3% body surface area) or with psoriasis associated with systemic symptoms e.g. arthropathy, or with a 1st degree relative with history of psoriasis that required medical intervention.
8) Significant uncontrolled intercurrent illness including, but not limited to:
   a. uncontrolled infection requiring antibiotics;
   b. clinically significant cardiac disease (class III or IV of the New York Heart Association [NYHA] classification, see Appendix 1);
   c. unstable angina pectoris;
   d. angioplasty, stenting, or myocardial infarction within 6 months;
   e. uncontrolled hypertension (systolic blood pressure >160 mm Hg or diastolic BP >100 mmHg, found on two consecutive measurements separated by a 1-week period) despite two anti-hypertensive medications;
   f. clinically significant cardiac arrhythmia; or
   g. uncontrolled diabetes.
9) Known or tests positive for human immunodeficiency virus (HIV), hepatitis B or hepatitis C.
10) Active herpes simplex or herpes zoster:
   a. Subjects with a history of herpes zoster who have had an outbreak within the last 3 months will also be excluded;
   b. Subjects on prophylaxis for herpes who started taking medication at least 30 days prior to study entry, should continue to take the prescribed medication for the duration of the study.
11) Experienced allergic reactions to monoclonal antibodies or other therapeutic proteins;
12) Known active autoimmune disease will be excluded (For example: Grave's disease; systemic lupus erythematosus; rheumatoid arthritis; Crohn's disease);
13) Is pregnant (confirmed by beta human chorionic gonadotrophin [β-HCG]) or lactating.