Kantonsspital St.Gallen

Interdisziplinäre Medizinische Dienste
Muskelzentrum/ALS clinic

Direkt 071 494 35 81
muskel-als@kssg.ch

Kantonsspital St.Gallen

CH-9007 St.Gallen
Tel. 071 494 11 11
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Cytokinetics - **Courage ALS** Protocol CY 5031 / Site 215069 / PI MW	**Inclusion / Exclusion**
ÄRZTIN / ARZT	Visitendatum:
Patientenname	
Geburtsdatum	
Patienten ID	

	Inclusion Criteria	**Ja**	**Nein**
1	Able to comprehend and willing to sign an ICF and willing to comply with all study procedures and restrictions for the duration specified in the Schedule of Activities (SoA; Section 1.3).		
2	Males and females between 18 and 80 years of age, inclusive, at screening.		
3	Diagnosis of familial or sporadic ALS (defined as meeting the laboratory-supported probable, probable, or definite criteria for ALS according to the World Federation of Neurology El Escorial criteria published in 2000 [Brooks 2000]). Patients who meet the possible criteria are eligible if they have lower motor neurone findings; those who have purely upper motor neurone findings are ineligible.		
4	First symptom of ALS ≤ 24 months prior to screening. The qualifying first symptoms of ALS are limited to manifestations of weakness in extremity, bulbar, or respiratory muscles. Cramps, fasciculations, or fatigue should not be taken in isolation as a first symptom of ALS.		
5	ALSFRS-R total score ≤ 44 at screening. Patients with a total score of 45 or higher may be rescreened 60±7 days following the original screening date and be deemed eligible if their ALSFRS-R total score is ≤ 44 or if their score is 2 or more points less than at initial screening. Such patients must continue to meet all other inclusion/exclusion criteria at the time of rescreening.		
6	Upright FVC ≥ 65.0% of predicted for age, height, sex and ethnicity at screening according to Global Lung Initiative equation (Quanjer 2012).		
7	Able to perform reproducible pulmonary function tests defined as being able to perform FVC at screening with variability of the 2 highest raw values of less than 10% with a maximum of 5 trials permitted. Screening FVC results must be reviewed and approved by the central review process prior to randomization.		
8	Must be either on riluzole for ≥ 30 days prior to screening or not have taken it for at least 30 days prior to screening		

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		Ja	Nein
9	Must have completed at least 2 cycles of edaravone at the time of screening or not have received it for at least 30 days prior to screening		
10	Clinical laboratory findings within the normal range, or if outside the normal range, not deemed clinically significant by the Investigator, except as specifically indicated as laboratory exclusion in Section 5.2.		
11	Able to swallow whole tablets.		
12	Male patients, who have not had a vasectomy with medical assessment of surgical success, or a confirmed sperm count of zero, are eligible to participate if they agree to the following during the trial and for at least 10 weeks after the last dose of study drug: a. Refrain from donating sperm Plus when their female partner is of childbearing potential must either: b. Be abstinent from heterosexual intercourse and agree to remain abstinent OR Must agree to use a male condom AND have his female partner use a highly effective method of contraception (as described in Appendix 3 [Section 10.3])		
13	A female patient is eligible to participate if she is not pregnant or breastfeeding, and at least one of the following conditions applies: a. Is not a woman of childbearing potential (WOCBP; as described in Appendix 3 [Section 10.3]) OR Is a WOCBP and using a highly effective method of contraceptive (as described in Appendix 3 [Section 10.3]) and her male partner must agree to use a male condom during the trial and for at least 4 weeks after the last dose of study drug. b. A WOCBP must have a negative pregnancy test (urine or serum as required by local regulations) within 3 days before the first dose of study drug. Note: The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy. Contraceptive use by men or WOCBPs should be consistent with the guidance in Appendix 3 (Section 10.3) and local regulations regarding the methods of contraception for those participating in clinical studies.		
14	Able to complete all screening procedures.		

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	Exclusion Criteria	**Ja**	**Nein**
1	Other medically significant neurological conditions that could interfere with the assessment of ALS symptoms, signs or progression.		
2	Presence at screening of any medically significant cardiac, pulmonary, gastrointestinal, musculoskeletal, or psychiatric illness that might interfere with the patient's ability to comply with study procedures or that might confound the interpretation of clinical safety or efficacy data, including, but not limited to: a. Poorly controlled systemic hypertension b. Clinically significant electrocardiogram (ECG) abnormalities that require medical attention (ie, persistent atrioventricular conduction block >first degree, or acute myocardial ischemic changes) c. New York Heart Association Class II or greater congestive heart failure d. Chronic obstructive pulmonary disease e. Gastrointestinal disorder that is likely to impair absorption of study drug from the gastrointestinal tract f. eGFRCysC < 45.0 mL/min/1.73 m2 at screening g. ALT or AST ≥ 3×ULN at screening h. Urine protein creatinine ratio > 1 mg/mg (113 mg/mmol) at screening i. Total bilirubin (TBL), direct or indirect bilirubin above the ULN. j. History of Gilbert's Disease, Dubin-Johnson syndrome, or Rotor syndrome k. Poorly controlled or brittle diabetes mellitus l. Amputation of a limb m. Cognitive impairment, related to ALS or otherwise that impairs the patient's ability to understand and/or comply with study procedures and provide informed consent n. Cancer currently being treated (other than basal cell carcinoma, carcinoma in situ of the cervix, or squamous cell carcinoma of the skin excised with clean margins) or a history of cancer with an expected survival of less than 5 years. Breast cancer survivors with an expected survival of ≥ 5 years who are on long-term endocrine therapy are eligible. o. Any other condition, impairment or social circumstance that, in the opinion of the Investigator, would render the patient not suitable to participate in the trial p. Patient judged to be actively suicidal or a suicide risk by the Investigator		
3	Known to have received reldesemtiv or tirasemtiv in any previous clinical trial		
4	Has received or is considering receiving during the course of the trial any form of gene therapy for the treatment of ALS		

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5	Has received or is considering receiving during the course of the study any form of stem cell therapy for the treatment of ALS		
6	Has received or is considering obtaining during the course of the trial a diaphragmatic pacing system		
7	Use of a strong cytochrome P450 (CYP) 3A4 inhibitor within 7 days prior to first dose of study drug or a strong CYP3A4 inducer within 14 days prior to first dose of study drug		
8	Use of a medication that is an OCT1/OCT2 substrate within 7 days prior to first dose of study drug per Appendix 4 (Section 10.4)		
9	Currently participating in another trial, managed access program, open label extension, early access program, or through the right to try act is receiving an investigational drug or received an investigational drug or device within 30 days (or 5 half-lives for drugs, whichever is longer) prior to screening. Patients also cannot be taking outside of a clinical trial certain investigational drugs (which includes drugs, supplements, and nutraceuticals) within 30 days of screening (or 5 half-lives for drugs, whichever is longer) that are currently being studied or have been studied for the treatment of ALS. Examples of excluded drugs include TUDCA, sodium phenylbutyrate, and ravulizumab. A full listing of excluded agents can be found in the Study Manual.		
10	Has a tracheostomy		

Comment:

Name PI / SI		**Datum:**	
Unterschrift PI / SI:			