Titolo del progetto: ***Riluzole in patients with spinocerebellar ataxia type 7: a randomized , double-blind, placebo-controlled pilot trial with a lead in phase***	
Responsabile	Prof. Giovanni Ristori
Tipo (Progetto di Ateneo, Progetto Esterno competitivo/Non competitivo, Studio Clinico, Linea di ricerca)	Bando competitivo nazionale - AIFA 2016
Enti Finanziatori	AGENZIA ITALIANA DEL FARMACO
Ambito di Ricerca	Neuorologia
Durata	48 mesi
Inizio	01/04/2020
Fine	20/02/2025
Budget Totale	€ 275.980,00
Sede	Dipartimento di Neuroscienze Salute Mentale e Organi di Senso
Gruppo di Ricerca	Prof. Giovanni Ristori
Partner di Progetto	
Sintesi dell'attività di Ricerca	Spinocerebellar ataxia type 7 (SCA7) belongs to the dominant forms of inherited cerebellar ataxias (CA), being one of the rarest form. SCA7 has no therapeutic options, so that the relentless course, the important visual deficit that accompanies CA, and the possibility of disease development in childhood are pressing unmet needs. We published encouraging data on riluzole in inherited CA other than SCA7. These results prompted off-label use of riluzole in single cases of SCA7 in Italy and United States, suggesting possible efficacy of the drug in this condition. We propose a clinical trial in SCA7 patients performing a serial evaluation of riluzole effects on stringent outcome measures: ophthalmological metrics, scale for the assessment and rating of ataxia (SARA) scores, and safety biomarkers. The study design will be a randomized , double-blind, placebo-controlled pilot trial with a lead-in phase. The design will include a run-in phase of 6 months for all the participants, assessing ophthalmological metrics and SARA scores at the month 0, 3, and 6. Then one arm will undergo riluzole for other 12 months, while the other will take placebo for 6 months, and riluzole for the following 6 months; from both groups the same evaluations will be obtained at the month 12, 15 and 18 of the study. Thirty-four patients will be enrolled at 4 clinical Centers (3 in Italy and one in U.S.). The clinical epidemiology aspects (design of the study, statistical analysis and enrollment process) will be followed by National Rare Diseases Centre and Complex Diseases Group of National Centre of Epidemiology, Surveillance and Health Promotion of National Institute of Health. Eligible

	subjects for this study are patients (at least 7-year old) with positive genetic test for SCA7. Serious systemic illnesses or conditions (cardiac, haematologic and hepatic diseases) known for enhancing the side effects of riluzole, pregnancy or breastfeeding will be exclusion criteria. Participants will be randomly assigned (1:1) to riluzole (50 mg twice daily) or placebo. In pre-pubertal subjects the dosage will be adjusted on a mg/m2 basis according to the recommended human daily dose (100 mg). At baseline and after 3, 6, 12, 15 and 18 months, symptoms, physical and neurological signs, and SARA score will be recorded. At the same time points the following quantitative ophthalmologic assessments will be performed: - corrected visual acuity (right eye and left eye measurements) expressed as logMAR units with the ETDRS chart (either back-illuminated or projected). -Color vision via a Farnsworth D15 Arrangement Test. -Visual evoked potential are elicited using transient Pattern Reversal stimuli and monocular stimulation. -Electroretinography -Optical Coherence tomography with macular map of both eyes. - Computerized visual field examination by standard automated perimetry and kinetic perimetry Every three months electrocardiogram and a laboratory profile will be obtained for drug safety. The co-primary endpoints will be the proportion of patients with stability of SARA score and visual acuity (in log MAR units) at 18 months, compared to the mean values of t0-t3-t6 evaluations. A sample size of 17 patients per group (a total of 34 patients) had 80% power and an value of 10% to detect a difference between the two groups of 35% in the co-primary end points. This calculation took into account published data on riluzole in CA. Data will be expressed as mean (SD) for continuous variables and as proportions for categorical variables. Comparisons between riluzole and placebo group will be assessed using the t test for unpaired data for continuous variables and odds ratio with a relative 95% CI for categorical data. An intention-to-treat analysis will be done adopting a last observation carried forward method. A logistic regression model will be done at 18 months to adjust the results for the main baseline characteristics; p values less than 0.05 will be considered significant.
Altre Informazioni	
Link utili di approfondimento	