

Everolimus for cardiac rhabdomyomas in children with tuberous sclerosis. The ORACLE study protocol (everOlimus for caRdiac rhAbdomyomas in tuberous sCLERosis): a randomised, multicentre, placebo-controlled, double-blind phase II trial

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Abstract

Introduction: Tuberous sclerosis complex is a rare genetic disorder leading to the growth of hamartomas in multiple organs, including cardiac rhabdomyomas. Children with symptomatic cardiac rhabdomyoma require frequent admissions to intensive care units, have major complications, namely, arrhythmias, cardiac outflow tract obstruction and heart failure, affecting the quality of life and taking on high healthcare cost. Currently, there is no standard pharmacological treatment for this condition, and the management includes a conservative approach and supportive care. Everolimus has shown positive effects on subependymal giant cell astrocytomas, renal angiomyolipoma and refractory seizures associated with tuberous sclerosis complex. However, evidence supporting efficacy in symptomatic cardiac rhabdomyoma is limited to case reports. The ORACLE trial is the first randomised clinical trial assessing the efficacy of everolimus as a specific therapy for symptomatic cardiac rhabdomyoma.

Methods: ORACLE is a phase II, prospective, randomised, placebo-controlled, double-blind, multicentre protocol trial. A total of 40 children with symptomatic cardiac rhabdomyoma secondary to tuberous sclerosis complex will be randomised to receive oral everolimus or placebo for 3 months. The primary outcome is 50% or more reduction in the tumour size related to baseline. As secondary outcomes we include the presence of arrhythmias, pericardial effusion, intracardiac obstruction, adverse events, progression of tumour reduction and effect on heart failure.

Conclusions: ORACLE protocol addresses a relevant unmet need in children with tuberous sclerosis complex and cardiac rhabdomyoma. The results of the trial will potentially support the first evidence-based therapy for this condition.

Palabras clave

Palabras clave de autor:[Everolimus](#); [cardiac rhabdomyoma](#); [tuberous sclerosis complex](#); [children](#)

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