

EP10.14 Fetal cardiac rhabdomyomas susceptible to prenatal treatment with mTOR inhibitors: literature review and management algorithm proposal

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Objectives
To identify criteria for fetal cardiac rhabdomyomas (FCR) susceptible to prenatal mTOR inhibitor (mTORi) treatment through a narrative review and institutional experience at the Instituto Nacional de Perinatologia (INPer). A classification system and a management algorithm are proposed.

Methods
A narrative review of prenatally treated FCR cases using PubMed, Scopus, Web of Science, and Google Scholar was conducted. Additionally, a retrospective analysis of FCR cases diagnosed at INPer (March 2017–August 2024) was performed. Clinical presentation, tumor characteristics, genetic findings, indications, outcomes, and eligibility for prenatal mTORi therapy were analyzed.

Results
Fifteen international cases of FCR treated with prenatal mTORi were identified, with sirolimus as the most used (86.7%). Indications included progressive tumor growth causing ventricular outflow obstruction, arrhythmias, or hydrops fetalis. All showed tumor reduction and improved cardiac function, with no neonatal mortality. Institutional data revealed 17 FCR cases, of which 23.5% could have benefited from prenatal mTORi. Five neonates required postnatal everolimus, with 80% improvement.

Conclusions
Prenatal mTORi therapy is promising for severe FCR cases. This study proposes specific fetal **candidate criteria and a management algorithm**, guiding clinicians in decision-making. Further studies are required to validate protocols and assess long-term outcomes.

Key findings from the literature review

Table 1. Echocardiographic and genetic characteristics of FCR

Echocardiographic characteristics and prenatal genetic testing of FCR	Total number of fetuses with CR n= 15
Number of FCR, n (%) - Single - Multiple	5 (33.3) 10 (66.7)
Largest FCR diameter (mm), median (IQR)	39.3 [18.53 – 45]
Location of the largest FCR, n (%) - Right atrium - Left ventricle - Apex - Tricuspid valve - Interventricular septum - Not reported	1 (6.7) 7 (46.7) 1 (6.7) 1 (6.7) 2 (20.0) 2 (13.3)
Prenatal TSC1/TSC2 genetic testing, n (%) - TSC1 - TSC2 - Negative - Not reported	1 (6.7) 7 (46.7) 1 (6.7) 6 (40.0)
Abbreviations: CR: cardiac rhabdomyoma, FCR: fetal cardiac rhabdomyoma, mTORi: mTOR inhibitor drug, TSC: Tuberous sclerosis complex	

Table 2. Main findings of prenatal mTORi therapy in FCR

Prenatal mTORi therapy in FCR	Total number of fetuses with CR n= 15
Indication for mTORi, n (%) - Progressive growth - OTS - Arrhythmia - Pericardial effusion - Atrioventricular valve insufficiency - Reduced ejection fraction - Hydrops - Cardiac function deterioration - Maternal TSC - Tumors in other anatomical sites	13 (86.7) 4 (26.7) 2 (13.3) 5 (33.3) 5 (33.3) 1 (6.7) 2 (13.3) 2 (13.3) 1 (6.7) 1 (6.7)
Type of mTORi, n (%) - Sirolimus - Everolimus	13 (86.7) 2 (13.3)
Target serum mTORi levels, n (%) 10 to 15 ng/ml 10 to 12 ng/ml 5 to 15 ng/ml 3 to 15 ng/ml 5 to 10 ng/ml 9.5 ng/ml - Not reported	6 (40.0) 2 (13.3) 1 (6.7) 1 (6.7) 1 (6.7) 1 (6.7) 3 (20.0)
Gestational age at initiation of mTORi (weeks), median (IQR)	30 [26.75 – 33.10]
Gestational age at discontinuation of mTORi, (weeks), median (IQR)	38 [36 – 39]
Gestational age at delivery, (weeks), median (IQR)	38.8 [36.85 – 39]
Mode of delivery, n (%) - Cesarean section - Vaginal delivery - Not reported	6 (40.0) 3 (20.0) 6 (40.0)
Umbilical cord mTORi levels at birth (ng/ml), median (IQR)	5.40 [3.30 – 11.30]
Maternal serum mTORi levels at delivery (ng/ml), median (IQR)	11.60 [6.90 – 16.70]
Maternal adverse effects, n (%) - None - Oral vesicles - Preeclampsia - Hypertriglyceridemia	11 (73.3) 2 (13.3) 1 (6.7) 1 (6.7)
Fetal growth restriction, n (%)	1 (6.7)
Reduction in FCR size, n (%)	15 (100)
Postnatal mTORi use, n (%)	6 (40.0)
Abbreviations: CR: cardiac rhabdomyoma, FCR: fetal cardiac rhabdomyoma, mTORi: mTOR inhibitor drug, OTS: Outflow tract obstruction, TSC: Tuberous sclerosis complex	