Reply

We thank Dr Russo and her colleagues for their interest in our recent Physician Alert. The authors highlight the urgent need for detailed analysis and meta-analysis of all completed STRIDER trials investigating the benefits and harms of sildenafil therapy for severe early-onset fetal growth restriction (FGR), and we are pleased to confirm that this is underway. Following the extensive international media and social media reporting on the interim analysis of the Dutch STRIDER trial, there has been debate over and some criticism of the STRIDER trials, and a meta-analysis would help put the findings in perspective.

Russo et al. also point out that the antenatal use of sildenafil is currently under investigation for a number of other indications, including the prevention of pulmonary hypertension in infants with congenital diaphragmatic hernia and the prevention of intrapartum fetal compromise in a much wider general obstetric population. Although we agree that the findings of a single trial of sildenafil for one indication in pregnancy (FGR) cannot be extrapolated to conclude a lack of efficacy for other indications in pregnancy, we believe that the statement ‘sildenafil is effective for the treatment of oligohydramnios’ is very premature, as it is based on one single-center open-label trial with methodological imperfections. There is little doubt that publication of case–control studies, case reports and underpowered randomized trials contributed to practice creep and unmonitored use of sildenafil for FGR, which stresses the importance of responsible reporting and interpretation of research findings.

Having made this cautionary remark, we agree with Russo et al. that the study of sildenafil in pregnancy for indications other than FGR may still be valuable as long as it is in the setting of high-quality randomized trials and stems from a clear rationale based on preclinical and animal data that support the hypothesis and favor overall benefit rather than harm to the mother and fetus. Such is the case for proposed trials of antenatal sildenafil to ameliorate the debilitating effects of congenital diaphragmatic hernia. It is imperative to continue to conduct high-quality clinical research in pregnant women to ensure that future care of mothers and babies is robust and evidence-based.

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References