**REBIRTH and Treatment of PPCM with Bromocriptine**

Research suggests that a hormone known as prolactin may play a role in the development of peripartum cardiomyopathy (PPCM). Prolactin levels are elevated in your body around the time of childbirth and stimulate the production of milk (lactation) required for breastfeeding. The stress of childbirth sometimes results in the breakdown of prolactin, creating small proteins in your blood which have a negative impact on both blood vessels and your heart. Preventing the release of this hormone with a drug called bromocriptine prevents the development of peripartum cardiomyopathy in laboratory models (Hilfiker-Kleiner, 2007), suggesting bromocriptine may be a potential treatment for PPCM.

Bromocriptine is a medication taken by mouth, once or twice daily. Bromocriptine was once commonly used in the United States to stop lactation (milk production). The medication is no longer used for this purpose; however, the medication is still available for other uses including the treatment of Parkinson's disease and to block prolactin release by pituitary tumors called prolactinomas.

**Clinical Studies of Bromocriptine in PPCM**: Three previous studies have evaluated bromocriptine as a potential treatment for PPCM. The first study was done in South African women with PPCM. Ten women were treated with standard therapy (heart failure medications), and 10 women received standard therapy plus 8 weeks of bromocriptine. Women receiving bromocriptine had better survival and were more likely to improve their heart function (Sliwa, 2010). A larger trial of 96 West African women with PPCM compared standard therapy to standard therapy plus 4 weeks of bromocriptine. The women who received bromocriptine demonstrated greater improvement in heart function and better survival compared with those women who did not receive bromocriptine (Yaméogo, 2017). A European trial of 63 German women with PPCM compared one week of bromocriptine therapy with eight weeks of bromocriptine. There was no significant difference in the recovery of heart function between the one-week and eight-week bromocriptine treatment groups, however the overall outcomes of both groups treated with bromocriptine were felt to be better than predicted based on several registries (Hilfiker-Kleiner, 2017). This led to the inclusion of bromocriptine in European guidelines for the treatment of PPCM (Bauersachs, 2019).

**REBIRTH Trial:** Although these three studies suggest potential benefits of bromocriptine, there remains uncertainty. Currently in the USA and Canada, bromocriptine is rarely used to treat PPCM. A larger clinical trial in a diverse group of patients with PPCM is required to determine if bromocriptine is an important addition to current medical therapy for PPCM. The National Institutes of Health funded **R**andomized **E**valuation of **B**romocriptine **I**n Myocardial **R**ecovery **TH**erapy (REBIRTH) for Peripartum Cardiomyopathy will determine the role of bromocriptine as a therapy for PPCM.

REBIRTH is sponsored by the National Institutes of Health (NIH) and will enroll 200 women at approximately 60 sites across North America. The women will be newly diagnosed with peripartum cardiomyopathy within 5 months postpartum. Women will be randomized to receive either eight weeks of bromocriptine or a placebo (a pill that does not contain any active drug) in addition to standard guideline directed medical therapy (what your main heart doctor thinks is the best medical regimen for the PPCM). The primary analysis will be to determine if women receiving bromocriptine have better heart function at 6 months after entering the trial. Secondary endpoints will evaluate whether women receiving bromocriptine have better clinical outcomes over three years of follow up.

## References:


Hilfiker-Keiner D, Kaminski K, Podewski E, et al. A cathepsin D-cleaved 16 kDa form of prolactin mediates postpartum cardiomyopathy. Cell. 2007; 128(3):589-600.

Sliwa K, Blauwet L, Tibazarwa K et al. Evaluation of bromocriptine in the treatment of acute severe peripartum cardiomyopathy: a proof-of-concept pilot study. Circulation. 2010 Apr 6;121(13):1465-73.

Yaméogo NV, Kagambèga LJ, Seghda A, et al. Bromocriptine in Management of Peripartum Cardiomyopathy: A Randomized Study on 96 Women in Burkina Faso. J Cardiol Clin Res 2017; 5(2): 1098.

Hilfiker-Kleiner D, Haghikia A, Berliner D, et al. Bromocriptine for the treatment of peripartum cardiomyopathy: a multicentre randomized study. Eur Heart J. 2017 Sep

Bauersachs J, König T, van der Meer P, et al. Pathophysiology, diagnosis and management of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Study Group on peripartum cardiomyopathy.Eur J Heart Fail. 2019 Jul;21(7):827-843