Current Project Brief

Objectives and Background

A phase III, randomized, double-blind, active, controlled, multinational, multicentre, non-inferiority trial using Carbetocin room temperature stable (RTS) for the prevention of postpartum haemorrhage during the third stage of labour in women delivering vaginally.

The objective of this trial is to evaluate if carbetocin RTS 100µg intramuscular (IM) is non-inferior to oxytocin 10 IU IM, as a uterotonic during the third stage of labour, in preventing postpartum haemorrhage in women delivering vaginally.

Postpartum haemorrhage (PPH) is the leading cause of maternal mortality in low-income countries and it contributes to nearly a quarter of maternal deaths globally. The majority of deaths due to PPH could be avoided through the use of prophylactic uterotonics during the third stage of labour and by timely and appropriate management. Oxytocin (IM/IV, 10 IU) is recommended as the uterotonic drug of choice. Based on the manufacturer’s recommendations, oxytocin should be stored under refrigeration. Carbetocin appears to be a promising agent in the prevention of PPH, is a more stable molecule and induces a prolonged uterine response, when administered postpartum. The manufacturer of carbetocin (Ferring Pharmaceuticals) has recently developed a room temperature stable formulation (carbetocin RTS) which makes it an attractive option for countries where maintaining the cold chain is problematic. Merck for Mothers, Ferring Pharmaceuticals and the World Health Organization would like to evaluate the room temperature stable carbetocin solution for injection as a promising intervention for reducing PPH particularly in settings where cold storage is difficult to achieve and maintain.

Geographic location

Argentina, Egypt, India, Kenya, Nigeria, Singapore, South Africa, Thailand, Uganda, United Kingdom.

Main deliverables

This multicentre trial showed the noninferiority of heat-stable carbetocin, as compared with oxytocin, for the primary outcome of blood loss of at least 500 ml or the use of additional uterotonics agents. Noninferiority was not shown for the primary outcome of blood loss of at least 1000 ml; however, the trial was underpowered for this outcome. There were no significant differences between the two groups in other measures of bleeding or in adverse effects. These data inform care of women in parts of the world where a lack of heat stability is a barrier to the effective prevention of postpartum hemorrhage. Avoiding the need for a cold chain will enable lower-cost transport and storage as well as reduce the waste associated with heat-exposure–related degradation and loss of active
ingredient. Within the labor-ward environment, eliminating a need for cold storage will facilitate easier access to the drug for patient care.

The trial finished recruitment on 30 January 2018. Results were published in June 2018 in the New England Journal of Medicine.

**Partners**
Merck for Mothers, Ferring Pharmaceuticals

**Sources of funding**
Merck for Mothers

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