Evaluate Vantage

April 14, 2015

GSK labours the point of addressing the unloved unmet needs

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The pharma industry is often criticised for its reluctance to invest in areas of high unmet need where development challenges and commercial considerations combine to make an unattractive proposition. So GlaxoSmithKline should probably be commended for embarking on an ambitious phase III programme for the management of preterm labour, where little innovation has been achieved in decades (see table below).

The company is setting out to show whether retosiban, an oxytocin antagonist, can improve neonatal outcomes of babies born to women who have gone into spontaneous preterm labour. It is also noteworthy that Glaxo's programme is designed to get the project registered in the US – where one of the handful of drugs that exist in this category failed to gain approval in the late 1990s and the FDA has withdrawn another class that is available elsewhere in the world.

Glaxo has just opened two registration trials with retosiban that will effectively test whether it can stop preterm labour and, if so, whether increasing the gestational age of the neonate can reduce complications of prematurity. Currently, there is no approved tocolytic medicine – one that stops contractions – which has been shown to improve neonatal outcomes.

The larger of the two studies tests retosiban, versus placebo, as an add-on to conventional therapy that includes corticosteroids and magnesium sulfate. It will enrol 900 patients and results are expected in July 2017.

The second compares retosiban to atosiban, an oxytocin/vasopressin antagonist which was approved in the EU in 2000, but is not available in the US. This study will enrol 330 women and should yield results in June 2016. Glaxo says the long-term safety, and outcomes of the infants born to mothers participating in the both trials, will also be assessed, and further studies are planned.

The FDA rejected atosiban in 1998 on the grounds that foetal safety was not proven; J&J, which held US rights, subsequently abandoned the project.

Lack of innovation

The co-primary endpoints of both studies are the same: time to delivery and the proportion of neonates with any diagnosis of neonatal morbidity and mortality. The trials also have a large number of secondary endpoints designed to assess the proportion of births at various time points, neonatal death rates, hospitalisations and safety and adverse events.

Both will enrol women of between 24 and just under 34 weeks' gestation with an uncomplicated, singleton pregnancy and intact membranes who have preterm labour. This will exclude women with premature rupture of membranes, which occurs in around 30% of all preterm pregnancies.

In both cases, women may be between 12 to 45 years old. Subjects must be diagnosed with preterm labour by virtue of having regular uterine contractions and cervical dilation.

Spontaneous preterm labour is considered to occur when the mother experiences uterine contractions and cervical changes before 37 weeks' gestation. It accounts for 40-50% of all preterm births – the other reasons including when preterm labour is medically induced, for example because of rupture of membranes or a condition such as pre-eclampsia. An estimated 15 million babies are born preterm every year worldwide, and this is the leading cause of morbidity and mortality in newborns and infants.

EvaluatePharma data suggest that there is little competition on the horizon, with only one other company having a programme in active development: ObsEva is focusing on the assisted reproduction space.

It is surprising that there are still areas of unmet need that affect large numbers of people yet where there is little pharmaceutical development activity. It would be heartening to think that if Glaxo is successful in this endeavour it would encourage other companies to tackle some of these areas where innovation has been so notably absent.

Management of spontaneous preterm labour - classes on the market and in the pipeline				
	Product	**Pharma class**	**Company**	**Ongoing trials**
Marketed	Tractocile (atosiban)	Oxytocin receptor antagonist†	Ferring (ex-US)	
	Utemerin (ritodrine hydrochloride)	Short-acting beta 2 adrenoreceptor agonist*	Kissei (Japan only)	
Phase 3	GSK22149 (retosiban)	Oxytocin receptor antagonist	GlaxoSmithKline	NCT02377466 (900); NCT02292771 (330)
Phase 2	OBE001	Oxytocin receptor antagonist	ObsEva	NCT02326142 (100)
†J&J failed to win US approval in 1998.				
**Various generics available worldwide, but class not present on the US market in this use.*				

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