Adocia announces positive topline phase 1 results for second Pramlintide Insulin - April 11, 2019

Significant 85% decrease in postprandial blood glucose vs. Humalog; Possible hypoglycemia concerns may persist; Three-week phase 1/2 trial to begin 2Q19

Adocia announced positive topline results from a phase 1 trial (n=24) for a second Pramlintide Insulin (7.5 U A21G human insulin/45 µg pramlintide), called ADO09. A21G human insulin - a rapid-acting analog that is the main metabolite of Sanofi's Lantus (insulin glargine) - replaces human insulin in the new co-formulation, which demonstrated a significant 85% decrease in blood glucose levels over the first two hours post-meal vs. Humalog (comparable to simultaneous, separate injections of Symlin and Humulin). For reference, Adocia's first Pramlintide Insulin (BioChaperone) demonstrated a 97% reduction on this endpoint against Humalog in an identical phase 1 study in September 2018.

	ADO09	**Humulin (human insulin) + Symlin (pramlintide)**	**Humalog (insulin lispro)**	**Adocia's 1st gen BC Pram Ins**
Mean Delta AUC Blood Glucose 0-2 hours after meal (mg*h/dL)	18 (p<0.0001 vs. Humalog)	26	119	4 (p<0.0001 vs. Humalog [126 mg*h/dL] in previous study)
Hypoglycemic events	2	2	0	4

Numbers of hypoglycemic events were small and similar across all three groups but trended toward an increase in both groups that involved pramlintide treatment (ADO09 and Humulin + Symlin groups). That said, its very hard to read into the hypoglycemia results this early on in the candidate's development. Of course, pramlintide is well-associated with increased hypoglycemia, and this concern will need to be monitored in further studies. Next up for ADO09 will be a three-week phase 1/2 trial, expected to begin in 2Q19.

We were unaware that Adocia was exploring other formulations of BC Pramlintide Insulin until now, and Adocia shared with us that they have considered many approaches - both with and without its BioChaperone technology - to find the best combination. Per Adocia, both A21G and pramlintide are stable at pH 4, while the prior insulin was stable at pH 7. As of 4Q18, the company's older version was set for a second, repeated administration trial in 2Q19, but ADO09 will be brought forward alone into additional studies for now, according to Adocia management.

Adocia's press release notably includes a quote from Georgetown's Dr. Robert Ratner on the implications of the results: "I believe this combination has the potential to finally deliver on the promise of pramlintide for a large number of patients, by addressing the significant unmet need for tighter postprandial control and lower glycemic variability without the burden associated with another product and a higher number of injections."

Importantly, these results provide another clinical demonstration of feasibility for a fixed-ratio co-formulation of pramlintide and human insulin, indicating that the known synergistic effects of the two when administered separately are maintained in a co-formulation. Full results from the trial have been submitted

for publication and will presented at a major diabetes conference later this year (hopefully EASD, according to management).

To date, commercial traction for the only marketed amylin analog (AZ's Symlin) has been slow, in part due to injection burden and difficulty in adjusting insulin dose when adding the analog. We're optimistic that a co-formulation could make pramlintide significantly easier to use and meaningfully increase its potential impact for patients.

-- by Martin Kurian, Peter Rentzepis, Ann Carracher, and Kelly Close