



Diabetes Close Up, V 2, #1
January 12, 2003

Observations on the ADA 50th Annual Postgraduate Sessions

Greetings! It's a beautiful day in New York City – sun shining, crisp winter air¹. Onward – much to discuss, as the American Diabetes Association's 50th Annual Postgraduate Sessions took place January 10-12 in New York City. This smaller diabetes meeting occurs annually in January² and tends to attract a terrific range of academics, endocrinologists, internists, GPs, nurses/diabetes educators, pharmacists, and dieticians, as well as industry participants spanning the pharmaceutical, biotech, and medical device (blood glucose monitor, insulin pump, insulin pen) worlds.

1. **One of the conference's most interesting general sessions focused on "Novel Therapeutic Targets in Diabetes: Science versus Promise."**
 - **Continued strong interest in GLP-1³ and GIP.** Dr. David Drucker from Toronto General Hospital gave an intriguing talk on incretins – gut peptides that prompt insulin secretion following meals. GLP-1 (glucagon-like peptide 1) and GIP (glucose-dependent insulinotropic peptide) represent two primary incretins, both of which exert their actions by stimulating distinct receptors in islet beta cells, prompting insulin gene transcription and glucose-dependent insulin release – i.e., these compounds stimulate insulin production.
 - **A new class of drug is hailed:** GLP-1 and GIP were praised as they appear to represent a novel new class of drug to treat Type 2 diabetes. Industry has been widely criticized recently for failure to discover new classes of drugs to treat what is now widely characterized as disease that has reached epidemic proportions⁴.

¹ Today's weather reminds me of one of my favorite literary passages of all time, in fact, from Joseph Conrad's "Youth": *It was January, and the weather was beautiful – the beautiful sunny winter weather than has more charm than in the summertime, because it is unexpected, and crisp, and you know it won't, it can't last long. It's like a windfall, like a godsend, like an unexpected piece of luck. Isn't that marvelous?*

² Location alternates annually between New York City and San Francisco.

³ Note that AMLN stock price began one of its several ascents in 2002 directly following the Postgraduate Sessions in late January. While companies do not present at this meeting, it is a gathering where many clinicians meet and discuss latest progress of companies in the industry.

⁴ Although many strides have been made in oral drugs to treat diabetes over the last decade, numerous oral drugs currently on the market, particularly sulfonylureas, are criticized for association with hypoglycemia, among other drawbacks.

- **Hypoglycemia less problematic with GLP-1 and GIP compounds:** Notably, unlike other beta cell secretagogues like the sulfonylureas, the beta cell incretin receptor signaling associated with insulin secretion appears to be tightly glucose-dependent, thereby appearing to reduce the likelihood of hypoglycemia. What does this mean? Seems to be that the drugs work when blood glucose levels are high but *not* when they are normal or low. If so, eureka! GLP-1, but not GIP, appears to potently inhibit gastric emptying, satiety, and glucagons secretion, complementary actions that lower blood glucose.
- **Beta cell regeneration – the gold ring:** In most Type 1 diabetics and many Type 2, significant or total beta cell destruction has occurred⁵. This new class appears to address this problem – technically, both GIP and GLP-1 appear to activate signal transduction pathways leading to beta cell proliferation and islet neogenesis. Additionally, GIP and GLP-1 appear to have protective tendencies (seem to confer resistance to beta cell apoptosis in experimental islet injury).
- **Who’s working on these compounds?** A range of companies is working on these compounds; the most notable include Amylin (has the only Phase III compound, AC2993, and is also working on a long-acting formulation with Alkermes, AC2993 LAR) and Novo Nordisk (behind Amylin, and has a BID formulation). Look for more data on GIP and GLP-1 compounds to be released at this year’s ADA in New Orleans⁶ - this is an extremely promising new class of drug.
- **Adverse Event data to come:** While data on these drugs looks highly promising, I don’t have enough info yet on AE profiles – large numbers from the Phase III trials will clearly be of benefit to us in this analysis.

2. **Booths are busy.** Booths at this meeting are open only at the coffee breaks! Particularly highly-traffic’d booths include Amylin (see above), Animas (showing insulin pumps and the popular EZ Manager), Becton Dickson (see below), Deltec (new pump manufacturer), LifeScan (showing already-approved and soon-to-be-launched UltraSmart – industry watchers are waiting for this meter, which should have strong data management capability⁷), Metrika (just received OTC clearance

⁵ Beta cell destruction causes insulin secretion to fail partially or totally. Type 2 diabetics have a twin problem, insulin resistance, which these drugs do not address.

⁶ Register for this year’s ADA, to take place June 8 – 14, at www.diabetes.org (click on *Professional*).

⁷ This meter won’t be marketed using big rebates and giveaways, as has been industry convention (razor/razor blade model). Industry watchers are very curious to see how UltraSmart meter sales go in particular. I expect that the keenest Ultra users will be the fastest converters and that the meter capabilities will likely prompt even more testing by the heavy users.

for A1C Now) and TheraSense (where the PDA Tracker is drawing positive marks⁸).

3. **On the medical device product front, one booth that drew lots of attention was Becton Dickinson, which launched two new diabetes products at this meeting.**

- **The BD Logic is the new “stand-alone” glucose meter**, which will be co-marketed by Medtronic; **the BD Latitude is the “all-in-one diabetes system”**, co-marketed by Lilly, that includes meter, insulin pen⁹, lancing device, lancets, pen needles.
- **Distribution will be interesting.** The BD sales force appears to be much smaller than sales forces at LifeScan, Roche, Abbott, Bayer, and TheraSense – it will be interesting to see how the co-marketing goes and exactly what kind of support Medtronic (Logic) and Lilly (Latitude) offer. The monitors will be sold by BD reps only.
- **Thinking big:** This year, BD says it will sell around \$40-50 million – the company is confident it can get to 10% of the market within five years – that’s a big percentage to steal – managed care contracts (and sales and marketing spending) will be key to watch, as will partnership support. BD has big ads in the January issues of several diabetes magazines (Diabetes Care, Diabetes, Diabetes Forecast) aimed both at the trade and at consumers.
- **Smart strategy:** BD is going after the most profitable patients – pump users (who use more strips a day than other patients) and those on insulin (where it can leverage its valuable database).
- **The sales pitch for the new monitor (same in both products):**
 - “5 seconds and accurate results *and*
 - 0.3 microliter *and*
 - 33-gauge lancet” – the thinnest-gauge on the market.¹⁰
- **Pricing:** According to a rep at the meeting, “likely” price points would be \$84.99 for the Latitude, \$74.99 for the Logic, with “big rebates.” Strips pricing said to be \$42-\$43 per 50 strips, similar to other manufacturers. Price cutting doesn’t appear likely, good news for competitors. The meters will be available in pharmacies in late March.
- **Meter product details:**
 - **Not approved yet for alternate site testing.** I imagine the approval will come in time, but stands as a disadvantage for now – nearly all manufacturers have sought to enter this market by this point. Still, nothing stops off label AST.

⁸ Notably, the Tracker is the only meter that offers standard deviation data – your focus-group-of-1 author finds this particularly useful. While A1C levels are important to watch, I feel that standard deviation of blood glucose levels is equally if not more important – a high standard deviation can result in an A1C that “looks” like a good score (e.g., 7 or below) but one that is created by averaging scores that are too high and too low. While the Tracker won’t appeal to every Freestyle tester (particularly for younger children testing on own, the FreeStyle may be a better monitor), I think TheraSense serves its heaviest users well with this product.

⁹ Most pens fit in the pen “slot” except some Novo pens (Novo is pen partner of competitor LifeScan.)

¹⁰ It is worth noting that although this comes across as an attractive sales point given aversion to pain, patients could use the BD lancets with most monitors. I did not notice major difference between old 30-gauge lancets and new 33-gauge ones, but the continued progress on this front is applauded – the lancet is a huge improvement compared to lancets used in the mid-1990s for example

- **Nice strips** – On the positive side, capillary action “sucks up” the patient’s blood drop, offering a clear visual assessment – patients seem to like this a lot. On the negative side, the strips may ultimately prove to be too small for elderly patients; although the small size of the strip bottle itself is appreciated especially by the “on-the-go” demographic, there does appear to be some difficulty in getting the strips out of a full bottle judging from my 60 seconds spent with a bottle¹¹. One unappreciated part of the strip is that it works no matter if the end is touched by a patient – many other strips that are touched still give results, but the accuracy isn’t maintained.
- **Memory** holds 250 blood glucose test scores and insulin doses.
- **Robust data management** - I didn’t have a chance to view data management capabilities in depth yet, but had two quick observations.
 - First, the data management system offers mealtime-specific blood glucose averages – this is a good idea, though in reality since the average is derived from only three numbers, it may not be as useful as a trend as other meters with this planned capability (e.g, UltraSmart, and others in time). Data management software, for those who take the time with it, could be useful for those on pumps and multiple injections, as they fine tune insulin rates – I will have to test the software before I have an opinion.
 - Second, although the opportunity to log insulin doses in the *meter* itself is being billed as a nice addition (this is included so that one can view impact of insulin on blood glucose scores), without building in data that includes carbs (insulin doses are either on carbs ingested or on insulin ‘correction’ needed), a full management picture is not provided. The data insertion process for insulin also strikes me as a little clunky, probably to be expected for a first product. Other products in which data on carbs, insulin, and blood glucose levels are used include both the TheraSense Tracker as well as the Animas EZ Manager. The BD system does allow quick analyses without using a PDA – on this front “YMMV” – different demographic groups have different preferences.
- **Size an advantage for Logic, but packaging not; packaging an advantage for Latitude, but size not.** Although the Logic looks to be about the same size as the smallest meters made by LifeScan, Roche, Abbott, and TheraSense, the packaging is bigger than with most systems – not a positive for many “on-the-go” diabetics in my opinion. Clinicians and CDEs noted that the Latitude might be

¹¹ LifeScan initially experienced this with its strips as well (FastTake/Ultra), and it changed bottle design to make it easier to get the strips out. BD’s bottle is very similar, but smaller.

too big a system; some said that women might carry in a purse – some doctors said they doubted men would use it outside of home. Unlikely in my view that kids would carry something so big. Note that the only users of Latitude would be pen users – so BD is pushing the pen – makes sense as the margins will go higher as volumes increase. Reps noted that the Latitude was tested intensively among focus groups, who loved having “everything in one place.” To be sure, it is very comprehensive system and seems like it may find a place among those who test at home most often. On the bright side, it will likely result in patients using more lancets – today, many patients change lancets in lancing devices only very infrequently – having the lancets right at hand will serve as a reminder.

- **New lancing device with Latitude is nice small size.** Unfortunately, this will not be sold separately “for now.” Perhaps it could be a proprietary tool, though users who really want to could just use this. If BD could figure out a way to make the lancet not give more than 1/3 drop of blood – that would be terrific.
- **BD said it won’t compete on the continuous marketing front** due to its partnerships, but I assume they are working with MiniMed on some interesting things on this front.
- **Everyone can win!** While some industry-watchers seemed quite occupied with the question of whether every glucose monitor manufacturer can survive, when thinking about growth prospects, I think more focus on the actual market size and trends is in order.
 - **Overall diagnoses growing:** Much more visibility on the epidemic has increased diagnoses – implications include clinicians urging testing sooner and more frequently. “Pre-diabetes” visibility continues to increase, as does educating of importance of blood glucose monitoring. This aids the entire industry.
 - **Intensive user population growing:** Lantus and more pumps both require more testing – as such, more of these users are becoming intensively managed diabetics. This aids the entire industry.
 - **Intensive users getting more intense!** Intensively managed diabetics used to be defined as using 4 strips/day, now, in the era of more frequent post-prandial testing, the intensive users tests 8-10 strips. This aids the entire industry.
 - **Average age of diagnosis moving down,** in the wake of Type 2 kids and increased diagnoses of those in their 20s and 30s¹², increasing the lifetime of the average diabetic. This aids the entire industry.
 - **Ethnic populations** in which diabetes is more prevalent are growing. This aids the entire industry, especially the companies

¹² Albeit from a smaller base, the most growth in 2000 for diabetics was in the 30-39-year-old demographic.

(there are several) at work on impressive targeted marketing to various ethnic groups.

- **I could talk about this for hours** – please e-mail me if you want to talk about other market trends.

4. Odds and Ends: I spent much of the conference speaking to a number of clinicians, all independent and not associated with industry. Some anecdotal highlights:

- **Lantus is hailed as a major breakthrough by clinicians**, receiving heaps of praise. This is not just from endos, but also from GPs and internists – clearly Lantus use has moved downstream.
 - **More Lantus = more syringes and strips sold → and bodes positively for other injected drugs coming down the pike and also for the pump:** Historically many Type 2 patients have been unwilling to use syringes; this has changed significantly with Lantus. In addition to Aventis, the manufacturer of Lantus, this has positive implications for Amylin (both its Phase III drugs, AC2993 and Symlin, are taken by injection) and more broadly, for blood glucose monitor and strip manufacturers (patients said to be testing more frequently once they are on Lantus) as well as for BD (#1 syringe manufacturer). In addition, more patients may be moving to pumps, having had positive experience with the new “basal” insulin – in particular, patients with more than one basal profile are said to be drawn to insulin pumps (Lantus assumes consistent basal requirement 24/7).
 - **Weight gain still a negative, but less hypoglycemia experienced:** Although, similar to other insulins, weight gain is frequently seen among those who go on Lantus, relatively less hypoglycemia appears to be experienced with the new basal insulin. From personal use, I believe this is because 1) Lantus necessitates no insulin “stacking” (ask me if you don’t know what this means) and 2) other longer-acting insulins were less stable than Lantus.
- **Interest heightened in islet cell progress.** Another trend I’ve witnessed in the show thus far seems to be clinicians interested in islet cell transplantation – clearly Edmonton (see NEJM,) has captured the attention of many and islet cell transplantation does not any longer appear to be viewed as experimental therapy. That said, significant barriers remain:
 - Supply of islet cells remains very limited, although there is talk of progress on this front;¹³

¹³ Stem cell progress appears exciting but “further out,” and xenotransplantation is widely perceived to be a less viable option at this stage, as the process can destroy organs in seconds.

- Immunosuppressive drug regime still a major drawback (though exciting work is being done on this front as well, in Canada and at UCSF, among other venues – Sirolimus use in particular has been interesting).
- Cost – high, to say the least.
- **Interest in inhaled insulin also heightened, and clinicians appear to eager to see next round of data.** Getting safety data appears paramount – whether inhaled insulin will be reimbursed also appears to continue to be a \$64 mm question. Although dosing specificity doesn't appear refined enough for Type 1 use, it is though that many Type 2's who have avoided syringes (either during the day or even at night, with Lantus) might warm to inhaling before meals.
- **Testing levels moving upward – (also see above.)** There is more talk here of postprandial testing as a trend, i.e., testing after meals (one hour after or two hours after) in addition to before meals. I keep saying this makes sense – if one attains a perfect score of 100 before lunch, but is at 180 after lunch – and lasts at that level for six hours, until dinner at 6:30 pm, this is NOT good for the A1C level! Also not good for long-term complication potential – seems a simple message and I believe this will help move average testing up. Remember we are still on average for the U.S. at one strip per diabetic used per day! I push up the average by using about eight tests and there are more and more like me – but still others who still test just once a week. Even if we just got to an average 2.0 tests per day, this would double this \$4.0 billion blood glucose market!
- **Education still needed:** some of the questions here are unbelievable. One presentation to primary care docs yesterday was as follows:
 - **DOC:** "My patients don't like fingersticks - they don't mind shots as much. Is it all right to just advise a small bolus before meals, even if they don't check the blood sugar?"
 - **Dr. Irl Hirsch (endocrinologist extraordinaire):** "We call this a blind bolus. What if the patient's blood glucose is 70? Clearly a shot wouldn't be a good idea."

Note: Kelly L. Close is a specialized consultant to the medical technology/pharmaceutical industries. All observations expressed are Kelly's opinions alone and should not be viewed as recommendations to investors on any companies in the industry. If you prefer not to be included on Diabetes Close Up mailings, or if you know others who would like to be on the mailing list for future occasional observations, please send a message to info@closeconcerns.com.