diaTribe®

research and product news for people with diabetes

in this issue

from the editor

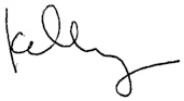
How are things going for you? And, more important, what can be done to make things better?

Broad questions, I know, but crucial in every part of life – especially diabetes. This month I've been thinking even more than usual about my own goals and strategies, thanks to a new position statement from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). It's called "Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach." Although the specific treatments discussed in the guidelines are for people with type 2 diabetes, many of the "patient-centered" principles apply to type 1 as well.

Ten authors and dozens of collaborators (many of whom we are honored to have on our advisory board at diaTribe) worked for two years to produce the document, which replaces a 2009 ADA/EASD "consensus algorithm" for type 2 diabetes. The 2009 algorithm (a flow chart), which was not actually officially endorsed by the ADA or EASD, gave clear preference to drugs that were more established and less expensive. This framework was introduced as part of a longer paper that explained the pros and cons of different therapies, but the main graphic did not make as clear why a patient might benefit from one combination versus another. By contrast, the main graphic of the new position statement gives a detailed picture of all the main drug classes based on glucose-lowering effectiveness, risk of causing hypoglycemia, effect on weight, risk of causing non-hypoglycemia-related side effects, and cost. In keeping with its "patient-centered approach," the position statement also includes recommendations for starting on insulin therapy, as well as guidance on A1c goals. The strong, consistent message throughout is that every individual with diabetes is different and deserves his or her own treatment plan. This, sadly, is not always the case in today's rushed healthcare system. But it is how things ought to be.

The new document is not simple, but of course neither is diabetes, especially given the large (and growing) number of medications available. We think that the document does a good job of guiding people through this complexity and of emphasizing the importance of the individual patient. To help you and your healthcare provider make the most of the new position statement, we drafted some questions that center on goals and medical treatments (available for download at http://bit.ly/JwI6dA). These are by no means recommendations – just five questions to start a conversation and aid your own thinking. I wish there were one single path that was best for everyone. But since there isn't, I will simply say: good luck as you continue to find your own way, and thank you for sharing that journey with us.

very best,



diaTribe staff

diaTribe advisory board

quotable quotes

"Currently, less than 5% of adults meet the recommended targets for physical activity."

-In a pre-screening of HBO's The Weight of the Nation documentary (available for free viewing online at http://theweightofthenation.hbo.com/films; see this issue's new now next) at CDC's Weight of the Nation: Moving Forward, Reversing the Trend, May 7-9, 2012, Washington, DC.

"Profit margin for soft drinks: 90%. Profit margin for fresh produce: 10%."

- In a pre-screening of HBO's The Weight of the Nation documentary.

"AACE [The American Association of Clinical Endocrinologists] now strongly asserts that obesity is a primary disease, and the full force of our medical knowledge should be brought to bear on the prevention and treatment of obesity as a primary disease."

- From a new position paper on obesity and obesity medicine issued by AACE, officially recognizing obesity as a primary disease, May 22, 2012, Philadelphia.

"10% of people with type 2 diabetes have changed or cancelled their plans in the last month due to diabetes."

- From a poster at Lilly Diabetes headquarters, Lilly Diabetes Blogger Summit, May 21, 2012, Indianapolis, (Lilly paid our expenses to Lilly HQ for this summit.).

fingersticks

ILLUSTRATION: DANIEL BELKIN

new now next

T1/2

FDA Advisory Committee Recommends Approval of Obesity Medication Lorqess

Several months after an FDA advisory committee delivered an overwhelmingly positive vote (20-2) in favor of approving Vivus' Qnexa for the treatment of obesity (see our new now next in diaTribe #40), the agency has done it yet again, voting 18-4 (with one abstention) earlier this month to approve Arena's Lorqess for the treatment of obesity. While the votes for the two drugs are similar at first glance, Lorqess had less enthusiasm, given its more modest efficacy (an average of 3-4% total body weight loss after one year of treatment –this is "average" and some patients experienced more weight loss and some less). Nonetheless, the day's deliberations reaffirmed that obesity is finally coming closer to being recognized on par with other diseases, worthy and in great need of additional treatment options.

During the FDA's first review of Lorqess in 2010, the agency decided not to approve the drug largely due to its potential cancer risk. Specifically, breast tissue (mammary) tumors and brain tumors (astrocytomas) were observed at higher rates in mice and rats treated with the drug (see our new now next in diaTribe #26). Since then, results from additional studies and analyses Arena performed have made the FDA more confident in the drug's safety (judging by the FDA briefing document), as its cancer risk was found to be lower than initially believed. This additional level of comfort with the drug's safety, combined with the recognition of the unmet need for the treatment of obesity, appeared heavily influence the positive vote by the advisory committee. We also believe the committee recognizes that while "average" weight loss wasn't that high, Lorqess will prompt higher-than-average weight loss for some patients (and lower than average for others), and availability of the therapy may be particularly positive for them. Also, having several alternatives would be a positive for healthcare providers, many of whom have, to date, been frustrated by the lack of current options.

Although the committee and the FDA noted some questions still remain regarding the drug's safety (e.g., whether Lorqess' cancer risk in animals is relevant to humans, and whether cardiovascular risk could definitively be ruled out), they seemed to be comfortable to wait to characterize the remaining uncertainties after Lorqess is on the market and these questions can be properly assessed (it is very difficult to do large enough trials before a drug is approved to assess cancer risk in particular). While approval is by no means guaranteed, Lorqess' prospects of approval are now much more encouraging, following the positive vote. The FDA now has until June 27 to consider the panel's recommendation and to make a decision on whether to approve Lorqess. Exciting times ahead – 13 years without any new drugs to treat obesity, and now two could potentially be approved by mid-summer! *–VW*

T2

DPP-4 Inhibitor Alogliptin Rejected by FDA

In April, the FDA denied approval of the DPP-4 inhibitor alogliptin in the US. Takeda (the drug's manufacturer) has not yet revealed the reasons behind the FDA's decision, although the company believes it can address the agency's concerns with already available data and results from ongoing studies. Takeda has indicated that it plans to reapply for approval shortly, with an expectation that the drug could be approved by early 2013. As a reminder, alogliptin has been available in Japan since 2010 under the brand name Nesina. DPP-4 inhibitors are type 2 diabetes therapies that help the body secrete insulin only when blood glucose levels are high – so there is no hypoglycemia associated with the drugs, and there is also no weight gain, unlike with a number of cur-

rent diabetes therapies. There are three currently approved DPP-4 inhibitors in the US, including Januvia (sitagliptin), Onglyza (saxagliptin), and Tradjenta (linagliptin).

Based on the studies we've seen, alogliptin appears to be quite similar to the already approved DPP-4 inhibitors in many respects. But what could distinguish alogliptin is that it may also become available in combination, in a single pill, with the type 2 diabetes therapy Actos (pioglitazone). Actos is a TZD (thiazolidinedione) and works to improve blood glucose control by increasing the body's sensitivity to insulin. Therefore, by targeting both insulin secretion (with a DPP-4 inhibitor) and insulin resistance (with a TZD), a combination alogliptin/Actos pill could form a very useful therapy for many people with type 2 diabetes. We note that some studies have associated use of Actos for more than one year with bladder cancer. In response, the FDA recently updated the medication's label and will be looking for further clarity as more extensive trial data becomes available. For more information, please see new now next in diaTribe #34.Over the coming months, we'll be keeping our ears to the ground for any more information surrounding alogliptin's rejection and Takeda's plans to resubmit the drug for approval in the US. Meanwhile, alogliptin is under review for approval in Europe, and a decision is expected in 2013. *–BK*

Dexcom's currently available Seven Plus CGM. The new Gen 4 sensor, which is now under FDA review, is over 20% more accurate than the Seven Plus and will feature an updated receiver design.

T1/2 **Dexcom Files New Gen 4 Sensor with FDA; Approval Optimistically Expected by the End of 2012**

Earlier in May, we were encouraged to hear that Dexcom has filed its new Gen 4 CGM sensor with the FDA. The review process typically takes six months or longer, meaning Dexcom might even see FDA approval of the new sensor before the end of 2012. As a reminder, the original Gen 4 sensor was approved in Europe in March 2011 (see new now next in diaTribe #31), though we understand that the US version has several incremental improvements over the currently available Gen 4 sensor in Europe (sold as part of the Animas Vibe integrated pump/CGM). Here in the US, Dexcom has been encouraged by early interactions with the FDA thus far, and we certainly hope this continues as the Gen 4 makes its way through the regulatory process. We'll be excited to give it a test drive once it becomes available (see diaTribe #15 for our test drive of the Dexcom Seven Plus). For those across the Atlantic, Dexcom is planning to launch the new updated Gen 4 CGM in Europe later this summer.

The new Gen 4 sensor is expected to be over 20% more accurate and 25% better in hypoglycemia detection relative to the current Seven Plus. The Gen 4 transmitter will also have a much longer communication range with the receiver – up to 30 feet normally and up to 50 feet (!) if it's in line of sight, compared to a range of five feet cited in the label for the Seven Plus. Dexcom's new sensor will feature a new receiver design as well, including a color screen, slimmer profile, and a different navigation interface. Down the road, the Gen 4 will also be integrated into the Animas Vibe and Insulet OmniPod insulin pumps, though Dexcom has not yet disclosed a timeline on when these might be filed with FDA. *–AB*

T1/2 **HBO's Weight of the Nation Documentary Hopes to Confront Public with Realities of the Obesity Epidemic**

On May 14, HBO premiered its four-part documentary series on obesity, *The Weight of the Nation*. Each part – entitled "Consequences," "Choices," "Children in Crisis," and "Challenges" – addressed head-on a different aspect of the obesity epidemic, featuring a powerful mix of personal stories, compelling statistics, and opinions from an array of leading experts. In a rare and extremely commendable move, HBO has also post-

ed all four hour-long films in their entirety online at http://theweightofthenation.hbo.com/films (go to the "Watch" tab to view all four films), plus videos explaining the overall project and a dozen bonus short films on such topics as "Poverty and Obesity," "The Biology of Weight Loss," and "Obesity and Type 2 Diabetes." We highly recommend watching this – we have seen it and were blown away by it. The site also has an impressive assortment of learning materials and a whole section on advocacy ideas, a clear (and refreshing) demonstration to us that the project has loftier goals than just making an of-the-moment movie. The documentary has an impressive list of co-presenters: the Institute of Medicine, NIH, CDC, the Michael & Susan Dell Foundation, and Kaiser Permanente. Executive producers Sheila Nevins and John Hoffman have won an Emmy Award for their previous public health documentary *The Alzheimer's Project*, and we expect this will be up for many awards as well.

We were moved, educated, angered, and inspired after seeing the film's fourth segment in a pre-screening at the CDC's recent Weight of the Nation Conference. We think HBO has done a most impressive job with this project, which executive producer John Hoffman hopes will be the largest public health campaign on obesity that America has ever seen. We hope so too. Notably, HBO is also sending out 40,000 DVD Screening Kits (complete with discussion guides) to community organizations around the US. Given this commitment and the high regard for the film's co-presenters, we believe *The Weight of the Nation* may well bring more widespread public attention to obesity – one comparison has been the way in which Rachel Carson's *Silent Spring* called environmentalists to action in the 1960s (she is credited with launching the environmental movement, and her work is said to have enabled a major pesticide ban in the early 1970s). – *AW/AB/KC*

test drive

T1/2 Sanofi's iBGStar: iPhone/iPod touch + blood glucose meter = a better testing experience

by Adam Brown

The consumer marketplace has a long history of inventions that combine two or more products – things like the spork, premixed peanut butter and jelly, and the clock radio. In these cases, the combination is often greater than the sum of the parts. In diabetes, the insulin pen did this for syringes and vials, and down the road, the artificial pancreas will hopefully do this for CGM and insulin pumps. This month, we had the opportunity to test drive the newest combination product in diabetes: Sanofi/AgaMatrix's iBGStar, the first blood glucose meter that connects directly to the iPhone and iPod touch.

The iBGStar is the first iPhone compatible blood glucose monitor.

We last wrote about the iBGStar when it was cleared by FDA in December 2011 (see new now next in diaTribe #39), and this month's US-wide launch of the meter gave us the chance to give it a try for the first time. As a reminder, the iBGStar blood glucose meter is about the size of a USB memory stick (2.2 in x 0.9 in x 0.4 in) – very small! – and attaches to an iPhone or iPod touch through a built-in dock connector (i.e., no cords or cables are needed to plug it in to an iPhone or iPod touch). When the iBGStar is plugged directly into the Apple device and a person tests his or her blood sugar, the screen displays the test result using the iBGStar Diabetes Manager App (a free download in the iTunes App Store). The iBGStar also has a small screen on the device itself, meaning it can be used to test glucose levels as a standalone meter independent of an iPhone or iPod touch.

Ease of Use

In my view, a major highlight of the iBGStar is that it improves and simplifies the whole experience of blood glucose testing, from downloading the App to viewing results to sharing them with a healthcare provider. After taking the iBGStar out of the box and plugging it into an iPhone, I was immediately prompted to download the Diabetes Manager App. Compared to many other diabetes software programs I've installed, this was refreshingly quick and hassle- free.

Checking blood glucose on the iBGStar – whether plugged into an Apple device or using the standalone meter (see below) – was also straightforward. When plugged into an iPhone or iPod touch (regardless of what I was doing on the device), the phone instantly recognized an inserted strip, opened the App, and automatically played an animation video demonstrating proper sample application technique. After a short wait for the six-second test time (accompanied by another animation – it actually counts to three, making the time seem closer to three seconds), the result was displayed in large, readable font on the Diabetes Manager App.

The scrollable glucose trend chart on the Diabetes Manager App.

The Diabetes Manager App

I was able to learn and navigate through the App within a few minutes of booting it up, something I sort of take for granted in a world increasingly full of intuitive touchscreen technology. The App has clearly marked sections for entering data (carb, insulin, and manual blood glucose entry), reviewing statistics and charts, as well as easily sharing results via email. Color-coding was also nicely incorporated: orange for hyperglycemia, blue for in-zone, and fuchsia for hypoglycemia (no red or green to be found!). This feature really shone in the data menu, where the glucose values could be viewed over time in a scrollable chart. The graphical display – with colors to differentiate high or low glucose values – made it especially easy to spot areas where hypoglycemic or hyperglycemic values clustered.

The App also simplified information gathering by auto-tagging results based on the time of day. As someone that generally avoids all forms of manual data entry, I definitely appreciated this automation. After pre-setting my meal times (e.g., Breakfast: 8-10 am, Lunch: 12-2 pm, etc.), the App automatically tagged my results appropriately: Post-Breakfast, Pre-Dinner, etc. When an auto-tag was not applicable due to a different mealtime, changing it took just a couple taps. The array of "notes" that could be added to a result was also quite comprehensive – everything from "air bubble" to "fatty meal" to "light exercise" was already in the app, with the additional capability to add my own customized notes. Notes still required manual entry (meters cannot read minds yet!), but I liked that the iBGStar seemed to simplify the process as much as possible.

When not plugged into an iPhone or iPod touch, the iBGStar can also be used as a standalone blood glucose meter.

Testing without an iPhone/iPod Touch

As previously mentioned, the iBGStar also works as a standalone meter when it's not plugged into an iPhone or iPod touch. Testing in this way is akin to using a standard blood glucose meter: insert the strip, apply blood, wait for the countdown, view the result on the meter's screen. The iBGStar as a standalone meter can store up to 300 results, which are automatically uploaded to the Diabetes Manager App the next time it is plugged into an iPhone or iPod touch.

The compact size of iBGStar was what immediately stood out when testing without an Apple device. This is easily the smallest meter I've ever used (2.2 in x 0.9 in x 0.4 in), and I appreciated that it looks like a high-tech consumer electronic rather than a more utilitarian medical device. The iBGStar also comes with a small cover/clip that hooks on

The iBGStar and associated supplies in the small carrying case.

to the built-in dock connecter, a nice way to avoid carrying the clunkier, all-in-one zipper case (though the case is definitely smaller than a typical blood glucose monitoring case). The meter's battery charges when plugged into the iPhone or iPod touch or through a micro-USB port on the bottom of the device.

The downside to using the iBGStar as a standalone meter is the screen. The font is quite small and the backlight is low – this device was really designed to be used with an iPhone or iPod touch, and the standalone feature seems more for convenience rather than optimal use. We understand this also helped for regulatory purposes. I did not find that the iBGStar unacceptably drained iPhone or iPod touch battery life.

The meter uses BGStar strips, which based on the data reported to FDA, are comparable in accuracy to other new strips and meters we've recently tested (see comparison table below or test drive in diaTribe #41 for our review of the LifeScan OneTouch VerioIQ, the Abbott FreeStyle InsuLinx, and the Telcare meter). The iBGStar strips' sample window and blood drawing action were not quite as impressive as the new OneTouch Verio strips or the FreeStyle Lite strips – those are great! - but I did not find it significantly worse.

The iBGStar uses BGStar strips, which are priced similarly to other major brands.

Pricing and where to get iBGStar

You can get iBGStar at Walgreens and at Walgreens.com ($74.99 and includes 10 test strips), at Apple retail stores (!) and at Apple.com ($99.95 and includes 50 test strips), and through Diabetic Care Services & Pharmacy ($71.99 and includes 10 test strips). If you prefer to get iBGStar at your local non-Walgreens pharmacy, they can also probably get it for you but it depends on their distributors. The BGStar strips are priced similarly to other major strip brands (Walgreens.com retail price of $64.99 for 50 strips). Notably, Sanofi is offering a co-pay savings program to limit out-of-pocket expenses to no more than $20 per purchase for one year, though certain restrictions may apply.

A new era of blood glucose monitoring?

In thinking about the three new meters we recently reviewed (see test drive in diaTribe #41) and now Sanofi's iBGStar, it's refreshing to see a healthy level of competition and innovation in blood glucose monitoring. For too long the data have often been hard to download, analyze, contextualize, and visualize, especially for on-the-go decision-making. In my view, this is one place where recent meters have made important strides. Managing diabetes is unquestionably challenging and frustrating, but it's made even worse when the data we laboriously collect do nothing to ease the burden. I have no doubt that this is changing for the better.

	Sanofi/ AgaMatrix iBGStar	**LifeScan OneTouch Verio IQ**	**Telcare**	**Abbott FreeStyle InsuLinx**
Accuracy under 75 mg/dl (% of points within 10 mg/dl of lab value)	100%*	100%*	95%*	92%*
Accuracy over 75 mg/dl (% of points within 10% of lab value)	92%*	95%*	98%*	90%*
Special Features	iPhone connectivity	Pattern recognition	Cellular (3G)-enabled	Touchscreen
Retail Cost of Meter (without insurance)	$71.99-$99.95	$69.99	$150 ($100 with a one-year strips subscription)	To Be Determined
Blood Sample Size	0.5 microliters	0.4 microliters	0.7 microliters	0.3 microliters
Test Time	6 seconds	5 seconds	5 seconds	5 seconds or faster
Battery	Rechargeable	Rechargeable	Rechargeable	Two replaceable coin cell batteries (lasts for 3,000 tests)
Size/Weight	2.2 in x 0.9 in x 0.4 in 0.3 ounces	3.5 in x 1.9 in x 0.5 in 1.66 ounces	3.9 in x 2.4 in x 0.6 in 4 ounces	3.8 in x 2.4 in x 0.6 in 2.3 ounces
Software	iPhone and iPod touch	PC only (stored on local computer)	Web and iPhone	PC and Mac (stored on meter)

**** Due to differences in study design, accuracy results may not be comparable. The higher the number reported, the more often the meter's value fell within 10 mg/dl of the true laboratory value (i.e., the more accurate the meter is). The current FDA requirements mandate that at least 95% of points must be within 15 mg/dl of the lab value for readings under 75 mg/dl and within 20% of the lab value for readings over 75 mg/dl. All four meters exceed this requirement.***

trial watch

T2

The Effectiveness of U-200 Insulin Degludec vs. Insulin Glargine in Adults with Type 2 Diabetes Requiring High Doses of Insulin
ClinicalTrials.gov Identifier: NCT#01570751
http://clinicaltrials.gov/ct2/show/NCT01570751

Tresiba (insulin degludec) is a novel ultra-long-acting basal insulin that was developed by Novo Nordisk. The drug is currently being reviewed for approval by the FDA with a decision expected by July 29, 2012 and by European and Japanese regulatory agencies around the same time. In previous trials compared to Lantus (insulin glargine), Tresiba was demonstrated to similarly lower blood glucose levels, but have a longer duration of action and a lower risk for hypoglycemia (both at night and overall). This phase 3 study will aim to confirm the effectiveness of Tresiba in people with type 2 diabetes and with high insulin dose requirements when delivered in the U-200 formulation (twice the usual concentration). Participants will be randomly assigned to receive U-200 Tresiba for 16 weeks followed by Lantus for 16 weeks, or vice versa. The primary goal of the study is to compare the abilities of Tresiba and Lantus to reduce A1c at weeks 16 and 32. The study is recruiting 144 adults with type 2 diabetes who have A1c levels ≥ 7.5%, who are taking Lantus once daily in vials (daily dose of 65-100 units), and who have been treated with metformin with or without one other oral antidiabetic drug for ≥12 weeks. Exclusion criteria for the study include the use of any other insulin therapy besides Lantus, treatment with a TZD or GLP-1 agonist within 12 weeks of the study's start, a previous major cardiovascular event (i.e., a heart attack, a stroke), and a current cancer diagnosis (with some exceptions). The trial is being conducted at 34 sites within the US. Those interested in enrolling can contact the Novo Nordisk Trial Call Center at 866-867-7178.—*NR/BK*

T1

Continuous Glucose Monitoring in Adolescents With Poorly Controlled Type 1 Diabetes
ClinicalTrials.gov Identifier: NCT#01586065
http://clinicaltrials.gov/ct2/show/NCT01586065

The Nemours Children's Clinic in Jacksonville, Florida, is currently recruiting for a six-month study to assess how continuous glucose monitors (CGM) may help children with poorly controlled type 1 diabetes. The experimental group will wear a CGM throughout the study while the control group will only use standard fingersticks to measure blood glucose. The purpose of the study is to evaluate how CGM affects both A1c levels and the frequency of hypoglycemia. Eligible volunteers must be 12-18 years old, have had type 1 diabetes for at least a year, have an A1c of 9% or higher, and be on either insulin pump therapy or multiple daily injections (MDI). Potential volunteers will be excluded from the study if they have experienced diabetic ketoacidosis (DKA), hypoglycemia unawareness, or severe hypoglycemia recently/frequently. For the full list of inclusion and exclusion criteria, visit http://clinicaltrials.gov/ct2/show/NCT01586065. If you or your child is interested in participating in this study, contact the principal investigator, Dr. Larry A. Fox of the Nemours Children's Clinic, at lfox@nemours.org or 1-904-697-3674. –*AW/AB*