Closer Look

MEMORANDUM

Medtronic Launches MiniMed Duo combination glucose sensor-insulin infusion set in Europe - June 3, 2014

Executive Highlights

- This morning, Medtronic announced the initial EU launch of MiniMed Duo, a three-day wear combined insulin infusion-CGM sensor set (a "snake bite" configuration under a single patch, separated by 11 mm). The device has an MARD of 15.5% vs. SMBG.
- The product will launch in the UK first and will subsequently become available in select European countries over the next few months (pending local approvals).
- The MiniMed Duo could be an especially good option for very young patients, who have less on-body real estate to wear separate sites for CGM and insulin delivery.

This morning, Medtronic announced the initial EU launch of the MiniMed Duo, a three-day wear combined insulin infusion-CGM sensor set (a "snake bite" configuration under a single patch, separated by 11 mm, with a 27-gauge steel insulin cannula); this comes following a CE Mark received "this week"! MiniMed Duo will launch in the UK first and will subsequently become available in select European countries over the next few months (pending local approvals). Perhaps unsurprisingly, there is no timeline to bring this product to the US. The launch news came somewhat unexpectedly, as Medtronic has not ever given an official timeline on the MiniMed Duo, although some data has been disclosed at conferences over the past year.

As we noted in our AACE 2014 Day #3 coverage two weeks ago (see below), the MiniMed Duo demonstrated an MARD of 15.5% vs. paired SMBG readings in a 48-patient, 15-day home study (77% of points fell in Zone A of the Consensus Error Grid). The accuracy was not particularly groundbreaking, especially considering there were an average of 4.7 calibrations per day. Of course, the combination form factor is a win for patients (especially pediatrics), and sensor accuracy is unquestionably a challenge given a short three-day length of wear. Indeed, day one MARD of 18.7% was really the stumbling point, as days two and three saw improved accuracy (13.1% and 14.1%). It's not clear whether this is the Enlite, Enlite 2, or another sensor. For comparison, the MiniMed 530G/Enlite's FDA label quotes an MARD of 13.6-14.7% vs. YSI; no accuracy data has been shared on Enlite 2. As a sidenote, MiniMed Duo accuracy data is compared to SMBG whereas the Enlite accuracy data is compared to YSI.

There is no pricing information at this time, though we assume the three-day-wear MiniMed Duo is at least somewhat more expensive for patients than buying the individual six-day-wear Enlite sensor and a separate infusion set (i.e., a patient would use twice as many sensors with MiniMed Duo).

We think MiniMed Duo could be an especially good option for very young patients, who have less on-body real estate to wear separate sites for CGM and insulin delivery. It will be most interesting to see how much/ if this device expands the CGM market to pumpers not currently wearing a sensor. Of course, many barriers to broader CGM adoption are frequently cited (cost, hassle factor, accuracy, constant reminder of diabetes, negative provider perceptions), and it's tough to know exactly what fraction of patients fall in the camp that refuses to wear CGM due to the challenge of wearing two separate devices. In any case, we do think some patients will appreciate this additional option, though since sensors get more accurate with longer wear, some will prefer longer-wear sensors. Now if pump sets could just be made to last longer than three days!

- **A key advantage of this technology is forced 24/7 CGM wear, which is of clear benefit to patients and HCPs who are struggling with patient adherence issues.** From a business perspective, the MiniMed Duo also seems like a win for Medtronic, assuming it is priced to reflect

that twice as many sensors will be used. Certainly, reimbursement for CGM is more challenging in Europe, so this product may not have a major impact on the business for some time. From an optics perspective, Medtronic does not break out CGM sales from pump sales, so we may never know how much this launch impacts the business.

- **Traditionally, steel needle sets have often been two-day-wear sets, though the duration of use in the AACE 2014 study appears to have been three days.** We assume MiniMed Duo's labeling will indicate it for up to three-day wear, though this remains to be seen.
- **Could the combined insulin-CGM set design change user behavior?** In one sense, users will be incentivized to wear sets as long as possible in order to get the most out of the sensor. However, wearing currently available infusion sets for too long (more than two or three days, depending on the person) can lead to absorption issues, higher occlusion rates, and scar formation. This is a challenging tradeoff from a patient perspective and one that we have not seen much data on from a behavioral perspective.
- **A related question is what will happen when users have infusion site issues or unexplained high blood glucose.** While needle sets tend to have fewer site issues, they still have them, and would more commonly occur if duration of use is extended beyond two or three days. The traditional troubleshooting approach puts the user's health above the cost of the infusion set, leading to replacement of the set as an early step when managing elevated blood glucose. Now, troubleshooting by replacing the site is a much more expensive proposition for the user - both in terms of material costs and giving up a sensor that may be in the sweet spot for accuracy. It is not clear how this will play out, but it puts the user in a more complicated situation than separable systems offer.
- **We wonder whether and how many current Medtronic pump+CGM users would switch to the MiniMed Duo,** given what seems like slightly lower accuracy and the potential for higher out of pocket cost relative to wearing the separate devices. As noted above, the value proposition seems most attractive for pediatric patients, which likely have more inelastic demand.
- **The MiniMed Duo uses a 27-gauge steel cannula for insulin delivery; the company has not officially shared what CGM sensor is being used in the MiniMed Duo**, though we assume it is the Enlite 2 sensor that launched in Europe following ATTD 2014. The glucose sensor and insulin cannula are housed under one adhesive and inserted using a single-button insertion device (with automatic needle retraction). In a Medtronic study (data on file), 96% of people using MiniMed Duo rated pain at the time of insertion at 0 or 1 out of 10 - the size of this study and methods were not detailed. The CGM calibration scheme is no different from that of the Enlite, which requires at least two (and ideally three to four) calibrations per day.
- **There is no timeline for bringing the MiniMed Duo to the US,** though Medtronic certainly hopes to bring a more frequent cadence of new technologies to the US market. Management made it clear on the last earnings call that recent collaboration with the FDA on the MiniMed 640G is moving things faster than expected on that next-gen insulin delivery product.

COMBINED INSULIN INFUSION-CGM COMPETITIVE LANDSCAPE

We are aware of the following companies and academic groups working on combined CGM-insulin infusion:

- **BD is developing a combined CGM-insulin infusion set -** this three-year collaboration with JDRF was announced on June 18, 2013. There is no official timeline, though we imagine this wouldn't come until after BD's CGM and insulin infusion sets come out - both individual components are still in the works. A clinical trial of the CGM is expected to be wrap up in fall 2014, with results expected in early 2015.
- **Insulet is attempting to integrate CGM into the OmniPod as well** - as of the company's 1Q14 call, an insertion study was complete, and data was being compiled. This project is still in early

stages and an update is expected later this year. We are much less optimistic about Insulet and integrated CGM anytime soon since their partnership with Dexcom dissolved - we hope very much to see the revived.

- **Pacific Diabetes Technologies (PDT) and Oregon State University** were using a flex circuit to dispose glucose sensors on a flat surface that can be wrapped into a catheter (i.e., each catheter is encased by a glucose sensor); as of the FDA-JDRF-NIH Workshop on Innovation Towards an Artificial Pancreas in April 2013, the device was in pre-animal testing. See page six here. More data from this team is expected at ADA 2014 in late-breaking poster 69-LB.
- **Sensile Medical** was developing a single port sensor in which a five-millimeter porous cannula simultaneously measures glucose and delivers insulin by changing the size of its pores in response to glucose concentration. The last update we heard on this came at ATTD 2012. See page 10 here.
- **Medical University of Graz** is working to integrate commercially available sensors into an insulin cannula. The last update we heard on this came at ATTD 2012. For more detail, see page 11 here. More data from this team is expected at ADA 2014 in poster 857-P.

CLOSE CONCERNS QUESTIONS

Q: How will the MiniMed Duo be priced? How much more expensive is the MiniMed Duo vs. purchasing a Medtronic CGM sensor and infusion set separately?

Q: What is the potential market for the MiniMed Duo? What fraction of current pumpers that don't use CGM will now be persuaded to use CGM via the MiniMed Duo?

Q: What fraction of current Medtronic pump + CGM users will switch to the MiniMed Duo?

Q: Will any Dexcom CGM + Medtronic pumpers elect to switch to the MiniMed Duo?

Q: Will Medtronic pursue FDA approval of this device?

Q: What impact will this launch have on Medtronic's international business?

AACE 2014 COVERAGE - INSULIN INFUSION AND GLUCOSE SENSING BY MINIMED DUO, A NEW COMBINATION DEVICE

Scott Lee, MD (Medical Director, Medtronic Diabetes, Northridge, CA)

Dr. Scott Lee shared new data from a 48-patient home study of the MiniMed Duo, a three-day wear combined insulin infusion-CGM sensor set (a "snake bite" configuration under a single patch, separated by 11 mm) - see a picture on twitter here. Patients wore five MiniMed Duo devices during the 15-day study and sensor accuracy was compared to SMBG values. The sensor's overall MARD was 15.5% and 77% of points fell in Zone A of the Consensus Error Grid (n=5,056 paired points) - the accuracy was not particularly groundbreaking, especially considering there were an average of 4.7 calibrations per day. Of course, the combination form factor is a win for patients (especially pediatrics), and sensor accuracy is unquestionably a challenge given the three-day length of wear. Indeed, day one MARD of 18.7% was really the stumbling point, as days two and three saw much improved accuracy (13.1% and 14.1%) - we wonder if the warm-up time could be extended to allow for improved day one accuracy. There were 44 total adverse events, with 98% classified as mild in severity and skin-related (e.g., "bruising and bleeding"); one patient had an abscess that was treated with antibiotics. Overall, this is the longest-term data we've seen on this device, and it certainly demonstrates its real-world feasibility. We look forward to hearing about future improvements and whether Medtronic plans to commercialize this device.

- **Overall, 75% of paired CGM-SMBG points were within 20% of one another, meeting the study's "primary success criteria" (>60% was the goal).** This struck us as an unconventional primary success criteria, as CGM accuracy is more typically described in MARD terms.

- **Dr. Lee shared the Duo's sensitivity and specificity, noting that the rate of false hypoglycemia alerts was somewhat high**. At a CGM alert setting of 70 mg/dl, 92% of hypoglycemia events were correctly detected within 30 minutes, though 57% of alerts were false. The rate of false alarms has been a complaint of the MiniMed 530G as well, and is something we expect will improve with Medtronic's next-gen sensors.
- **The study enrolled current pump + CGM users (94% on Enlite), and the acceptability ratings looked encouraging:** 75% of patients indicated "no pain" at the time of insertion; 74% of patients preferred the Duo device to the two-site configuration; and 89% agreed that the overall device experience was acceptable.
- **The MiniMed Duo combines a glucose sensing electrode and a steel insulin infusion cannula under a single adhesive pad.** The electrode and the cannula are separated by 11 mm, an "important point" - Dr. Lee said that insulin boluses typically go out ~7 mm into the subcutaneous tissue.
- **Three prior studies paved the way for this study:** O'Neal et al., *JDST* 7(2); Frid et al., *Pediatr Diabetes* 14(S18); Norgaard et al., *Diabetes* 61(S1). These studies showed: (i) an 11 mm separation between the insulin cannula and sensor electrode result in acceptable sensor accuracy; (ii) sensor performance and longevity are not affected when recurrent large boluses are delivered during device use; and (iii) there was a reliable correlation between sensor and meter blood glucose values in a three-day outpatient study.

--by Adam Brown and Kelly Close