



Therapeutic Thursdays: Therapeutic Thursdays: Type II Diabetes and GLP1-RAs
Episode Transcription

Speaker 1: Welcome to the ASHP official podcast, your guide to issues related to medication use, public health, and the profession of pharmacy.

Zach Weber: Hello and thank you for joining us for the Therapeutics Thursdays ambulatory care pharmacy podcast. This podcast is hosted by the ASHP Section of Ambulatory Care Practitioners and provides updates on hot topics and ambulatory care pharmacy. My name is Zach Weber and I serve as a clinical associate faculty member with Purdue college of pharmacy and I'm currently the chair of the ASHP section of ambulatory care practitioners. And I'll be your host for today's podcast. And with me today, we're really excited to welcome Kristi Kelley, she is a clinical professor at Auburn university, Harrison School of Pharmacy and a clinical pharmacist with Brookwood Baptist Health. So thank you for joining us today, Kristi we're certainly happy to have you on board. So let's go ahead and get talking about today's topic, which is type 2 diabetes and the GLP one receptor agonists. And so as a bit of a kind of a unique way to start this particular conversation. I think it'll be fun if you could just go ahead and introduce us to a brief patient case.

Kristi Kelley: Great, thanks Zach. So I just wanted to tell you about a patient we've had in clinic over the last several months. It's a 45 year old African American male that presented to the emergency department. At that admission was diagnosed with type two diabetes. He presented with an A1C of 10.5 which equated to an average blood glucose of 296 his c-peptide was 2.5 so he was still within the normal range but because he was symptomatic he was placed on Lantus, Solostar Pen, 35 units once a day, and Metformin 1000 milligrams twice a day. He came back to clinic a few weeks later and reported that he was having difficulty tolerating Metformin due to GI upset and was really concerned about being able to get his new type 2 diabetes under control and being able to return to work when we look at labs and such to see how he is and what we might could do to help optimize his care.

Kristi Kelley: At this point we see that his renal function was maybe a little bit elevated, but where we would expect it to be his eGFR or was 71 random microalbumin was 15.1 and his blood pressure was remaining elevated when he was coming to see us post emergency department follow up with his systolic blood pressures in the 140s to 150s so at this point he was also started on



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amlodipine 10 and because of his elevated lipids including triglycerides that were greater than 600 mg/dL, his elevated blood glucose, at that initial presentation, he was started on atorvastatin, which was appropriate because his ASCVD risk score was greater than 7.5% at this point.

Kristi Kelley: Has only other complaints really were associated with signs and symptoms of depression and so he was diagnosed with depression and he was started on bupropion a hundred and milligrams once a day. And really the conversation at the subsequent visits post follow up from the emergency department and our clinic or just about his ability to afford his medications. There were so many that had been added of note, he does have private commercial insurance. But it still is a consideration to figure out what would we do for him and what would be most appropriate given that he's got so many comorbidities right now.

Zach Weber: Sure, thank you. Yeah, definitely sounds like as we see and so many of our patients with diabetes, there's a lot of things that we need to consider and take into account as we think about what might be the best plan for them going forward. And so I'm wondering from your perspective, would you consider this patient to have been managed appropriately during that initial phase for his type 2 diabetes by starting Metformin?

Kristi Kelley: Yes, I really would. That's something that we talk a lot about on the clinic side of things about how do we manage a patient, but I think it's equally important to consider when they're presenting to the hospital whether they're actually just managed in the emergency department or whether they're admitted. His blood glucose was very high initially I did result in a brief hospitalization for him. It was appropriate to go on and start him on Metformin and at that point in time he actually was placed on dual therapy to be on Metformin, does align with the American Diabetes Association recommendations, which we frequently follow in primary care and our ambulatory care settings. But it also aligns with the AACE/ACE guidelines (the American Association of Clinical Endocrinologists /American college of endocrinology). These both recommend Metformin first-line. So I think we can feel confident that he was appropriately managed in addition to emphasize comprehensive lifestyle interventions, which is something we did even during his follow up appointments.



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Zach Weber: Definitely, yeah. Certainly seems like it was a good initial choice. And then if we look at some of the other medications that he was on, was the use of insulin glargine initially in this patient considered to be appropriate?

Kristi Kelley: Yes, I really think so. I kind of pause talking about that the last with thinking about Metformin, but really it's important for these patients when their blood glucose is so elevated, we know we're going to need to approach it from multiple perspectives. The advantage of using Metformin is the fact probably low hypoglycemia, the potential to help with some weight loss. We know that it's going to lower A1C appropriately, in contrast when we think about using insulin glargine, you know it's no longer a pill we're talking about the patient's got to inject themselves. There's a potential for weight gain. We hope that that balances out with the use of Metformin when the patients are very symptomatic, when they initially present, it is appropriate to go on and use insulin.

Kristi Kelley: And so when we think about what makes the most sense, a lot of times in these newly diagnosed patients, it makes sense to use a basal insulin like glargine, which is what was done with him. In patients that have an A1C of greater than 10 (depending on what source you look at) or greater than nine if you're looking at the AACE/ACE guidelines, support starting insulin. So that's not usually the first thing patients want to hear is that they've got to give themselves an insulin injection. But when we're needing to do something relatively quickly, we know that insulin is going to get their blood glucose down and we'll do it more quickly than waiting for several weeks for the effects to take place.

Zach Weber: Sure, thank you. Yeah, I definitely think it certainly makes the point for starting these two medications that were certainly likely inappropriate option for this particular patient. And so if we shift gears just slightly away from the treatment options and start thinking about treatment targets, what is the target A1C in a patient like this that is young, newly diagnosed and really doesn't have any other comorbidities?

Kristi Kelley: Yeah, I think that's a great consideration. You know, we certainly think about that from the clinician side, but I think it's really important for us to be able to talk to patients about that, what's our target in a patient like this. I would say that both the AACE/ACE guidelines as well as the ADA guidelines really



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emphasize the need to have an individualized target. And so that can mean lots of different things of course for lots of people, but the ADA recommendations would say that we would target an A1C of less than 7% and a non pregnant patient with no other comorbidities. They make the case that we could potentially push to a lower target to an A1C of less than 6.5 if the patient's really not at risk for significant problems related to hypoglycemia or ADRs because we know that to get patients to less than 6.5 for A1C we would have to use multiple agents in most cases in addition to lifestyle modifications.

Kristi Kelley: They make the argument that this is appropriate and patients that have had type 2 diabetes for short duration. So really this patient falls into that category. We expect that at his age of mid-forties that he's probably got a long life expectancy and need at this point in time we have no documentation that he's got significant cardiovascular disease. This would align to with the AACE/ACE guidelines that make the argument that we should go on and be more aggressive and have the A1C goals of less than or equal to 6.5 for those same reasons. In a patient like this, it gives us something to talk to him about, to know what we're working towards. We always talk in the clinic about we're not trying to be the numbers police, but we know that by targeting these lower A1Cs that we're providing that overall protection for these patients, we're providing care for them. I like to say from their head to their toes that we know that that results in less micro and macro vascular complications.

Zach Weber: For sure, yeah. And then once we're able to identify potentially what his goal or target A1C would be, we of course have to begin to think about how we're going to get him there and keep him there. And so when would you consider adjusting his therapy?

Kristi Kelley: I think that's a great question and it really hits home with this patient in particular so it's real easy for a patient to come back and to say, "Oh, we need to do lots of other things." We certainly do, but we know that on some level and these patients when they first get diagnosed, especially, it's kind of a moving target. And so if we think from a guideline perspective, they would say that we can give it three months before we start adding lots of other therapies because we know that there's many things that are playing into this. These patients are newly diagnosed, we're adding therapy, we're trying to talk to them about lifestyle



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changes, the patients we hope we're trying to make those modifications. And so we know that there's lots of things that can impact their target and their ability to obtain that A1C targets.

Kristi Kelley: So I would say probably wouldn't add additional therapy in him until we hit kind of that three month mark. Especially if we see that he's coming in and we're checking blood glucose in the clinic he's bringing us a blood glucose log and it's showing that he's, as I like to say headed in the right direction, that those values are coming down, that he's not having or experiencing too much hypoglycemia. I think that one of the things that came very apparent with this patient is that he tried to titrate his Metformin quickly and went to that max dose pretty much initially even though it was documented that he had been counseled to titrate it up to start at 500 once a day for a few days to go to 500 twice a day. Kind of go from there so I think that to me is a little different that if we talked to a patient about titrating a dose or trying to use what they have rather than just adding lots of other medications and that initial three-month time period.

Zach Weber: Yeah, that sounds good. And I think if we continue kind of the thought process of where we're at in approaching a diabetes patient like this, we've kind of identified what those initial medications are, we've begun to consider what his initial targets would be and maybe when we would want to adjust therapies. And so if we get to the point where additional options might need to be added in his care, what would be appropriate to add and why?

Kristi Kelley: Yeah, I think that's a great question and something we talk a lot about in the clinic and I work in a clinic with internal medicine residents, and so a lot of times we're trying to think one step ahead for them to be able to kind of get the game plan together. And so in this case, for this patient if we're looking at the ADA guidelines, which is what we consult a lot in clinic, we really have to think about their approach from a standpoint. Does that patient have established ASCVD or CKD? And if not, then we can look at the other recommendations that they have and think about, are we most concerned about the patient experiencing hypoglycemia? Are we most concerned about trying to minimize weight gain or even promote weight loss or is cost a big concern? This patient was concerned about cost initially, but as I mentioned, he does have commercial insurance.



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Kristi Kelley: So that sometimes is different than a percentage of our patients we have in the clinic where I work that don't have any insurance coverage and so we're definitely restricted on what we're able to do. I think the other thing that becomes apparent is when we think about the other recommendations, we can guideline recommendations. We can look at the AACE/ACE recommendations talk about what are those first and second line agents that they would recommend, how do we rank those? They actually rank their medications, but in that compilation of medications that they list the GLP-1 receptor agonists or the SGLT-2 inhibitors are there as well as the DPP-4 inhibitors. We see those in clinic.

Kristi Kelley: It does vary depending on some of the patient's other comorbidities, but the AACE/ACE recommendations actually talk about the alpha- glucose inhibitors, colesevelam or bromocriptine. We don't routinely use those in our clinic. So while I think about those being an option, I think we really come back to thinking about the GLP-1 the SGLT-2 and the DPP-4s. Another consideration in a patient like this because he was started on insulin initially, that basal insulin is really to think about would you continue that basal insulin or do you get to a point that we've gotten his blood glucose is lower and so would we want to consider maybe switching from that basal insulin to something else instead of that basal insulin but still continuing that Metformin. So those are some of the things we would think about in our clinic... In this patient when we're kind of brainstorming what would be the next best option for him.

Zach Weber: For sure, yeah. And you definitely did a great job of bringing up many specific medication classes that we would consider at this place in therapy for this type of patient. And so we know that we've had a handful of new medication classes for diabetes that have been introduced in recent years that have definitely picked up an interest in use among many providers and clinicians. And one of those is that everybody really seems to be kind of getting on the GLP-1 receptor agonist bandwagon. And so I'm wondering if you kind of... Do you agree with this for this particular patient in terms of considering this type of medication and do you think he might be a good candidate for one?

Kristi Kelley: Yeah, I think that's a great question and one that we are facing on a regular basis in our clinic. For a long time, I felt like it was just something that



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we would talk about in pharmacy circles and I would get really excited about and we really didn't have the option to use that in clinic. And the residents are coming back from working with some of the private practice physicians where they do rotations and they are all about the GLP-1 RA and it's like they're trying to find patients to start the GLP-1 receptor agonist. And I think the good news is that with this evidence that we've continued to have come out, there's lots of patients that really would fit the criteria and be good candidates for GLP-1 receptor agonists. One of the things that really has come to mind from my perspective is just the proven cardiovascular benefits and we know have several agents on the market here in the United States that have completed cardiovascular outcome trials that have shown benefit.

Kristi Kelley: When we think about how we approach those agents clearly liraglutide, dulaglutide, injectable semaglutide and exenatide ER are coming to mind. We could talk a lot of data about the benefit of these agents. They've been studied in patients with a history of cardiovascular disease as well as increasingly we're seeing some data come out and patients that don't have a history of cardiovascular disease and still seeing benefits collectively across the GLP-1 class, to date we've seen that we see a decrease in those major cardiovascular events. When we treat patients we've seen numbers needed to treat in the ballpark of 75 over 3.2 years. So that's powerful when we're thinking about how to manage these patients. This gentleman that we were talking about in this patient case does not have a history of ASCVD however, I could make a strong case that we're seeing some evidence that's showing that we could use these agents potentially to permit ASCVD.

Kristi Kelley: And so is that strong enough to use in a patient like this? I think we can make that case. We're going to have to add something a lot of times in a patient like this anyway. So why not trust something like the GLP-1 receptor agonist? I think trying to decide what would you use gets into another discussion. But we know we have options for giving these agents either orally with the oral semaglutide that has recently been approved and brought to market to an injectable that we could do either daily or weekly. So we've got several options. And I think the other thing for me and him especially that could potentially be a benefit is the fact that we do expect them to call some weight loss and that would



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be a benefit in him. His BMI was 41 so we know we'd like to see a decrease in that if at all possible to help his overall health.

Zach Weber: Yeah, for sure. Yeah, it definitely seems like this one might be a good option on for many reasons for this particular patient and it certainly doesn't appear that he has any contra-indications or restrictions for using a GLP-1. And so if you were to decide to start one of those agents, do you think you would initiate one of the injectable ones or perhaps try the new oral semaglutide?

Kristi Kelley: Yeah, I think that's a great question and something that I've already started thinking about in clinic a good bit. I think if the patient's willing to inject on some level can make the case for having stronger evidence with some of our injectable agents. I think some of it depends on what does the patient want to do, is it burden for the patient to have to take a pill every day. Some patients are like, "I'm already taking something. I might as well just add another pill to it." Some patients would prefer to be able to do an injection that's once a week. And so in that vein I would think something like liraglutide or the injectable semaglutide potentially would rise to the forefront. Another thing that we have to consider when we're thinking about this, are any of these approved for cardiovascular benefit?

Kristi Kelley: Right now we only have that for liraglutide. My understanding is that some of the other agents are seeking approval for use to prevent cardiovascular events and so that may change the dynamics. I know some of our patients in clinic don't like needles. This patient's already having to attach a pin needle to his Lantus SoloSTAR pen. So that may not be a big deal for him. But in our patients that don't like needles, some of the different devices give them options where they may not have to see that needle or it's easier for them to use something like dulaglutide would be a good option for him. As far as the oral option with semaglutide or Rybelsus, I believe that's the way you're supposed to say that, is approved for adjunct therapy with diet and exercise, we've got evidence to show that it's appropriate to use in combination with Metformin with or without insulin and that aligns with where our patient is.

Kristi Kelley: Majority of the GLP-1 receptor agonists, we have the same type of data. So I think it's reasonable if he gets excited and wants to try the newer agent



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wants to trust something orally. I think that would be a reasonable option. Probably the last thing that kind of comes to mind about that is just thinking about the titration schedule and the fact that we do have to take the oral semaglutide very specifically, at least 30 minutes before any food or other beverage or other medications. And you can only have take it with four ounces of water. So this patient was somebody that was on the go. So that would be a consideration we'd have to talk about. Does that slow down his routine if he has to do that first thing in the morning to be able to get to his job?

Zach Weber: Yeah. Thank you. Yeah, you've definitely done a great job of outlining the considerations for these types of medications for this patient. And then as we think about those medications and others, we always think about medication access and something that you kind of mentioned earlier on in the patient case. As this patient had some concerns about the affordability of his medications and so which could potentially have an influence on the decision and what you were to add. And so how would you address this issue related to affordability and access to medications for this patient?

Kristi Kelley: Yeah, I think that, that's something I feel like we face on a daily basis probably in all of our practices. We talk a lot about that the best medication doesn't work if the patients can't access it. So I think that's something we need to think about from the forefront, you know the ADA suggests that if cost is an issue that you can consider using therapy with sulphonylurea or TZDs in combination with Metformin. I feel like here because the patient has commercial insurance that we might have some other options that might potentially target his overall care. So I think that's where we would come into play to think about something like the GLP-1 receptor agonist. We could think about DPP-4s or even the SGLT-2s. We're really don't have a lot of generic options for any of these.

Kristi Kelley: There's only one DPP-4 inhibitor that's available as a generic. So then you're coming back to okay, if we're going to give a GLP-1 receptor agonist and there's no generic available, which one's covered by his insurance? And so trying to figure that out certainly would be helpful. But then just being aware of those resources that are out there to help a patient like this to think about, is there a copay card that would help reduce the cost and make it more reasonable? We would definitely have to think about not only the cost of the



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medication but the cost of if it was an injectable, the cost of the pen needles. Interestingly with Rybelsus, it's actually already got copay cards that are out there. And I found it interesting when we started thinking about this in the clinic that that copay card is less than what we're seeing the out-of-pocket costs would be for patients and what we're seeing with the injectable agents.

Kristi Kelley: And then one of the other kind of final things to keep in mind about the cost of all of this is that there are patient assistance programs that are available. That's something we use pretty routinely in our clinic. I mean there are standard requirements that patients must meet. These are relatively clear and those requirements are and spelled out on the various company websites. Patients are required to provide some documentation to be able to qualify for some of these programs. And so for some of our patients, some of that can be a challenge, but it's really a neat option to be able to partner as healthcare providers to be able to get these medications to patients and not to simply be restricted about what they can afford to pay out of pocket. And I think one of the final things that I thought about with this patient in particular is just making sure that we're keeping him on the meds that he needs to be on, but as we should with any patient.

Kristi Kelley: Just making sure that we have them on the least amount of medications that are needed so that, that actually helps not only with the cost but just minimizes the number of medications that the patient's having to keep up with. So those were things that I kind of thought about when I was thinking of his overall approach because the cost is probably not only a consideration for if we added GLP-1 receptor agonists, but does he need something else? You know, for his blood pressure, is he going to require eventually additional lipid lowering therapy or is all this kind of being fixed so to speak, by getting his blood glucose under control. So is there things that came to mind for me.

Zach Weber: Yeah, it's definitely a lot to consider and I think you've done a wonderful job kind of working through this patient case of certainly bringing to the forefront of all these things that go into just trying to provide the best care for a patient like this. And obviously the complexity of the decisions that have to be made, not only in terms of choosing what medications might be best, what treatment targets do we want to get to, but then of course there's always this



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factor of cost that comes into play in making sure that we can provide access to those decisions that we think would help our patients the best. And so with that, I think that's all the time that we have for today. And so I certainly want to give a big thank you to Kristi Kelley again for joining us today to discuss our considerations of GLP-1 receptor agonists and how they might help our patients with type 2 diabetes. And so please be sure to join us here every Thursday where we will be talking with ASHP member content matter experts on a variety of other clinical topics.

Speaker 1: Thank you for listening to ASHP official, the voice of pharmacists advancing healthcare. Be sure to visit [ASHP.Org](https://www.ashp.org) forward slash podcast to discover more great episodes, access show notes, and download the episode transcript. If you love the episode and one of your more, be sure to subscribe, rate, or leave a review. Join us next time on ASHP official.