

Overcoming Challenges in Treatment of Patients With Type 2 Diabetes

A Q&A With Robert A. Gabbay, MD, PhD, FACP



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AJMC®: Over the past decade, we have seen the arrival of several new type 2 diabetes (T2D) therapeutic drug classes, including dipeptidyl peptidase-4 (DPP4) inhibitors, sodium-glucose transport protein 2 (SGLT2) inhibitors, and glucagon-like peptide-1 (GLP1) receptor agonists. How does the availability of these different options help the physician in clinical practice?

GABBAY: I think it's been almost revolutionary, particularly the SGLT2 inhibitors and the GLP1 receptor agonists. It's really changed the way we think about managing T2D, and that's largely because the cardiovascular benefits that were demonstrated with those 2 drugs were a bit of a surprise [and] were really discovered through required FDA cardiovascular outcome trials. They demonstrated reduction in cardiovascular disease. If you look at the American Diabetes Association (ADA) clinical practice guidelines and you compare it with what it looked like before these drugs were available versus now, it's a completely different algorithm that really focuses on the presence or absence of cardiovascular disease, and then everything flows out of that. It really has changed quite a lot the way we think about managing diabetes.

AJMC®: Can you discuss the challenge of hypertension in T2D? How can this be addressed with combination therapy?

GABBAY: In the end, the number 1 killer of people with T2D is cardiovascular disease. Although glucose control probably has a small impact on that, it largely is not about glucose control and it's about blood pressure and lipids as the biggest predictors and the biggest ways to reduce the risk. These 2 newer SGLT2 inhibitors and GLP1 receptor agonists lower cardiovascular disease, but, their impact on cardiovascular disease is probably not around lowering glucose. We also know that for most people with diabetes, it takes at least 2 and often 3 medications to be able to manage their hypertension and get them to goal. Getting to this idea of combination therapy, you know that people are going to need at least 2 medications. [We add drugs] slow step wise; we'll try 1 at a low dose [and] gradually go up and add the second drug low dose [and] gradually go up. There's a lot of time lost. Essentially people are not at goal. The advantage of combination therapy is it's simpler in so many ways. It's easier to, in many cases, get individuals with diabetes on board. [With] combination therapy, you start [with] a combination, use a low dose for safety, but then all you're really having to do is titrate that 1 tablet and you're not adding to the pill burden of people with diabetes.

AJMC®: What are the specific clinical advantages of a combination DPP4 inhibitor/SGLT2 inhibitor? What are the advantages for a payer?

GABBAY: The clinical advantage again is that same idea of not having to titrate [a] second drug, and it really gets back to a big effort that the ADA is taking with a number of partners, patient groups, pharma, physician groups, [and] payers to tackle this idea called therapeutic inertia, [or] the observation that people are not at goal and they come to see their health care provider and nothing seems

to happen in terms of a change. Combination therapy is one way to attack that. Now, more specifically [with] DPP4 and SGLT2 inhibitors, we know that more people need to be on SGLT2 inhibitors based on the benefit it can provide for cardiovascular disease. Some studies have suggested from database review, there is only about 10% of people that would benefit from these drugs are actually on these drugs. DPP4 inhibitors are nice drugs because they're extremely well tolerated, they're easy to use, and you don't need to titrate it. From the clinical side there [are] some real advantages. From the payer side [of] combination tablets... in the end, payers are looking to ensure that we reduce the overall cost of care for people with diabetes, and a huge driver that cost of care is cardiovascular disease. Better blood sugar control prevents blindness, kidney failure, amputations, and SGLT2 inhibitors lower hospitalizations for congestive heart failure; those hospitalizations obviously are very costly.

AJMC®: For a patient with A_{1c} above 8%, how does the availability of combination therapy increase the chances of glycemic control?

GABBAY: It gets at this idea of therapeutic inertia; you're tackling things more aggressively upfront. We also know that managing people with T2D earlier in the course of their disease has what is called a legacy effect: good glucose control in [the] first period of time translates to even better benefit down the line, and so treating aggressively makes sense. With the exception of insulin, all of the medications for diabetes, in essence, lower A_{1c} 0.5 to 1.5 at most, and that's only if people really have very high A_{1c}.

AJMC®: What are the barriers to medication adherence to patients with poorly-controlled T2D?

GABBAY: For some, it's competing demands. For [others], it's a lack of understanding of why just prescribing something typically [isn't] enough to ensure adherence. Medication adherence is really a challenge. Cost is a huge potential barrier. I would say for most providers, it they're not always sure what would be on formulary or not for a given patient at the moment they're prescribed, it's really not as accurate as it could be.

Overcoming therapeutic inertia has a number of different components. One is aimed at the health care team and that's educating them about what therapeutic inertia is and why we need to tackle it, and then giving them some tools to be able to deal with that. The other equally important part is on the [side of the] individual

with T2D, and that [means] educating them as to what it is and that T2D is a progressive disease. One needs to continue to advance therapy and a whole host of [other] things. It's not just education, it's also problem solving, and that's where diabetes care and education specialists really come into play and increasing the engagement with those individuals and others are really important, including the whole health care team. It's educating patients about the importance of participating with those other members of the team, and also engaging the health care team about making sure you include it. [On] the system side, how do you remove barriers? Maybe it's making a combination therapy more available, formularies more transparent and increasing access.

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AJMC®: Centers for Medicare & Medicaid Services has invited comment on the problems of prior authorization in Medicare Advantage. What are the specific challenges with prior authorization in diabetes care that you would like to see addressed?

GABBAY: It drives health care providers nuts. It is it is one of the biggest pain points after electronic health records, which is the biggest pain point for them, and it really slows the whole process down and honestly contributes [to] therapeutic inertia. It creates a lot more work. It delays things. We all understand the reasons why you need to have some sort of appropriate controls around spending, but there could be more innovative ways of doing that. The other challenge of course, is that often every payer has a different way of documenting that prior authorization, and that drives people nuts. ♦