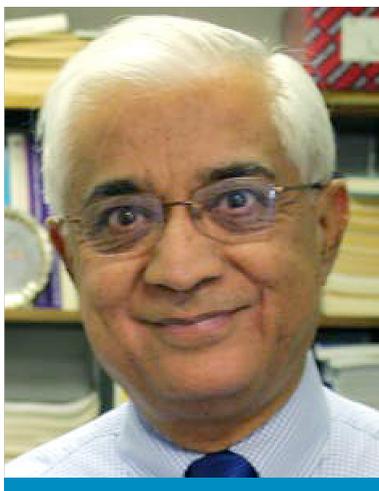


Treatment Selection for Patients With Type 2 Diabetes

A Q&A With Om P. Ganda, MD



OM P. GANDA, MD

Senior Physician, and Medical Director, Lipid Clinic Chair, Clinical Oversight Committee Joslin Diabetes Center, Associate Professor of Medicine, Harvard Medical School
Boston, MA

AJMC®: In your experience, what are the most common characteristics that patients with type 2 diabetes (T2D) share?

GANDA: T2D is a very common problem that we are facing these days and is on the increase because one of the main factors that govern T2D is obesity; two-thirds of the United States is overweight or obese. Only a minority of the population, one-third, is what can be called normal weight by the current body mass index criteria. The more we have to deal with obesity, the more we have to deal with diabetes because T2D is really dependent on several risk factors of which obesity is the most important. Of course, the genes are important. You have [to have] the gene before you can get diabetes; not all obese people get diabetes, There are other factors: family history, which indirectly is related with the genes and having a set of metabolic risk factors such as hypertension, high triglycerides, low high-density lipoprotein cholesterol, increasing waist circumference.

AJMC®: In general, what is your treatment approach to patients with T2D? If patients fail the American Diabetes Association standard of care (metformin), what is your next approach?

GANDA: Everything I say is, of course, going to be on top of the lifestyle intervention that has to be there not only for prevention of T2D; people with diabetes have to always think about lifestyle changes like diet, exercise, cessation of smoking, and so forth. Prior to 1995, we had only 1 class of oral drug that could be used, called sulfonylureas, and if that didn't work, the only other choice was insulin. Now we are at the phase where we have lots of choices, and some of the newer classes of drugs that we're using more and more for good reason, include 3 classes of drugs, namely dipeptidyl peptidase-4 (DPP4) inhibitors, glucagon-like peptide-1 (GLP1) receptor agonists and sodium-glucose transport protein 2 (SGLT2) inhibitors. I think these 3 classes or drugs have become very popular, mainly because some of the drawbacks of sulfonylureas and insulin, at least in the early stages of T2D. While we are using all these choices, in general, we always start with metformin first because that has really been the basis of treatment for a very long time and is quite effective in the early stages. Of course, in many cases, within 5 years after the onset of T2D, most people will require a second drug, and some will require a third drug after another couple of years. We often end up using 2 or 3 drugs in a given patient.

Some of the concerns have been related to the adverse effects of the older drugs, for example, sulfonylureas can cause hypoglycemia, weight gain, and there has been some lingering question about whether they are not so protective of the cardiovascular system. On top of metformin, the other 3 classes of drugs that I mentioned have the advantage because they don't cause hypoglycemia, they don't cause weight gain, and they seem to be cardioprotective in the sense that they don't cause any cardiovascular toxicity, which has been an ongoing concern with sulfonylureas and even with insulin.

AJMC®: What about newer classes of drugs DPP4 inhibitors, SGLT2 inhibitors, and GLP1 receptor agonists?

GANDA: After metformin, most of us are using 1 of these 3 agents. However, Sulfonylureas are not going to be withdrawn from the market; as in many parts of the world, cost is an issue. Sulfonylureas, like metformin, are all generic and very cheap. For the cost issue, many people still use those drugs and they do have efficacy in improving hyperglycemia. If you have choices, then the first option these days after sulphonylurea is one of those 3 agents, particularly if you have cardiovascular background. No matter which guideline you look at these days, after starting metformin, the next question should be: does the patient have any atherosclerotic cardiovascular disease? If that is the case, there have been significant advantages of these newer drugs, particularly GLP1 receptor agonists and SGLT2 inhibitors in protecting the cardiovascular system, and even some renal benefits have been reported. DPP4 inhibitors are a preferred choice after metformin in the absence of ASCVD, due to their excellent tolerability. There was an FDA mandate in 2008 that all new drugs must undergo a phase 4 trial where they must show non-inferiority, compared with placebo, in protecting the cardiovascular system. In other words, they should be safe and not cause any cardiovascular drawbacks.

AJMC®: Can you compare the costs of DPP4 inhibitors, SGLT2 inhibitors, and GLP1 receptor agonists?

GANDA: In general, DPP4 inhibitors have been around the longest, and they have proven their safety record; they seem to be less costly than the newer classes, the GLP1 receptor agonists and the SGLT2 inhibitors. If cost is an issue and safety is an issue, DPP4 inhibitors would be a very appropriate drug to add on top of metformin, in the absence of ASCVD.

AJMC®: What are some of your biggest challenges with current treatment of T2D?

GANDA: There are indeed a number of challenges. Long-term lifestyle changes can be difficult for people. We always tell our patients to at least meet us halfway with efforts to lose weight. I tell all my patients that even if you can't lose weight, at least exercise every day because exercise improves insulin resistance, and you end up with less medication and half the dose of the medication. Even if you don't lose weight, don't be disheartened. Just exercise regularly, which means 4 to 5 days a week, at least 30 to 40 minutes of brisk walking. Another challenge, of course, is adherence to drugs. This has been a big problem, not only with drugs for diabetes, but for any chronic disease. There was a big study done from the VA population a number of

years ago. It was a long term randomized controlled trial, called the ALLHAT study, and there were other studies with blood pressure drugs and statins and showed that people who do not take their cardioprotective drugs regularly, actually end up in the hospital more often, increasing the health care cost, and they actually end up with higher mortality. The same has now been shown in people with poorly-controlled T2D who are not adhering to their medication regimen. There is increased risk of hospitalization and there's increased risk of mortality.

“ DPP4 inhibitors have been around the longest, and they have proven their safety record. If cost is an issue and safety is an issue, DPP4 inhibitors would be a very appropriate drug to add on top of metformin, in the absence of ASCVD. ”

AJMC®: Have you seen any initiatives that affect patient adherence (either improve or decrease)?

GANDA: I think every new patient with diabetes should sit down with an educator. I know not every physician has the availability of educators, but if they can be approached; and the patient should learn the proper diet, and why the medication is being given. Part of the nonadherence to the drug is because patients may not understand the need for the drug, and they are not properly educated about the importance of the medication. Cost is an issue we talked about it. Then there are personal issues like psychological factors; patients may not want to take too many medications because they think that this is their personal failure. We need to encourage them, and we don't need to enforce all at the same time; rather gradually get them into better control by ensuring that they take the drugs properly. We have to take the social, economic, and cultural factors into account. Teaching the patient about the importance of medications, and reminding them about the need to prevent complications goes a long way. When you see a newly diagnosed patient, you should try to get them to learn the right habits from the very beginning. There's a lot of data we have seen in both type 1 and type 2 diabetes that the earlier you control diabetes, the better in the long-term outcome. ♦