Optimizing Diabetes Management
An educational update for providers

In June 2012, the American Diabetes Association (ADA) with the European Association for the Study of Diabetes (EASD) issued a position statement advocating a patient-centered approach to management of hyperglycemia in patients with type 2 diabetes.[1] The statement encourages addressing individual patient needs, preferences, values, and tolerances and takes into account the age of patients and disease progression. The recommendations parallel the January 2012 ADA guidelines and are closer to glycemic control algorithms from the American Association of Clinical Endocrinologists and American College of Endocrinology.[2] The statement focuses on customizing glycosylated hemoglobin (A1C) goals, emphasizing lifestyle modifications for all patients, and selecting appropriate drug therapy based on A1C levels.

Metformin is still recommended as the optimal first-line treatment for most patients.[1] If metformin cannot be used, up to three drugs may be needed. Desired AIC levels, patient characteristics/preferences, and drug side effect profiles help guide choice of agents. Initial options may include sulfonylureas/meglitinides, pioglitazone, dipeptidyl peptidase 4 inhibitors, or glucagon-like peptide (GLP-1) receptor agonists.

For patients who require additional glycemic control after an initial 3-month trial with metformin monotherapy, the statement discusses advancing to dual combination therapy.[1] After the initial trial with metformin, the next step would include addition of a second oral agent, a GLP-1 receptor agonist, or basal insulin. The higher the A1C, the more likely insulin will be required.

In terms of triple combination therapy, the position statement notes that once patients require the addition of a third agent, "the most robust response will usually be with insulin."[1] Most patients will need to be transitioned to insulin, which should be favored in circumstances where the degree of hyperglycemia (defined as an AIC $\geq$ 8.5%) will make it unlikely that another drug will be of sufficient benefit. If triple combination therapy without insulin is used, patients need to be closely monitored. Ongoing months of uncontrolled hyperglycemia should be avoided. Problems with increasing the number of medications such as increased potential for adverse events, drug-drug interactions, increased costs, and negative impacts on patient adherence are highlighted.

If combination therapy that includes basal insulin fails to achieve an A1C target after 3 to 6 months with fasting glucoses at target and postprandial glucose levels exceeding 180 mg/dL, then clinicians should incorporate prandial (mealtime) rapid-acting insulin injections (basal-bolus therapy) or premixed insulins. The more complex insulin regimens can be used in combination with 1 or 2 non-insulin agents.[1] The position statement noted that although some non-insulin agents may be continued, with addition of prandial insulin, the insulin secretagogues (i.e., sulfonylureas, meglitinides) are usually stopped and pioglitazone doses reduced or

discontinued to avoid edema and excessive weight gain. Only select patients with large insulin requirements due to severe insulin resistance may still require pioglitazone continuation to aid in reducing their insulin dose. Incorporation of prandial insulin necessitates a decrease in basal insulin doses. Finally, the position statement noted that positive data on combination therapy with incretin-based therapies and basal insulin are accumulating; however, the costs of these types of combination regimens must be considered.

Take home points for management:

- **Metformin is the optimal first-line treatment.**
- **If metformin monotherapy fails, addition of a second oral agent, a GLP-1 receptor agonist, or basal insulin is recommended.**
- **Once 3 drugs are needed, the addition of insulin as the third agent will produce the best results.**
- **If combination therapy that includes basal insulin fails, then patients should be transitioned to a more complex insulin regimen.**
- **Once patients are on a complex insulin regimen, then, ideally they should ONLY be on 1 or 2 additional non-insulin agents. Secretagogues (i.e., sulfonylureas, meglitinides) are usually stopped and the dose of pioglitazone is reduced or the agent is discontinued in patients receiving complex insulin regimens.**

References

1. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 2012;35(6):1364-1379.
2. Rodbard HW, Jellinger PS, Davidson JA, et al. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology Consensus Panel on Type 2 diabetes mellitus: An algorithm for glycemic control. *Endo Pract*. 2009;15(6):540-559.