Therapeutic inertia in type 2 diabetes: getting from where we are to where we want to be

Inerzia terapeutica nel diabete di tipo 2: arrivare da dove siamo a dove vogliamo essere

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It's impressive what AMD is doing in the area of therapeutic inertia to modify the assessment and care of patients with diabetes. I'm going to update you on what the American Diabetes Association is doing in this field.
The topic for ending this session is: "Therapeutic Inertia in Type 2 Diabetes: Getting from where we are to where we want to be," and again, I think AMD is doing a great job moving in that direction. I'm here representing the position of the American Diabetes Association (ADA) and will discuss their multi-pronged strategy and approach to address therapeutic inertia. The ADA's campaign "Connecting for life: Therapeutic inertia - Treating the Whole Patient" has four pillars of activity. The first is reframing the conversation; the second is precision medicine going forward; the third is removing the hurdles or barriers that exist; and finally, we will focus on disease state campaigns.
Let's review each of these pillars sequentially. The first is: "Reframing the Conversation." For millions of affected people, diabetes is a silent disease, a disease that is asymptomatic and not apparent. But once the disease progresses and comorbidities arise it becomes more evident. Therefore, education is incredibly important in terms of informing the patient. Another element that I don't think is being adequately addressed is changing human behaviour. We can educate patients infinitely in what diabetes is and how to manage their disorder but changing the patient's behaviour remains a challenge for all of us in the clinical space. Patients need to be heard, whether that is a child with type 1 diabetes or her mother, other family member or caretaker. Finally, we need to acknowledge that we don't have to brave this alone. Treating diabetes successfully needs a team approach and diabetologists in Italy appear to be implementing this on a daily basis.
So, let's move to the second pillar: "Precision Medicine" which is transforming practice. Over the last 15 years much progress has been made and precision medicine

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will likely be the standard of care in another decade or two. Right now, we need to continue to understand the disease, the natural history of the disease, and who is at risk. We need to develop a better framework of biomarkers that can be used to assess risk for diabetes and risk of complications. We then need to develop algorithms related to these biomarkers that can be used to predict risk, complications and what medications will work best for a given patient. Those predictions could be genetically based or environmentally influenced. They may also be based on so called "epigenetic phenomena", where DNA sequences don't change but gene expression is modified individually. We also need to consider regulatory engagement and how regulations within Italy, the United States or globally can be modified to adopt this personalized approach to patient care. We also need to think about precision approaches related to health and environmental assessment. Ultimately, we need to translate ongoing investigations into clinical care so we can modify prescriptions for each individual patient, and then and inform the patient what we're trying to accomplish.

The third pillar of this therapeutic inertia is "Removing the Hurdles or Barriers." Here we are looking at practice optimization, improving patient access, doing research on what works best to modify therapeutic inertia, and looking at policy and partnerships to support our efforts. Practice optimization implies addressing the full range of barriers affecting therapy and decision-making related to it. Improving patient access requires focusing on identifying solutions to address barriers for access to medicines and devices and non-medical therapies like diabetes education. It also involves understanding addressing social and emotional barriers to patient adherence to therapies. Research implies developing a deeper understanding of what works and refining metrics and milestones to assess progress and success. And finally, it will be important to identify and establish collaborations with partnerships with relevant organizations like AMD.

The fourth pillar is "Disease Specific Campaigns." I've been very much a part of a program called "Know Diabetes by Heart", which was instituted a in November of 2018. This is a joint-venture between the American Diabetes Association and the American Heart Association, with the goal of increasing the knowledge of heart disease risk in patients with diabetes and ultimately implementing effective evidence-based strategies to modify that risk. This is a $40 million initiative that is supported by pharmaceutical industry partners who have drugs and devices in diabetes space. The next disease specific campaigns will include eye health, or the ophthalmological complications of diabetes, followed by renal disease and obesity, all important issues for this patient population. Changing the obesity epidemic in the U.S., much less globally, is a tremendous challenge. However, even a 5 to 10% weight loss can provide significant benefit to patients. Modifying this identifiable biomarker related to cardiovascular disease and diabetes really is an important next step. As for renal disease, it is clear we now have new therapeutic agents that modify the natural history of the decline in eGFR that occurs in patients at risk for progressive nephropathy. In the fourth quarter of 2020, the emphasis is going to be on non-alcoholic fatty liver disease. All of these components related to type 2 diabetes can be modified to benefit our patients downstream.

Dr. William Cefalu, the former Chief Science and Medical Officer for the American Diabetes Association said, "despite the availability of 40 new branded medications developed in the past 20 years, as well as a wealth of education and information resources for people who have diabetes, the hard truth we must face is that the average A1c in the United States (and by the way in Italy), has not substantially changed". So, what's wrong with this picture? We need to do better.

Will Cefalu made an interesting observation – he evaluated time-related change in HbA1c in participants with type 2 diabetes who received conventional therapy (i.e. metformin) with add-on therapy going forward versus those who were treated initially with triple drugs therapy (Khan A, Cefalu WT. Diabetes Care 2016; S2:S137-45). You can think of any triple drug therapy that might be appropriate for your own implementation, but ultimately if you follow these people for the first six months, there's a greater fall in A1C when triple therapy is prescribed at baseline. At 24 months, A1C was 0.55% lower, on average, with triple therapy.

So, what's the solution to this problem? Well, we think a big part of overcoming this inertia is removing the hurdles to optimal diabetes care. There are three pillars to this approach. First is to work to cure diabetes. I think this is an inappropriate goal and that in another decade or two we will, in fact, be able to cure diabetes. Second is preventing diabetes in patients with pre-diabetes, which is an important part of the mission of the American Diabetes Association, as I'm sure it is for AMD. Third is to directly reduce of prevent therapeutic inertia by promoting adoption of evidence-based practices, strategies, programs and tools that address key determinants of therapeutic inertia in diabetes care, leading to improved, timely treatment modification and improved overall glycaemic control in diabetes patients.

So here are the objectives of the solution to reducing therapeutic inertia that the ADA is facing, and you are facing here: 1) Improve baseline understanding of therapeutic inertia and what it stands for; 2) Identify and promote activities, skills, and methodologies that are closely aligned with improved glycemic control; 3) Provide skill-based education, tools and other resources to improve adherence to the ADA guidelines (or the AMD guidelines); 4) Develop user-friendly solutions to support point of care clinical decision-making; 5) Identify the most critical policy barriers contributing to therapeutic inertia, and develop a long-term strategy to promote changes through coalition building and active advocacy support; 6) identify and support ongoing initiatives led by other coalitions, associations and governmental organizations that are determined to have a direct impact on therapeutic inertia.

So why the ADA? The American Diabetes Association's Standards of Medical Care is internationally recognized and trusted as the authority in diabetes care. These Standards of Medical Care that come out in January of each year are intended to be the Bible, if you will, for the next year related to diabetes assessment and care. In addition, the Standards of Medical Care are now updated on a rolling basis when the evidence changes, further supporting our ability to assess and treat diabetes using the best available evidence. Here are some facts about the ADA and the Standards of Medical Care:

- Sixty-four thousand primary care providers in the US are using and turning to the Standards of Medical Care for Diabetes;
- 1.2 million website visitors per month over more than half a million are active subscribers;
- 400,000+ volunteers nationwide including Healthcare Professionals are active in ADA related activities;
- 35,000 ADA Journal subscribers to "Diabetes", "Diabetes Care", and "Clinical Diabetes";
- 874,000 social media followers;
- 6 million readers of Diabetes Forecast, that reaches all our patients who are on the mailing list for the journal, a very informative lay-level publication of the ADA;
- Nearly 50,000 Health Care Professionals who are certified to use the ADA in-person and online programming;
- We have over 15,000 professional members and all of you are welcome to join in any time. Yes, there is a fee, but nevertheless there are a lot of benefits to occur being a member of the ADA.

The ADA's essential role in addressing therapeutic inertia is ultimately: 1) convening and aligning stakeholders related to diabetes and modifying therapeutic inertia through that mechanism; 2) collecting and assessing what works (and what doesn't work) going forward; and 3) disseminating and evaluating the impact of this transition from therapeutic inertia at rest and therapeutic inertia that is more proactive. Part of the solution also includes building patient engagement and trust, optimizing and personalizing care and leveraging tools and technology that relate to better care.

What's the timeline? The first step is a modification of our understanding based on an extensive literature review, landscape scan and meta-analysis. The second is the development of a market research survey to understand how clinicians currently think about clinical inertia. This will be followed by a robust awareness campaign aimed at increasing urgency of addressing therapeutic inertia now. We will then move into a best practice collection pathway and continue to track progress, monitoring and evaluating the data gathered. Finally, we will report our outcomes of modifying therapeutic inertia and share what works. This is the plan for the next one year as we work to change therapeutic inertia as we currently understand it.

Here is an overview of current therapeutic inertia projects conducted by the ADA. In November of 2018 the ADA convened an "Overcoming the Therapeutic Inertia Summit" that brought together all stakeholders in the diabetes environment to examine this problem from many angles. Then, in October 2019, ADA began a series of regional clinical workshop pilot programs aimed at helping clinicians optimize office workflow and improve patient communication to reduce therapeutic inertia. Planning is underway to create an awareness campaign that promotes the urgency of this issue and engages critical alliance partners. I see no reason why AMD can't join as a partner, ultimately to globalise the importance of addressing therapeutic inertia. The ADA also plans to publish a white paper detailing its entire plan to address therapeutic inertia in detail. In addition, they will be taking the findings form the systematic literature review I mentioned earlier and turning this into a journal article to discuss what seems most effective in addressing therapeutic inertia in clinical practice. So, this is the current list of projects the ADA has in the therapeutic inertia space and we hope to see favourable outcomes to follow.

Finally, I would like to discuss an approach clinical decision-making by healthcare professionals that I believe helps improve patient engagement

and outcomes. First, it is critical to address patient characteristics, assessing where they are right now, how much knowledge they have, understanding what the next step may be, and modifying our approach to address their needs. Second, we must consider specific factors that impact the choices of treatment. Remember, lifestyle remains important, including nutrition, physical activity, and the absence of tobacco and other illicit drug use. Third we need to create a personalized diabetes management plan for each patient that considers the current state of their diabetes, as well as their personal challenges, strengths and values. Fourth, we need to use shared decision making to agree on the management plan with the patient him/herself. Finally, we need to implement the plan, provide ongoing monitoring and support, and ultimately reassess regularly as time goes on to assure that the patient continues progress toward goal.

So, in summary, ADA priorities in the area of therapeutic inertia include: 1) looking at research including systematic review and possible pragmatic trial addressing issues in the therapeutic inertia space; 2) Practice optimization; 3) Patient access and engagement, and 4) the Standards of Medical Care and patient-centered research and care. This is ADA's effort to continue to modify therapeutic inertia in a favourable way so that the outcomes for a patient to follow are ultimately favourable.