The T2D is a complex and heterogeneous disease, with multiple variables that might influence on its treatment. For example, it can appear in a wide range of ages, the evolution time is very variable, the patients usually have overweight or obesity, but they can also have a normal weight, concomitant diseases can occur that contraindicate the use of certain antihyperglycemics, the tolerance of the drugs is individual, etc. On the other hand, its prevalence is alarmingly high, with a constant growth during the last years. It seems that it will not stop at least during the next decade, with an estimate of more than 300 million patients with T2D worldwide. Only these two last characteristics explain the reason of the deluge of consensus and guidelines published recently about the treatment of T2D. Its heterogeneity might make us doubt about which is the best therapeutic option for a certain patient, and its high prevalence make the health/governmental authorities take an active part with the intention of avoiding a pharmaceutical bulky invoice. Moreover, at present we count with more than 30 antihyperglycemic agents corresponding to nine different therapeutic groups (biguanides, alpha glucosidase inhibitors, sulphonylureas, glinides, glitazones, dipeptidyl peptidase-4 inhibitors [DPP-4], glucagon-like peptide-1 analogues [GLP-1], basal insulin and fast acting insulin), which need to find their place at the therapeutic scheme of the T2D.

During 2008, we have attended to the almost simultaneous publication of an important number of consensus and guidelines about the treatment of T2D that though addressed to a same objective; differ in the way of achieving it. Of all of them, perhaps the most known one is the consensus of the American Diabetes Association-European Association for the Study of Diabetes (ADA-EASD), published at the end of 2008, and which caused certain controversy within the scientific community. However, there are other guidelines and consensus that have also come out during the same year and that deserve our attention. Therefore, the characteristics of the already mentioned consensus ADA-ESAD and the National Institute for Clinical Excellence (NICE)² are detailed below as well as the consensus of the Canadian Diabetes Association (CDA)³ the guidelines of the Ministry of Health (MH) of Spain and the Diabetes in Primary Care Study Group (GEDAPS). In order to compare them, we shall discuss about the first, second and third stage of the treatment.
Therapeutic objective
The glycosylated hemoglobin (HbA1c) determines the therapeutic objective. Practically, all of them base themselves in their therapeutic actions in achieving a HbA1c lower than 7%. Only the NICE looks for HbA1c lower than 6.5% initially, passing onto an objective of HbA1c <7.5% once the biotherapy fails. The comparisons among the recommendations of the different consensus and guidelines according to the different therapeutic stages are summarized in table 1.

Special characteristics of the analyzed consensus and guidelines
In the ADA-EASD consensus, it is advised against the glibenclamide due to the high incidence of hypoglycemias it entails, the sulphonylureas are suspended when starting the treatment with basal insulin, and the rest of the treatments are included in a second level of lower scientific evidence. The pioglitazone is placed in this level, but not the rosiglitazone due to its potential cardiovascular risk, and also the exenatide. The consensus includes the DPP-4 inhibitors in “other treatments” as well as the alpha-glucosidase inhibitors, the glinides and the pramlintide, due to its lower or equivalent hypoglycemicant power, its scarce experience and its high cost.

The NICE consensus advises to use sulphonylureas as treatment starting in case of normal weight or high glycemias, and the possibility of treatment with exenatide is included in the third stage if the body mass index (BMI) is >35 kg/m² and if there are psychological repercussions arisen from obesity. In case of considering the treatment with glitazones, the pioglitazone is recommended. The treatment with DPP-4 inhibitors is not considered either with insulin detemir, which shall be analyzed in a specific document that will come out in the next months.

Importance is given to the control of the post-prandial glycemia in the Canadian consensus and it is explained which are the specific drugs that can control it. The rosiglitazone is not excluded because it is considered that there are no clear evidences about the implication in a higher cardiovascular risk. The GLP-1 agonists are not included, without specifying the reason, nor are the sulphonylureas suspended when starting the basal insulin.

The possibility of sulphonylureas are considered in the MH guideline as starting of the treatment in case of normal weight; the treatment with glitazones is recommended only as a second option in case of intolerance / contraindication to other drugs, and the use of pioglitazone is recommended. In case of intolerance to the metformin in the first stage, the sulphonylureas are recommended and pioglitazone in the second stage. Neither the GLP-1 nor the DPP-4 inhibitors are included, due to the lack of data about its safety at long term.

Finally, the GEDAPS Network does not recommend to suspend the sulphonylureas when starting the basal insulin, it does not include
the insulin in the second stage or incorporate the GLP-1 agonists. These two last aspects are being evaluated again, with a high probability to be included in the next guideline update.

This analysis might conclude with the following phrase: “same problem, different consensus”. The main discrepancies would turn around the administration or not of metformin as from the diagnosis, how to act when the first therapeutic option fails (some authors recommend to add sulphonylureas and others to choose the drug according to the characteristics of the patient) and what to do in the third therapeutic stage (third drug versus adding insulin). As regards to the common weaknesses, we could mention that all the consensuses recommend starting in the same way, without taking into account the initial HbA1c, except for the Canadian consensus, which categorizes according to the HbA1c level (≤9 or >9%). There are not either many specifications about what to do if metformin is contraindicated or it is not tolerated, as it does not seem logical from a physiopathology point of view to restart to sulphonylureas directly. It has not been studied in depth about the differences that exist among the different sulphonylureas that we might choose if they are indicated, except for the recommendation of avoiding glibenclamide. Finally, everything is based in the HbA1c. However, we know that when we get closer to the therapeutic objective, for example with HbA1c <7.3%, the postprandial control becomes more important, which has to be taken into account when choosing a drug or the other. It is not known with accuracy if other parameters (HOMA-R, HOMA-B, C-peptide, glycemic variability, etc.), might be useful when taking the decision, though all this can be history if finally the investigation in pharmacokinetics allows us to choose the treatments à la carte.

In conclusion, it is evident that up to date there are different strategies with the objective of achieving the best glycemic control of the patient with T2D, which might probably reflect the own heterogeneity of such disease. Perhaps this datum is the one that offers more cohesion to the treatment individualization, as regards to the different characteristics of the patients (weight, evolution time, age, HbA1c, etc.). One of the most important current limitations of the treatment algorithms for the T2D is the shortage of well-designed randomized and controlled studies, which compare the different strategies of treatment, particularly the different combinations of drugs among them. In view of all this, the starting of head-to-head studies of the different therapeutic options might be very useful, as well as others addressed to assess the effects on the cardiovascular risk factors, that determine the first causes of mortality of most the patients with T2D.

As a personal opinion, the central objective when issuing any therapeutic consensus has to be the patient, and other factors (financing, etc.) should not constitute the main argument for it. Moreover, we should not forget that most of the health expenses caused by the diabetes arise from the chronic complications. An adequate and early treatment of this disease might prevent the onset of many of them, though it might not be necessary (or yes?) to reach the proposal of Dr. DeFronzo (metformin, pioglitazone and exenatide since the diagnosis of T2D).

Declaration of potential conflict of interests
F.J. Escalada San Martín states that there are no conflicts of interest as regards to the content of this article.

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