COMMENT ON FERRANNINI AND ROSENSTOCK

Clinical Translation of Cardiovascular Outcome Trials in Type 2 Diabetes: Is There More or Is There Less Than Meets the Eye? Diabetes Care 2021;44:641–646

Stavros Liatis

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I read with great interest the recent Perspective by Ferrannini and Rosenstock (1), which provides thoughtful insight on the interpretation of the numerous recent cardiovascular outcome trials (CVOT) in the field of type 2 diabetes.

As far as I understand, though, there are some numerical mistakes in both Table 1 and Fig. 2*A* and *B* that may seriously affect the overall understanding of the article. Specifically, in Table 1, although the incidence rates (IRs) of all the reported outcomes are expressed per 1,000 patient years (py), the corresponding values derived from the Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) trial, in the row "HHF" (hospitalization for heart failure) and below, clearly represent events per 100 py, possibly because this is the way they are reported in the original publication (2). Moreover, to my understanding, the reported IR of "HHF or CV death" from LEADER is further mistaken (6.0 per 1,000 py instead of 30.0 per 1,000 py). These mistakes have affected accordingly the next column of the table, where ΔIRs are also shown as 10ths of the correct values (since they represent events per 100 py).

Unfortunately, the aforementioned mistaken values have been transferred to Fig. 2*A* and *B*), where the base risk rate (*x* axis) of the majority of the outcomes of the LEADER trial (yellow dots) are erratically depicted on the extreme left side of the graphs. This misdistribution results in an erroneously elongated span of the base risk rate. If the correct IRs and ΔARs (Δ of absolute risks) from LEADER were put onto the correct positions, this would most probably affect (possibly strongly) the *r* and *P* values of the reported correlation between IR and ΔAR in Fig. 2*A* and, undoubtedly, would also modify the shape and position of fit lines, shaded areas, and arrows. According to my calculation, the Pearson correlation between IR and ΔAR for all the outcomes provided in Table 1 using the correct values from LEADER is $r = -0.429$ ($P = 0.002$), which is much lower than the reported value ($r = -0.72$, $P < 0.000001$).

In conclusion, although the authors correctly emphasize that absolute risk reduction and number needed to treat are crucial in interpreting the CVOT results, the supporting evidence provided in the text and depicted in Fig. 2 should be recalculated using the correct data from the LEADER trial.

I express my thanks for considering these remarks, which hopefully will contribute to further highlighting this important article.

Duality of Interest. During the last 3 years, S.L. has received honoraria for providing consultancy on advisory board meetings and speaking at symposia and has had travel/registration/accommodation support for conferences from Boehringer Ingelheim, Novo Nordisk Hellas, Sanofi Hellas, AstraZeneca, Novartis, and Pharmaserv Lilly. No other potential conflicts of interest relevant to this article were reported.

References

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Diabetes Center, First Department of Propaedeutic Medicine, National and Kapodistrian University of Athens, Athens, Greece

Corresponding author: Stavros Liatis, sliatis@med.uoa.gr