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LETTER TO THE EDITOR

# Teplizumab: Not all that glitters is gold

To the Editor,

We read with interest the work by O'Donnell et al.,[1] which provides valuable real-world insights into the experiences of individuals and caregivers using teplizumab for stage 2 type 1 diabetes. Their findings suggest a generally positive perception of teplizumab, particularly in delaying disease onset, that could feed into discussions with patients regarding decision-making on whether or not to take the therapy. However, as we consider the implications of widespread teplizumab use, especially in the context of emerging screening programmes like Italy's national initiative,[2,3] a balanced perspective is crucial.

We recognize that teplizumab represents a significant advance as the first disease-modifying therapy for type 1 diabetes.[4] Nevertheless, its practical implementation warrants careful consideration. As noted by O'Donnell et al., the efficacy of teplizumab appears most pronounced in individuals with diminished β-cell function, notably children and adolescents.[5] Nevertheless, the high cost of treatment and the need for robust screening programmes to identify eligible individuals present substantial barriers to widespread adoption. Specifically, the economic burden of teplizumab, approaching $200000 for a single course, mandates comprehensive cost-effectiveness analyses to justify its widespread use. Indeed, the COMPASS patient support programme reported in O'Donnell et al. assisted individuals in obtaining insurance authorization and also provided tools and educational resources related to teplizumab. As a result, the vast majority (>85%) of patients in the United States that have received teplizumab have been through COMPASS, raising the issue of the sustainability of teplizumab in the long term, especially if many more subjects become candidates. Indeed, the reimbursements for the drug costs described in O'Donnell study[1] do not apply to countries other than the United States and will be subject to different rules depending on the healthcare system. For this reason, at the moment, regardless of efficacy or perception, it is difficult to envisage widespread adoption without serious consideration of reimbursement issues.

Like any therapy, teplizumab also has safety concerns, including potential side effects such as cytokine release syndrome, transient lymphopenia, and hypersensitivity reactions. Of course, it is important to contextualize these risks. For instance, cytokine release syndrome has been reported in <6% of people and it is typically mild to moderate, resolving within a few days and requiring only non-prescription medication.[4,6] Similarly, the reported neutropaenia is often transient and does not necessarily translate to a significant increase in severe infections.[7] Anaphylaxis is rare (0.1%).[4] Nevertheless, careful monitoring is essential, particularly given the immunosuppressive effects that necessitate pre-treatment vaccination and caution with administering live-attenuated vaccines. Reassuringly, clinical trials have shown that infection rates do not significantly differ between individuals taking teplizumab and controls, alleviating some concerns regarding broad immunosuppression. It is also important to acknowledge that immunomodulatory therapies are commonly used in other autoimmune diseases with comparable side-effect profiles. This context helps to normalize the discussion around teplizumab's safety, emphasizing the need for informed risk–benefit assessments. This broader perspective is crucial to avoid an isolated and overly negative view of teplizumab's safety profile. Nevertheless, concerns about the safety of the drug in children and adolescents, especially in relation to growth and development, need to be confirmed in larger samples.[8]

In the context of compassionate use (i.e., the opportunity to use unlicensed drug whilst waiting for the approval by the relevant drug regulatory agency, subject to review and assessment of the individual patient), especially within European countries like Italy where teplizumab is only available for patients meeting specific criteria, it is essential to weigh these risks against the potential benefits. The desire to delay the onset of Stage 3 type 1 diabetes, as highlighted in O'Donnell et al.'s survey,[1] is a compelling motivation. This delay can provide crucial time for both physical and emotional development, potentially easing the transition to insulin therapy and allowing for advances in diabetes management technologies like automated insulin delivery (AID) systems. For example, delaying the need for intensive insulin therapy can allow children to develop greater cognitive maturity, improving their capacity to manage the complexities of type 1 diabetes.

While O'Donnell et al.'s study[1] was limited by a potential for bias due to the response rate and the demographic profile of the participants, it also offers valuable insights into patient perceptions. The observation that many respondents had a family history of type 1 diabetes suggests a heightened awareness of the disease burden within the cohort, which may have influenced their decision-making. This familial awareness can lead to a more informed and perhaps more motivated approach to early intervention that might not be present in other contexts or groups.

While the aim of screening programmes is to prevent diabetic ketoacidosis (DKA) and delay disease onset, we must also consider the psychological impact of prediabetes. The potential for increased

  

anxiety and disease burden from early medicalization is a valid concern. However, as O'Donnell et al.'s survey[1] suggests, teplizumab can provide a sense of control, even if it does not eliminate all worries.

In conclusion, teplizumab offers a promising avenue for delaying type 1 diabetes onset. Its emerging use must be approached with a balanced understanding of its benefits and risks. Clear and honest communication between healthcare providers and patients is essential to ensure informed decision-making. Future research should focus on long-term outcomes, cost-effectiveness,[9] and the psychological impact of teplizumab therapy.

## CONFLICT OF INTEREST

The authors have no conflicts of interest.

## PEER REVIEW

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## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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