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Peer Review

Review of: "The Multifaceted Nature of Pain in Sickle Cell Disease: From Molecular Mechanisms to Emerging Therapeutic Frontiers"

Pagona Flevari[1]

1. Thalassemia Unit, Haemoglobinopathies Expertise Center, Member of EuroBloodNet, Laiko General Hospital of Athens, Athens, Greece

The review article entitled “The Multifaceted Nature of Pain in Sickle Cell Disease: From Molecular Mechanisms to Emerging Therapeutic Frontiers” addresses an important clinical topic that concerns many health care providers and even more patients, since pain represents one of the most significant and common manifestations of SCD. It is acknowledged that SCD pain has a complex pathophysiology and heterogeneous presentation. This manuscript aims to connect molecular mechanisms with potential therapeutic approaches.

However, in its current form, the manuscript requires major revision. The English language needs substantial improvement, as several sentences are difficult to follow due to grammatical and syntactic issues. It is recommended that a native English speaker or a professional language editor provide a thorough revision.

The manuscript is also excessively long and includes too many details. Although it is a review article and the title refers to a broad and multifaceted approach, it is recommended that the text be more concise in order to facilitate overall readability. In particular, the sections discussing the physiology and pathophysiology of pain are overly analytical and not easy to read. These parts could be shortened to emphasise the most significant mechanisms directly related to pain in SCD.

Additionally, the discussion of agents already well presented in the literature but no longer available or withdrawn, such as crizanlizumab and voxelotor, should be more limited to a brief context.

In conclusion, the manuscript has great potential. However, major revisions are required before publication: extensive English language editing, substantial reduction in length, reduction of repetitive

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content, clearer organisation, and emphasis on the key messages regarding pain mechanisms and management may ensure a more reader-friendly presentation.

Declarations

Potential competing interests: No potential competing interests to declare.