Letter to Editor

A New Frontier of Hope: Highlighting the Promising Potential of Spliceosome Inhibitor E7107 in Treating SF3B1 Mutant Uveal Melanoma

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Dear Editor

This letter highlights the promising nature of spliceosome inhibitor E7107 in SF3B1 mutant uveal melanoma and warrants future research to establish its clinical application, safety, and efficacy for these patients.

Uveal melanoma originates from the melanocyte of the uvea and has a metastasis rate of about 25-34% within a span of ten years leading to poor prognosis and a death rate of 80% at 1 year following metastasis.[1] This shows the horrible nature of these melanomas and demand for an inevitable urge of definitive treatment options for these patients. However, unfortunately, the treatment options are very limited and poor. Various prognostic factors have been identified for uveal melanoma including mutations in genes encoding BRCA-1 associated protein (BAP1) being worst, splicing factor 3b subunit 1 (SF3B1) being intermediate, and eukaryotic translation initiating factor 1A X-linked (EIF1AX) being best prognostic factor.[2,3]A large percentage of about 15%-35% of uveal melanomas have SF3B1 mutations which make it an important prognostic feature however there is no well-established pharmacological agent targeting or utilizing this major prognostic mutation as a therapeutic fortune. A recently introduced protein Tebetafusp though showed prolonged survival in metastatic carcinoma but available only for metastatic uveal melanoma.[4]

Till date, no successful therapy has been launched specifically for SF3B1-mutated uveal melanoma.Thisshows the utter need for the development of a safe, efficient, and clinically practical therapy for thisnotorious type of uveal melanoma. Recently a pilot study published by Erasmus MC Medical CenterRotterdam, CA Rotterdam, The Netherlands, showed a hope for patients with SF3B1-mutated uveal melanomas uncovering the hidden therapeutic potential of spliceosomes inhibitors like E7107 in these tumors.[5]According to this study, SF3B1-mutated uveal melanomas are comparatively more sensitive to splicing inhibitor E7107 than wild SF3B1 uveal melanomas which is a beacon of therapeutic hope for the patient suffering from this notorious melanomas.[5]

Though this study has shown that SF3B1-mutated uveal are more sensitive and less viable to splicing inhibitor E7107, but the goal has not yet achieved because this study has only established an ex vivo and in vitro splicing inhibitory effect of the splicing inhibitor E7107. Despite the amazing therapeutic potential of this splicing inhibitor, certain hurdles are yet to be addressed. The study relies only on in vitro and ex vivo models, and so is a call for extensive in vivo trials for the validation to establish thorough efficacy and patient safety. Though E7107 is well tolerated, it is necessary for the patient safety that the toxicity of the spliceosome inhibitor E7107 should be thoroughly investigated as recently two phase 1 trials on pharmacologic investigation of E7107 have been terminated due to visual impairment of the 3 out of 66 patients, which alerts us about the E7107 being a therapeutic option for uveal melanoma in vivo.[6,7] Beyond this, exploring other spliceosome modulators like H3B-8800 may prove similar or even better results with no reported risk of adverse effects like visual impairments as recently phase 1 trials on H3B-8800 have provided safety profiles boosting confidence in wide class of splicing inhibitors.[8]

In short, this breakthrough aligns with the broader trends towards the goals of precision in oncology,

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however, translating these potential powers into clinical practice requires extensive and rigorous validation and innovative delivery strategies. After validation and solid establishment of safety and efficacy, the clinical translation of spliceosomes inhibitors including E7107 could redefine the therapeutic paradigm for this challenging tumor opening new frontiers of hope for the patients.

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