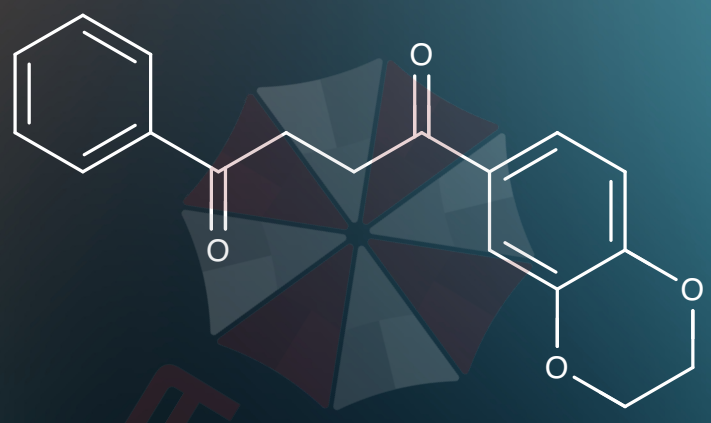


Dalosirvat (SM04554): : A WNT Pathway Modulator for the Treatment of Androgenetic Alopecia

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History

Dalosirvat (also known as SM04554) was first described in the scientific literature in 2017. It was originally discovered by Samumed which was later renamed to Biosplice Therapeutics. It entered clinical studies to treat androgenetic alopecia in the mid- 2010s. The relevant patent (WO2014130869) was published in 2014.

Dalosirvat and other WNT modulators are also been discussed in some publications as possible treatment for inflammatory skin diseases such as atopic dermatitis and psoriasis.[1,2]

Mechanism of Action

Dalosirvat is a modulator the WNT signalling pathway, which is an important cellular mechanism that plays crucial roles in embryonal development, but also in clinically relevant processes in adults, including cancer and diabetes. The activation of the WNT-signalling pathway seems to lead to an increases hair growth in hair follicle cells, which makes activators of this pathway to a potential remedies for hair loss.

Preclinical Trials

In mice, dalosirvat increased markers for WNT signalling and cell proliferation specifically in hair follicles, indicating localized follicular activation of Wnt signalling and proliferation, not generalized to the epidermis. In rodents and mini-pigs, dalosirvat increased follicle numbers and hair growth compared to vehicle.

Within 4-days treatment, dalosirvat increased total hair-follicle counts 2-fold compared to vehicle. In depilated mice, dalosirvat induced hair growth with 10 days of treatment. In other type of mouse, hair growth was observed after 3 weeks of treatment with dalosirvat compared to >5 weeks with vehicle.[3]

Clinical Trials

4 clinical trials have been completed so far that study the applicability of dalosirvat in the treatment of androgenetic alopecia. Only of these has results posted.[4]

A phase 2 trial with 49 participants used dalosirvat at concentrations of 0.15% and 0.25% (NCT02503137). Another phase 2 trial used the same concentrations in a topical solution and enrolled 310 participants. (NCT02275351)

The phase 3 study used the same concentrations as the previous phase 2 trials and enrolled 675 participants, it ended in December of 2020.

(NCT03742518)

A post from Samumed does however give some information about the results of the earlier clinical trials. No serious adverse events (SAEs) were reported.48 adverse events (AEs) were experienced by 29 subjects:14 in the 0.15% SM04554 group,16 in the 0.25% SM04554 group and 18 in the vehicle group. AEs considered related to study treatment were application site erythema, application site paraesthesia, application site pruritus, and skin exfoliation. No trends or imbalances were noted between all treatment and vehicle groups. Laboratory parameters and vital signs were unremarkable during the study. No clinically significant values or changes from baseline were reported in any of the subjects. The subjects that received the 0.25% concentration of dalosirvat had highest increase in hair follicle counts, both after 91 and 135 days. The results presented here were barely statistically significant and hence studies with a higher count of participants were needed.

Conclusion

There is limited information available about dalosirvat. From the clinical studies, it can be assumed it is safe for human use at concentrations of 0.15% and 0.25% in topical solutions. The effect seen in clinical trials is statistically significant, but relatively small. To better understand the effect strength of dalosirvat, the currently unavailable results of the phase III trials must be analysed.

References

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[3] Deshmukh V, Pedraza M, Barroga C, Seykora J, Yazici Y. 712 A small molecule modulator of the wnt pathway (SM04554) as a potential topical treatment for androgenetic alopecia (AGA). *Journal of Investigative Dermatology.* **2017**;137:S122. doi: 10.1016/j.jid.2017.02.735.

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