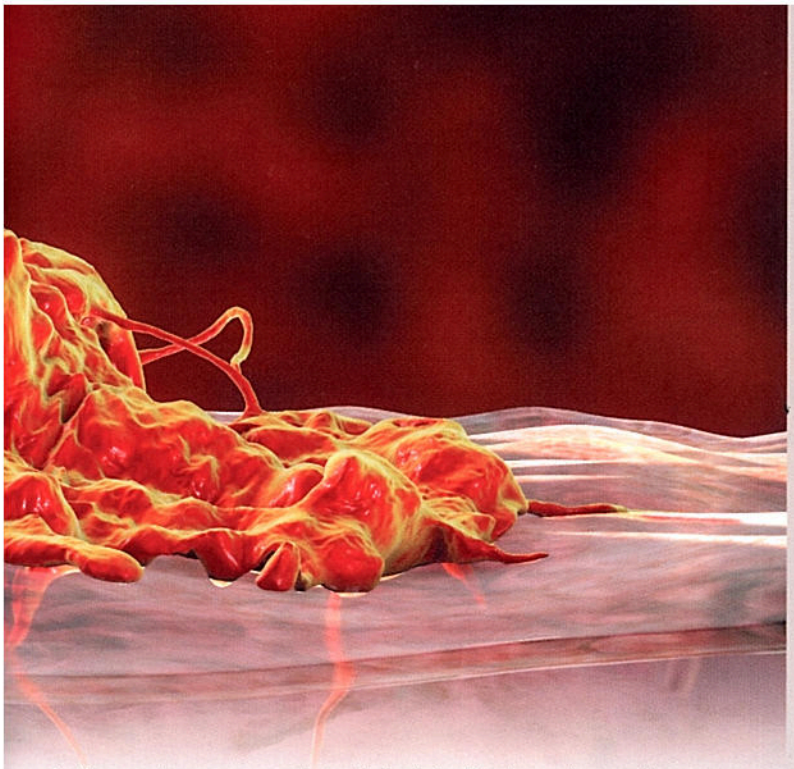

In the past year, several preclinical studies based upon the synergistic responses with combination regimens of BRAF/MEK inhibitors with immune checkpoint blockade got underway.[4]

What therapies are there beside MAPK pathway and immune checkpoint inhibitors in 2021? Intralesional oncolytic virotherapy, T-VEC, transfects tumor cells with a granulocyte macrophage colony-stimulating (GM-CSF) factor encoding plasmid, resulting in high local concentrations in the tumor microenvironment that has resulted in significantly improved durable response rates compared with systemically administered GM-CSF.[4] It has also been noted recently that the melanoma glycome is composed of complex carbohydrates, termed glycans, and it has been suggested that glycans may play a major role in influencing melanoma progression and could be used for prognostication of metastatic activity as well as therapeutic targets.[6]

Because epigenetic markers have been noted to be able to predict response to cancer immunotherapy, what is their role in melanoma immunotherapy? Histone methyltransferase EZH2 has been associated with treatment resistance to anti-CTLA4 or interleukin (IL)-2 therapy.[4] A potential for combining immunotherapy with epigenetic modulators to achieve better treatment efficacy is being explored and hopefully will be news in the top story of melanoma in 2022.

Genetic testing and personalized medicine are almost here! Although not yet FDA approved, a 31-gene two-class molecular test is available for cutaneous melanoma. Finally, the measurement of circulating tumor DNA is gaining in popularity for melanoma surveillance and to measure response to therapy.[5] My hope is that in future melanoma updates, this kind of testing will be part of melanoma management protocol improving patient care.

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Tofacitinib for Facial Hair Alopecia Areata

By Robert T. Brodell MD, FAAD

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There is growing belief that topical use of the JAK inhibitor tofacitinib can provide effective treatment for alopecia areata affecting facial hair

What makes an article of the year? I have chosen a small study that provides convincing evidence for a safe, novel drug that will have a solid impact on the field of dermatology.[1] The jury is still out on the use of systemic tofacitinib because of dose-related safety concerns. The use of topical tofacitinib on a small, easily visible surfaces such as patchy involvement of alopecia areata (AA) on the face and scalp, however, would logically be expected to be very safe. This is especially true when compared with current use of super-potent topical steroids. Considering the devastating psychological effects of hair loss in young people commonly affected by AA, the potential impact of this drug is great. This study adds to the growing body of evidence that topical tofacitinib is effective for some patients.[1-5]

In September 2021, the first topical JAK inhibitor, ruxolitinib, was approved for atopic dermatitis. This gives me confidence that topical tofacitinib will soon be approved. It is likely there will be a black box class warning emphasizing heart-related events, cancer, blood clots, and death, as is the case with all JAK inhibitors, including topical ruxolitinib.

I believe this is a highly promising therapy. As evidence for efficacy builds, I anticipate FDA approval and rapid uptake in the field of dermatology, although we should be careful not to overpromise – it is clear that this drug will not work for everyone.

There are two factors remaining: the anticipated high cost of the drug and the potential for hair loss when the topical agent is discontinued. Again, judging by the cost of developing new drugs and the high price of topical ruxolitinib, one could expect that tofacitinib will be expensive. With regard to recurrence, there are likely resident T cells in the areas of involvement that may well lead to recurrence at the previously affected sites when treatment is discontinued.

My choice for article of the year was also meant to send a message: even small studies, of the type that could be done by any dermatologist, can be impactful!

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