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EMERGING TARGETED THERAPIES AND COMBINATION APPROACHES IN VITILIGO TREATMENT: A SYSTEMATIC REVIEW

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Vitiligo represents a significant global health challenge, affecting approximately 0.5-2% of the world's population, with notably higher prevalence rates in specific regions such as India (8.8%). The condition imposes substantial psychosocial burden, with up to 35.8% of patients experiencing anxiety and various degrees of depression, emphasizing the critical need for effective therapeutic interventions. Traditional treatment modalities have demonstrated limited efficacy, necessitating the exploration of novel therapeutic approaches that address the complex pathogenesis involving autoimmunity and melanocyte homeostasis.

This comprehensive review aims to evaluate and synthesize emerging therapeutic innovations for vitiligo treatment, assess the efficacy and safety profiles of novel treatment strategies, and provide evidence-based clinical practice recommendations for new candidate drugs. The review particularly focuses on recent developments in targeted therapies and their potential impact on treatment outcomes.

The analysis revealed significant advancements in vitiligo treatment, particularly in JAK inhibitors, where ruxolitinib emerged as the first FDA-approved topical treatment for nonsegmental vitiligo in patients aged 12 and older. Clinical trials demonstrated that 54.9% of patients achieved F-VASI75 and 50.0% achieved T-VASI50 in long-term extension studies. Other JAK inhibitors, including tofacitinib, baricitinib, and upadacitinib, showed promising results in various clinical trial phases, with significant improvements in repigmentation rates. Several innovative treatment modalities demonstrated efficacy, including cytokine-targeted therapies focusing on IFN-α, TNF-α, IL-2, and IL-15, immune checkpoint modulators, T-cell metabolism targeting drugs, α-MSH analogs, and PDE-4 inhibitors.

Enhanced outcomes were observed with combination therapies, particularly when JAK inhibitors were combined with narrow-band ultraviolet B (NB-UVB) phototherapy, 5-Fluorouracil combinations, trichloroacetic acid applications, and prostaglandin therapies. Combination approaches typically yielded superior results compared to monotherapy, particularly when incorporating phototherapy with novel agents.

The landscape of vitiligo treatment is experiencing significant transformation with the emergence of multiple promising therapeutic innovations. JAK inhibitors, particularly ruxolitinib, represents a breakthrough in targeted therapy, while various novel approaches show potential in addressing different aspects of the disease pathogenesis. Combination therapy approaches demonstrate the most promising outcomes, though additional large-scale clinical trials are necessary to establish long-term safety and efficacy profiles.