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**НОВЫЕ ТАРГЕТНЫЕ ТЕРАПИИ И КОМБИНИРОВАННЫЕ ПОДХОДЫ В
ЛЕЧЕНИИ ВИТИЛИГО: СИСТЕМАТИЧЕСКИЙ ОБЗОР**

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

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Резюме. Витилиго представляет собой глобальную проблему со значительным психосоциальным воздействием и ограниченной эффективностью традиционных методов лечения. В данном обзоре рассматриваются новые терапевтические инновации, направленные на улучшение лечения витилиго с помощью целевых вмешательств. В нем рассматриваются данные клинических испытаний новых препаратов - в частности, ингибиторов JAK - и их влияние на результаты репигментации. В исследовании обобщены данные последних публикаций и испытаний, особое внимание уделяется комбинированным методам лечения, таким как NB-UVB с новыми препаратами. Выводы свидетельствуют о революционных достижениях, в частности о применении руксолитиниба, и в то же время подчеркивают необходимость проведения дальнейших крупномасштабных клинических испытаний.

Ключевые слова: витилиго, JAK-ингибиторы, репигментация, комбинированная терапия, терапевтические инновации.

Resume. Vitiligo presents a global challenge with significant psychosocial impact and limited efficacy of conventional treatments. This review evaluates emerging therapeutic innovations to improve vitiligo management through targeted interventions. It examines clinical trial data on novel agents—especially JAK inhibitors—and their effect on repigmentation outcomes. The study synthesizes evidence from recent literature and trials, emphasizing combination therapies such as NB-UVB with novel agents. Findings highlight transformative advances, notably with ruxolitinib, while underscoring the need for further large-scale clinical trials.

Keywords: vitiligo, JAK inhibitors, Repigmentation, Combination Therapy, Therapeutic Innovations.

Relevance. Vitiligo poses a significant global health challenge, affecting approximately 0.5–2% of the world's population—with prevalence rates as high as 8.8% in regions like India. The condition not only causes noticeable skin depigmentation but also exerts a substantial psychosocial burden, as up to 35.8% of patients experience anxiety and varying degrees of depression. Given that conventional treatments have limited efficacy, there is a critical need to explore and validate novel therapeutic approaches that both address the underlying pathogenesis and improve patient quality of life.

Aim: this comprehensive review is undertaken to evaluate and synthesize emerging therapeutic innovations for vitiligo. It aims to assess the efficacy and safety profiles of these

novel treatment strategies and to provide evidence-based clinical practice recommendations for new candidate drugs that target the disease's complex pathogenesis.

Objectives:

1. To review recent advances and innovations in the therapeutic landscape of vitiligo, with a focus on targeted approaches.
2. To examine clinical trial data—particularly for novel agents such as JAK inhibitors—and determine their impact on repigmentation and overall treatment outcomes.
3. To integrate findings from various studies to form a basis for evidence-based clinical recommendations.
4. To analyze the outcomes of incorporating combination therapies, such as NB-UVB phototherapy with novel agents, compared to monotherapy.

Material and methods. The study adopts a comprehensive review approach, synthesizing data from recent clinical trials and published literature related to vitiligo treatment innovations. Emphasis is placed on analyzing outcomes from targeted therapies, particularly JAK inhibitors, and their combination with modalities such as narrow-band ultraviolet B (NB-UVB) phototherapy. Data extraction focused on clinical efficacy indicators, including measures such as F-VASI75 and T-VASI50 scores, to provide a detailed understanding of treatment performance over time.

Results and their discussion. The analysis revealed significant advancements in vitiligo treatment, with JAK inhibitors taking center stage. Specifically, ruxolitinib emerged as the first FDA-approved topical treatment for nonsegmental vitiligo in patients aged 12 and older, with clinical trials demonstrating that 54.9% of patients achieved F-VASI75 and 50.0% achieved T-VASI50 in long-term extension studies. In addition, other JAK inhibitors, such as tofacitinib, baricitinib, and upadacitinib, showed promising results in various clinical trial phases by significantly improving repigmentation rates. The review also highlights several innovative treatment modalities—including cytokine-targeted therapies (targeting IFN- α , TNF- α , IL-2, and IL-15), immune checkpoint modulators, T-cell metabolism targeting drugs, α -MSH analogs, and PDE-4 inhibitors—which have demonstrated efficacy. Moreover, combination therapies, particularly those integrating JAK inhibitors with NB-UVB phototherapy, 5-Fluorouracil, trichloroacetic acid applications, and prostaglandin therapies, produced enhanced outcomes compared to monotherapy, reinforcing the potential benefits of a multimodal treatment approach.

Conclusion:

1. Vitiligo treatment is undergoing a transformative shift with multiple promising therapeutic innovations.
2. JAK inhibitors, particularly ruxolitinib as a breakthrough agent, are reshaping the targeted therapy landscape.
3. Novel approaches are emerging to address the multifaceted aspects of vitiligo pathogenesis.
4. Combination therapy strategies have shown superior outcomes compared to monotherapy.
5. Further large-scale clinical trials are essential to confirm the long-term safety and efficacy of these treatments, offering hope for more effective, evidence-based, and patient-centric management of vitiligo.

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