MORE OTHERARIO AF GIA



Future-Proofing Businesses

Innovative Solutions in Pediatric Rheumatology:

Bridging Treatment Gaps with Advanced Modalities

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Pediatric Rheumatology Therapies: Evolution of Treatment Approaches

	< 2010 > 2010 - 13	2014 - 17 > 2018 - 2021 > 2022-2025
Small Molecule	 Methotrexate Sulfasalazine Hydroxychloroquine Leflunomide Azathioprine Thalidomide (off-label) 	 Mycophenolate Mofetil Tofacitinib Apremilast Upadacitinib
Biologic Therapies	 etanercept Adalimumab Infliximab Rituximab 	 Tocilizumab Golimumab Golimumab Ustekinumab Ixekizumab Secukinumab Guselkumab
Advanced Biologics	Rilonacept	 Canakinumab Belimumab Belimumab Dupilumab Risankizumab
Antibody Drug Conjugates	mainstream, with Methotrexate and leading disease- modifying antirheumatic drugs (DMARDs) that have been the mainstay of treatment. The	• Dacetuzumab • Belantamab • Mirvetuximab (experimental) mafodotin soravtansine
Cell and Gene Therapies	2nd Wave : Introduction of biologics that specifically target inflammatory cytokines like TNF, IL-1, and IL-6, revolutionizing the management of juvenile idiopathic arthritis (JIA) and other pediatric rheumatologic conditions.	 Mesenchymal Stem Cells (early trials) CAR-T Cell Therapy (research phase) CAR-T Cell Therapy (research phase) CRISPR Therapies AAV Gene Therapy
Personalized Medicine	3 ^{re} Wave : The most recent developments, including IL-17 and IL-23 inhibitors and the emerging field of gene therapy, which hold promise for more targeted and potentially curative treatments.	 Biomarker-driven Treatments (pilot NGS-guided Therapy Precision Medicine

Optimizing Pediatric Rheumatology Therapies: Overcoming Treatment Challenges

	Off-target	Treatment	Disease	Long-term Safety	Limited Treatment	Immune
	Toxicity	Resistance	Heterogeneity	Concerns	Efficacy	Exhaustion
•	Methotrexate Cyclophosphamide Etanercept	 TNF Inhibitors (e.g., Adalimumab, Etanercept) Methotrexate 	 NSAIDs (e.g., Ibuprofen, Naproxen) Corticosteroides (e.g., Prednisone) 	 Steroids (e.g., Prednisone) Cyclophosphamide Azathioprine 	 JAK Inhibitors (e.g., Tofacitinib) DMARDs (e.g., Leflunomide) 	 Corticosteroids High-dose Biologics
	High Specificity	Combination	Personalized	Novel	Advanced	Immune
	Biologics:	Therapies:	Medicine:	Therapeutics:	Monitoring:	Modulation:
	Use targeted therapies like IL-6 inhibitors (e.g., Tocilizumab) to minimize off-target effects and adverse events in children.	Combine biologics with DMARDs (e.g., Methotrexate + Adalimumab) or new modalities like JAK inhibitors to overcome resistance.	Implement biomarker- driven diagnostics and targeted therapies (e.g., Anakinra for) to address diverse disease presentations.	Adopt therapies with better long-term safety, such as biologics (e.g., Anakinra, Tocilizumab) and JAK inhibitors (e.g., Baricitinib).	Use advanced imaging and telemedicine for real- time monitoring, enabling timely adjustments to improve efficacy.	Investigate therapies that modulate immune response without causing immune exhaustion, such as low-dose biologics along with adjunctive therapies

Therapies



Solutions

Challenges

Hype Cycle for Pediatric Rheumatology Treatment Options



Biomarker-Driven Personalized Medicine: Impact: Likely to advance significantly, enabling tailored treatments that improve outcomes and reduce side effects, with increasing clinical integration expected within the next 2-5 years.

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Biologic Therapies Targeting IL-17 and IL-23:

Impact: Anticipated to gain wider acceptance as ongoing trials solidify their efficacy and safety, potentially becoming mainstream treatments in the next 3-5 years.

Telemedicine and Remote Monitoring:

Impact: Expected to become a standard component of pediatric rheumatology care within the next 2 years, driven by the need for continuous, accessible patient management.

Continual R&D Efforts to Improve Efficacy and Safety in Pediatric Rheumatology



	Advancements	Examples
	• Subcutaneous Administration: Enhances patient compliance by reducing the frequency and invasiveness of treatments.	• Tocilizumab (IL-6 inhibitor): Effective in treating systemic juvenile idiopathic arthritis (sJIA) and polyarticular JIA.
Small	 Longer Half-life Biologics: Reduces dosing frequency, thereby improving convenience and adherence. 	• Secukinumab (IL-17 inhibitor): Emerging option for refractory cases of juvenile idiopathic arthritis.
Molecules	• Newer Cytokine Targets: Targeting specific cytokines such as IL-17, IL-23, and IL-1 for more precise treatment of inflammatory pathways.	Canakinumab (IL-1 inhibitor): Used for systemic JIA with good results in reducing inflammation.
Biologics	 Selective JAK Inhibitors: Target specific pathways (e.g., JAK1) to reduce side effects while maintaining efficacy. Combination with DMARDs: Enhances efficacy by targeting multiple pathways simultaneously. 	 Baricitinib: JAK1/2 inhibitor, currently being studied for JIA, showing promise in reducing disease activity. Upadacitinib: A selective JAK1 inhibitor, offering a new avenue for patients who do not respond well to TNF inhibitors.
Gene Therapy	 CRISPR-Based Approaches: Potential to correct genetic mutations causing autoimmune conditions. Gene Replacement Therapy: Aimed at replacing defective genes in monogenic autoimmune diseases. 	• Experimental Therapies: Still in early stages but showing promise for conditions like autoinflammatory syndromes.
Personalized Medicine	 Biomarker-Driven Therapy Selection: Utilizing specific biomarkers to predict response to treatment, leading to more tailored and effective therapies. Pharmacogenomics: Understanding the genetic factors that influence a patient's response to specific medications, allowing for dose adjustments and medication choice based on individual genetic. 	 Next-Generation Sequencing (NGS) for JIA: Helps in identifying specific genetic mutations and tailoring therapies accordingly. Personalized Dosing Protocols: Adjusting doses based on pharmacogenomic data to minimize side effects and maximize efficacy.

Advancing Pediatric Rheumatology Through Innovating Therapy Modalities and Targeting Multiple Pathways



Note: Small circles depicts the associated benefits with the respective treatment strategy

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