Aster HOSPITALS & CLINICS
We'll Treat You Well

HealthNews DIGEST

APRIL 2026

38th Edition

Dr. Sherbaz Bichu

CEO & Specialist Anaesthetist
Aster Hospitals & Clinics,
UAE, Oman, and Bahrain

On behalf of Aster's leadership, I am immensely delighted to address you in the 38th edition of HealthNews as we celebrate yet another significant milestone.

We're proud to be once again recognised in **Newsweek's World's Best Hospitals Rankings.** In the 2026 list, we're in the **top 10,** with Aster Hospital, Mankhool, maintaining its strong 4th position, and Aster Hospital, Al Qusais, making an impressive jump from 16th to 10th. These achievements reflect our ongoing dedication, clinical expertise, and the trust our patients place in us every day.

These recognitions reaffirm our position among the world's leading hospitals, driven by a culture of excellence, innovation, and patient-centred care. They reflect the collective efforts of our clinicians, nursing teams, and support staff, whose dedication continues to set benchmarks in the healthcare ecosystem.

As we celebrate these accomplishments, let's stay committed to innovation, teamwork, and upholding the highest standards of care for the communities we serve.

Dr. Ramanathan V

Medical Director
Aster Hospitals & Clinics,
UAE

As the Group Medical Director of Aster Hospitals and Clinics, I am pleased to address you in the 38th edition of HealthNews, celebrating yet another year of consistent excellence and clinical achievement across our hospitals with our continued recognition in **Newsweek's World's Best Hospitals Rankings.**

I am also delighted to highlight the expansion of our neurological services, led by **Dr. Jaffer Vali Sayyed, Neurology (Specialist),** whose specialised expertise in the use of Botox in Therapeutic Neurological Applications beyond aesthetics is enhancing our capabilities in advanced neurosciences. With this, we're redefining the scope and depth of care we deliver to our patients in our Neurosciences Department, ensuring comprehensive, precise, and innovative care.

Together, let's continue elevating standards and shaping the future of healthcare.

Methotrexate Overdose and Toxicity identified and treated effectively at Aster Cedars Hospital and Clinic, Jebel Ali, Dubai

Dr. Rakesh Kumar Mishra
Dermatology (Specialist)

PRESENTATION

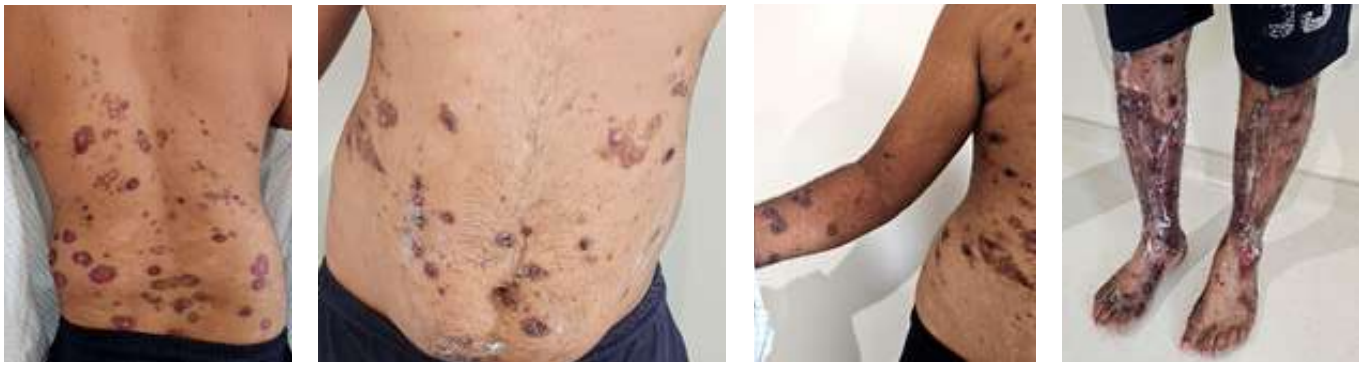
- 30-year-old male with no known comorbidities
- Presented to the hospital emergency with:
  - Multiple ulcerative, painful, non-healing ulcers on the body, along with a few lip/oral cavity ulcers for one week
  - Difficulty in swallowing food and generalised malaise
  - Fever, tiredness and severe body pain

FINDINGS

During examination:

- Febrile with pale appearance
- Conscious and oriented
- Dehydrated
- Multiple polysized, tender, dull red ulcers with bizarre margins and a few with necrotic slough at the base, on the front and back of the trunk and hands and legs
- Large confluent ulcers below the knee on both legs
- Skin tenderness

Upon further discussion, it was identified that the patient had been consuming a few medications along with **Methotrexate 5 mg tablets twice a day for more than a week.**



Pre-treatment images

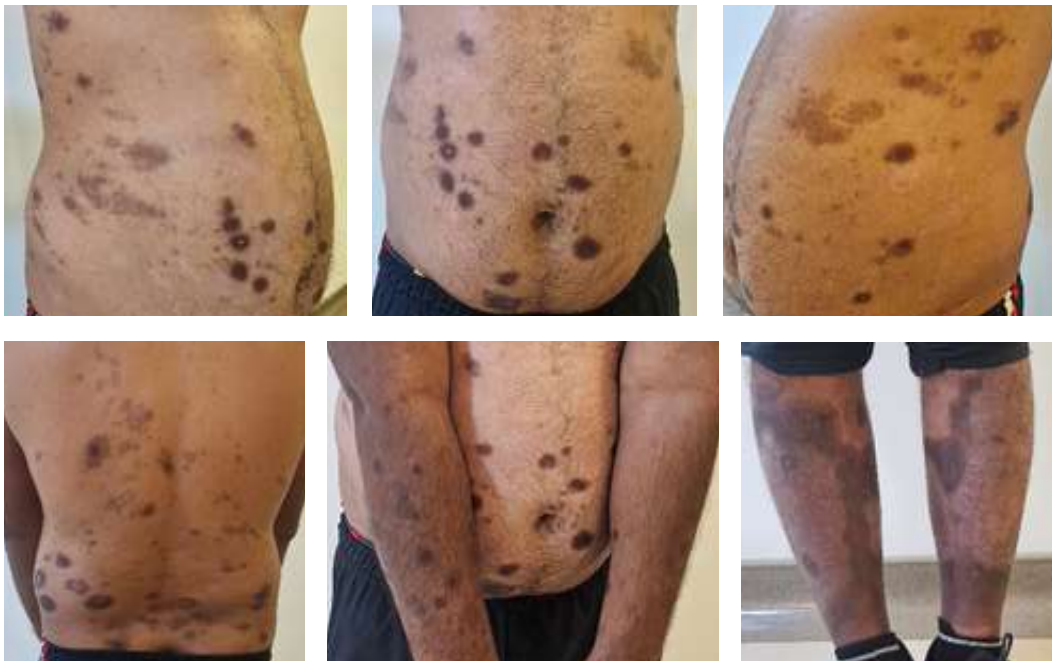
MANAGEMENT

The patient was admitted as a suspected case of an adverse drug reaction (ADR). Blood investigations revealed increased SGOT/PT indicating liver damage, and severe leukopenia (1.3/µL), anaemia and thrombocytopenia (87000). The blood picture was suggestive of drug-induced myelosuppression, with all three lines suppressed. This was a classic case of Methotrexate induced myelosuppression. The patient was admitted and kept under observation with ICU standby for any emergency support. He was started on IV Steroid bolus, IV fluids, antibiotics and other supportive topical dressings to cover the ulcers. The possible requirement for Folinic acid was discussed and kept ready.

The patient was managed with IV Solu-Medrol and other supportive medical care.

Over the following days, with supportive care, the patient responded well, and the ulcers began to heal. Serial blood counts began to improve, and the patient felt better. Interestingly, blood counts improved with "overexpression" or compensatory hyperplasia of marrow, leading to increased counts, with platelet counts reaching up to 9 lacs. However, the patient did not present with any fresh problem. Eventually, in the next few weeks, the counts stabilised to within normal limits.

Blood Investigations	Day 1	Day 2	Day 3	1 Week	1 Month
WBC (4 - 10)	**1.38**/µL	**1.63**/µL	**2.70**/µL	19.82/µL	8.38/µL
RBC (4.5 - 5.5)	**3.83**/µL	**3.73**/µL	**3.78**/µL	4.54/µL	4.36/µL
Haemoglobin (13.6 - 17.7)	**11.0** g/dl	**10.7** g/dl	**10.8** g/dl	13.1 g/dl	12.8 g/dl
Haematocrit (40 - 50)	**31.0**%	**30.4**%	**31.1**%	38.7%	37.8 %
Platelets (150 - 410)	**87**/cu.mm	**101**/cu.mm	**129**/cu.mm	899/cu.mm	204/cu.mm



Post-treatment images at 2 weeks

DISCUSSION

Methotrexate is the most commonly used cytotoxic drug for widespread, recalcitrant psoriasis, with doses ranging from 7.5 mg to 30 mg per week [1]. It inhibits mitosis of the cells by inhibiting dihydrofolate (DHF) reductase, an enzyme responsible for the conversion of dihydrofolate (DHF) to tetrahydrofolate (THF), leading to a reduction in thymidylate and purine biosynthesis. It is polyglutamylated to its active form inside the cell and thereby remains in the cell for a long time when taken daily or in divided doses. The cells that effectively polyglutamate Methotrexate include leukemic myeloblasts, synovial macrophages, lymphoblasts and dividing epithelial cells [1].

In psoriasis, it acts by inhibiting the DNA synthesis of T lymphocytes and epidermal keratinocytes [2]. Higher doses can often have toxic effects on various systems, causing reduced blood counts, deranged liver function (increased enzyme levels), and skin and mucosal necrosis. The mechanism of acute toxicity from Methotrexate is the inhibition of DNA synthesis in rapidly proliferating cells, i.e., the gastrointestinal (GI) tract, haematopoietic cells, and cells in psoriatic lesions. Hence, acute methotrexate toxicity causes decreased blood counts, nausea, vomiting, black stool, skin and mucosal erosion and ulceration [3]. It takes six to ten weeks for the post-inflammatory hyperpigmentation to disappear completely.

Methotrexate is a cheap and highly effective systemic drug prescribed for psoriasis. Methotrexate toxicity is rare with low dose, correct scheduling of the dose and adherence to the recommended guidelines [4]. Acute methotrexate toxicity manifests itself in several forms, including hepatotoxicity, pulmonary toxicity, acute renal failure, stomatitis, ulceration/erosion of the GI and pancytopenia [5].

CONCLUSION

Treatment of methotrexate toxicity is usually by folinic acid rescue therapy. Ideally, the dose of folinic acid is determined by the level of serum methotrexate and the duration of overdosing [6]. However, the facility for measuring serum methotrexate levels is not available in resource-poor settings. Ideally, all patients are treated with intravenous folinic acid (leucovorin) 20 mg 6 hours on day 1, followed by 10 mg 6 hourly till blood counts return to normal. However, in this case, the total dose of Methotrexate consumed by the patient was not very clear, and the patient was observed with serial blood monitoring, which showed improvement with conservative management, and the skin ulcers started healing with re-epithelialisation. This case also concludes that the swift stoppage of offending drugs and conservative management can reverse the myelosuppression.

REFERENCES

1. Roenigk HH Jr, Auerbach R, Maibach HI, Weinstein GD. Methotrexate in psoriasis: revised guidelines. J Am Acad Dermatol. 1988 Jul;19(1 Pt 1):145-56. doi: 10.1016/s0190-9622(88)80237-8.
2. Czarnecka-Operacz M, Sadowska-Przytocka A. The possibilities and principles of methotrexate treatment of psoriasis - the updated knowledge. Postepy Dermatol Alergol. 2014 Dec;31(6):392-400. doi: 10.5114/pdia.2014.47121.
3. Agarwal KK, Nath AK, Thappa DM. Methotrexate toxicity presenting as ulceration of psoriatic plaques: a report of two cases. Indian J Dermatol Venereol Leprol. 2008 Sep-Oct;74(5):481-4. doi: 10.4103/0378-6323.44305.
4. Morgan SL, Baggott JE, Vaughn WH, Austin JS, et al. Supplementation with folic acid during methotrexate therapy for rheumatoid arthritis. A double-blind, placebo-controlled trial. Ann Intern Med. 1994 Dec 1;121(11):833-41. doi: 10.7326/0003-4819-121-11-199412010-00002.
5. Olsen EA. The pharmacology of methotrexate. J Am Acad Dermatol. 1991 Aug;25(2 Pt 1):306-18. doi: 10.1016/0190-9622(91)70199-c.
6. Madke B, Singh AL. Acute Methotrexate Toxicity. Indian Journal of Drugs in Dermatology. 1(1):p 46-49, Jul–Dec 2015. doi: 10.4103/WKMP-0110.170764.

Key Vaccines for Respiratory Infections

Dr. Raiza Hameed KH
Pulmonology (Specialist)
Aster Clinic, Bur Dubai, Dubai

INTRODUCTION

Respiratory infections remain a primary cause of morbidity and mortality in patients with chronic respiratory diseases (CRD) (1). This burden has persisted despite substantial advances in antimicrobial therapy, vaccination programs, and supportive care over recent decades. Recent global estimates indicate that CRD affected more than 540 million individuals worldwide in 2021 and was responsible for over 3.5 million deaths (2). These figures demonstrate that historical improvements in treatment have not yet translated into a proportional reduction in infection-related complications (1,2).

Specifically, chronic obstructive pulmonary disease (COPD) remains among the leading causes of respiratory-related mortality globally. In these patients, recurrent infection-driven exacerbations continue to accelerate lung function decline, worsen long-term prognosis, and drive substantial healthcare utilisation (3). Respiratory viral pathogens, including influenza, respiratory syncytial virus (RSV), and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), are recognised as the major precipitants of these exacerbations. In vulnerable respiratory populations, these agents are directly associated with increased risks of hospital admission, ventilatory support, and death (3).

The coronavirus disease 2019 (COVID-19) pandemic further underscored the systemic and long-term consequences of viral insults. Accumulating evidence reveals persistent inflammation and prolonged post-acute sequelae following SARS-CoV-2 infection, particularly in individuals with underlying lung disease (4). In response to the recognised severity and systemic impact of these infections, contemporary respiratory guidelines, including the SEPAR (Spanish Society of Pulmonology and Thoracic Surgery) recommendations and international expert consensus, have increasingly positioned vaccination as an essential component of chronic disease management, aimed not only at preventing infections but also reducing exacerbations, disease progression, and long-term complications (5,6).

Vaccination is therefore positioned as a cornerstone preventive strategy in chronic respiratory disease, supported by evidence linking immunisation against major respiratory pathogens to reductions in severe infections, exacerbations, hospitalisation, and mortality, while acknowledging persistent gaps between clinical trial populations and real-world respiratory cohorts (3). Accordingly, integration of vaccination into longitudinal respiratory disease management pathways is increasingly emphasised in contemporary respiratory recommendations (3).

This article reviews key advances in respiratory vaccination, focusing on differences across vaccine platforms, risk-stratified strategies for respiratory phenotypes, and practical considerations for timing, sequencing, and safety in high-risk patients.

CONTEMPORARY VACCINE PLATFORMS AND THEIR CLINICAL IMPLICATIONS IN RESPIRATORY CARE

Vaccines utilised in respiratory practice differ substantially by platform, immune mechanism, and clinical performance, with important implications for the durability of protection and patient outcomes, particularly in high-risk respiratory populations (7). Recognising these platform-specific differences is essential for aligning vaccine selection with disease phenotype, immune competence, and long-term preventive goals in CRD management (7).

Current influenza vaccines include inactivated, recombinant, and live-attenuated formulations (8). Vaccine effectiveness (VE) varies across seasons and populations due to antigenic mismatch, viral evolution, and host-related factors such as age and immune status (8). To address waning immunity in vulnerable groups, enhanced influenza vaccine platforms, such as high-dose vaccines containing increased antigen content, have been developed (7,8).

In addition to injectable options for influenza prevention, the live attenuated influenza vaccine (LAIV), administered via nasal spray, providing a needle-free alternative for seasonal flu prevention, is available (9). This formulation is approved for individuals between 2 and 49 years old and offers efficacy comparable to injectable vaccines (9). However, the nasal spray is not recommended for use during pregnancy (9).

Similarly, pneumococcal vaccination strategies involve distinct vaccine platforms that differ in immune response characteristics and clinical application across respiratory risk groups (7,8). These platform-specific differences directly influence booster requirements, long-term effectiveness, and optimal vaccine sequencing strategies in respiratory clinical practice (7).

Figure 1 provides an illustrative example comparing major respiratory vaccine platforms and summarises key immunological and clinical distinctions relevant to respiratory practice.

Platform-Specific Characteristics of Vaccines in Respiratory Care (7,10,11)

Comparing immune strength and protection across influenza vaccines

Characteristics	Standard Influenza Vaccine	High-Dose / Adjuvanted Influenza Vaccine
Primary immune mechanisms	Antigen-based antibody response	Higher antigen content or immune-enhanced activation
Immunogenicity profiles	Moderate	Higher and more sustained antibody responses
Durability of protection	Seasonal protection requires annual vaccination	Improved durability compared with the standard dose
Booster considerations	Annual revaccination recommended	Annual revaccination recommended
Clinical relevance in respiratory care	Baseline protection against seasonal influenza in CLD	Enhanced protection in older adults and CLD

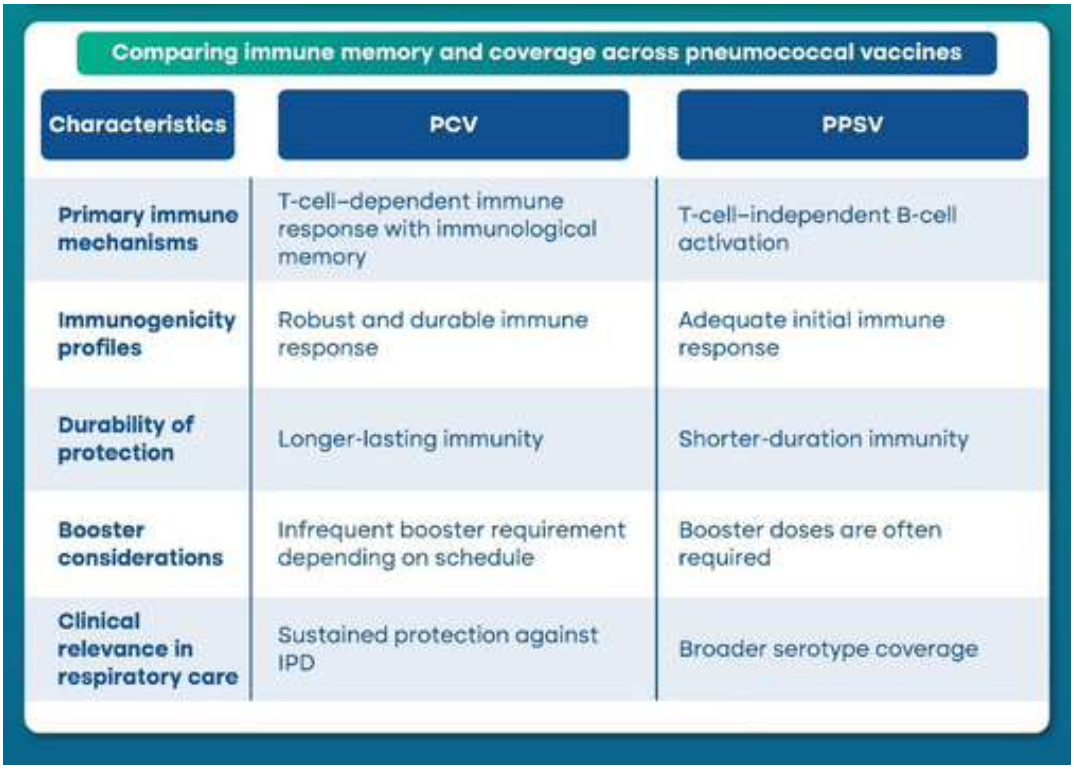


Figure 1. Comparison of key vaccine platforms used in adult respiratory practice (7,10,11)

(Abbreviations: PCV- Pneumococcal conjugate vaccine; PPSV- Pneumococcal polysaccharide vaccine; CLD – chronic lung disease; IPD – invasive pneumococcal disease; T-cell – thymus-derived lymphocyte; B-cell – bone marrow-derived lymphocyte)

Across various respiratory populations, vaccination against major pathogens has been consistently associated with reductions in severe respiratory infections, acute exacerbations of chronic lung disease, hospitalisation, and mortality (7). In patients with COPD, specifically, influenza and pneumococcal vaccination are linked to lower rates of exacerbation-related hospital admissions and improved survival outcomes (7).

Despite these benefits, important gaps remain between clinical research and real-world respiratory practice (7). Several pivotal vaccine trials that inform adult respiratory vaccination strategies, including the high-dose versus standard-dose influenza vaccine efficacy trial in older adults and large pneumococcal conjugate vaccine trials evaluating protection against invasive pneumococcal disease, have under-represented patients with severe airflow limitation, advanced multimorbidity, or markedly impaired pulmonary reserve (7). As a result, trial populations often differ substantially from routine respiratory cohorts, creating uncertainty when extrapolating vaccine efficacy, durability of protection, and booster requirements to patients with advanced chronic lung disease and frequent exacerbations (7).

RISK-STRATIFIED VACCINATION IN RESPIRATORY PATIENT POPULATIONS

Vaccination strategies in respiratory medicine should extend beyond broad disease categories to phenotype-specific risk stratification (3). This transition enables the direct translation of vaccine science into patient-level clinical decision-making within specialist respiratory practice (11).

Among these high-risk phenotypes, patients with COPD who experience frequent exacerbations face a significantly higher risk of infection-related hospitalisation and mortality (11). This underscores the value of intensified preventive vaccination in high-risk respiratory phenotypes (11). This clinical reality underscores the vital need for intensified preventive vaccination in high-risk respiratory phenotypes(11). Similarly, individuals with eosinophilic asthma receiving biologic therapies represent a distinct immunological subgroup (7). In these patients, the inhibition of cytokines involved in B-cell differentiation and plasma cell maintenance may negatively affect vaccine-induced humoral immunity (11).

The use of long-term immunomodulatory therapies, including anti–IL-5 (interleukin-5) and anti–IL-4 (interleukin-4) receptor biologics, systemic corticosteroids, and post-transplant immunosuppression, is closely associated with reduced vaccine-specific antibody responses and impaired immunogenicity (12). Clinical evidence indicates that patients receiving biologic therapies demonstrate significantly lower antibody levels following SARS-CoV-2 vaccination compared with healthy adults (12). These differences have been shown to persist over time, making it essential to maximise protection by aligning vaccine platform potency, administration timing, and dosing intensity with the specific respiratory phenotype and immune status of the patient (12).

To support clinical decision-making on vaccine selection and timing across respiratory risk phenotypes, a practical clinical action matrix is presented in **Figure 2.**

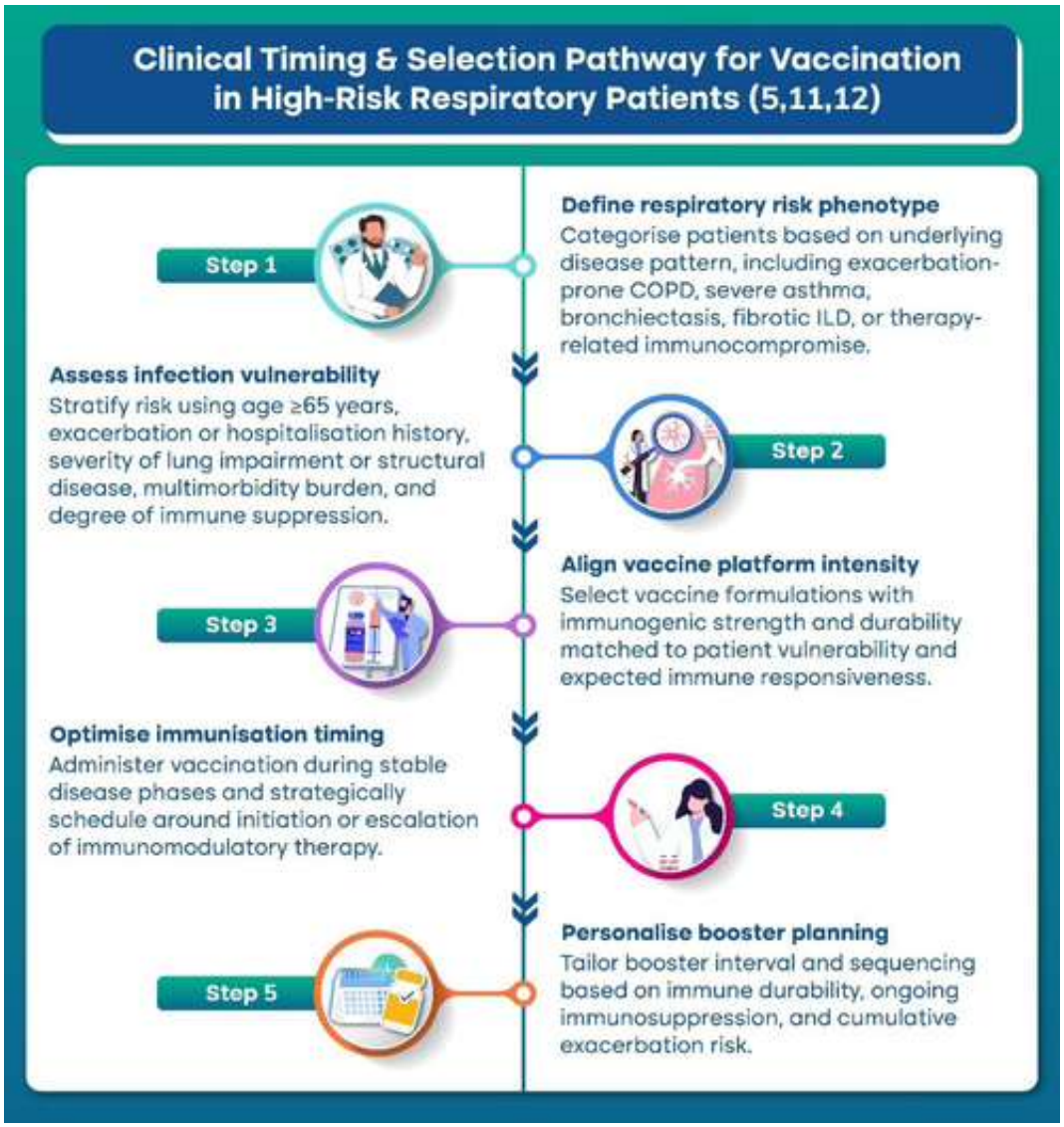


Figure 2. Simple vaccine decision pathway for high-risk respiratory patients (5,11,12)

(Abbreviations: COPD- chronic obstructive pulmonary disease; ILD- interstitial lung disease)

TIMING, SEQUENCING, AND INTEGRATION INTO RESPIRATORY PRACTICE

To maximise efficacy, vaccination for chronic respiratory diseases should be scheduled during periods of clinical stability (5). Immunisation during acute exacerbations or uncontrolled illness may reduce both patient tolerability and the overall immune response (3). Furthermore, because systemic corticosteroids, biologics,

and post-transplant immunosuppressive therapies are associated with reduced vaccine immunogenicity, clinicians should prioritise vaccination before treatment initiation or during windows of lower immunosuppressive burden (5). Evidence consistently shows that immune responses are attenuated in immunocompromised populations, which reinforces the need for optimised timing and strategic booster administration in high-risk cohorts (12).

Vaccine sequencing must adhere to established adult immunisation principles to prevent interference and ensure long-term protection (13). This includes maintaining minimum dose intervals, following appropriate conjugate–poly–saccharide pneumococcal sequencing, and avoiding the unnecessary restarting of vaccine series (13) While sequencing is vital, the co-administration of indicated vaccines is considered acceptable and often necessary to improve uptake within busy clinical schedules (14). In such cases, vaccines should be administered at separate anatomical sites to monitor for local reactions effectively (8).

To support clinical interpretation, **Figure 3** summarises the integration of timing, sequencing, and safety principles within specialist practice.

Figure 3. Respiratory vaccine timing and selection based on the CDC adult immunisation schedule and SEPAR recommendations (3,8,13,14)

(Abbreviations: COPD- chronic obstructive pulmonary disease; ILD- interstitial lung disease; PCV20- 20-valent pneumococcal conjugate vaccine; PCV15- 15-valent pneumococcal conjugate vaccine; PPSV23- 23-valent pneumococcal polysaccharide vaccine; RSV- respiratory syncytial virus; COVID-19- coronavirus disease 2019)

Vaccination is generally well tolerated, even in patients with severely impaired pulmonary reserve (7). In cases of severe chronic respiratory disease, the protective benefits of preventing infection-related lung injury significantly outweigh the risks of potential side effects (7).

Despite the clear benefits, significant gaps in evidence remain (5). Uncertainty persists regarding the optimal intervals for multi-dose regimens, the complex immune interactions between concurrent vaccines, and the long-term durability of protection in multimorbid respiratory cohorts (5). Furthermore, current vaccination strategies are often influenced by variability in guideline recommendations and differing levels of implementation across healthcare centres (3).

Because of this variability, respiratory specialists play a central role in the longitudinal care pathway (15). They are responsible for interpreting evolving evidence, optimising individual vaccine schedules, and providing tailored counselling to high-risk patients to ensure maximum protection within their specialist care (15).

EMERGING EVIDENCE AND FUTURE DIRECTIONS IN RESPIRATORY VACCINATION

The landscape of respiratory immunology is evolving rapidly, with expanding clinical evidence reinforcing the effectiveness of RSV, influenza, pneumococcal, and COVID-19 vaccines in high-risk respiratory cohorts (16). Recent data specifically highlight the profound impact of these interventions on older adults and individuals with chronic lung disease or immunocompromise (16). A landmark achievement in this field includes the recent approval of RSV vaccines for older adults and maternal immunisation strategies, which represent a significant stride in preventing RSV-associated morbidity across the most vulnerable age groups (16).

Innovation is moving toward next-generation vaccine platforms, such as nanoparticle-based constructs, to provide broader and more durable protection (7). These platforms have demonstrated enhanced immunogenicity, characterised by increased neutralising antibody titers and more robust memory T-cell responses, which effectively reduce lung viral loads compared to conventional formulation (17).

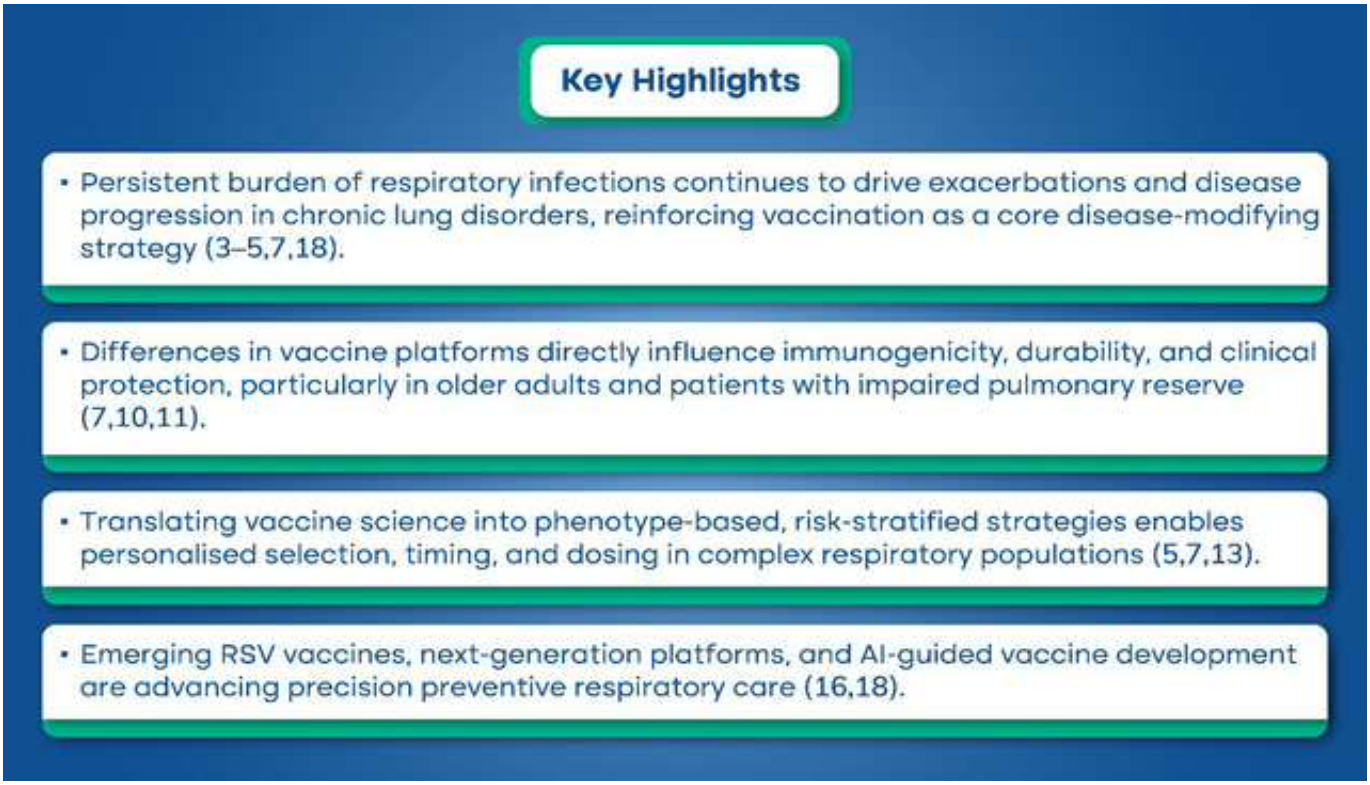
Complementing these structural advances is the integration of artificial intelligence (AI) (17). AI is now instrumental in:

- **Antigen Discovery:** Identifying novel targets with high precision.
- **Epitope Optimisation:** Refinement of vaccine components for maximum immune recognition.
- **Predictive Modelling:** Assessing immune durability and adaptive vaccine updates across heterogeneous patient populations (17).

Emerging data further suggest that expanded vaccination against respiratory viruses may reduce viral-triggered exacerbations and long-term disease burden in chronic obstructive pulmonary disease by limiting inflammatory disease activation (7).

Beyond preventing acute infection, vaccination is increasingly recognised for its role in modifying the course of chronic respiratory diseases (18). Emerging data suggest that comprehensive vaccination against respiratory viruses can reduce viral-triggered exacerbations, a primary driver of disease progression in COPD (18). By limiting inflammatory disease activation, these vaccines play a potential role in reducing long-term lung function decline and the burden of recurrent exacerbations, ultimately improving the quality of life and mortality rates for patients with chronic lung conditions (18).

Despite this scientific progress, real-world vaccine uptake remains a persistent challenge. Coverage for pneumococcal and RSV vaccines is often suboptimal due to barriers such as safety concerns, access limitations, and inconsistent healthcare provider recommendations (18). These findings emphasise that technical innovation alone is insufficient; there is a critical need for strengthened specialist engagement, improved guideline implementation, and data-driven policy refinement to optimise future strategies (18).



REFERENCES

1. Micheletto C, Aliberti S, Andreoni M, Blasi F, Di Marco F, Di Matteo R, et al. Vaccination Strategies in Respiratory Diseases: Recommendation from AIPO-ITS/ETS, SIMIT, SIP/IRS, and SItI. Respiration. 2025 Mar 9;104(8):556–74.
2. Zhai Y, Zhu C, Zhu T, Song W, Tang Y, Jiang L, et al. Global, regional, and national burden of chronic respiratory diseases,1990–2021 and predictions to 2035: analysis of data from the global burden of disease study 2021. Annals of Medicine. 2025 Dec 31;57(1):2530225.
3. Micheletto C, Aliberti S, Andreoni M, Blasi F, Di Marco F, Di Matteo R, et al. Vaccination Strategies in Respiratory Diseases: Recommendation from AIPO-ITS/ETS, SIMIT, SIP/IRS, and SItI. Respiration. 2025 Aug;104(8):556–74.
4. Mazzanti S, Barchiesi F, Pallotta F, Luchetti I, Giacometti A, Brescini L. Severe Acute SARS-CoV-2 Infection and Long COVID: What Do We Know So Far? New Challenges in Diagnosis and Management. Diseases. 2025 Oct 13;13(10):337.
5. Maggi S, Launay O, Dawson R. Respiratory Virus Vaccines: Pathways to Recommendations and Enhanced Coverage for At-Risk Populations. Infect Dis Ther. 2025 Jan;14(Suppl 1):99–114.
6. de Miguel-Díez J, Torres-Castro R, Sanz Herrero F, Menéndez Villanueva R, Solís Gómez B, Quirós Fernández S, et al. SEPAR Recommendations on Vaccination for Chronic Respiratory Patients. Archivos de Bronconeumología. 2025 Jun;S0300289625002182.
7. Kwok WC, Wong JNC, Cheung A, Tam TCC. Vaccination in Chronic Obstructive Pulmonary Disease. Vaccines (Basel). 2025 Feb 22;13(3):218.
8. Wei CJ, Crank MC, Shiver J, Graham BS, Mascola JR, Nabel GJ. Next-generation influenza vaccines: opportunities and challenges. Nat Rev Drug Discov. 2020;19(4):239–52.
9. CDC. Influenza (Flu). 2025 [cited 2026 Feb 17]. Live Attenuated Influenza Vaccine [LAIV] (The Nasal Spray Flu Vaccine). Available from: https://www.cdc.gov/flu/vaccine-types/nasalspray.html
10. DiazGranados CA, Dunning AJ, Kimmel M, Kirby D, Treanor J, Collins A, et al. Efficacy of High-Dose versus Standard-Dose Influenza Vaccine in Older Adults. New England Journal of Medicine. 2014 Aug 14;371(7):635–45.
11. Mao J, Li Y, Lv D. Impact of influenza on chronic obstructive pulmonary disease: pathophysiology, exacerbations, and preventive approaches. Ther Adv Respir Dis. 2025 Sep 9;19:17534666251363308.
12. Runnstrom MC, Morrison-Porter A, Ravindran M, Quehl H, Ramonell RP, Woodruff M, et al. Reduced COVID-19 Vaccine Response in Patients Treated with Biologic Therapies for Asthma. Am J Respir Crit Care Med. 205(10):1243–5.
13. CDC. Vaccines & Immunizations. 2025 [cited 2026 Jan 27]. Adult Immunization Schedule. Available from: https://www.cdc.gov/vaccines/hcp/imz-schedules/adult.html
14. de Miguel-Díez J, Torres-Castro R, Sanz Herrero F, Menéndez Villanueva R, Solís Gómez B, Quirós Fernández S, et al. SEPAR Recommendations on Vaccination for Chronic Respiratory Patients. Arch Bronconeumol [Internet]. [cited 2025 Dec 22]; Available from: http://www.archbronconeumol.org/en-separ-recommendations-on-vaccination-for-articulo-S0300289625002182
15. Rickards T, Kitts E. The roles, they are a changing: Respiratory Therapists as part of the multidisciplinary, community, primary health care team. Can J Respir Ther. 2018;54(4):10.29390/cjrt-2018–24.
16. Jiang J, Hu H, Cao L, Mao N, Zhu Z, Wang N, et al. Comparative Evaluation of Three Nanoparticle Vaccines Targeting the Prefusion F Protein of Respiratory Syncytial Virus: Immunogenicity and Protective Efficacy. Int J Nanomedicine. 2025 Aug 15;20:9945–61.
17. Bhandar S. The Role of AI in Accelerating Vaccine Development. International Journal of Scientific Research. 2022;8(6).
18. https://www.nfid.org/ [Internet]. [cited 2025 Dec 22]. 2025 NFID National Survey on Respiratory Diseases. Available from: https://www.nfid.org/resource/2025-national-survey-on-respiratory-diseases/

Dr. Masoodh Basha
Orthopaedics (Specialist)

Dr. Yuvaraj Karthick Rajaji
General and Laparoscopic Surgery (Specialist)

An Extremely Rare Diagnosis for Hip Pain diagnosed and treated successfully at Aster Hospital, Muhaisnah, Dubai

PRESENTATION

- 42-year-old male
- History of falling from stairs
- Presented to ER with complaints of:
  - Severe back pain and left hip pain
  - Unable to sit/lie down

FINDINGS

During examination:

- Afebrile
- Conscious and oriented
- Tenderness in the lumbar spine and left gluteal region
- Painful movements

An X-ray was done to rule out fractures of the spine and hip. It was normal, with no obvious fractures. Hence, he was given oral pain medications, and the patient went back home.

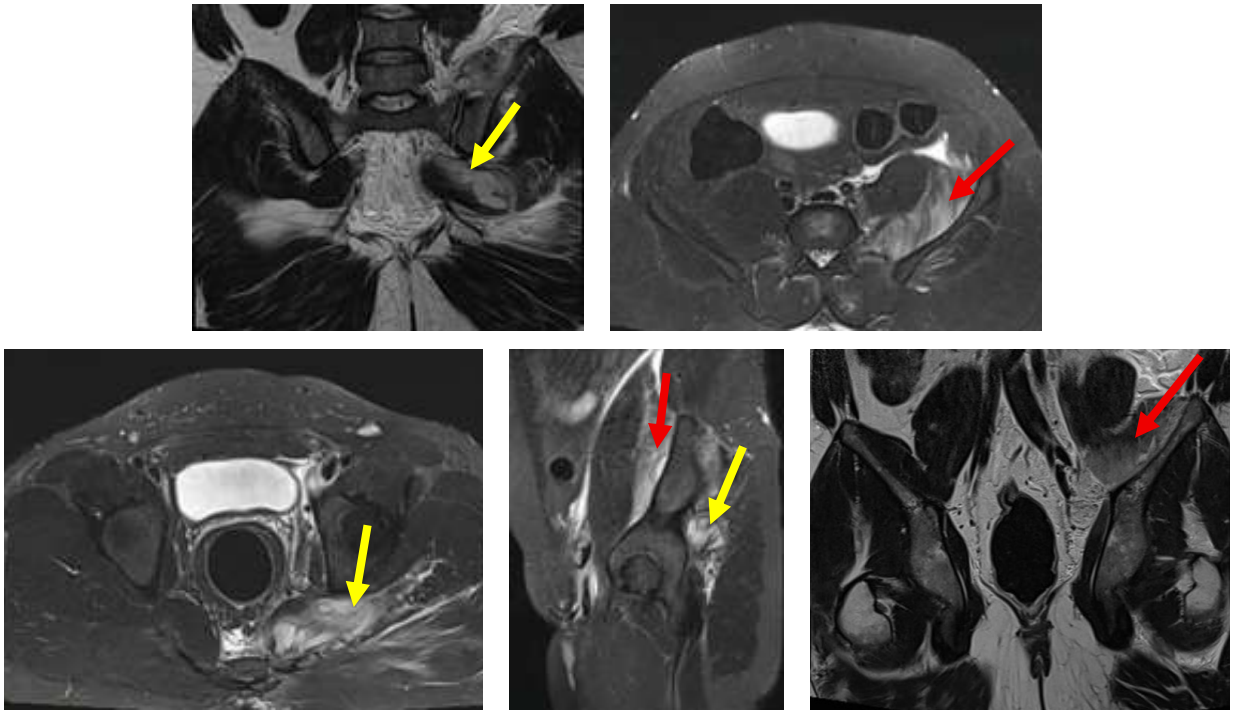
He presented to the OPD after 3 days with atypical severe pain localised to the left gluteal region with severe tenderness. Since the pain persisted, CT and MRI were ordered to rule out fractures of the spine and hip and look for other causes of the atypical pain that was not responding to painkillers.

As the pain was severe, he presented in the ER again the next day, following which blood investigations were done to look for infections, a CT for fractures, and an MRI was expedited.

CT Pelvis and Lumbar Spine showed:

- No obvious fracture in the spine and hip
- Fat stranding and oedema were noted along the left hemipelvis adjacent to the S1 and S2 nerve roots, extending into the region of the superior border of the left piriformis

MRI showed:



MRI images showing pus in the piriformis (yellow arrows) and iliacus (red arrows) areas

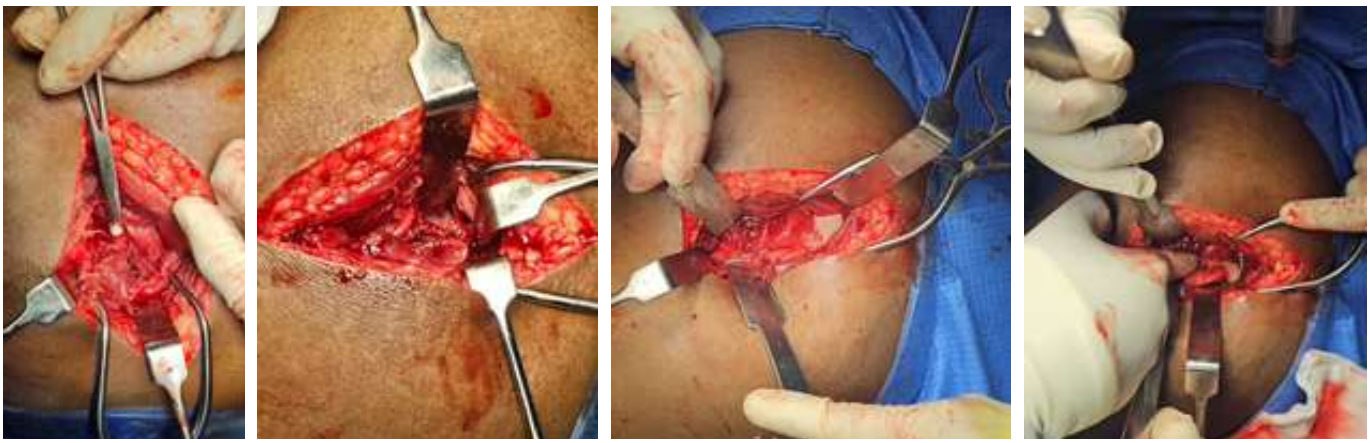
- Multiloculated intramuscular collections involving the left hemipelvis, including the visualised sections of the lumbar portion of the iliacus muscle; the largest in the left piriformis measuring up to 6.9 x 2.6 cm, and minimal bone marrow oedema of the left sacral ala at the S1 and S2, and focally reaching the SI joint.
- No widening or involvement of the sacral neural foramina.
- Lower LS spine T2 image showed intraspinal canal signal heterogeneity.
- Further evaluation with postcontrast enhanced MRI pelvis and LS spine was advised.
- Clinical correlation with blood count and CRP evaluation was advised.

He was started on antibiotics while awaiting approval for surgery. Surgery was done 3 days later.

DURING PROCEDURE

The patient underwent **Incision and Drainage of Pyomyositis of the left Piriformis:**

- The patient was positioned and draped.
- The incision was deepened into the gluteus maximus and was split bluntly.
- The piriformis was identified by its insertion into the greater trochanter.
- The same was split bluntly, and frank pus was drained.
- Multiple loculi present beneath were broken, and lavage was given.
- Subsequently, another loculi of pus was noted tracking into the pelvis through the greater sciatic notch.
- The same were deroofed and saline lavage was done.
- The piriformis tenotomy was done.
- The medial meniscus was normal.
- Haemostasis was achieved.
- A corrugated drain was placed, and the skin was closed in layers.



Intra-op Images

POST PROCEDURE

The patient responded well after surgery. Intra-op and post-op periods were uneventful. The patient tolerated the procedure well and was in a stable condition with a significant reduction in pain after surgery.

He was started on oral Clindamycin 300 mg TDS for 2 weeks. The CRP dropped from 167.31 to 18.93, and the WBC count from 16190 to 9590 in 5 days post op. Gram stain and AFB were negative, and pus culture from surgery showed scanty growth of Staphylococcus aureus.

Daily dressings were done for 3 days. The drain was applied and removed on day 3 on discharge. The dressings were done every 3 days, and the sutures were removed after 2 weeks.

The wound was healthy and healed well 3 weeks after surgery.

DISCUSSION

Piriformis Pyomyositis is an extremely rare bacterial infection, usually caused by Staphylococcus aureus. Common manifestations include fever, buttock or gluteal pain, lower back pain, limited ambulation, raised inflammatory markers (ESR, CRP), and leukocytosis.

In the systematic review by Abu Bakar Siddiq & Johannes Jacobus Rasker, 21 articles describe 23 cases of piriformis pyomyositis. A more recent review (2021) identified 32 cases (including abscess formation in 21).

In a systematic review of causes of piriformis syndrome, pyomyositis of the piriformis accounted for about 9.4% (20/212) of cases in one retrospective collection of case reports. Because of this, there's no reliable "incidence per population" number; the condition is so rare that most literature is case reports or small series.

The mean age found was ~26.98 ± 17.5 years (range 3-69) in the 32-case review, with a slight female predominance (~52.4%). The most common pathogen found in the 32-case review was Staphylococcus aureus (~57%).

Predisposing factors include muscle overuse/trauma, pelvic/gynaecologic manipulations, other infections or immunocompromise. However, associations weren't always statistically significant. Imaging (particularly MRI) is helpful for early diagnosis, given its deep location.

CONCLUSION

Since Piriformis Pyomyositis is so rare, one must maintain a high index of suspicion when a patient presents with gluteal/buttock pain, fever, possible sciatica symptoms, raised inflammatory markers, and no obvious source. Early imaging (MRI or CT) is important, especially when the pain is deep and the presentation is atypical. Early diagnosis and treatment (antibiotics ± drainage) lead to good outcomes in documented cases.

Delayed diagnosis risks abscess formation, complications such as sciatic nerve compression, and septic spread. In the absence of large-scale incidence data, we can only rely on case series and reviews for guidance.

REFERENCES

1. Siddiq MAB, Rasker JJ. Piriformis pyomyositis, a cause of piriformis syndrome-a systematic search and review. Clin Rheumatol. 2019 Jul;38(7):1811-1821. doi: 10.1007/s10067-019-04552-y.
2. Salehi M, Ghiasvand F, Feizabadi MM, Zarei M, Yazdi NA, Alijani N, Qaempanah M, Seyedpour S. The piriformis abscess: a case-based review. Iran J Microbiol. 2021 Apr;13(2):252-256. doi: 10.18502/ijm.v13i2.5988.
3. Jayanthan S, Rajkumar S, Kumar V, Shalini M. Pyomyositis of the Piriformis Muscle—A Case of Piriformis Syndrome. Indian Journal of Radiology and Imaging. 2021 Nov;31(01). doi: 10.1055/s-0041-1739183.
4. Kraniotis P, Marangos M, Lekkou A, Romanos O. Brucellosis presenting as piriformis myositis: A case report. J Med Case Reports. 2011 Mar;5(1):125. doi:10.1186/1752-1947-5-125.

Aster
HOSPITAL
We'll Treat You Well

BOTOX IN NEUROLOGY

Advanced, targeted treatment for complex neurological conditions

- Chronic migraine & pill-resistant headaches
- Movement disorders
- Hemifacial spasm
- Spasticity & disability management

Dr. Jaffar Vali Sayyed
Specialist Neurology

Aster Hospital, Qusais

Clinical Applications and Therapeutic Impact of Tolebrutinib in Multiple Sclerosis (MS)

Dr. Ponnu Sankara Pillai
Neurology (Specialist)
Aster Hospital, Mankhool, Dubai

INTRODUCTION

Multiple sclerosis (MS) is an immune-mediated disease of the central nervous system (CNS) characterised by a degenerative component involving both adaptive and innate immune responses (1). While current disease-modifying therapies (DMTs) effectively reduce relapses and magnetic resonance imaging (MRI) activity, they often fail to slow disability progression and are associated with significant adverse events (1). Evidence indicates that neuroaxonal loss is present from the early stages, leading many patients to experience clinical deterioration despite a lack of overt inflammatory activity (2). This smouldering MS, or progression independent of relapse activity (PIRA), is thought to be driven by chronic, non-resolving neuroinflammation within the CNS (2).

Because targeting a state of 'no evident inflammatory disease activity' (NEIDA) does not sufficiently prevent disability accumulation, treatment must address the pathological processes in the brain and spinal cord that drive functional loss (2,3). B cells and microglia have emerged as major contributors to this pathogenesis (6). Consequently, Bruton's tyrosine kinase (BTK), a downstream mediator of B-cell receptor signalling, has become a critical therapeutic target for modulating both peripheral and central inflammation (1,4).

Tolebrutinib is an oral, brain-penetrant BTK inhibitor designed to cross the blood-brain barrier (BBB) (3). By targeting myeloid cells (including microglia) and B cells in both the periphery and the CNS, tolebrutinib addresses the diffuse inflammation that current therapies may not adequately control (1,4).

This article examines the biological rationale for BTK inhibition and the distinct pharmacological profile of tolebrutinib, including its effects on humoral immunity and CNS penetration. Furthermore, we review the clinical evidence from the GEMINI, HERCULES, and PERSEUS trials to evaluate their safety, tolerability, and potential role in redefining treatment algorithms for the MS spectrum.

BIOLOGICAL RATIONALE FOR BTK INHIBITION IN MULTIPLE SCLEROSIS (MS)

As MS evolves toward a progressive phenotype, inflammatory activity becomes increasingly compartmentalised within the CNS, where chronic active or "smouldering" lesions persist due to sustained activation of microglia and macrophages (5). These lesions feature persistent innate immune activation, iron-laden microglia, and ongoing neuroaxonal injury, all contributing to irreversible disability accumulation (6). This shift underscores why conventional DMTs show limited efficacy against such CNS-sequestered inflammation, reinforcing the hypothesis that progression is driven by immune mechanisms trapped behind the BBB, independent of peripheral relapses (6).

Figure 1 illustrates immune activity across the BBB and depicts how BTK-dependent signalling in B cells and myeloid cells perpetuates inflammatory cascades leading to demyelination, axonal degeneration, and neuronal injury in MS.

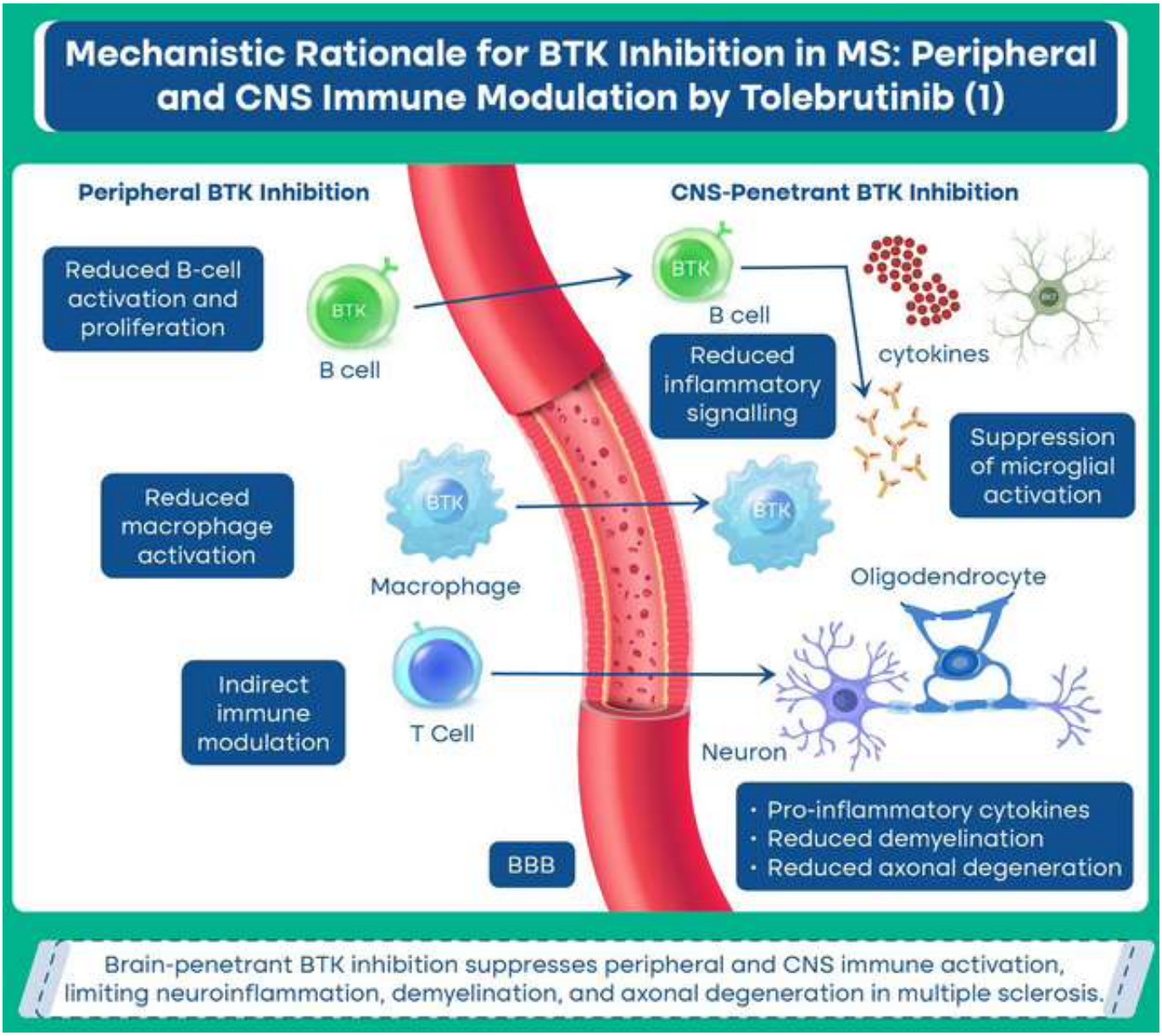


Figure 1. Schematic illustrating how brain-penetrant BTK inhibition suppresses peripheral B-cell activation and CNS microglial inflammation to reduce neurodegeneration in MS (6)

(Abbreviations: MS - multiple sclerosis; BTK - Bruton's tyrosine kinase CNS - central nervous system; BBB - blood–brain barrier; B cell - B lymphocyte; T cell - T lymphocyte)

BTK is expressed in B cells and myeloid lineage cells such as macrophages and microglia, where it regulates Fc receptor signalling, cytokine production, and amplification of innate immune responses (6). Beyond antibody production, B cells drive MS pathology through antigen presentation to T cells, proinflammatory cytokine secretion, and modulation of myeloid cell function, fuelling a self-sustaining inflammatory loop (7). Within chronic active lesions, microglial BTK signalling exacerbates compartmentalised neuroinflammation via cytokine release, oxidative stress, complement activation, and neurotoxic pathways (7). This CNS-trapped activity explains the unmet need for therapies that penetrate the brain (7).

Tolebrutinib meets this need by achieving sustained CNS target engagement. Phase I pharmacokinetic data demonstrate cerebrospinal fluid (CSF) concentrations exceeding thresholds required to inhibit BTK in MS-relevant immune cells (8,9). Comparative analyses indicate higher potency and CSF exposure than other BTK inhibitors, supporting effective modulation of peripheral B-cell activation and microglial neuroinflammation (6,10).

PHARMACOLOGY AND DRUG CHARACTERISTICS OF TOLEBRUTINIB

The development of tolebrutinib represents a strategic shift toward targeting the compartmentalised inflammation found within the CNS (6). As an oral, covalent BTK inhibitor, its molecular structure has been optimised for potency and BBB penetration (10).

This design allows tolebrutinib to reach CNS-resident cells, such as microglia, which play a pivotal role in the "smouldering" disability progression seen in MS (10). Laboratory assays confirm its efficiency, showing that tolebrutinib binds to its target substantially faster than evobrutinib and demonstrates superior cellular potency compared to both evobrutinib and fenebrutinib (10).

Data from CSF studies validate that tolebrutinib achieves the concentrations necessary for meaningful therapeutic impact (10). Phase I volunteer studies further showed that these concentrations remain above biologically relevant thresholds required to inhibit immune signalling pathways implicated in MS pathology (9).

Figure 2 summarises key pharmacologic differences among emerging BTK inhibitors, including binding mode, potency, CNS penetration, and CSF exposure relative to BTK IC_{90} (10).

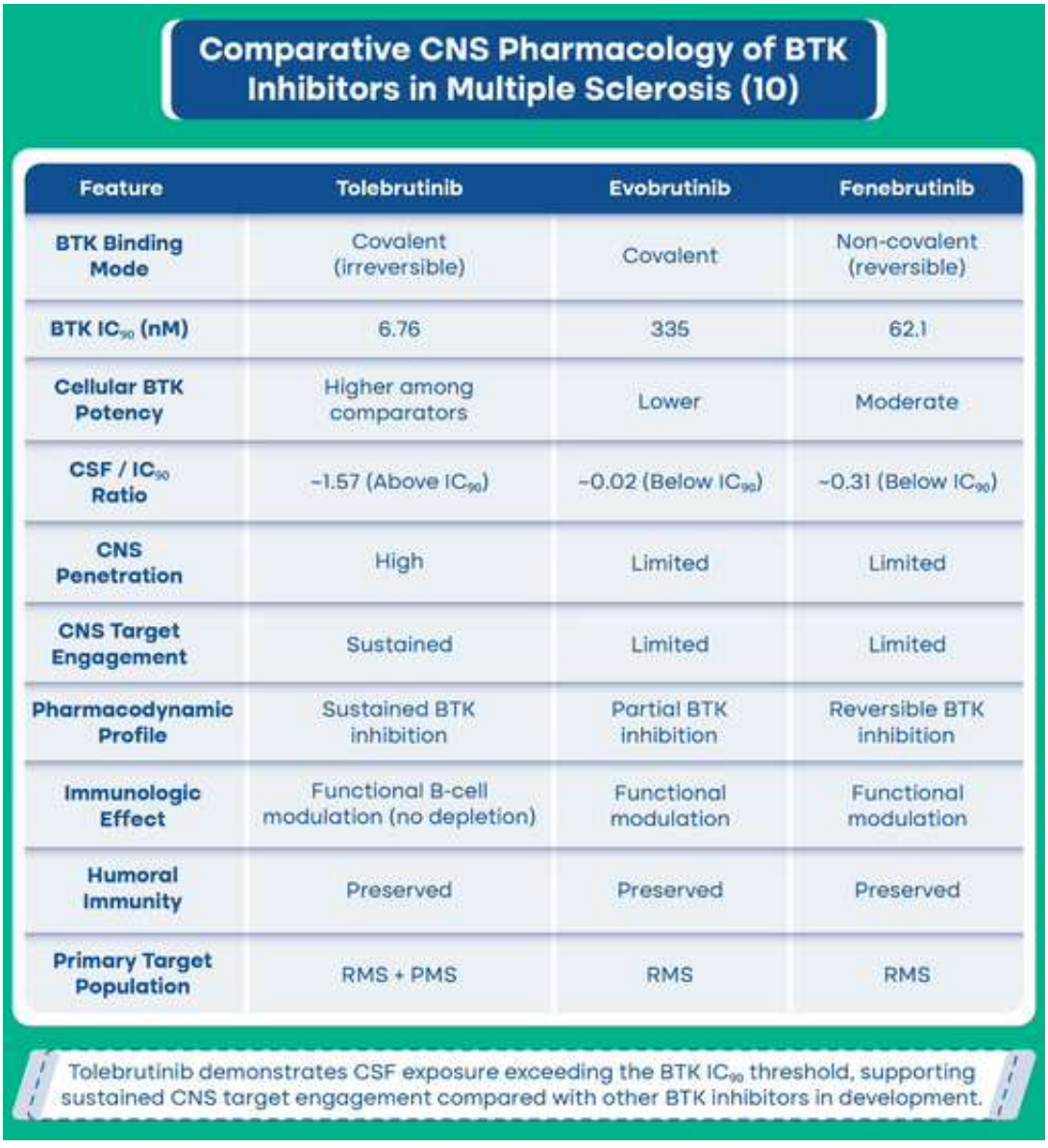


Figure 2. Comparative CNS pharmacology of BTK inhibitors in MS (10)

(Abbreviations: MS - multiple sclerosis; BTK - Bruton's tyrosine kinase; CNS - central nervous system; CSF - cerebrospinal fluid; IC_{90} - 90 percent inhibitory concentration; RMS - relapsing multiple sclerosis; PMS - progressive multiple sclerosis)

A significant advantage of tolebrutinib is its high selectivity (6). Unlike first-generation BTK inhibitors, which often affect multiple kinases and lead to off-target effects, tolebrutinib demonstrates a more targeted pharmacologic profile, supporting a cleaner safety and immunologic impact (6).

The drug's mechanism also marks a departure from traditional B-cell–depleting therapies. Instead of eliminating the B-cell population, Tolebrutinib focuses on functional modulation (10):

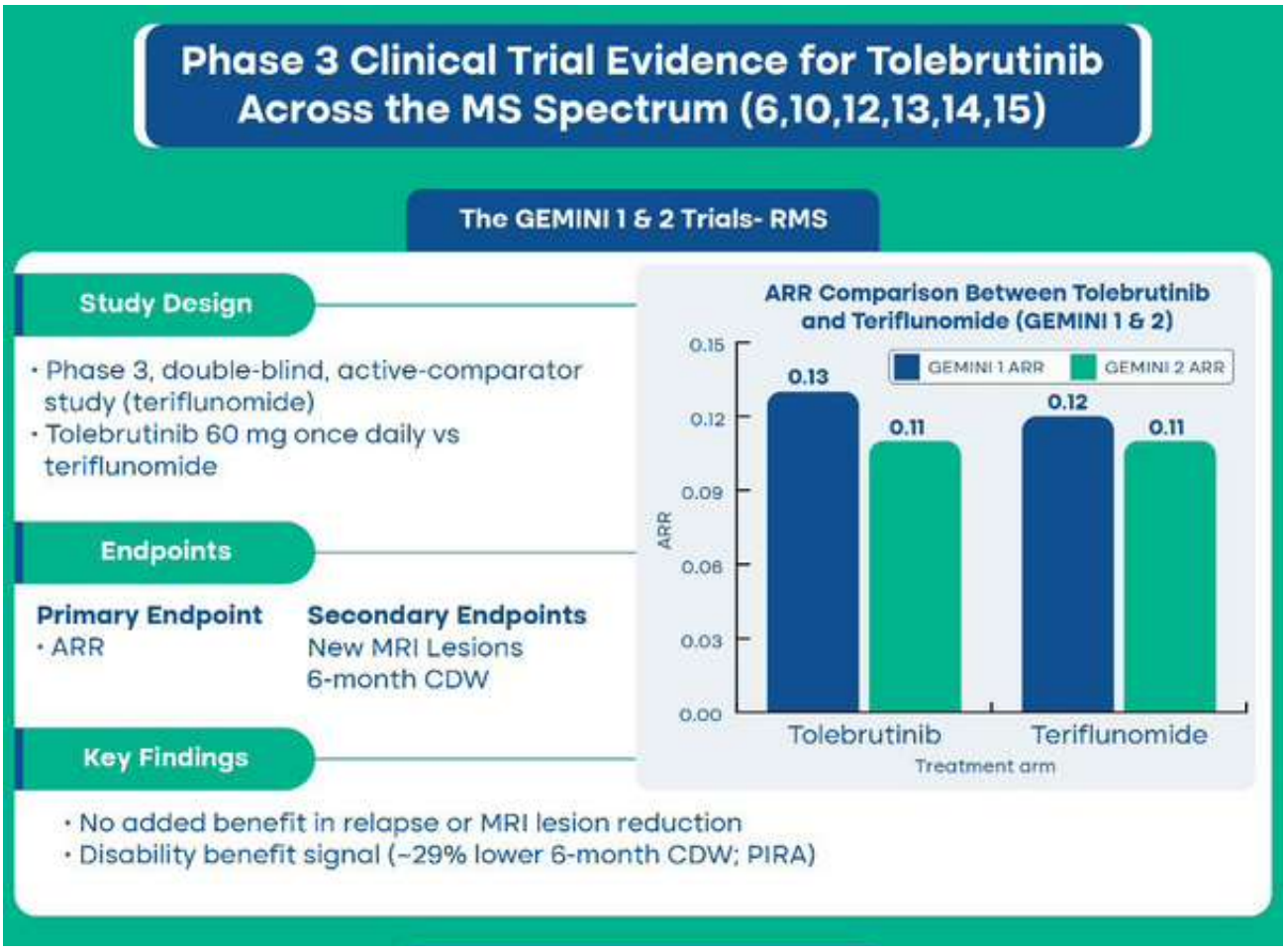
- It dampens B-cell activation, cytokine release, and antigen presentation without destroying the cells themselves (11).
- It modulates innate immune activity, including myeloid cells and microglia within the CNS (6).
- By preserving B-cell populations, it supports maintenance of humoral immunity and immunologic memory, with potential implications for infection risk and vaccine responsiveness (6).

Together, these pharmacologic features position tolebrutinib as a differentiated BTK inhibitor with potential relevance across relapsing and progressive MS phenotypes, where CNS-compartmentalised inflammation contributes to ongoing disease activity (10).

CLINICAL TRIAL EVIDENCE ACROSS THE MULTIPLE SCLEROSIS (MS) SPECTRUM

The Phase III development program for tolebrutinib characterises its efficacy across the MS spectrum, revealing a phenotype-dependent profile (12). Data synthesised from the GEMINI, HERCULES, and PERSEUS programs indicate that the clinical impact of BTK inhibition is significantly more pronounced on disability progression than on acute focal inflammatory activity (5,12).

Figure 3 summarises the design, endpoints, and principal findings from the GEMINI, HERCULES, and PERSEUS Phase III trials, highlighting differential clinical responses across relapsing and progressive MS phenotypes.



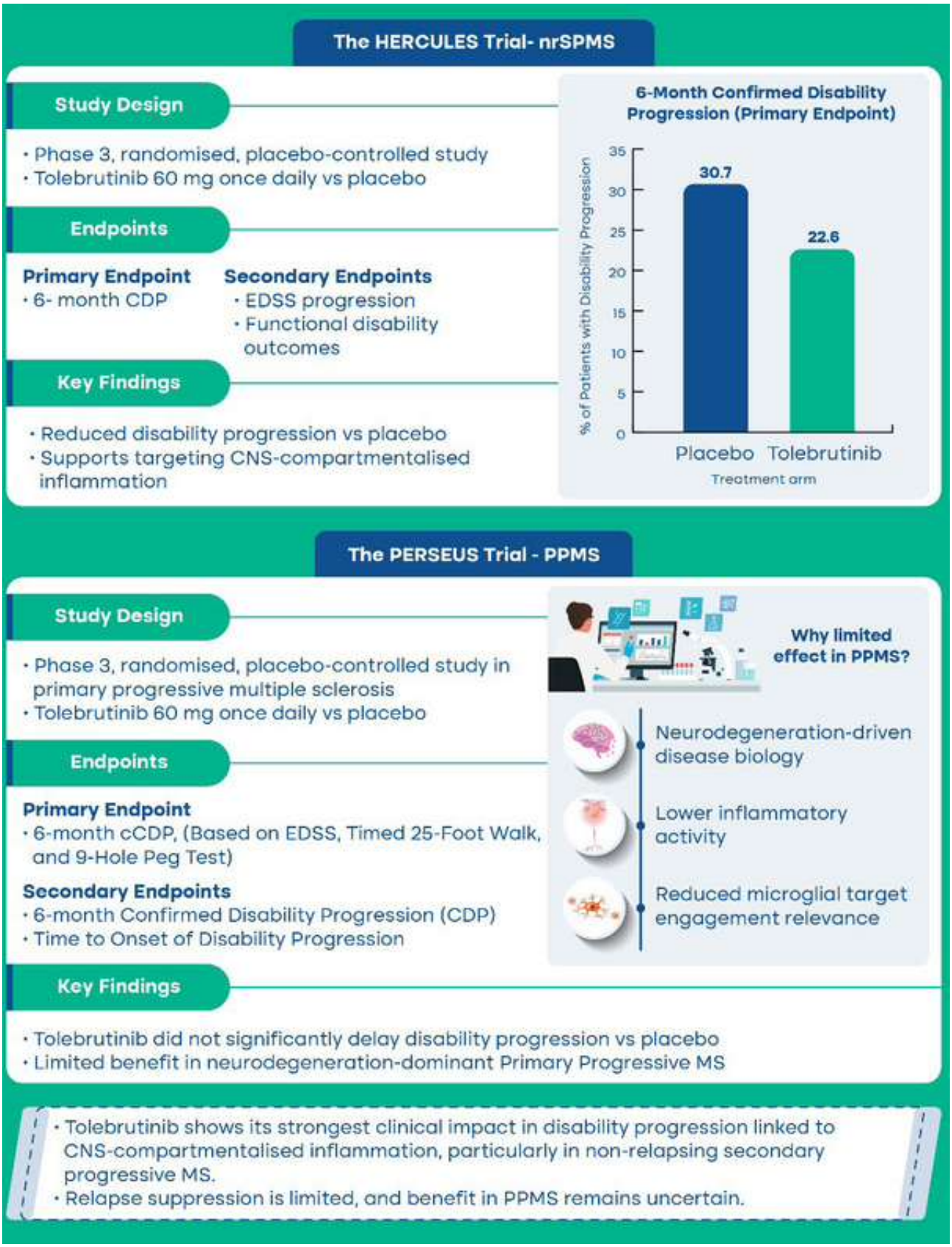


Figure 3. Phase 3 clinical trial evidence for Tolebrutinib across the MS spectrum (6,10,12,13,14,15)

(Abbreviations: MS - multiple sclerosis; RMS - relapsing multiple sclerosis; SPMS - secondary progressive multiple sclerosis; PPMS - primary progressive multiple sclerosis; BTK - Bruton's tyrosine kinase; CNS - central nervous system; ARR - annualized relapse rate; MRI - magnetic resonance imaging; CDW - confirmed disability worsening; CDP - confirmed disability progression; EDSS - Expanded Disability Status Scale; PIRA - progression independent of relapse activity)

Across relapsing MS, results from the GEMINI 1 and 2 trials indicate that tolebrutinib does not confer meaningful additional benefit in relapse suppression or focal MRI lesion control, suggesting limited impact on acute inflammatory disease activity (13). However, the observed disability signal supports a potential effect on progression independent of relapse activity (PIRA), consistent with mechanisms linked to CNS-compartmentalised inflammation (10).

In non-relapsing secondary progressive MS (nrSPMS), findings from the HERCULES trial provide the strongest evidence of clinical benefit, reinforcing the relevance of BTK inhibition in disease states driven by innate immune activation and microglial-mediated neuroinflammation (12). These results align with emerging biological models that identify compartmentalised CNS inflammation as a key driver of disability accumulation in progressive MS (8). The success in this progressive population is supported by specific clinical and biological rationales.

In contrast, evidence from the PERSEUS trial in primary progressive MS (PPMS) suggests limited or uncertain therapeutic benefit, implying that tolebrutinib may not substantially modify disease progression in phenotypes dominated by neurodegenerative pathology and lower inflammatory activity (6,14).This divergence highlights the importance of underlying disease biology in determining responsiveness to BTK inhibition (6).

Collectively, cross-trial evidence positions tolebrutinib as a potential disability-modifying therapy with the greatest relevance in nrSPMS and relapsing MS populations exhibiting PIRA, while its clinical utility in PPMS appears more constrained (1,15).

SAFETY, TOLERABILITY, AND PRACTICAL POSITIONING IN MULTIPLE SCLEROSIS (MS) PRACTICE SPECTRUM

Across Phase III development, tolebrutinib demonstrated an adverse event profile characterised by hepatic enzyme elevations and infection risk that necessitate structured safety monitoring (8). While efficacy varies by disease phenotype, the safety findings remain consistent across the MS spectrum, reflecting a class-wide consideration for BTK inhibitors and reinforcing the need for integrated pharmacovigilance strategies in clinical practice (1,3).

In the HERCULES trial, elevations in alanine aminotransferase (ALT) were reported more frequently in the tolebrutinib arm than in the placebo group, prompting a strong clinical emphasis on liver function surveillance (8). Approximately 4% of treated patients experienced ALT values above three times the upper limit of normal, with the most severe elevations (>20× ULN) occurring almost exclusively within the first 90 days of treatment (3).

To mitigate the risk of drug-induced liver injury (DILI), safety protocols were revised during the pivotal trials to implement intensive monitoring strategies (8). The current clinical consensus suggests a structured surveillance approach:

- **Initial intensive phase:** Weekly liver function testing during the first 3 months of therapy to capture early-onset elevations (8).
- **Long-term surveillance:** Continued monthly monitoring following the initial 90-day window to ensure sustained hepatic safety (8).

Safety findings from the GEMINI 1 and 2 trials in relapsing MS similarly identified treatment-emergent infections and laboratory abnormalities, with no unexpected signals beyond known class effects (13). Independent pooled analyses confirm that while hepatotoxicity represents a relevant safety signal, overall serious infection rates remained comparable to other high-efficacy disease-modifying therapies (DMTs) (1). The therapeutic appeal of BTK inhibition lies in its differentiated impact on immune modulation compared with existing high-efficacy agents (11).

Unlike anti-CD20 therapies, which induce prolonged B-cell depletion and are associated with hypogammaglobulinemia and increased infection risk, BTK inhibition modulates B-cell signalling while

preserving circulating B-cell populations and humoral immunity (15). This mechanism supports immune competence and vaccine responsiveness while limiting pathogenic immune activation pathways implicated in MS progression (5). Comparative class-level analyses suggest that BTK inhibitors may offer a differentiated balance between immunologic efficacy and infectious risk relative to S1P modulators and other oral agents, which are frequently associated with broader lymphocyte suppression (5).

Tolebrutinib may be particularly advantageous in patients with progression independent of relapse activity and evidence of CNS-compartmentalised inflammation, where microglial-driven pathology contributes significantly to disability accrual (14). This aligns with emerging concepts that smouldering neuroinflammation and CNS-resident immune activation represent key drivers of long-term disease progression (2).

As treatment paradigms increasingly shift toward long-term disability prevention and targeting of CNS-resident immune cells, BTK inhibition represents a potential evolution in MS therapeutic algorithms beyond relapse-focused disease control (14).

Figure 4 illustrates patient populations, biological rationale, and safety considerations guiding the clinical positioning of tolebrutinib in MS practice.

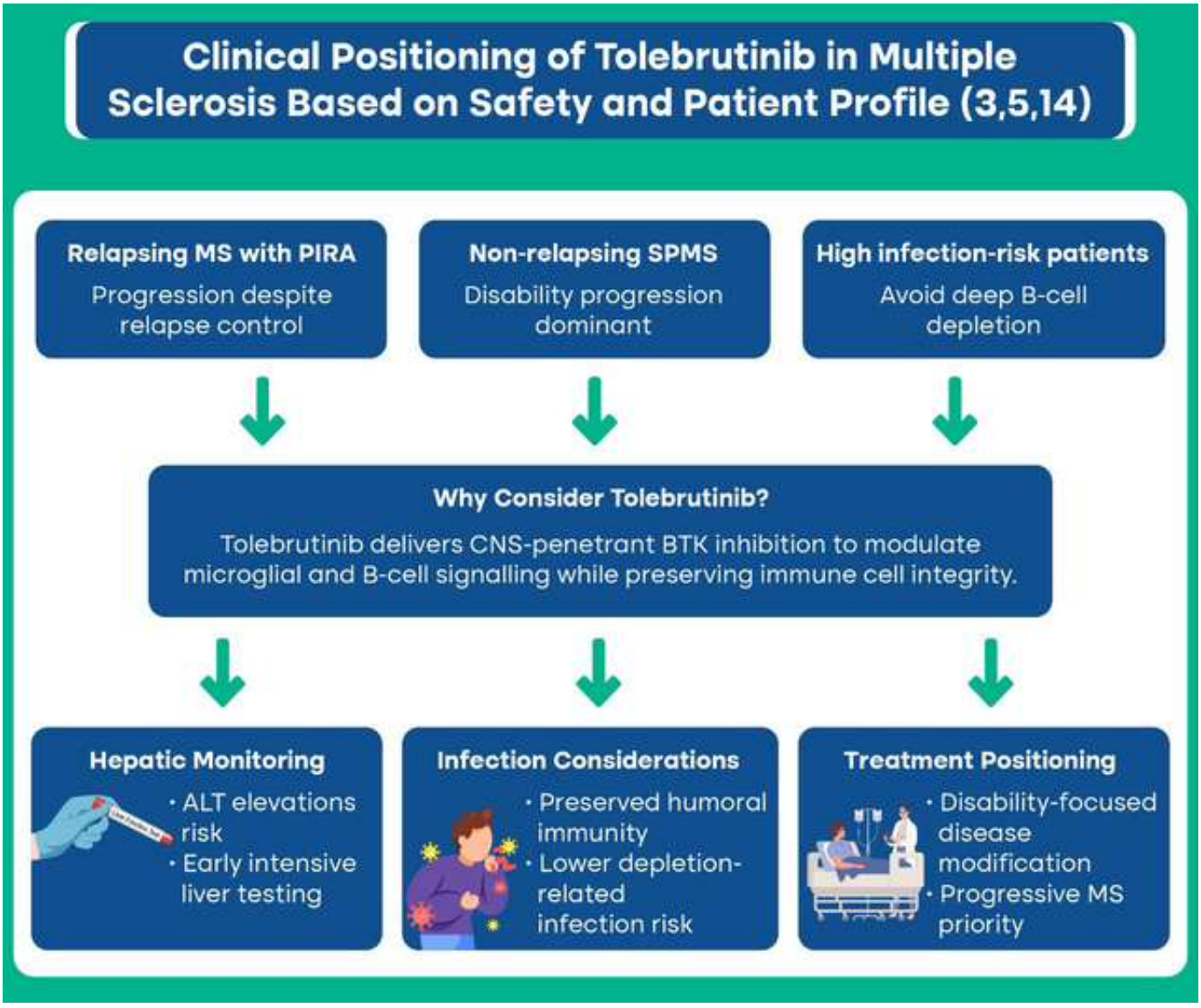
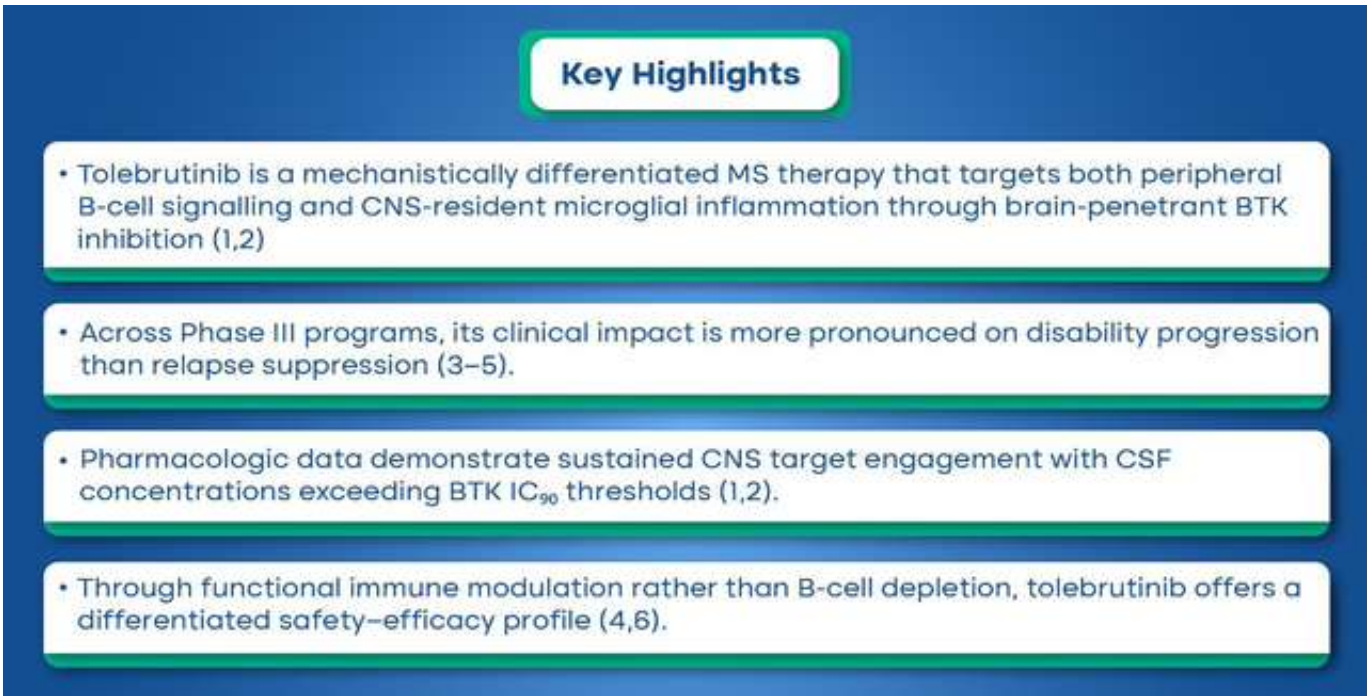


Figure 4. Clinical positioning and safety-guided use of Tolebrutinib in MS (3,5,14)

(Abbreviations: MS - multiple sclerosis; PIRA - progression independent of relapse activity; SPMS - secondary progressive multiple sclerosis; CNS - central nervous system; BTK - Bruton's tyrosine kinase; ALT - alanine aminotransferase; B cell - B lymphocyte)

Collectively, the emerging biological, pharmacological, clinical, and safety evidence position tolebrutinib as a differentiated BTK inhibitor with potential relevance for disability-focused disease modification in MS (5). Its capacity for CNS penetration, functional immune modulation without B-cell depletion, and clinical efficacy in non-relapsing secondary progressive disease reflects a mechanistic alignment with compartmentalised neuroinflammation and progression independent of relapse activity (14). As of 2025, the FDA has declined to approve Tolebrutinib, citing risks of drug-induced liver injury (DILI) (16). While hepatic safety monitoring remains essential and efficacy in primary progressive MS appears limited, ongoing long-term outcome data will further define its role within evolving treatment algorithms (3).



REFERENCES

1. Abbas A, Sabet H, Abouelmagd ME, El-Moslemani M, Ewis DK, Soliman SM, et al. Safety and efficacy of Bruton's tyrosine kinase inhibitors in multiple sclerosis: A systematic review and network meta-analysis of randomized controlled trials. Brain Network Disorders. 2025 Aug 18. doi:10.1016/j.bnd.2025.06.003.
2. Giovannoni G, Popescu V, Wuerfel J, Hellwig K, Iacobaeus E, Jensen MB, et al. Smouldering multiple sclerosis: the 'real MS.' Ther Adv Neurol Disord. 2022 Jan 25;15:17562864211066752. doi:10.1177/17562864211066751.
3. Mohammed Fahim S, Lin GA, McQueen B, Zemplenyi A, Richardson M, Agboola F. Tolebrutinib for secondary progressive multiple sclerosis: A summary from the Institute for Clinical and Economic Review's California Technology Assessment Forum. J Manag Care Spec Pharm. 2025 Dec;31(12):1320–5. doi:10.18553/jmcp.2025.31.12.1320.
4. D'Egidio F, Kacem H, Lombardozzi G, d'Angelo M, Cimini A, Castelli V, et al. The Potential Therapeutic Role of Bruton Tyrosine Kinase Inhibition in Neurodegenerative Diseases. Applied Sciences. 2025 Jul 24;15(15). doi:10.3390/app15158239.
5. Reidy M, Khan M, Mills EA, Wu Q, Garton J, Draayer DE, et al. New Frontiers in Multiple Sclerosis Treatment: From Targeting Costimulatory Molecules to Bispecific Antibodies. International Journal of Molecular Sciences. 2025 Apr 19;26(8). doi:10.3390/ijms26083880.
6. Krämer J, Bar-Or A, Turner TJ, Wiendl H. Bruton tyrosine kinase inhibitors for multiple sclerosis. Nat Rev Neurol. 2023;19(5):289–304. doi:10.1038/s41582-023-00800-7.
7. Langlois J, Lange S, Ebeling M, Macnair W, Schmucki R, Li C, et al. Fenebrutinib, a Bruton's tyrosine kinase inhibitor, blocks distinct human microglial signaling pathways. J Neuroinflammation. 2024 Oct 27;21(1):276. doi:10.1186/s12974-024-03267-5.
8. Fox RJ, Bar-Or A, Traboulsee A, Oreja-Guevara C, Giovannoni G, Vermersch P, et al. Tolebrutinib in Nonrelapsing Secondary Progressive Multiple Sclerosis. New England Journal of Medicine. 2025 May 14;392(19):1883–92. doi:10.1056/NEJMoa2415988.
9. Cabanis M, Nicolas O, Vitse O, Jan C, Brun P, Soubayrol P, et al. A phase I trial assessing the safety, pharmacokinetics, cerebrospinal fluid penetrance, and food effect of BTK inhibitor tolebrutinib in healthy volunteers. Clin Transl Sci. 2024 Feb 6;17(2):e13693. doi:10.1111/cts.13693.

10. Turner TJ, Brun P, Gruber RC, Ofengeim D. Comparative CNS Pharmacology of the Bruton's Tyrosine Kinase (BTK) Inhibitor Tolebrutinib Versus Other BTK Inhibitor Candidates for Treating Multiple Sclerosis. Drugs R D. 2024 Jun;24(2):263–74. doi:10.1007/s40268-024-00468-4.
11. Comi G, Bar-Or A, Lassmann H, Uccelli A, Hartung HP, Montalban X, et al. The role of B cells in Multiple Sclerosis and related disorders. Ann Neurol. 2021 Jan;89(1):13–23. doi:10.1002/ana.25927.
12. GA L, B M, SM F, M R, A Z, F R. Tolebrutinib for Secondary Progressive Multiple Sclerosis [Evidence Report] [Internet]. Institute for Clinical and Economic; 2025 Jul. Report. Available from: https://icer.org/assessment/multiple-sclerosis-2025/
13. Oh J, Arnold DL, Cree BAC, Ionete C, Kim HJ, Sormani MP, et al. Tolebrutinib versus Teriflunomide in Relapsing Multiple Sclerosis. New England Journal of Medicine. 2025 May 14;392(19):1893–904. doi:10.1056/NEJMoa2415985
14. Vermersch P, Airas L, Berger T, Deisenhammer F, Grigoriadis N, Hartung HP, et al. The role of microglia in multiple sclerosis: implications for treatment with Bruton's tyrosine kinase inhibitors. Front Immunol. 2025 May 15;16. doi:10.3389/fimmu.2025.1495529
15. Airas L, Bermel RA, Chitnis T, Hartung HP, Nakahara J, Stuve O, et al. A review of Bruton's tyrosine kinase inhibitors in multiple sclerosis. Ther Adv Neurol Disord. 2024 Aug 1;17:17562864241233040. doi:10.1177/17562864241233041
16. National Multiple Sclerosis Society. National Multiple Sclerosis Society [Nonprofit Health Organization Website] [Internet]. 2025 [cited 2026 Feb 20]. Update: FDA Issues Complete Response Letter for Tolebrutinib. Available from: https://www.nationalmssociety.org/news-and-magazine/news/tolebrutinib-phase-3-trial#:~:text=24%2C%202025The%20U.S.%20Food,at%20a%20future%20medical%20meeting.

Good Functional Recovery after Open Reduction and Internal Fixation of Comminuted Holstein–Lewis Fracture Complicated by High Radial Nerve Palsy at Aster Cedars Hospital and Clinic, Jebel Ali, Dubai

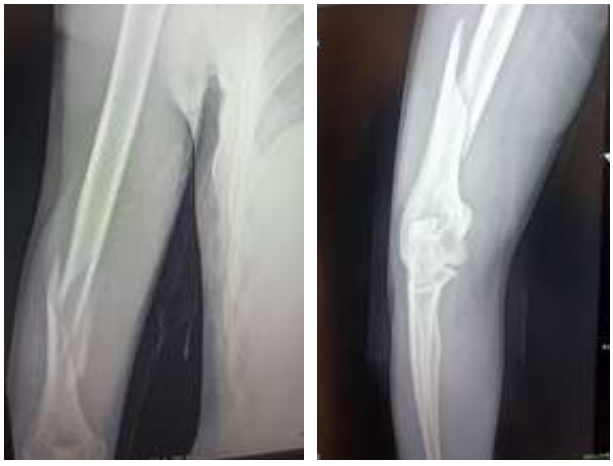
Dr. Shafeed Thadathil Parambil
Orthopaedics (Specialist)

PRESENTATION

- 22-year-old male
- No medical history
- No family history of medical illness
- Presented with pain, swelling and deformity of the right lower arm following a fall at the work site

FINDINGS

- Physical examination revealed abrasions and ecchymosis over the right lower arm
- An X-ray showed a comminuted spiral fracture of the lower 3rd humerus
- High radial nerve palsy with wrist drop and finger drop

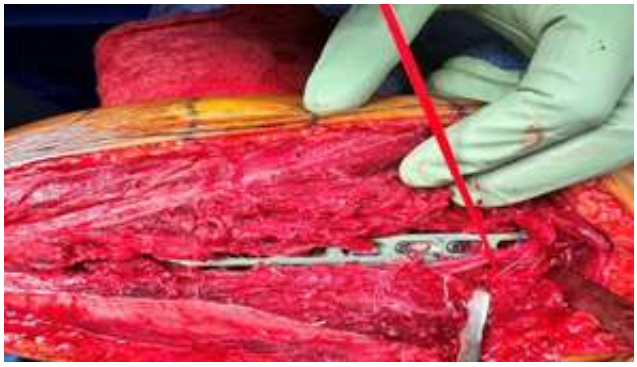


Pre-op X-ray images

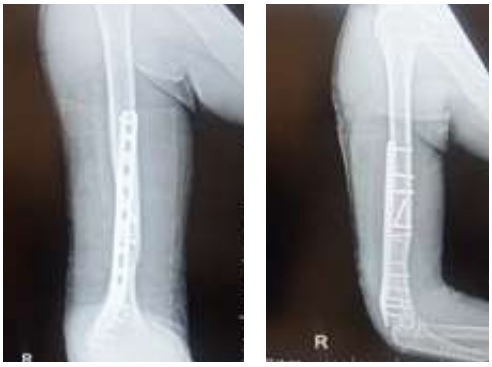
DURING PROCEDURE

- The procedure was done under general anaesthesia.
- The patient was positioned laterally with the affected limb on the side support.
- The right elbow and upper limb were prepared and draped.
- Posterior approach – the triceps were split.
- The radial nerve was found to be contused, released, and isolated along with the vascular bundle.

- The fracture ends were freshened, held in reduction temporarily with K-wires and fixed with a postero-lateral locking plate and screw.
- The wound was closed in layers after haemostasis was achieved.
- The dressings and a splint were applied.



Intra-op image showing the radial nerve



Post-op X-ray images

POST PROCEDURE

The right elbow was immobilised in an above-elbow splint for 3 weeks, and thereafter a structured physiotherapy regimen was initiated, including passive and active-assisted range-of-motion exercises for the elbow, wrist, and fingers, alongside specific radial nerve gliding exercises to prevent tethering and promote neural recovery.

DISCUSSION

While humerus fractures are common, the Holstein-Lewis variant accounts for only about 10-15% of these cases. It remains a classic but challenging clinical entity, necessitating a high index of suspicion for radial nerve involvement due to the unique anatomy of the distal third of the humerus. In contrast, the majority of radial nerve palsies associated with humeral shaft fractures are neuropraxias that resolve with conservative treatment. Spiral geometry and distal location of the Holstein-Lewis variant increase the risk of mechanical nerve entrapment or interposition. In this case, the patient achieved complete neurological recovery within one month following surgical stabilisation. Such a rapid timeline suggests that the injury was high-grade neuropraxia, likely exacerbated by fracture instability or subtle mechanical compression that was relieved upon open reduction and internal fixation (ORIF).

REFERENCES

1. Holstein A, Lewis GM. Fractures of the humerus with radial-nerve paralysis. J Bone Joint Surg Am. 1963 Oct;45:1382-88. PMID: 14069777.
2. Shao YC, Harwood P, Grotz MR, Limb D, Giannoudis PV. Radial nerve palsy associated with fractures of the shaft of the humerus: a systematic review. J Bone Joint Surg Br. 2005 Dec;87(12):1647-52. doi: 10.1302/0301-620X.87B12.16132.
3. Ekholm R, Ponzer S, Törnkvist H, Adami J, Tidermark J. The Holstein-Lewis humeral shaft fracture: aspects of radial nerve injury, primary treatment, and outcome. J Orthop Trauma. 2008 Nov-Dec;22(10):693-7. doi: 10.1097/BOT.0b013e31818915bf.
4. Bishop J, Ring D. Management of radial nerve palsy associated with humeral shaft fracture: a decision analysis model. J Hand Surg Am. 2009 Jul-Aug;34(6):991-6.e1. doi: 10.1016/j.jhsa.2008.12.029.
5. Gerwin M, Hotchkiss RN, Weiland AJ. Alternative operative exposures of the posterior aspect of the humeral diaphysis with reference to the radial nerve. J Bone Joint Surg Am. 1996 Nov;78(11):1690-5. doi: 10.2106/00004623-199611000-00008

Aster
CLINIC
We'll Treat You Well

SHOW THE WORLD YOUR REAL SMILE!

Smyl Please!

Aster smyl AI Powered by LogyAI

Introducing SmylAI

Powered by LogyAI

Your personal AI dental health assistant that checks your oral health

in 2 minutes

Scan the QR Code to get your Dental Report NOW!