PULSE

A Mission to Make an Impact on Patients' Lives
www.vpulsehk.com

HIV/AIDS Care Advance

Road to Cure: From Daily Management to Long-Acting Prevention and Immune-Guided Remission

033
ISSUE
DEC 2025

Feature Story: Rare Genomic Targets in NSCLC: 2025 Breakthroughs in Precision Therapy and Future Directions

Optimising Long-Term Renal Health in Chronic Hepatitis B Management

Navigating Management of Low-Grade NHLs: Recent Advances in CLL/SLL Treatment

Cardiovascular-Kidney-Metabolic (CKM) Syndrome: Why and How It Matters for Every Primary Care Physician

HKDU CME
Accredited Articles Inside

V.Pulse App Now Available!

GET IN ON Google Play

Download on the App Store

THE WISE CHOICE

FOR YOUR CHB PATIENTS

Product photo shown is not actual size.
The person depicted is not an actual healthcare professional.

Your patients deserve better care with Vemlidy®:*

- Higher rates of ALT normalization and high rate of viral suppression[1-3]
- Less impact on renal and bone function[1-3]
- 0% resistance detected at 5 years[1]
- No dosage adjustment for patients with eCrCl≥15mL/min or ESRD receiving chronic hemodialysis[4]

ALT: Alanine Aminotransferase CHB: Chronic Hepatitis B; eCrCl: Estimated Creatinine Clearance; ESRD: End Stage Renal Disease

*Comparison of ALT normalization, viral suppression, and impact on renal and bone function were made between tenofovir aladenamide and tenofovir disoproxil fumarate.[1-3]

Reference:

1. Chan HLY, Buti M, Agarwal K, et al. Maintenance of high levels of viral suppression and improved safety profile of tenofovir alafenamide relative to tenofovir disoproxil fumarate in chronic hepatitis B patients treated for 5 years in 2 ongoing phase 3 studies. Poster presented at: AASLD; November 13-16, 2020. Vitual 803.
2. Buti M, Gane E, Seto WK, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of patients with HBeAg-negative chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial. Lancet Gastroenterol Hepatol. 2016;1:196-206.
3. Chan HL, Fung S, Seto WK, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of HBeAg-positive chronic hepatitis B virus infection: a randomised, double-blind, phase 3, noninferiority trial. Lancet Gastroenterol Hepatol. 2016 Nov;1(3):185-195.
4. Vemlidy Prescribing Information. (Version HK-JUN22-US-SEP21).

VEMLIDY® Abbreviated Prescribing Information (Version: HK-JUN22-US-SEP21) Presentation: Tablets: 25 mg of tenofovir alafenamide - yellow, round, film-coated tablets, debossed with "GSI" on one side of the tablet and "25" on the other side. **Indications:** VEMLIDY is indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease. **Dosage:** Prior to initiation of VEMLIDY, patients should be tested for HIV-1 infection. VEMLIDY alone should not be used in patients with HIV infection. Adults: The recommended dosage is 25 mg (one tablet) taken orally once daily with food. Patients with Renal Impairment: No dosage adjustment is required in patients with estimated creatinine clearance greater than or equal to 15 mL/min, or in patients with end stage renal disease (ESRD; estimated creatinine clearance below 15 mL/min) who are receiving chronic hemodialysis. On days of hemodialysis, administer VEMLIDY after completion of hemodialysis treatment. VEMLIDY is not recommended in patients with ESRD who are not receiving chronic hemodialysis. Patients with Hepatic Impairment: No dosage adjustment is required in patients with mild hepatic impairment (Child-Pugh A). Not recommended in patients with decompensated (Child-Pugh B or C) hepatic impairment. **Contraindications:** None. **Warnings and Precautions:** Severe acute exacerbation of Hepatitis B after discontinuation of treatment: Discontinuation of VEMLIDY, may result in severe acute exacerbations of hepatitis B. Patients who discontinue VEMLIDY should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, resumption of anti-hepatitis B therapy may be warranted. Risk of development of HIV-1 resistance in patients coinfected with HBV and HIV-1: Due to the risk of development of HIV-1 resistance, VEMLIDY alone is not recommended for the treatment of HIV-1 infection. The safety and efficacy have not been established in patients coinfected with HBV and HIV-1. HIV antibody testing should be offered to all HBV-infected patients before initiating therapy with VEMLIDY, and, if positive, an appropriate antiretroviral combination regimen that is recommended for patients coinfected with HIV-1 should be used. New onset or worsening renal Impairment: Prior to or when initiating VEMLIDY, and during treatment with VEMLIDY on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus. Discontinue VEMLIDY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. Lactic acidosis/severe hepatomegaly with steatosis: Treatment with VEMLIDY should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations). **Adverse reactions:** Refer to warning and precautions for severe acute exacerbation of hepatitis B, new onset or worsening of renal impairment, and lactic acidosis/severe hepatomegaly with steatosis. Headache, abdominal pain, cough, back pain, fatigue, nausea, arthralgia, diarrhea and dyspepsia were reported in ≥ 5% of subjects in clinical studies. **Drug interactions:** Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin. Antimycobacterial: rifabutin, rifampin, rifapentine. Herbal Products: St. John's wort. Drugs that reduce renal function or compete for active tubular secretion such as acyclovir, cidofovir, ganciclovir, valacyclovir, valganciclovir, aminoglycosides (e.g., gentamicin), and high-dose or multiple NSAIDs. **Before prescribing, please consult full prescribing information which is available upon request.** VEMLIDY is a registered trademark of Gilead Sciences, Inc., or its related companies.

For medical enquiries, please send your request to asiamedinfo@gilead.com or call 800 908 348 (toll-free number).

HK-VEM-210321, 2/1, dated 09/05/2024

GILEAD
Creating Possible

Gilead Sciences Hong Kong Limited
26/F, Hysan Place, 500 Hennessy Road,
Causeway Bay, Hong Kong
Tel: (852) 3129 2000 Fax: (852) 2856 2611

Vemlidy® tenofovir alafenamide 25mg tablets

CONTENTS

ISSUE 033 DEC 2025

Publisher:
Ronnie Kong

Managing Editor:
Dr. Feng Xue

Editors:
Jasmine Lai
Michelle Lee
Migee Tang

Sales & Marketing:
Kit Lam

Digital Marketing:
Russell Mau

Designer:
Albert Lau

www.vpulsehk.com

vpulsehk vpulsehk

Vital Base International Limited

Unit A, 17/F, Mai Wah Industrial Building,
1-7 Wah Sing Street, Kwai Chung, Hong Kong
Tel: (852) 2741 6265 Fax: (852) 2370 9932
Email: enquiry@vital-base.com

Dear Reader,

Welcome to this issue! Precision oncology is rewriting the playbook for non-small cell lung cancer. From BRAF and HER2 breakthroughs to KRAS and MET innovations, rare genomic targets are driving survival gains and reshaping treatment strategies. Our Feature Story distills 2025's biggest updates—clinical trials, CNS-active agents, ctDNA monitoring, and what's next for resistance profiling and early-stage designs.

In Focus, global HIV control is accelerating with long-acting regimens and bold steps toward cure, even as funding shocks threaten progress. We spotlight twice-yearly PrEP, real-world Cabenuva data, and cutting-edge science—from bNAbs to CRISPR.

The Industry Update dives into Hong Kong's aging chronic hepatitis B population—over 410,000 people—facing rising comorbidities like diabetes and kidney disease, as Prof. Desmond Y. H. Yap shares strategies to optimize care. And in Epoch, we unpack the health risks of dining out, backed by large-scale evidence and practical strategies for clinicians.

Enjoy the read!

Dr. Feng Xue
MPH, PhD
Managing Editor, V.Pulse

What are your preferred topics?

To provide articles that match your interest, a V·Pulse Reader Survey has been launched to collect your opinions on the preferred topics. Please provide your views by completing the online questionnaire at the link here https://forms.gle/Qan6ZPoijnKbVTvW8

SCAN ME!

Scan the QR code to read more articles or visit
www.vpulsehk.com

Equfina® 50mg
FILM COATED TABLETS
(Safinamide mesilate)

FOR PATIENTS WITH PARKINSON'S DISEASE-
MOTOR CONTROL KEEPS THEIR FEET STEADY, IMPROVEMENT IN MOOD AND PAIN KEEPS THEM DANCING.

ADDING EQUFINA® AS PART OF L-DOPA TREATMENT

Significantly improves motor symptoms[1-3]

- Daily ON time without troublesome dyskinesia[1-3]
- UPDRS Part III (motor) score[1-3]

Significantly improves non-motor symptoms[4-6]

- Pain[4,5]
- Mood disorders, such as depression[6]

References
1. Equfina® Hong Kong prescribing information. 2. Borgohain R, et al. Mov Disord. 2014 Feb;29(2):229-237. 3. Schapira AH, et al. JAMA Neurol. 2017 Feb 1;74(2):216-224. 4. Cattaneo C, J Parkinsons Dis. 2017;7(1):95-101. 5. Hattori N, et al. Front Neurol. 2022 Feb 7;12:752632. 6. Tsuboi Y, et al. J Neurol Sci. 2021 Oct 15;429:118070.

Abbreviated Prescription Information
1. NAME OF THE MEDICATION. Equfina Tablets 50 mg. 2. QUALITATIVE AND QUANTITATIVE COMPOSITION. Equfina is supplied in film-coated tablet containing Safinamide mesilate (Safinamide mesylate, Safinamide methanesulfonate) equivalent to 50 mg Equfina. 3. PHARMACEUTICAL FORM. Film-coated tablet. Equfina Tablets 50 mg: White film-coated tablet, printed with "€284" on one side. 4. CLINICAL PARTICULARS. 4.1 Therapeutic Indications. Equfina is indicated for the treatment of adult patients with idiopathic Parkinson's disease (PD) as add-on therapy to a stable dose of levodopa (L-dopa) alone or in combination with other PD medicinal products in mid-to late-stage fluctuating patients. 4.2 Posology and method of administration. Treatment should be started at 50 mg per day and may be increased to 100 mg/day on the basis of individual clinical need. No change in dose is required for elderly patients, hepatic impairment and renal impairment population. 4.3 Contraindications. Hypersensitivity to the active substance or to any of the excipients. Concomitant treatment with other monoamine oxidase (MAO) inhibitors or pethidine. Use in patients with albinism, retinal degeneration, uveitis, inherited retinopathy, severe progressive diabetic retinopathy, or severe hepatic impairment. 4.4 Special warnings and precautions for use. Caution should be exercised when initiating treatment with safinamide in patients with moderate hepatic impairment. In case patients progress from moderate to severe hepatic impairment, treatment with safinamide should be stopped. Safinamide should not be administered to patients with ophthalmological history that would put them at increased risk for potential retinal effects. Safinamide treatment has not been associated with any increase in the appearance of ICDs. Safinamide used as an adjunct to levodopa may potentiate the side effects of levodopa, and pre-existing dyskinesia may be exacerbated, requiring a decrease of levodopa. 4.5 Interaction with other medicinal products and other forms of interaction. In view of the MAO inhibitory activity of safinamide, concomitant administration of safinamide with sympathomimetics or dextromethorphan requires caution. Antidepressants may be administered but used at the lowest doses necessary. Safinamide may transiently inhibit BCRP in vitro and also inhibits OCT1 in vitro at clinically relevant portal vein concentrations in adult populations. 4.6 Fertility, pregnancy, and lactation. Equfina is not recommended during pregnancy and should not be given to women of childbearing potential unless adequate contraception is practiced. Equfina should not be used during breast-feeding. 4.7 Effects on ability to drive and use machines. Somnolence and dizziness may occur during safinamide treatment, therefore patients should be cautioned about using hazardous machines. 4.8 Undesirable effects. Dyskinesia was the most common adverse reaction when used in combination with L-dopa alone or in combination with other PD treatments. Serious adverse reactions are known to occur with the concomitant use of selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic/tetracyclic antidepressants and MAO inhibitors, such as hypertensive crisis, neuroleptic malignant syndrome, serotonin syndrome, and hypotension. Impulse control disorders can occur in patients treated with dopamine agonists and/or other dopaminergic treatments. 4.9 Overdose. Symptoms of confusion, sleepiness, forgetfulness and dilated pupils were reported in a patient suspected to consume more than the daily prescribed dose of 100mg for a month. These symptoms resolved on discontinuing the medicinal product, without sequelae. There is no known antidote to safinamide or any specific treatment for overdose. 5. PHARMACEUTICAL PARTICULARS. 5.1 List of excipients. Refer to full local prescribing information. 5.2 Incompatibilities Not applicable. 5.3 Special precautions for storage. To be stored away from moisture after opening of the aluminium pillow and under 30°C. 5.4 Nature and contents of container. Aluminium bag with 2g of desiccant and 2 blisters; each blister contains 14 tablets. PLEASE REFER TO FULL PRESCRIBING INFORMATION.

Eisai

Eisai (Hong Kong) Company Limited
Unit A, 29/F, Lee & Man Commercial Centre,
169 Electric Road, North Point, Hong Kong
Tel: (852) 2516 6128 | Fax: (852) 2561 5042

HK-EQ-VB-23J-01

by Dr. Feng Xue

Rare Genomic Targets in NSCLC: 2025 Breakthroughs in Precision Therapy and Future Directions

Non-small cell lung cancer (NSCLC) has entered a new era of precision oncology, where increasingly *rare* genomic targets—such as BRAF V600E, HER2 (ERBB2) activating mutations, ROS1 fusions, KRAS G12C/G12D, MET exon 14 skipping, and EGFR exon 20 insertions—are reshaping clinical outcomes for subsets of patients historically underserved by standard therapies.[1] Drawing on 2025 updates from multi-center trials and regulatory decisions, this article synthesizes the latest efficacy, safety, and translational insights across these targets, highlights milestones such as near 4-year median overall survival (OS) in frontline BRAF inhibition, head-to-head phase III trajectories in HER2 tyrosine kinase inhibitor (TKI) development, robust intracranial control with lorlatinib after first-line ROS1 TKI failure, and emerging central nervous system (CNS) activity with novel KRAS inhibitors. We further summarize progress for KRAS G12D, MET exon 14, and EGFR exon 20 insertions and articulate practical implications for diagnostic standardization, treatment sequencing, ctDNA-guided response assessment, and equitable access. Finally, we outline future priorities—combination strategies, resistance profiling, trial designs for earlier disease stages, and biomarker refinement—to accelerate benefit across the NSCLC rare-target landscape.

Introduction

Lung cancer remains among the leading causes of cancer morbidity and mortality worldwide, with NSCLC constituting the majority of cases. As molecular subtyping and targeted therapeutics advance, the umbrella term *rare targets* increasingly denotes a clinically significant aggregation of patients who harbor low-frequency but actionable alterations. In 2025, several pivotal analyses and regulatory actions have converged to redefine standards of care for NSCLC patients with rare genomic drivers, spanning BRAF V600E, HER2 TKD mutations, ROS1 fusions, KRAS G12C/G12D, MET exon 14 skipping, and EGFR exon 20 insertions.

ROS1 Fusions: Lorlatinib as a Post-TKI Strategy With Strong Intracranial Control

The IFCT-2003 ALBATROS study addressed an unmet need: what to do after first-line ROS1 TKI failure (commonly crizotinib). In 54 patients (median age 63; 57.4% with baseline brain metastases; 94.4% previously treated with crizotinib), lorlatinib achieved investigator-assessed objective response rate (ORR) 30% and disease control rate (DCR) 84%, Blinded Independent Central Review (BICR) ORR 34% and DCR 74%. Median duration of response (DoR) was 20.4 months, median progression-free survival (PFS) 7.4 months, and median OS 42.3 months, reflecting durable systemic control.[2]

Crucially, intracranial efficacy was striking: among 13 patients with measurable brain metastases at baseline, intracranial ORR reached 92.3% and intracranial DCR 100%—a hallmark of third-generation TKI performance against CNS disease. Safety was manageable despite ≥grade 3 treatment-related adverse events (TRAEs) in 45.3%; permanent discontinuation was rare (~1%), and dose reductions (30%) addressed hypercholesterolemia, hypertriglyceridemia, and peripheral edema.[2]

In summary, after earlier-line ROS1 TKI failure, lorlatinib delivers substantial intracranial control and prolonged response duration, reinforcing a continuum-of-care model for ROS1-positive NSCLC with attention to lipid management and dose modifications.[2]

KRAS G12C: CNS Activity and Combination Horizons

KRAS G12C occurs in roughly 12–14% of NSCLC and carries a high burden of brain metastases (approximately 25–42%), historically portending poor outcomes. The LOXO-RAS-20001 cohort focused on olomorasib, a novel G12C inhibitor, in patients with active, untreated brain metastases. Among 21 patients (median age 65; 52% prior cranial radiotherapy; 67% prior platinum plus immunotherapy), intracranial ORR was 43% (9/21, including five complete responses), and DCR was 86%; responders had DoR >6 months at analysis.[3]

Safety was favorable: diarrhea (28%, ≥grade 3 ~1%), nausea (12%), fatigue (9%); dose reductions (7.5%) and permanent discontinuations (1.0%) were infrequent. Global registration trials—SUNRAY-01 (NCT06119581) and SUNRAY-02 (NCT06890598)—are exploring frontline combinations with pembrolizumab in advanced and earlier-stage NSCLC.[3]

As a whole, demonstrated CNS activity in untreated brain metastases represents a meaningful advance for KRAS G12C inhibitors. The evolving competitive edge will hinge on chemotherapy-free regimens (e.g., immunotherapy combinations) and on systematically overcoming resistance.[3]

HER2 Mutations: Two TKIs Reshape First-Line Possibilities

Zongertinib: Irreversible HER2 TKI Optimized for Selectivity

Zongertinib, designed to irreversibly inhibit HER2 while sparing wild-type EGFR, demonstrated compelling first-line activity in Beamion LUNG-1 cohort 2. Among 74 advanced HER2-mutant NSCLC patients (median age 67; 50% female; 30% with baseline brain metastases), the BICR-assessed ORR was 77% (95% confidence interval [CI]: 66–85), with 8% complete responses and 69% partial responses; DCR reached 96%. Six-month DoR and PFS rates were 80% and 79%, respectively; median treatment duration was 10.3 months, with 47% of responders still on therapy at cutoff.[4]

Safety was favorable: TRAEs in 91%, grade 3 in 18%, with predominant events of diarrhea, rash, transaminase elevations, taste disturbance, and nausea; no grade 4–5 events were observed.[4] In 2025, the FDA granted accelerated approval for zongertinib (August 8) in HER2 TKD-mutant non-squamous NSCLC,[5] and China's National Medical Products Administration (NMPA) issued conditional approval (August 29) for previously treated locally advanced/metastatic disease.[6] A head-to-head phase III Beamion LUNG-2 (NCT06151574) is enrolling to compare zongertinib versus standard chemotherapy in the first line.

Sevabertinib: Reversible HER2 TKI With CNS Activity

SOHO-01 evaluated sevabertinib across three cohorts: D (post-line, HER2-targeting naïve; n=81), E (post-line after HER2-ADC; n=55), and F (first-line; n=73). BICR-assessed ORR values were 64% (D), 38% (E), and 71% (F); median PFS was 8.3 months (D), 5.5 months (E), and not reached (F). In cohort D, patients with baseline brain metastases achieved ORR 61%, comparable to those without (65%), and only 6% of patients without baseline brain metastases experienced intracranial progression—underscoring CNS penetration.[7]

Biomarker granularity matters: HER2 TKD mutation carriers had superior outcomes; notably, Y772_A775dupYVMA patients reached ORR 78% and median PFS 12.2 months, outperforming other TKD variants (median PFS ~7.0 months). Dominant TRAE was diarrhea (any grade up to 87%; grade 3 ranging 5–23% across cohorts), with no grade 4 events, no ILD/pneumonitis, and no discontinuations attributed to diarrhea.[7]

Taken together, with zongertinib and sevabertinib demonstrating high response rates and encouraging CNS control, HER2-mutant NSCLC is shifting from a therapeutic desert to a landscape of multiple first-line options. Next steps involve defining optimal patient selection by mutation subtype, and exploring rational sequences or combinations with antibody–drug conjugates (ADCs).[4,7]

BRAF V600E: Dual Targeting Delivers Durable Survival

Trial Signal and Design

PHAROS, a phase II single-arm study, evaluated encorafenib (BRAF inhibitor) plus binimetinib (MEK inhibitor) in advanced BRAF V600E-mutant NSCLC, enrolling distinct cohorts of treatment-naïve (n=59) and previously treated (n=39) patients. The goal was descriptive assessment of efficacy and safety across first-line and post-line settings.[8]

Long-Term Outcomes

By the 2025 analysis cut (March 14, 2025), with median follow-up approaching four years (PFS follow-up ~38.8 months; OS follow-up ~52.3 months), the regimen achieved median OS of 47.6 months and a 4-year OS rate of 49% in the frontline cohort; in previously treated patients, median OS was 22.7 months with a 31% 4-year OS rate. Median PFS reached 30.4 months (first-line) and 9.3 months (post-line)—the longest survival signals reported to date for this target in NSCLC (**Figure 1,2**). Objective responses were robust: ORR 75% and median DoR 40 months in first-line; ORR 49% post-line. These results informed regulatory approval and guideline endorsement of encorafenib + binimetinib as a frontline standard for metastatic BRAF V600E NSCLC.[8]

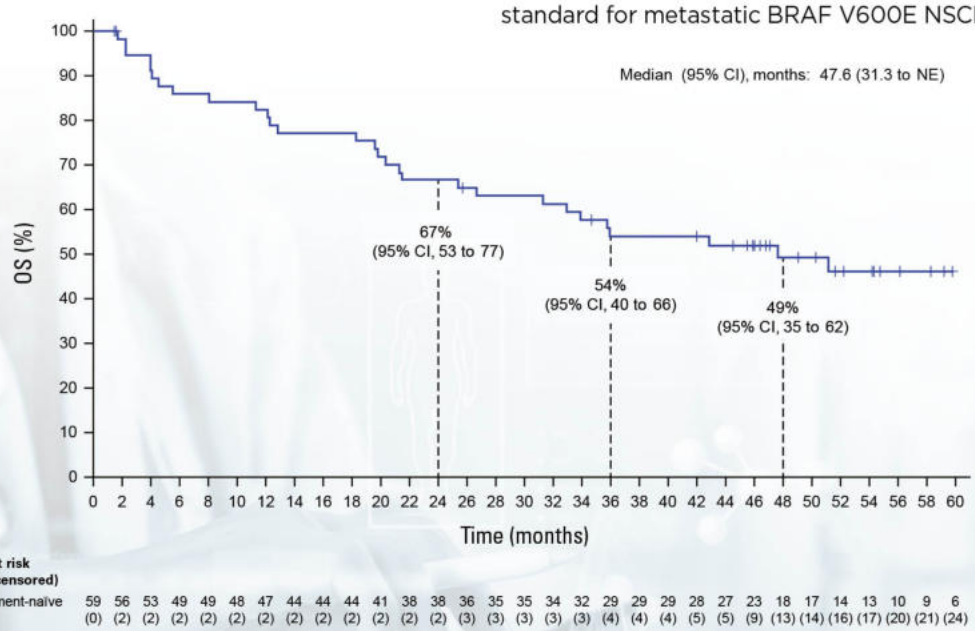


Figure 1. OS in treatment-naive patients[8]

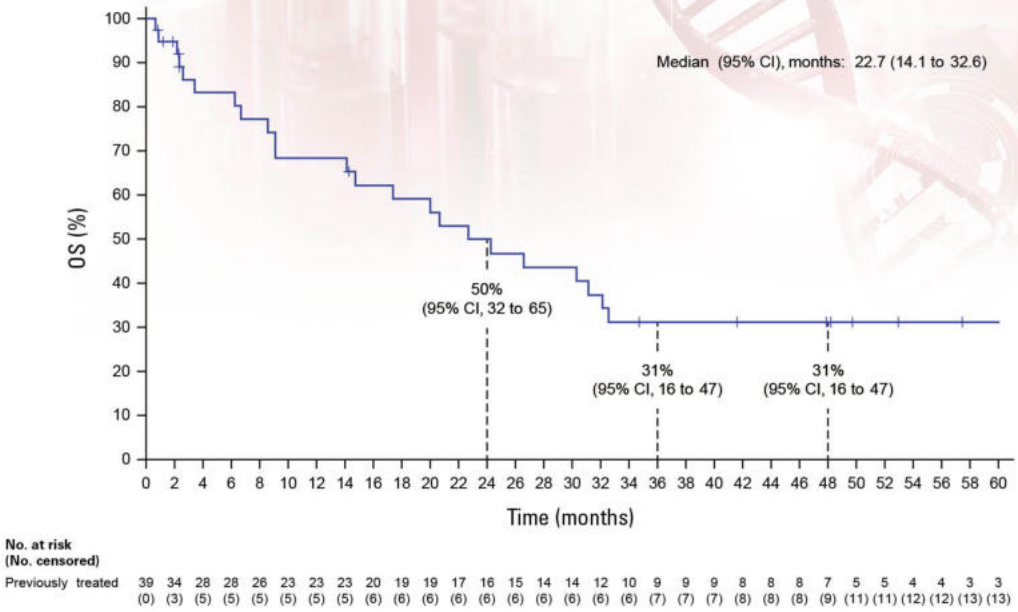


Figure 2. OS in previously treated patients[8]

Safety and Sequencing Considerations

Treatment-related adverse events (TRAEs) were manageable; common events included nausea, diarrhea, fatigue, and vomiting, with no emergent safety signals. Notably, 58% of frontline and 26% of post-line patients received subsequent systemic therapy after discontinuation, frequently immune checkpoint–based regimens or re-challenge with BRAF±MEK inhibitors—informing real-world sequencing strategies.[8]

In summary, dual BRAF/MEK inhibition sets a high durability benchmark, motivating research into resistance mechanisms and extending dual-targeted therapy into perioperative settings (neoadjuvant/adjuvant) for broader patient benefit.

Other Rare Targets: Rapid Gains and New Tools

KRAS G12D

In pretreated NSCLC, GFH375 showed promising activity: ORR 57.7% and DCR 88.5%, with enhanced outcomes at 600 mg QD (ORR 68.8%; DCR 93.8%)—a notable step against a historically "undruggable" mutation.[9]

MET Exon 14 Skipping

Dynamic ctDNA monitoring offers prognostic value. At week 4, patients achieving ctDNA clearance of MET ex14 demonstrated ORR 80%; conversely, longitudinal ctDNA positivity (≥2 positive time points) predicted early progression—supporting ctDNA as a practical tool for early on-treatment assessment.[10]

EGFR Exon 20 Insertions

For patients previously treated with amivantamab, zipalertinib achieved ORR 30% and DCR 96.7%; median DoR 14.7 months and median PFS 7.6 months, with 12-month OS 66.1%, signaling utility in subsequent lines.[11]

As a whole, the pipeline for traditionally difficult targets is diversifying, while ctDNA-based response kinetics are sharpening the precision of therapeutic evaluation.

Practical Implications: Diagnostics, Access, and Sequencing

Standardizing Detection

Rare-target identification depends on comprehensive molecular profiling. Ensuring broad NGS panels that cover BRAF, HER2 TKD variants, ROS1 fusions, KRAS G12C/G12D, MET exon 14 skipping, and EGFR exon 20 insertions is critical to unlock targeted options early—particularly in community settings where under-testing can preclude timely therapy.[12]

Access and Affordability

Regulatory approvals (e.g., zongertinib in the US and China) expand availability, but cost, reimbursement, and geographic disparities remain barriers. Strategic deployment of patient assistance programs, real-world evidence to support health-technology assessments, and regional guidelines can improve uptake.

Treatment Sequencing

Data from PHAROS, ALBATROS, and HER2 programs suggest viable post-progression strategies: immune checkpoint inhibitors or targeted re-challenge after BRAF/MEK; lorlatinib after ROS1 TKI failure; and potential HER2 TKI–ADC sequences. Formal comparative trials and prospective sequencing studies, including CNS-focused endpoints, are needed.

ctDNA-Guided Care

Early ctDNA dynamics (e.g., MET ex14 clearance at week 4) can inform on-treatment decisions—supporting treatment continuation or adjustment. Integration into routine care requires harmonized assays, defined time points, and education across care teams.[13]

Health-System Integration: Building a Rare-Target Pathway

To operationalize these gains, institutions can formalize a "rare-target pathway":[14,15]

- Comprehensive Baseline Profiling: Reflex NGS on all advanced NSCLC, including fusion panels and copy-number changes.
- Molecular Tumor Board: Rapid adjudication of rare targets, considering trial eligibility and sequencing.
- CNS Protocols: Standard brain imaging, scheduled intracranial response assessments, and targeted agents with CNS activity prioritized when relevant.
- ctDNA Monitoring: Early on-treatment (e.g., week 4) ctDNA checks for dynamic response in applicable targets like MET ex14; define thresholds and action plans.
- Access Navigation: Alignment with reimbursement pathways, clinical trial offices, and patient support programs to mitigate barriers.
- Data Capture: Real-world outcomes registries to refine sequencing and resistance strategies.

Limitations and Future Perspectives

Despite promising results, several gaps remain:

- Heterogeneity of Mutations: Even within a target class (e.g., HER2 TKD), variant-specific efficacy necessitates granular biomarker interpretation.
- Comparative Evidence: Many data derive from single-arm or cohort studies; randomized trials (e.g., Beamion LUNG-2) will solidify first-line standards.
- Real-World Generalizability: Older, comorbid patients and those with multi-site CNS disease are under-represented in trials, underscoring the value of pragmatic registries.
- Resistance Playbooks: Prospective algorithms to address acquired resistance (switching within class vs. combinatorial targeting) require validation.

Conclusion

The 2025 landscape for rare targets in NSCLC reflects tangible clinical momentum: BRAF V600E dual inhibition achieves near 4-year median survival in the frontline; HER2 TKIs (zongertinib, sevabertinib) deliver high response rates with manageable toxicity and emerging CNS activity; lorlatinib offers a compelling post-ROS1 TKI option with exceptional intracranial control; and KRAS G12C inhibitors like olomorasib demonstrate meaningful CNS responses in untreated brain metastases. Progress across KRAS G12D, MET exon 14, and EGFR exon 20 insertions further broadens the therapeutic armamentarium, while ctDNA dynamics begin to inform early treatment decisions.

Translating these gains into everyday practice demands standardized testing, equitable access, thoughtful sequencing, and integration of CNS and ctDNA-guided management. Looking ahead, priorities include rigorous randomized trials, earlier-stage applications, resistance-directed strategies, and variant-specific biomarker refinement. If pursued systematically, these directions can reshape outcomes for patients whose tumor biology previously offered few options—cementing rare-target precision therapy as a durable pillar of NSCLC care.

References

1. MMina SA, et al. Cancers. 2025; 17(3): 353. **2.** Duruisseaux M, et al. Efficacy of lorlatinib after failure of a first-line ROS1 TKI in patients with advanced ROS1-positive NSCLC: IFCT-2003 ALBATROS trial. 2025 ESMO. Abstract 5524. **3.** Cassier P, et al. Intracranial efficacy of Olomorasib in patients with KRAS G12C-mutant NSCLC and active, untreated brain metastases. 2025 ESMO. Abstract 1846MO. **4.** Popat S, et al. Zongertinib as first-line treatment in patients with advanced HER2-mutant NSCLC: Beamion LUNG-1. 2025 ESMO. LBA74. **5.** Lung Cancer Research Foundation. Zongertinib for HER2+ lung cancer. 28 August 2025. Available from: https://www.lungcancerresearchfoundation.org/sms250827/. [Accessed 25 November 2025]. **6.** Pharmaceutical Technology. China's NMPA conditionally approves Boehringer's tablets for NSCLC. 2 September 2025. Available from: https://www.pharmaceutical-technology.com/news/boehringer-nsclc-nmpa/. [Accessed 25 November 2025]. **7.** Le X, et al. Sevabertinib in advanced HER2-mutant non-small-cell lung cancer: results from the SOHO-01 study. 2025 ESMO. LBA75. **8.** Johnson ML, et al. J Clin Oncol. 2025 Oct 19:JCO2502023. doi: 10.1200/JCO-25-02023. Online ahead of print. **9.** Yoshinari T, et al. Commun Chem. 2025;8(1):254. **10.** Mazieres J, et al. Clin Lung Cancer. 2023;24(6):483-97. **11.** Dorta-Suárez M, et al. Cancer Treat Rev. 2024;124:102671. **12.** Liu X-D, et al. Heliyon . 2024;10(6):e27591. **13.** Xia Y, et al. EClinicalMedicine. 2025;81:103099. **14.** D'Aiello A, et al. Cancers (Basel). 2023;15(3):844. **15.** Kokkotou E, et al. Cancers (Basel). 2024;16(7):1414.

Join the HKDU

Hong Kong Doctors Union

The Hong Kong Doctors Union ("HKDU") is the one and only trade union specially designed for all medical doctors in Hong Kong, with the mission to fending for the welfare and rights of doctors.

About HKDU

Founded in 1966 as the "Low-Cost Clinics Doctors Management Committee" serving as the liaison body among its members, professional organisations, and the Government. With the expansion of its scope of services and professional roles, the organisation changed its name to Hong Kong Doctors Union Ltd. (HKDU) in 2000.

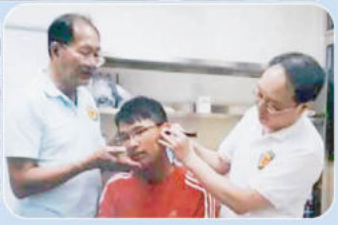
In future, the HKDU will continue humbly listening and keep on improving in our role as the channel between local medical doctors and our society.

Please join us by scanning the QR code

CME seminar in the past

Sport events for members in the 1970s

Community services



The liaison body between medical doctors and government departments

Member activities

by Michelle Lee

Optimising Long-Term Renal Health in Chronic Hepatitis B Management

Prof. Desmond Y. H. Yap
Specialist in Nephrology

Chronic Hepatitis B (CHB) remains a substantial public health burden in Hong Kong, with recent data indicating approximately 5.6% of the local population living with the infection, affecting over 410,000 individuals[1]. While antiviral therapies have significantly improved liver-related outcomes, the clinical landscape is transforming as the CHB population ages[2]. With the median age of CHB patients in Hong Kong now exceeding 50 years, this demographic shift has led to increased prevalence of comorbidities such as diabetes mellitus (DM) and chronic kidney disease (CKD)[3]. This creates a complex clinical challenge of achieving sustained viral suppression while also preserving renal function in an increasingly vulnerable population[4]. In a recent interview, Prof. Desmond Y. H. Yap, a specialist in nephrology, shared his expert perspective on optimising treatment strategies in this complex patient population.

The Evolving Challenge: An Ageing CHB Population with Comorbidities

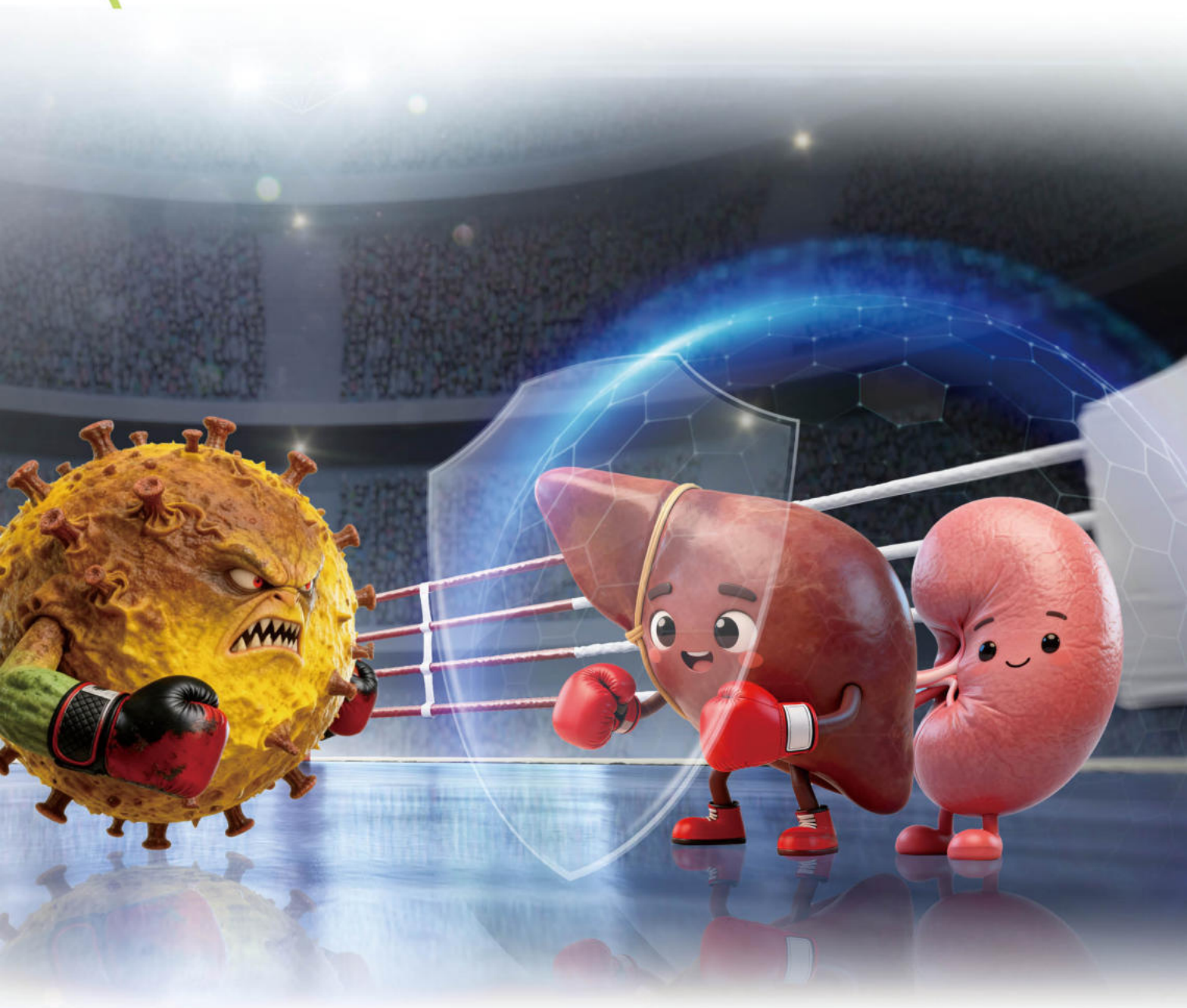
Prof. Yap explained that the clinical management of ageing CHB patients requires expanding focus beyond liver-specific complications to include antiviral-related nephrotoxicity. "We are managing a dual challenge: controlling viral replication while protecting renal function in patients who are already at risk," he noted. He emphasised that many patients now present with age-related conditions like diabetes and hypertension, which substantially increase their vulnerability to renal impairment.

This demographic challenge is underscored by data showing that CKD prevalence in CHB patients doubled with age: from 5.3% in patients aged 30-39 to 11.3% in those aged 50-59[5]. This trend, which aligns with Hong Kong's current patient profile, signals a growing burden on the healthcare system[1,5]. Real-world evidence indicates that CHB patients with concurrent comorbidities such as diabetes and hypertension have a substantially greater likelihood of developing kidney disease. The confluence of ageing chronic viral infection and these comorbidities has a synergistic effect leading to a cumulative probability of kidney disease that surpasses the additive risk from the individual factors alone[6].

Navigating Antiviral Selection: The Renal Safety Imperative

This evolving patient profile necessitates a critical re-evaluation of antiviral selection. Tenofovir disoproxil fumarate (TDF), while highly effective, has been associated with dose-dependent renal toxicity and reduced bone mineral density during long-term therapy[7,8]. This safety profile presents significant limitations for patients with existing renal risk factors.

Prof. Yap emphasised that renal safety considerations should fundamentally guide antiviral selection in



patients with comorbidities. The treatment goal is not only to suppress the virus but also to protect the patient's organs long-term, requiring careful monitoring of serum creatinine, estimated glomerular filtration rate (eGFR), proteinuria, and phosphate levels.

Crucially, emerging evidence suggests that renal impairment in this context is not necessarily irreversible. Recent studies demonstrate that timely intervention with renally safe antiviral regimens can lead to meaningful improvements in eGFR and a reduction in proteinuria[9].

A Strategy for Renal Protection: Long-Term Evidence

In response to this clinical imperative, long-term data provide strong support for Tenofovir Alafenamide (TAF). The final 8-year analysis from two global phase 3 trials, which included a majority of Asian patients, offers robust evidence for renal protection[10]. TAF's improved safety profile stems from its more targeted delivery, resulting in lower systemic tenofovir levels. This analysis demonstrated that patients receiving TAF maintained remarkable renal stability over the entire study period, with only small decline in eGFR from baseline of approximately 5 mL/min (median, ranging from 4.9 to 5.4 mL/min) after 8 years of continuous TAF treatment[10]. This minimal decrease is consistent with the expected rate of decline from normal ageing[10]. Furthermore, hip and spine bone mineral density also remained stable over the 8-year period (**Figure 1**)[10]. This sustained safety profile supports the concept of early renal protection and aligns perfectly with the goal of optimising lifelong management for the ageing CHB population in Hong Kong[10].

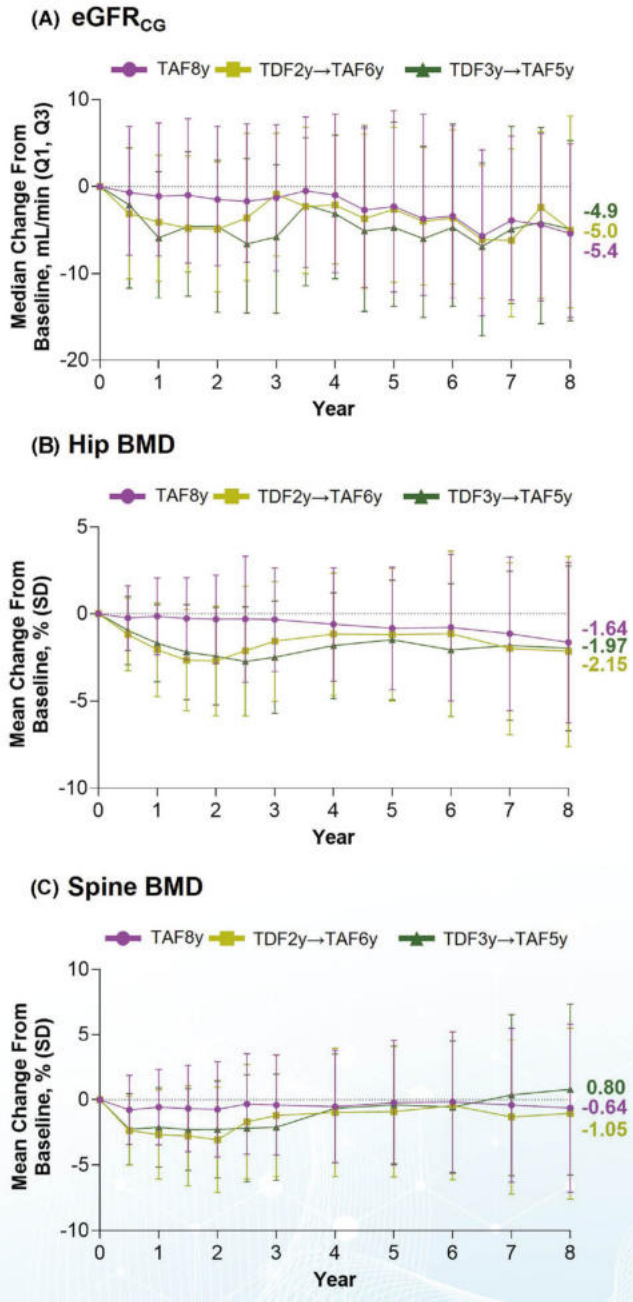


Figure 1: Pooled changes in renal and bone safety parameters over 8 years. (A) Pooled median change in $eGFR_{CG}$ (mL/min) from baseline by year. (B) Pooled mean percent change in hip BMD and (C) spine BMD from baseline by year[10]. BMD, bone mineral density; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault; Q, quartile; SD, standard deviation; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

Prof. Yap highlighted the practical advantages of this approach in routine clinical practice. "The simplified dosing of TAF across various stages of renal impairment streamlines management for most CKD patients," he stated, noting this represents a significant advantage over agents requiring complex dose adjustments and aligns with the goal of protecting renal function from the very start of therapy.

Expanding the Benefit: TAF in Special Populations

The management of CHB in kidney transplant recipients requires an antiviral strategy that meets several specific criteria for optimal patient outcomes. Prof. Yap outlines that an ideal prescription must provide effective hepatitis B virus (HBV) suppression, demonstrate low resistance rates, prevent both short- and long-term hepatic complications, and exhibit a lack of nephrotoxicity. These considerations are particularly crucial given the concurrent use of nephrotoxic immunosuppressants and the paramount importance of preserving allograft function.

Recent clinical evidence confirms the renal safety profile of TAF in this vulnerable population. A 2025 retrospective cohort study demonstrated stable serum phosphate levels over 2-year TAF treatment, with mean values remaining at 1.1 mmol/L at baseline through 12 months and showing only minimal decline to 1.0 mmol/L at 24 and 36 months. Similarly, renal allograft function remained stable, with mean eGFR maintained at 43.6 mL/min before treatment and 47.4 mL/min after 2-year TAF treatment, demonstrating no significant deterioration in renal function. Overall, this study showed that TAF provides favourable efficacy, renal safety, and tolerability in kidney transplant recipients (**Figure 2**)[11].

The European Association for the Study of the Liver (EASL) clinical practice guidelines have accordingly positioned TAF as a first-line treatment option, recognising its favourable safety profile[12]. Prof. Yap affirmed that TAF is fundamental to their management strategy, as it delivers potent antiviral control while supporting the maintenance of renal allograft function. This combination of efficacy and renal safety is critical for protecting both the liver and the transplanted organ. Furthermore, TAF may offer additional advantages for long-term management, such as a high genetic barrier to resistance that minimises concern over viral resistance, and it does not require dose adjustment based on eGFR levels[11].

Take Home Message

For an ageing CHB population like Hong Kong's, the treatment paradigm must expand beyond viral suppression to proactively preserve renal function from the outset[4]. As Prof. Yap emphasised, "Our therapeutic strategy should simultaneously target viral suppression and organ preservation." Utilising antiviral agents such

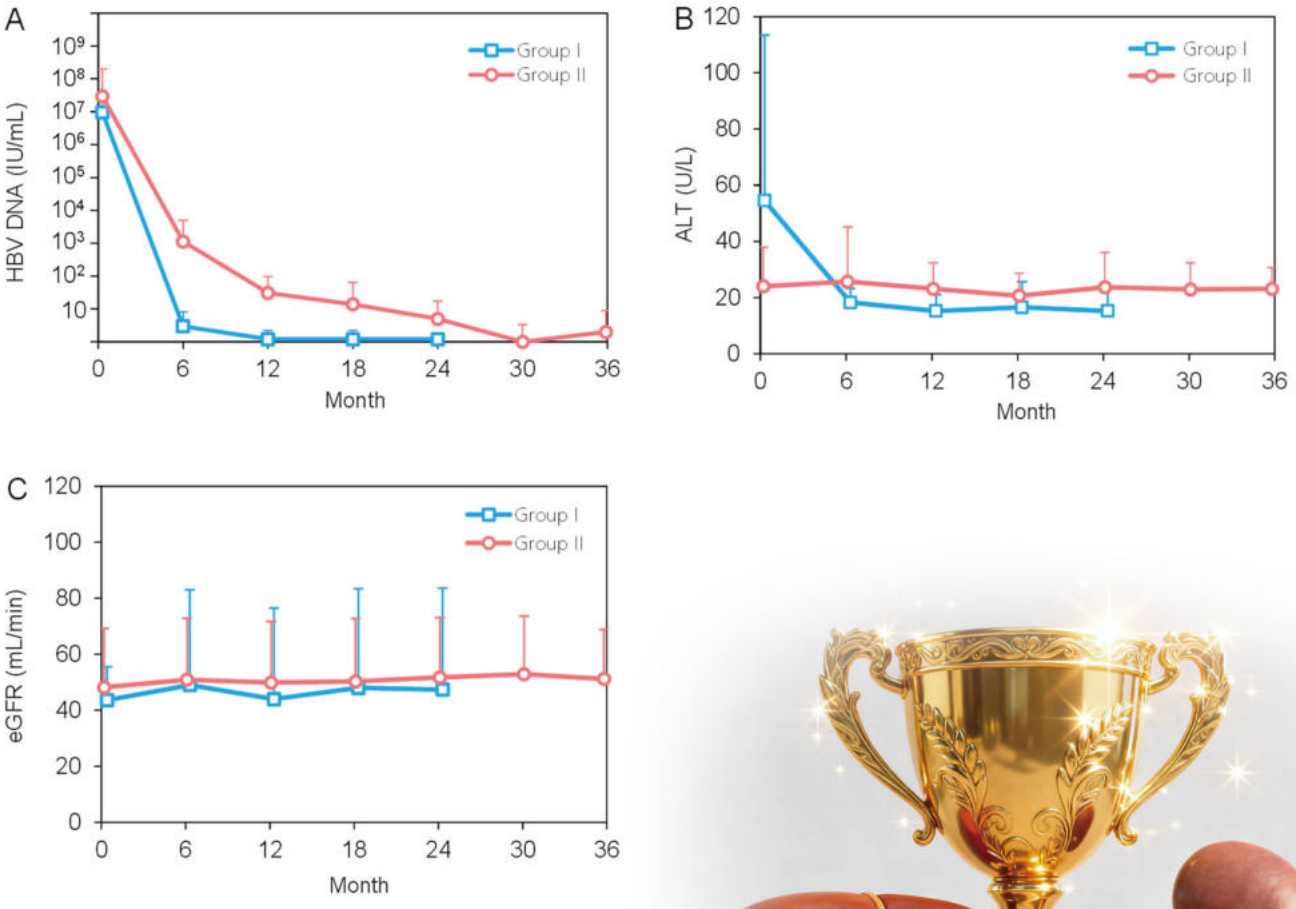


Figure 2: *Longitudinal changes in (A) HBV DNA (B) ALT levels and (C) renal allograft function in treatment-naïve (Group I) or treatment-experienced (Group II) HBsAg-positive kidney transplant recipients[11]. ALT, alanine transferase; DNA, deoxyribonucleic acid; eGFR, estimated glomerular filtration rate; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus.*

as TAF, which has demonstrated long-term renal safety profile supported by 8-year data showing minimal impact on kidney function, is fundamental to this approach[10]. This dual-protection strategy is essential for ensuring long-term patient well-being[10,11].

SCAN ME!

Scan the QR code to read more articles or visit
www.vpulsehk.com

References

1. Centre for Health Protection, Department of Health, Hong Kong SAR. Hepatitis B prevalence in Hong Kong. Available from: https://www.hepatitis.gov.hk/english/health_professionals/files/iCE_HBV_prevalence.pdf **2.** Rodríguez & Martinez, International Journal of Hepatology Research, 2024 **3.** ePulse – June 2025, Hong Kong Adventist Hospital **4.** Chen et al., BMC Gastroenterology, 2025 **5.** Ning l. apasl 2016. Poster P-0497 Abstract. **6.** Ito et al., BMC Nephrology, 2025 **7.** Liu, Z., Zhao, Z., Ma, X. et al. Renal and bone side effects of long-term use of entecavir, tenofovir disoproxil fumarate, and tenofovir alafenamide fumarate in patients with Hepatitis B: a network meta-analysis. BMC Gastroenterol. 2023;23:384. Available from: https://bmcgastroenterol.biomedcentral.com/articles/10.1186/s12876-023-03027-4 **8.** Casado JL, Bañón S, Andrés R, et al. Renal and bone toxicity with the use of tenofovir: understanding at the end. AIDS Rev. 2016;18(2):59-68. Available from: https://www.researchgate.net/publication/303787479 **9.** Ogawa E, Kohjima M, Koyanagi T, et al. Five-Year Effectiveness and Renal Safety Following Switching to Tenofovir Alafenamide in Chronic Hepatitis B Patients With Renal Impairment. J Gastroenterol Hepatol. 2025;40(10):2560-2567.Available from: https://aasldpubs.onlinelibrary.wiley.com/doi/10.1002/hep.31793 **10.** Buti M, et al. Aliment Pharmacol Ther. 2024;60(11-12):1573-1586. **11.** Desmond Y.H. YAP, et al, Biomedical Journal. 2025;100833. https://doi.org/10.1016/j.bj.2025.100833. **12.** European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol. 2025;83(2):502-583. Available from: https://www.hepb.org/assets/Uploads/EASL-guidelines-May-2025.pdf

by Dr. Feng Xue

Navigating Management of Low-Grade NHLs

Recent Advances in CLL/SLL Treatment

Dr. Chandramouli Nagarajan

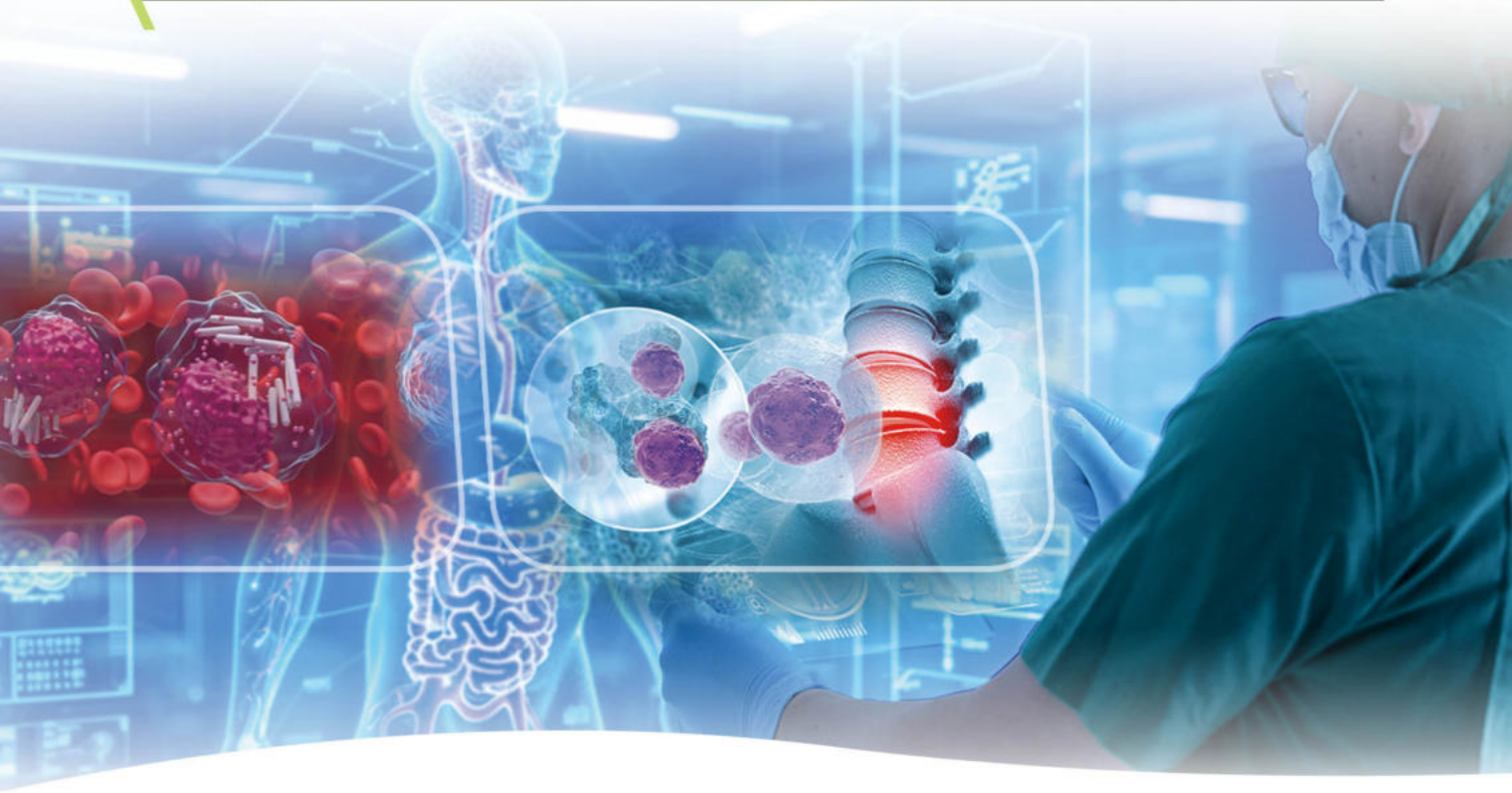
Senior Consultant Haematologist and Transplant Physician
Department of Haematology
SingHealth Duke-NUS Blood Cancer Center,
Singapore General Hospital and National Cancer,
Singapore

CLL (chronic lymphocytic leukemia) and SLL (small lymphocytic lymphoma) are of the same disease. But, in CLL cancer cells are mostly found in the blood and bone marrow; while in SLL cancer cells are mostly found in the lymph nodes. CLL/SLL belongs to a group of blood cancers known as non-Hodgkin lymphoma (NHL).[1] According to the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute in the United States, CLL is a disease primarily affecting older adults; the median age at diagnosis is 70 years. The age-adjusted incidence was 4.6 per 100,000 inhabitants per year. The 5-year relative survival was 65.1% in 1975 and has steadily increased over the past decades; it is estimated at 88.5% in 2024.[2] Only patients with active or symptomatic disease or with advanced Binet or Rai stages require therapy. When treatment is indicated, several therapeutic options exist, including monotherapy with one of the inhibitors of Bruton tyrosine kinase (BTK).[2] To understand the recent development in CLL/SLL management and provide an updated guide for therapeutic decisions in daily practice, at a recent symposium in Hong Kong, Dr. Nagarajan, a renowned hematologist in Singapore, was invited to share latest research findings on CLL therapy innovations.

Introduction

Due to the advancements in our understanding of CLL's pathogenesis, the management of the disease continues to experience significant and meaningful improvements. Chemoimmunotherapies have already improved overall survival when used as first-line therapy. More recently, specific inhibitors interrupting important pathways for CLL cell survival, such as BTK, have now replaced chemoimmunotherapy in first- and second-line settings.[2,3]

Dr. Nagarajan stated that BTK inhibitors have become a new and very active class of therapeutic agents in B-cell malignancies.[4] According to Dr. Nagarajan, newer-generation BTK inhibitors have demonstrated improved safety and efficacy versus their predecessors due to key differences in their mechanism of action. For example, although ibrutinib, a first-generation BTK inhibitor, changed the treatment landscape of CLL, cardiovascular toxicity limited its use.[5] Ibrutinib is generally considered as an irreversible inhibitor. However, in certain scenarios, notably with the acquisition of specific mutations like C481S, it can become reversible[6]. In contrast, zanubrutinib, an irreversible second-generation BTK inhibitor, is designed to maximize BTK occupancy and demonstrate less off-target kinase inhibition than ibrutinib.[2,7] Complete/sustained BTK occupancy may improve efficacy outcomes and increased BTK specificity may minimize toxicities related to off-target inhibition, Dr. Nagarajan stressed.[7] In addition, among the approved BTK inhibitors, zanubrutinib is less prone to pharmacokinetic modulation, leading to more consistent, sustained therapeutic exposures and enhanced dosing convenience. This can be translated into durable responses and improved safety, representing an important new treatment option for patients who benefit from BTK therapy.[8]



Various biological and genetic markers provide additional prognostic information. Deletions of the short arm of chromosome 17 — del(17p) and/or mutations of the TP53 gene predict a shorter time to progression with most targeted therapies.[2] Among CLL patients with a del(17p), a TP53 mutation, or both, those treated with zanubrutinib demonstrated longer progression-free survival (PFS) compared to those receiving ibrutinib.[9] Furthermore, in the Arm D of the SEQUOIA study (where treatment-naïve patients with CLL/SLL received zanubrutinib from cycle 1 and venetoclax from cycle 4 [ramp-up] to cycle 28, followed by continuous zanubrutinib monotherapy until disease progression, unacceptable toxicity, or meeting undetectable minimal residual disease [uMRD]-guided stopping criteria), the 24-month PFS rate achieved in patients with the del(17p)/TP53 mutation was comparable to that in patients without.[10] As a result, zanubrutinib has been recommended as a preferred regimen regardless of the del(17p)/TP53 mutation status in the first-line setting for CLL/SLL in the National Comprehensive Cancer Network (NCCN) guidelines.[11]

Clinical Research Evidence

Dr. Nagarajan then presented some clinical data derived from zanubrutinib-related research. The ALPINE Phase 3 study was designed to perform a head-to-head comparison between zanubrutinib and ibrutinib in patients with relapsed/refractory CLL. After a median follow-up of 29.6 months, the results indicated that zanubrutinib was superior to ibrutinib in terms of PFS. At 24 months, the investigator-assessed PFS rates were 78.4% for zanubrutinib and 65.9% for ibrutinib; and as mentioned earlier, in patients with a del(17p), a TP53 mutation, or both, those treated with zanubrutinib demonstrated longer PFS compared to those receiving ibrutinib (**Figure 1**). Additionally, PFS rates consistently favored zanubrutinib across other major subgroups. The safety profile of zanubrutinib was also better than that of ibrutinib, with fewer adverse events leading to treatment discontinuation and a lower incidence of cardiac events, including those that resulted in treatment discontinuation or death.[9]

Another Phase 3 study SEQUOIA was an open-label trial that compared zanubrutinib and bendamustine plus rituximab (BR) in treatment-naïve patients with CLL/SLL. The initial prespecified analysis (median follow-up 26.2 months) and subsequent analysis (43.7 months) revealed superior PFS (primary end point) in the zanubrutinib group compared with BR. At a

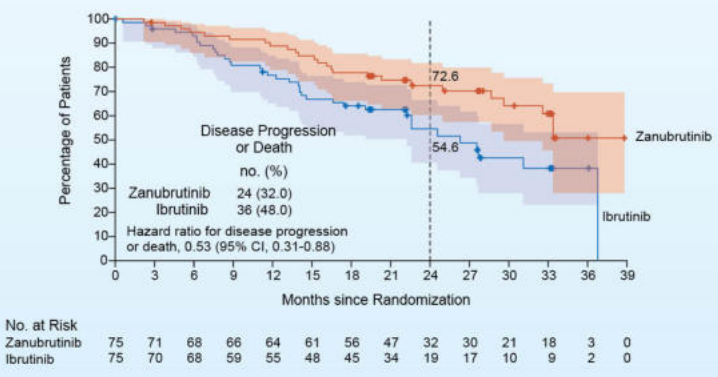


Figure 1: PFS in patients with a del(17p), a TP53 mutation, or both[9]

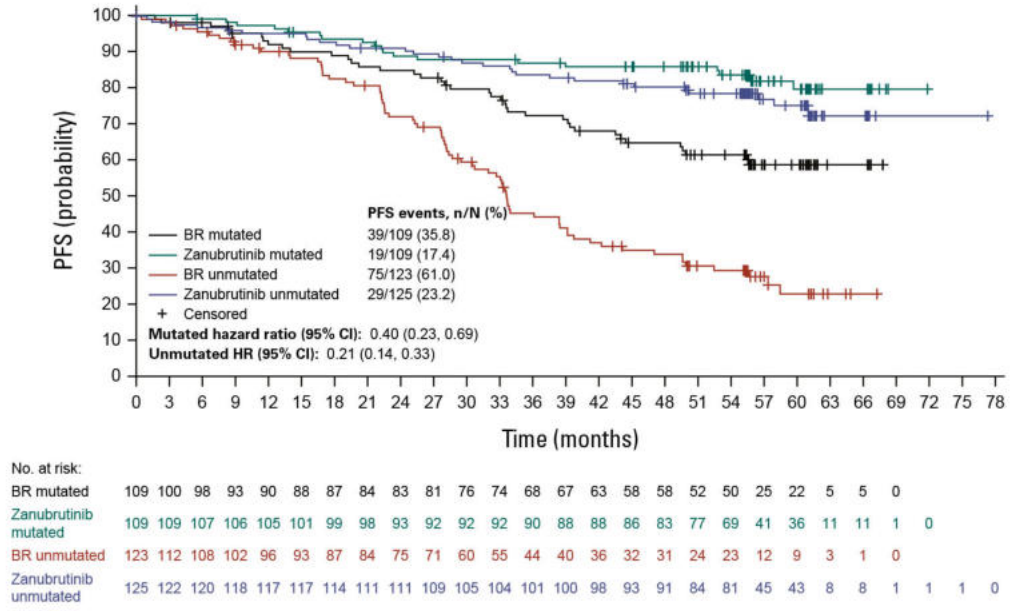


Figure 2: PFS in patients with mutated and unmutated IGHV genes[12]

median follow-up of 61.2 months, median PFS was not reached in zanubrutinib-treated patients; and median PFS was 44.1 months in BR-treated patients (hazard ratio [HR], 0.29; one-sided P = 0.0001). Prolonged PFS was observed with zanubrutinib versus BR in patients (**Figure 2**) with mutated immunoglobulin heavy-chain variable region (IGHV) genes (HR, 0.40; 95% confidence interval [CI], 0.23 to 0.69; one-sided P = 0.0003) and unmutated IGHV genes (HR, 0.21; 95% CI, 0.14 to 0.33; one-sided P < 0.0001). Median overall survival (OS) was not reached in either of the treatment arms. No new safety signals were detected.[12]

Also as mentioned earlier, according to a recent analysis of the Arm D of SEQUOIA (a non-randomized cohort of patients aged 65 years and older, or 18-64 years with comorbidities), regardless of del(17p)/TP53 mutational status, similar 24-month PFS rates were observed (94% in patients with TP53-aberrant disease and 89% in patients without TP53-aberrant disease), indicating the effectiveness of zanubrutinib across these genetic risk factors (**Figure 3**).[10]

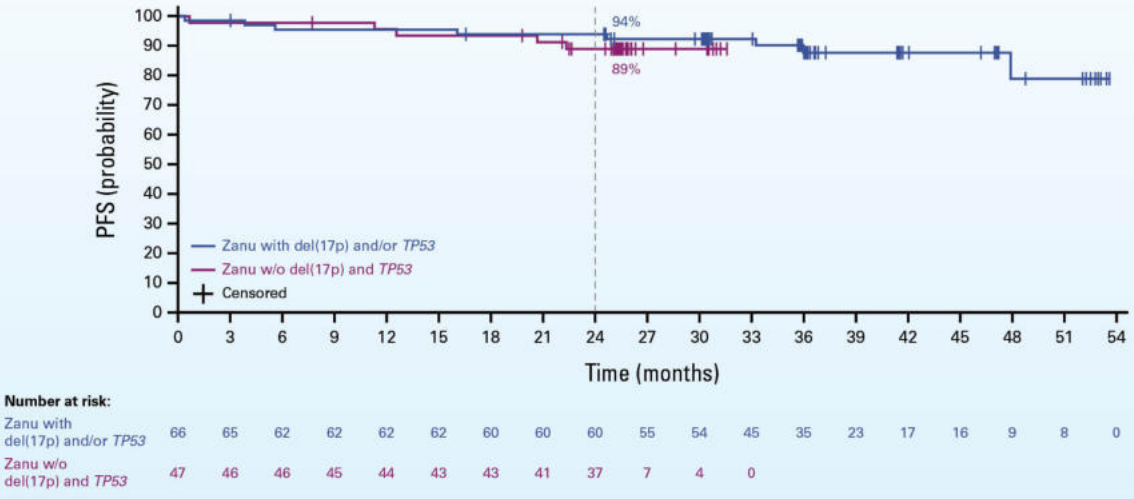


Figure 3: PFS in patients with and without the del(17p)/TP53 mutation[10]

Case Presentation

Dr. Nagarajan then presented a case to illustrate how advances in targeted therapies—specifically second-generation BTK inhibitors—were reshaping the treatment landscape for CLL.

Background Information

- 81-year-old male in 2019; T2DM with retinopathy, albuminuria, gall stones, fatty liver with transaminitis, BPH, HTN, HLD
- ED (Aug 2019): Symptomatic anemia and raised TWC with smear cells
- FBC: Hb 3.8; WBC 41.0; platelets 240; ALC 37.8 - Atypical lymphocytes and few smear cells seen
- Haptoglobin <0.1, LDH 809, total bilirubin 12, direct bilirubin 2, reticulocyte count 0.23
- B12, folate normal; thyroid functions normal; DAT 3+ (C3d, IgG 3+), suggesting the potential for AIHA
- Peripheral blood flow: Expanded population of atypical B-lymphocytes (69.94%), characterized by CD19+, CD5+, CD20w+, CD10-, CD38-, CD43 dim+, CD23 partial+, CD200+, CD45+, kappa light chain restricted. The findings were consistent with the diagnosis of B-LPD, favoring CLL
- Started 1mg / kg prednisolone + AcV and sulfamethoxazole/trimethoprim prophylaxis

Case Vignette

- IGHV mutation frequency: 1.40% (Unmutated)
- FISH for CLL: Negative
- Karyotyping: 46,XY, t(5;14)(q35;q11.2), inv(9)(p11q13) - Normal human variant
- Modified Rai I; Binet B Stage
- Watched and waited for CLL; but on tapering doses of steroids as AIHA was controlled (<10mg /day)
- Increasing ALC and downtrending platelets
- CT (performed in 2021 prior to treatment): Multiple areas of abdominal adenopathy and splenomegaly

Treatment

- 84-year-old male with unmuted CLL in 2021
- Commenced ibrutinib 420 mg OM
- Hb improved, WBC and ALC normalized

Ongoing Management

- 2022: Chest pain - MIBI showed mild ischemia, commenced on aspirin
- Zanubrutinib approval in Singapore in 2023
- Switched to zanubrutinib 160mg BID
- No neutropenia
- No CVS effects
- Mild peripheral bruising; No mucosal / orificial bleeding
- Well controlled HTN on bisoprolol

The patient case illustrated the benefits of zanabrutinib in managing CLL, including reduced cardiotoxicity and a lower risk of major hemorrhage versus ibrutinib.[7] During the discussion, Dr. Nagarajan also mentioned the challenges of using together BTK inhibitors and dual antiplatelet therapy (DAPT), which may increase bleeding risk, especially in patients on BTK inhibitors who also require DAPT after percutaneous coronary intervention.[13]

Conclusion

In conclusion, the management of CLL has been markedly transformed by a deeper understanding of its pathogenesis and the emergence of targeted therapies. Chemoimmunotherapy once served as the backbone of first-line treatment, but the rise of BTK inhibitors—particularly second-generation agents like zanubrutinib—has redefined clinical outcomes through improved efficacy and safety profiles. As highlighted by Dr. Nagarajan, zanubrutinib offers enhanced BTK occupancy with reduced off-target effects and pharmacokinetic variability, leading to consistent therapeutic benefits and a favorable toxicity profile. Clinical trials such as ALPINE and SEQUOIA have further validated zanubrutinib's superiority over older therapies, including ibrutinib and BR, across diverse patient populations and genetic subtypes, including high-risk features like del(17p)/TP53 mutations. The integration of these findings into international guidelines positions zanubrutinib as a preferred first-line option, marking a significant advancement in individualized treatment and long-term disease control for untreated patients with CLL/SLL.

References

1. NIH National Cancer Institute. NCI Dictionary of Cancer Terms: CLL/SLL. Available from: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/cll-sll. [Accessed 2 June 2025]. **2.** Hallek M. Am J Hematol. 2025;100(3):450–80. **3.** Jaglowski S and Jones JA. Expert Rev Anticancer Ther. 2011;11(9):1379–90. **4.** Wen T, et al. Leukemia. 2021; 35: 312–32. **5.** Ke L, et al. Front Pharmacol. 2024;15:1413985. **6.** Woyach JA, et al. N Engl J Med. 2014;370(24):2286–94. **7.** Hillmen P, et al. J Clin Oncol. 2023;41(5):1035–45. **8.** Tam CS, et al. Expert Rev Clin Pharmacol. 2021;14(11):1329–44. **9.** Brown JR, et al. N Engl J Med. 2023;388(4):319–32. **10.** Shadman M, et al. J Clin Oncol. 2025; 43(21):2409–17. **11.** NCCN Guidelines. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 3.2025. **12.** Shadman M, et al. J Clin Oncol. 2025;43(7):780–7. **13.** Mendez-Ruiz A, et al. J Soc Cardiovasc Angiogr Interv. 2023;2(3):100608.

by Dr. Feng Xue

HIV/AIDS Care Advance

Road to Cure: From Daily Management to Long-Acting Prevention and Immune-Guided Remission

Global human immunodeficiency virus (HIV) control has accelerated, yet uneven access and financing shocks threaten recent gains. In 2024, an estimated 40.8 million people were living with HIV; 77% received antiretroviral therapy (ART) and 73% had suppressed viral loads—contributing to dramatic reductions in new infections and deaths since 2010.[1] At the same time, innovation has shifted from daily management toward lighter, longer-acting regimens and credible steps towards cure. Twice-yearly lenacapavir for pre-exposure prophylaxis (PrEP) gained regulatory approvals in 2025 after exceptional trial efficacy, while Cabenuva (cabotegravir/rilpivirine) expanded monthly or every-other-month treatment options with real-world effectiveness. Immune-based strategies—including broadly neutralizing antibodies (bNAbs) paired with lenacapavir, CRISPR gene editing, and mRNA latency reversal—are advancing, moving cure research from concept to cautious human studies. Yet UNAIDS warns that 2025 funding shocks are disrupting prevention programs, underscoring an urgent need for sustainable financing.[2] This article synthesizes the latest global statistics, long-acting tools, cure-oriented science, patient-centered formulations, and access realities—ending with a discussion of health policy and financing.

Global HIV/AIDS Epidemiology Update

At the end of 2024, the world counted 40.8 million people living with HIV (PLHIV). ART coverage reached 31.6 million (77%), and 73% of PLHIV achieved viral suppression. New HIV infections fell by 40% since 2010; and acquired immunodeficiency syndrome (AIDS)-related deaths dropped by 54% (from 1.4 million to 630,000). Compared to the peak in 2004, the global HIV epidemic claimed 70% fewer lives in 2024 — landmarks achieved through testing, treatment scale-up, and prevention (**Figure 1**).[1]

These gains coexist with significant regional contrasts. For example, China saw a 15-fold rise in newly reported cases between 2005 and 2019. While HIV/AIDS-related deaths in China rose more modestly—by 25%, from 40,711 in 2005 to 51,250 in 2019—this slower growth may be largely attributed to improved access to antiretroviral drugs. Nevertheless, China continues to face significant challenges in curbing transmission and managing the evolving epidemic.[3]

Although substantial progress has been achieved, enduring challenges underscore the need for transformative treatment strategies and integrated health policy frameworks to accelerate the path toward an HIV cure.

The Prevention Revolution: Twice-Yearly Lenacapavir and More

Lenacapavir (twice-yearly PrEP)

In June 2025, the U.S. FDA approved lenacapavir as the first twice-yearly injectable PrEP, backed by PURPOSE 1 and PURPOSE 2 phase-3 trials that demonstrated near-complete protection when administered as directed.[4,5] WHO welcomed the approval and issued global guidelines in July 2025 recommending lenacapavir as an additional PrEP option, highlighting its potential to overcome adherence barriers.[6]

Roll-outs followed in several countries, with WHO prequalification and national fast-track authorizations enabling access, particularly across parts of Africa. Early implementation has underscored both transformative potential and urgent affordability/financing questions, given funding disruptions and price debates.[7]

What makes lenacapavir different? Two subcutaneous injections every six months, preceded by a brief oral loading dose, can initiate protection rapidly; high adherence is achievable because the regimen minimizes clinic touchpoints—an advantage for people who struggle with daily oral PrEP.[8,9]

Cabotegravir for PrEP (CAB-LA) and the expanding toolkit

Long-acting cabotegravir for PrEP laid critical groundwork for injectable prevention from 2021 onward, and manufacturers have tripled supply commitments for low- and middle-income countries in 2025–2026, under not-for-profit pricing in prioritized geographies. These actions complement lenacapavir's entry, broadening choices across daily, bi-monthly, and twice-yearly models of prevention.[10]

Long-Acting Treatment: Matching Efficacy, Easing Life

Cabenuva (cabotegravir/rilpivirine)

For treatment, Cabenuva enables monthly or every-other-month injections as a complete regimen for virologically suppressed patients aged ≥12 years—with dosing schedules validated in labeling and guidance. Clinical experience shows comparable safety and effectiveness across dosing intervals and practical pathways for missed injections—key for real-world continuity.[11]

Six-monthly combinations in development

To reach twice-yearly treatment, developers are pairing lenacapavir with bNAbs. Phase-2 studies presented at CROI 2025 and EACS 2025 indicate that lenacapavir + teropavimab + zinlirvimab can maintain suppression in carefully selected, bNAb-sensitive patients—hinting at future six-monthly regimens if resistance screening, dosing optimization, and access logistics are solved.[12]

Cure Research and Immune-Based Strategies: Credible First Steps

Broadly neutralizing antibodies (bNAbs)

bNAbs target conserved regions of HIV's envelope, neutralizing diverse strains. Recent clinical studies report post-intervention control for subsets of participants after pausing ART, implicating stem-like CD8+ T-cell qualities that synergize with antibody therapy. These results—though not generalized yet—validate a path toward functional remission supported by immune mechanisms.[13]

Gene editing (CRISPR)

Early human trials (e.g., EBT-101) using CRISPR-Cas systems to target integrated proviral DNA show promising safety and on-target activity; while viral rebound occurred after ART interruption in most participants, delayed rebound and reservoir decreases in at least one case encourage next-generation vectors and improved delivery. Parallel laboratory advances continue to demonstrate excision of HIV DNA from infected cells and protection against reinfection, setting the stage for safer, scalable delivery strategies.[14]

mRNA and latency reversal

A major barrier to cure is the latent reservoir in resting CD4+ T cells. In 2025, researchers demonstrated efficient mRNA-lipid nanoparticle (LNP) delivery to these cells (LNP X), using Tat mRNA to awaken latent virus ex vivo—without broad cell activation. This approach also carried CRISPR activation machinery, opening precision "kick-and-kill" strategies that could pair with immune clearance. Prior studies showed synergy between Tat mRNA and classical latency-reversing agents, reinforcing combination logic for future trials.[15]

Taken together, cure research is multi-pronged—antibodies, cellular immunity, gene editing, and mRNA

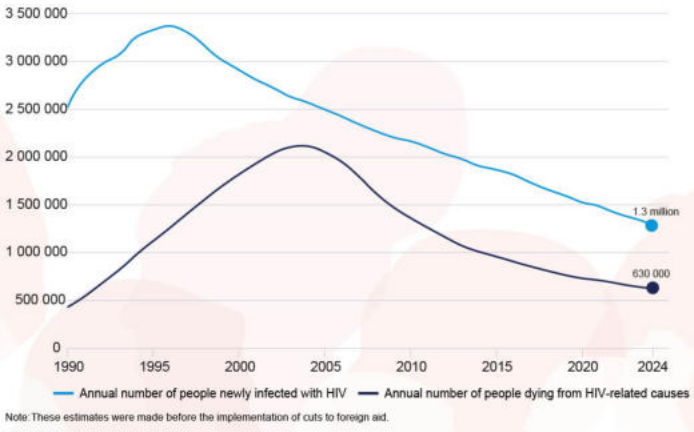


Figure 1: Global trends in people acquiring HIV and people dying from HIV-related causes (1990–2024)[1]

platforms—progressing from proof-of-concept toward cautious human experimentation. None is ready for routine care, but together they are shifting the horizon from indefinite daily management to durable remission strategies.

Access and Equity: The Promise and the Achilles' Heel

UNAIDS warns that 2025 funding cuts triggered a global prevention crisis, with projected 30–40% declines in external health assistance and widespread closures of community-led services. Without rapid policy and financing fixes, models project millions of additional infections and deaths by 2029. United Nations reporting notes some countries are increasing domestic budgets, but these efforts cannot fully replace long-standing international support; the call is for renewed solidarity to avoid reversing gains.[2]

On the innovation side, WHO and partners are using prequalification and collaborative registration procedures to accelerate access to long-acting lenacapavir; foundations and procurement mechanisms are negotiating generic pathways aiming for ~$40/year pricing from 2027 across >100 countries—still with gaps for middle-income settings. Similarly, CAB-LA supply expansions target high-burden regions through not-for-profit pricing and voluntary licenses.[6]

The science is ready to transform prevention and lighten treatment. Only fair pricing, sustainable financing, and community-centered delivery can ensure these tools reach those most at risk.

Policy and Financing: What Systems Must Do Next

- Bridge the funding gap: Reconstitute international assistance for prevention and community services to avert projected backsliding.
- Accelerate regulatory harmonization: Use WHO prequalification and collaborative registration to speed safe access to lenacapavir and future long-acting regimens.
- Advance equitable pricing: Support generic pathways with fair price targets and expand to middle-income settings that often face exclusion despite high burden.
- Invest in cure research: Sustain funding for bNAb, CRISPR, and mRNA platforms and for combination immunotherapies that aim for ART-free remission, moving from small trials to pragmatic studies.

Conclusion

The HIV response stands at a transformative juncture. By 2024, global metrics showed formidable progress in treatment coverage, viral suppression, and declines in infections and deaths. In 2025, science delivered twice-yearly PrEP and promising six-monthly treatment combinations, alongside immune-guided remission signals from bNAbs, first-in-human CRISPR efforts, and mRNA-based latency reversal. The arc is bending from daily management to long-acting, closer-to-cure strategies.

But innovation will matter only if access keeps pace. The 2025 funding crisis is a stark reminder: without solidarity, sustainable financing, and fair pricing, lifesaving advances can remain out of reach, threatening to reverse hard-won gains. The road to cure is not just scientific; it is political and operational.

For individuals, the next steps can be personal and practical: ask about long-acting options, review clinic schedules, and weigh PrEP choices—including whether twice-yearly lenacapavir or bi-monthly cabotegravir align with your life. For health systems and funders, the mandate is clear: protect prevention, scale equitable access, and invest in the cure pipeline. If we meet those commitments, the coming decade can deliver lighter care today and durable remission tomorrow—a road to cure that is credible, inclusive, and within reach.

Scan the QR code to read more articles or visit
www.vpulsehk.com

Reference

1. WHO. HIV statistics, globally and by WHO region, 2025. Available from: https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/who-ias-hiv-statistics_2025-new.pdf. [Accessed 25 November 2025]. **2.** UNAIDS. UNAIDS releases its 2025 World AIDS Day report: Overcoming disruption, transforming the AIDS response. 25 November 2025. Available from: https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2025/november/wad-2025-report. [Accessed 3 December 2025]. **3.** Xu JJ, et al. Chin Med J (Engl). 2021;134(23):2799–809. **4.** Bekker L-G, et al. N Engl J Med. 2024;391(13):1179–92. **5.** Kelley CF, et al. N Engl J Med. 2025;392(13):1261–76. **6.** PrEP Watch. Guidelines on Lenacapavir for HIV Prevention and Testing Strategies for Long-Acting Injectable Pre-Exposure Prophylaxis. 18 July 2025. Available from: https://www.prepwatch.org/resources/guidelines-on-lenacapavir-for-hiv-prevention-and-testing-strategies-for-long-acting-injectable-pre-exposure-prophylaxis/. [Accessed 25 November 2025]. **7.** Adepoju VA, et al. Int J Equity Health. 2025;24(1):270. **8.** Sah S, et al. J Int Assoc Provid AIDS Care. 2025 Nov 11;24:23259582251390622. **9.** Zhang J, et al. Lancet HIV. 2022;9(4):e254–e268. **10.** Jamieson L, et al. Lancet HIV. 2022;9(12):e857–e867. **11.** Pinto RM, et al. J Assoc Nurses AIDS Care. 2023;34(2):216–20. **12.** Eron JJ, et al. J Infect Dis. 2025 ;231(6):1440–4. **13.** Liu Y, et al. Emerg Microbes Infect. 2020;9(1):194–206. **14.** Hussein M, et al. Int J Mol Sci. 2023;24(2):1563. **15.** Cevaal PM, et al. Nat Commun. 2025;16(1):4979.

PULSE

The V.Pulse APP
Now Available !

Register today to access articles of Medical Breakthroughs, CME and Event Schedule...

Free Coffee Coupon

For new members who **successfully register** via the V.Pulse app, please **send your registration no. and the screenshot of V.Pulse app in your devices to enquiry@vital-base.com** to redeem your HK$50 coffee coupon as a token of our gratitude for your support !

Download V.Pulse App today at

GET IN ON Google Play

Download on the App Store

by Michelle Lee

The Hidden Health Cost of Dining Out

The habit of consuming meals prepared away from home is increasingly common in urban environments like Hong Kong. A large-scale prospective cohort study provides compelling evidence that a high frequency of eating meals prepared outside the home is significantly associated with an increased risk of death from all causes. While associations with cardiovascular and cancer-specific mortality require further investigation, the findings underscore an important public health consideration. This article reviews the context of dining out in Hong Kong, summarises the key evidence linking it to mortality risk, and explores potential strategies for mitigation aimed at healthcare professionals.

The Dining Out Culture in Hong Kong

Hong Kong is a city renowned for its vibrant culinary scene and fast-paced lifestyle. A confluence of factors drives the high frequency of dining out among its residents. Long working hours and extensive commuting times often leave little opportunity for meal preparation at home. The dense urban environment offers unparalleled convenience with a vast array of dining options from quick service restaurants and cha chaan teng (Hong Kong-style café) to high-end establishments at nearly every corner. Furthermore, smaller living spaces in many households can make cooking and storing groceries less practical. This cultural and socioeconomic landscape has made consuming meals away from home a norm rather than an exception for a large segment of the population.

Evidence Linking Away-from-Home Meals to Mortality

The relationship between frequent consumption of meals prepared away from home and health outcomes has been systematically examined in major studies. A key investigation analysed data from over 35,000 American adults followed for nearly two decades. The study accounted for variables including age, sex, socioeconomic status, dietary quality, lifestyle factors, and body mass index. The results revealed that participants who consumed two or more meals prepared away from home per day had 49% higher risk of death from any cause compared to those who ate such meals less than once per week (**Figure. 1**).

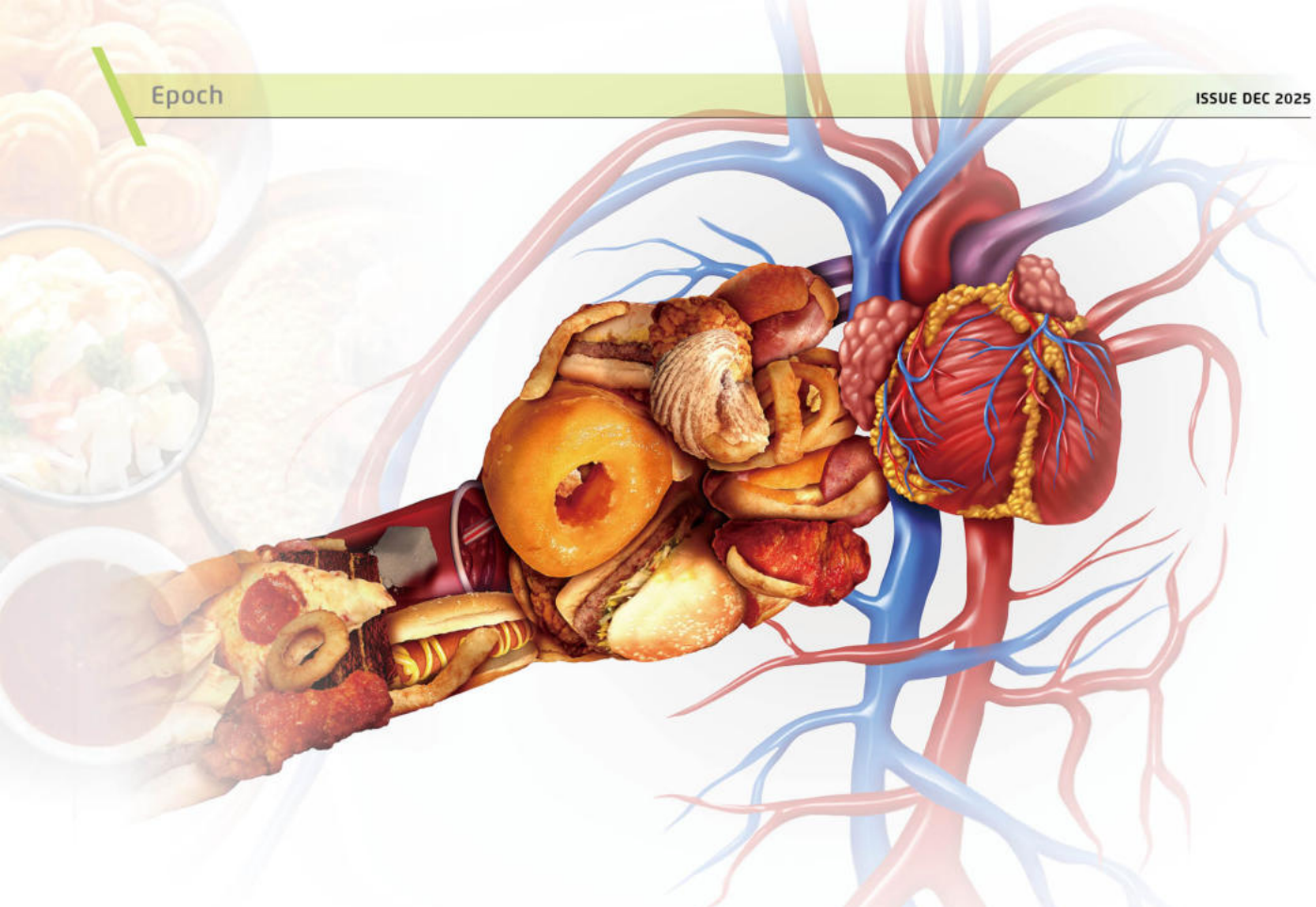
This elevated risk can be attributed to several nutritional and environmental factors. Meals prepared away from home are consistently documented to be higher in energy density, saturated fat, and sodium while being lower in dietary fibre, fruits, vegetables, and whole grains. This nutritional profile aligns with known risk factors for chronic diseases. Additionally, the overall dietary quality, as measured by indices like the Healthy Eating Index, is generally lower for food consumed away from home. Beyond nutrition, some research suggests exposure to certain chemicals like phthalates may be higher when dining out, which could pose additional health risks. The study also noted that the association with all-cause mortality appeared stronger among individuals with lower family incomes, highlighting a potential disparity in access to healthy food or choices when eating out.

Regarding cause-specific mortality, the same study found hazard ratios of 1.18 for cardiovascular mortality and 1.67 for cancer mortality for the most frequent consumers of away-from-home meals. However, these results were not statistically significant, likely due to the smaller number of specific cause deaths. This indicates a clear need for more research with larger sample sizes and longer follow-up to definitively establish these links.

Strategies for Risk Mitigation and Public Health Action

For healthcare professionals in Hong Kong, these findings present an opportunity to guide patients toward healthier lifestyles without demanding an unattainable complete avoidance of dining out. The goal should be a reduction in frequency and an improvement in the quality of choices when meals are consumed away from home.

Public education is paramount. Patients can be encouraged to view dining out as an occasional treat rather than a daily routine. Practical advice can include reviewing menus online beforehand to identify healthier options, prioritising dishes that are steamed, boiled, or



grilled over those that are deep fried or heavily sauced, and requesting for sauces and dressings to be served on the side. Increasing the consumption of vegetables and whole grains with each away-from-home meal can also help improve dietary balance.

At a broader policy level, there is a role for initiatives that improve the nutritional quality of food served in restaurants. While menu labelling laws that require calorie and nutrient information on most prepackaged foods have been implemented in Hong Kong, their effectiveness can be limited if consumers do not notice or understand the labels. More impactful may be government-led partnerships with the food and restaurant industry to reformulate recipes, reducing sodium, saturated fats, and sugars in commonly offered dishes. Subsidies or support for restaurants that incorporate healthier ingredients and cooking methods could also foster a more health-conscious food environment.

Frequency of Eating Out	Hazard Ratio (HR) for Death from Any Cause
<1 time/week	1.00 (Reference)
1-3 times/week	1.04 (Not Significant)
4-6 times/week	0.90 (Not Significant)
7-13 times/week	0.85 (Not Significant)
≥2 times/DAY	**1.49 (95% CI: 1.05 - 2.13)**

Figure 1: Association of frequency of eating meals prepared away from home with all-cause mortality among US adults from 1999-2014.

Conclusion

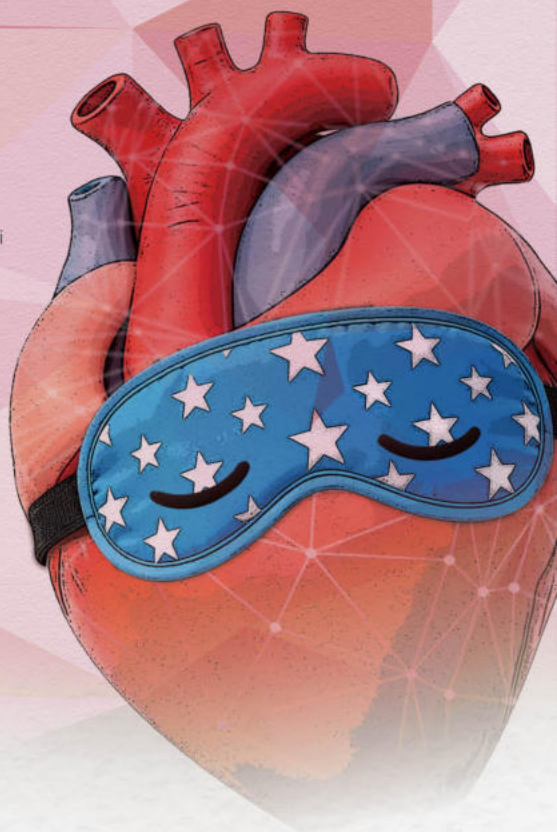
The convenience of meals prepared away from home is an integral part of modern life in Hong Kong. However, emerging evidence signals that over-reliance on this practice carries a tangible risk, notably an increased likelihood of all-cause mortality. While the connections to specific causes of death like cardiovascular disease and cancer are still being unravelled, the current evidence provides a strong foundation for preventive action. Healthcare professionals are well-positioned to advocate for a cultural shift towards more home-cooked meals and smarter restaurant choices, while supporting broader public health policies that make the healthy option the easier option for all residents of Hong Kong.

Reference

1. Du Y, et al. Association Between Frequency of Eating Away-From-Home Meals and Risk of All-Cause and Cause-Specific Mortality. J Acad Nutr Diet. 2021 Sep;121(9):1741-1749.e1. doi: 10.1016/j.jand.2021.01.012.

Melatonin: Heart Failure's Friend or Foe?

by Jasmine Lai



Synthetic melatonin is widely available as an over-the-counter (OTC) supplement in many regions including Hong Kong (and by prescription elsewhere) as an aid for sleep issues like insomnia and jet lag[1]. However, new findings have linked chronic melatonin use to a higher risk of heart failure, hospitalization, and all-cause mortality, based on a comparison of the health records from over 130,000 adults with insomnia and a melatonin prescription for at least a year and those without (though it is unclear if it excluded OTC melatonin consumption)[1].

This comes as a surprise for many as melatonin was previously understood to be safe, with experimental studies demonstrating the cardioprotective effects of endogenous melatonin[2-4]. While we wait for the full study results to be published, the concerning association prompts re-examining of previous research. One such study includes a systematic review and meta-analysis published in March 2025 that looked at melatonin's potential as a 'novel drug treatment' for heart failure patients[5].

What is the current evidence on melatonin and heart health?

Background

- **Endogenous melatonin is known to be cardioprotective** against ischemic injury, oxidative stress, apoptosis, and cardiac remodeling[3]
- Melatonin may slow down the heart rate at night and reduce hypertension[4]
- Experimental studies support the potential use of melatonin as preventive/ adjunctive curative therapy in heart failure[3]

What was the study aim?

Study objectives

To investigate the positive effect of melatonin on heart failure development[5]

How was the study conducted?

Methods

Systematic review and meta-analysis of randomised controlled trials[5]

What was studied?

Results

3 articles were selected for data analysis on:[5]

- Quality of life
- Ejection fraction
- New York Heart Association Functional Class (NYHA FC)

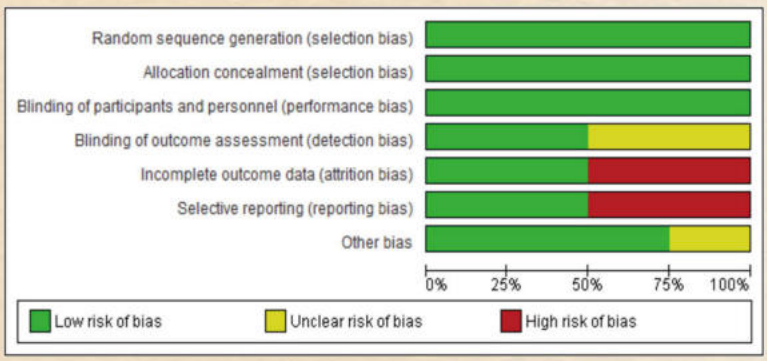


Fig. 1. *Risk of bias assessment*[5]

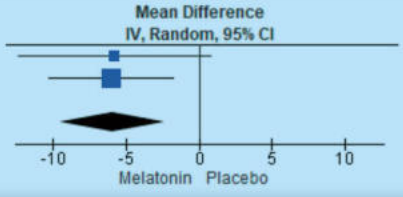
What did they find?

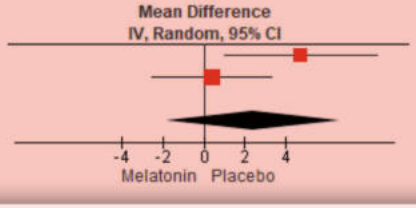
Results

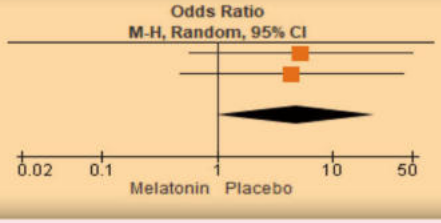
Study characteristics:[5]

	Melatonin (n)	Placebo (n)	Gender M/F (n)	Age (mean) Melatonin/Placebo	Intervention
Garakyaraghi et al. 2012	23	16	27/12	63.6 (±6.6)/ 65.8 (±12.5)	3 mg/day for 8 weeks
Hoseini et al. 2022	42	43	80/12	63.5 (±22.89)/ 58.5 (±15.15)	10 mg/day for 24 weeks
Jafari-Vayghan et al. 2022	18	17	25/10	55.78 (±11.57)/ 50.82 (±11.22)	20 mg/day for 24 weeks

Outcome vs placebo[5]	Mean difference/Odds ratio[5]	Quality of evidence[5]
1 Improved quality of life by 5.95 [CI −9.54, −2.35] *P*=0.001	Hoseini et al. 2022 Jafari-Vayghan et al. 2022 I^2=0%	Moderate*
2 Higher ejection fraction by 2.39 [CI −1.82, 6.59] *P*=0.27	Hoseini et al. 2022 Jafari-Vayghan et al. 2022 I^2=0%	Low**
3 Lower NYHA FC by 4.84 [CI 1.00, 23.44] *P*=0.05	Garakyaraghi et al. 2012 Hoseini et al. 2022 I^2=0%	Low**







*Moderate: the true effect is likely close to the effect estimate, but it could be substantially different from the effect estimate[5].
**Low: the true effect may be substantially different from the estimate of the effect[5].

What does this study tell us?

Conclusion

- Although the study looked at randomised controlled trials, the sample size was small[5]
- The results for heart-related outcomes are insignificant but it suggests that that melatonin consumption may be slightly protective[5]
- Overall, synthetic melatonin may not play a significant role in cardiac protection
- **Currently there is a lack of strong evidence supporting its role in heart failure**

Abbreviations: CI, confidence interval; NYHA FC, New York Heart Association Functional Class

References: 1. American Heart Association. Newsroom. Long-term use of melatonin supplements to support sleep may have negative health effects. https://newsroom.heart.org/news/long-term-use-of-melatonin-supplements-to-support-sleep-may-have-negative-health-effects [Accessed 27 November 2025]. **2.** Medical News Today. Long-term melatonin use linked to 90% greater heart failure risk. Available at: https://www.medicalnewstoday.com/articles/long-term-melatonin-use-linked-to-90-greater-heart-failure-risk [Accessed 27 November 2025]. **3.** Nduhirabandi F, Maarman GJ. Molecules 2018;23:1819. **4.** Simko F et al. J Pineal Res 2016;61(2):127-37. **5.** Daliri AS et al. Clin Cardiol. 2025 Mar;48(3):e70107.

by Dr. Roy Lau

Cardiovascular-Kidney-Metabolic (CKM) Syndrome: Why and How It Matters for Every Primary Care Physician

Dr. Chow Kai Ming
Council Member
Hong Kong Kidney Foundation
and Hong Kong Society of Nephrology

The epidemic of non-communicable diseases, including obesity, type 2 diabetes mellitus (DM), cardiovascular disease (CVD), and chronic kidney disease (CKD), is escalating and widely acknowledged in industrialized nations, while the interconnection of these diseases has been collectively conceptualized as the Cardiovascular-Kidney-Metabolic (CKM) syndrome[1]. The conceptualization of CKM syndrome enables a multidisciplinary approach in the risk stratification, early prevention, and treatment of the vicious circle generated by the interaction among disease components. In addition to specialist care, the involvement of primary care is vital for providing holistic care for patients with CKM syndrome. Accordingly, in a recent symposium titled "Cardiovascular-Kidney-Metabolic (CKM) syndrome: Why and How It Matters for Every Primary Care Physician" jointly organized by the Hong Kong Society of Nephrology (HKSN), the Hong Kong Kidney Foundation (HKKF), and the Hong Kong Association of Renal Nurses (HKARN), Dr. Chow Kai Ming was invited to discuss the pathophysiology of CKM syndrome and practical issues in managing the disease.

CKM Syndrome – A Multidisciplinary Challenge

Dr. Chow emphasized that metabolic disorders often occur together. For instance, approximately 25%–40% of patients with heart failure (HF) have DM, and approximately 40%–50% of patients with HF have CKD. Both DM and CKD are associated with increased risk of incident HF. Importantly, the combination of these 3 comorbidities is associated with a substantially increased risk for hospitalization and mortality[2]. Given that patients would suffer from complications in various

organs, Dr. Chow highlighted that multidisciplinary care is essential in managing CKM syndrome. In particular, primary care physicians are the initial point of care for patients with various chronic diseases. "There may be limited treatment options available if the patients were referred to specialty care after advanced complications have developed," Dr. Chow expressed. Thus, the roles of primary care physicians in identifying CKM patients and facilitating early treatment are crucial.

Given the complex interaction among the disease conditions, managing CKM syndrome is clinically challenging. However, Dr. Chow further noted that the challenge can be intensified by clinical inertia of physicians, which refers to the phenomenon of failing to initiate or intensify treatment for patients who are not achieving evidence-based therapeutic goals[3]. Accordingly, regular review and optimization of the management protocol for CKM patients is required.

Urine Albumin-creatinine Ratio - A Cost-effective and Essential Test Indicating CVD Risk

The clustering of condition under the umbrella of CKM syndrome not only highlights the risk of comorbid conditions but also establishes a holistic framework that incorporates screening, staging, and management to facilitate the early identification of potential CKM-related events[4]. In view of the conglomeration of metabolic disorders, Dr. Chow noted that CKM syndrome cannot be managed by a single specialty alone, whereas primary care physicians who have the patients' comprehensive clinical information are helpful in providing holistic care. Notably, a recent consensus recommendation on the management of CKD in Hong Kong advocated that primary care plays a core role in the strategies to improve patient awareness of CKD, adherence to treatment, and achievement of CKD care goals[5].

In evaluating the risk of CVD, Dr. Chow specifically recommended the PREVENT™ risk calculator formulated by the American Heart Association (AHA) in 2023, which includes urine albumin-creatinine ratio (ACR), body mass index (BMI), and glomerular filtration rate (GFR) as predictors[6]. Remarkably, Dr. Chow emphasized that the ACR test is cost-effective for accurately estimating the risk of CKM syndrome.

Dr. Chow illustrated the clinical significance of ACR test with the case of a female patient aged 60 years, who was a non-smoker and had hypertension with a history of gout. The patient was non-diabetic, with fasting glucose of 6.2 mmol/L and HbA1c of 5.7%. The cholesterol and LDL-C levels were 4.9 mmol/L and 2.4 mmol/L, respectively. Also, normal computed tomography coronary angiography (CTCA) is reported. Based on the AHA 2013 formula, which focuses on CV parameters only, the estimated 10-year CVD risk for the patient was 6.5%, suggesting statin therapy was not needed. In contrast, using the PREVENT™ risk calculator with the ACR test result, the estimated CVD risk was significantly higher (>10%), indicating the need for statin treatment. In this regard, the updated calculation of risk coupled with the appropriate clinical test will guide the appropriate treatment decision.

Moreover, an analysis of the data from NHANES III by Afkarian *et al.* (2013) revealed that the presence of albuminuria significantly increased mortality risk among DM patients (**Figure 1**)[7]. Hence, albuminuria has been included as one of the markers of kidney damage in the KDIGO 2024 Clinical Practice Guideline[8].

Overcoming Clinical Inertia

Despite effective clinical tests and treatments being available, it takes an average of 17 years to move them from clinical evidence to daily practice[9]. For instance, while an ACR test is crucial for guiding evidence-based treatments to mitigate CKD progression and CV morbidity, a meta-analysis by Shin *et al.* (2021) suggested that the ACR screening rate was only 35.1% in diabetes and 4.1% in hypertension[10]. Dr. Chow highlighted that about 60% of local DM patients in 4 general medical clinics under the Hospital Authority (HA) had not been screened for urine ACR in 2022. This reflects that improving the detection of CKM syndrome by enhancing the ACR screening rate is urgently needed. "I place 10-20 urine bottles in a "kidney dish" on my consultation desk everyday as a visual cue reminding myself to test ACR for my patients," Dr. Chow suggested.

Apart from ACR screening, therapeutic inertia can be another clinical problem. Dr. Chow particularly addressed the issue of intensive control in managing hypertension. According to the SPRINT trial, which involved 9,361 with a systolic blood pressure of 130 mmHg or higher and an increased cardiovascular risk,

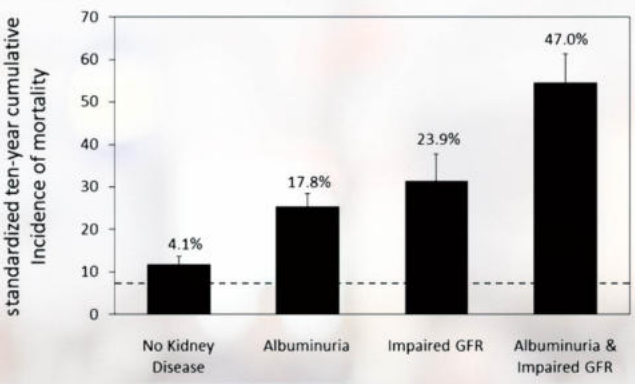


Figure 1: 10-year mortality in DM by kidney disease manifestation[7]

intensive control targeting a systolic blood pressure (SBP) of <120 mmHg resulted in significantly lower rates of fatal and nonfatal major CV events (**Figure 2**) and death from any cause as compared to standard control, which targeted systolic blood pressure at 140 mmHg[11]. Moreover, a subgroup analysis of the SPRINT trial indicated that intensive control of SBP to <120 mmHg resulted in significantly lower rates of fatal and nonfatal major cardiovascular events and death from any cause. Remarkably, the impact of intensive control was more pronounced among older patients with higher frailty[12]. Hence, Dr. Chow commented that a lenient hypertension treatment for frail patients is not advisable.

More recently, a meta-analysis of 6 randomized controlled trials (RCTs) accounting for 80,220 participants by Guo *et al*. (2025) confirmed that, after a median follow-up of 3.2 years, intensive blood pressure control provides a net benefit between the reduction in CV events and the increase in adverse events, including renal events, compared with standard control[13]. "Although there may be potential harm for intensive control, it has to be 3 times more adverse events to outweigh the harm from its benefits. Thus, withholding intensive blood pressure control is not good for patients," Dr. Chow commented.

The Role of Medications in Managing CKM Syndrome

To demonstrate the clinical management of patients with established CKM syndrome, Dr. Chow shared the case of another female patient aged 77 years who had been diabetic since 1997 and had triple-vessel coronary disease requiring coronary artery bypass graft (CABG) in 2010. The patient's left ventricular ejection fraction (LVEF) was 45% and eGFR was 33 ml/min/1.73m^2. The patient was initially treated with losartan, carvedilol, linagliptin, and rosuvastatin since 2015. Upon the addition of empagliflozin to the treatment regimen, the urine ACR decreased from 28.7 mg/mmol in July 2019 to 9.96 mg/mmol in July 2023. Finerenone was then

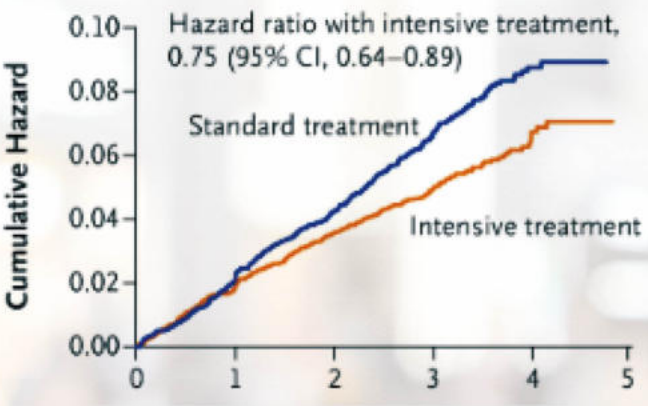


Figure 2: Primary outcome at 1 year in the SPRINT trial[11]

prescribed and the urine ACR was further reduced to 4.40 mg/mmol in April 2024. "Even for advanced CKM diseases, there are still many effective treatment options available," Dr. Chow noted.

Together with renin-angiotensin system (RAS) blockade, sodium-glucose co-transporter-2 inhibitors (SGLT2i), non-steroidal mineralocorticoid receptor antagonists (ns-MRA), and glucagon-like receptor-1 receptor agonists (GLP-1RAs) are collectively the 4 pillars of pharmacotherapies in CKM management. Importantly, the KDIGO Clinical Practice Guidelines recommend initiating an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) for patients with DM, hypertension, and albuminuria, and the medications should be titrated to the highest approved dose that is tolerated[14].

In the patient with established CKM symptoms above, hyperkalemia (serum potassium 5.4 mmol/L) and a serum creatinine of 330 µmol/L were observed after prolonged treatment. In this regard, recent clinical studies suggested that discontinuation of RAS inhibitors in patients with advanced CKD was not associated with favorable outcomes[15]. On the contrary, the treatment should be continued to control further CKD progression, with monitoring and maneuvers to control potassium level.

In addition to RAS inhibitors, SGLT2i was prescribed to the patient as well. A key recommendation in the updated KDIGO Guidelines is to prescribe SGLT2is for patients with DM, CKD, and eGFR ≥20 mL/min/1.73m^2 by virtue of the significantly reduced risk of mortality and extended time to dialysis[14]. Notably, Dr. Chow stated that an initial reversible decrease in eGFR can be observed after initiating SGLT2i, which is generally not an indication for discontinuing therapy. Requesting renal function test soon after initiating SGLT2i is therefore not a must. "Apart from the patients, the healthcare sector will be benefiting from the saved treatment costs and time associated with SGLT2i treatment," Dr. Chow opined.

Besides, ns-MRA is a relatively new therapy for managing CKM syndrome. The KDIGO 2024 Guidelines recommend ns-MRA for DM patients with eGFR >25 ml/min/1.73m^2, normal serum potassium concentration, and albuminuria (>3 mg/mmol)[8]. The efficacy of finerenone, a ns-MRA, in reducing CV and kidney events was demonstrated in the FIDELITY pooled analysis (**Figure 3A and 3B**). Remarkably, finerenone was reported to reduce urine ACR by 30% from baseline to 4 months[16]. Dr. Chow reminded us to monitor serum potassium at 1 month, then every 4 months, after initiating finerenone. Finerenone should be withheld when serum potassium

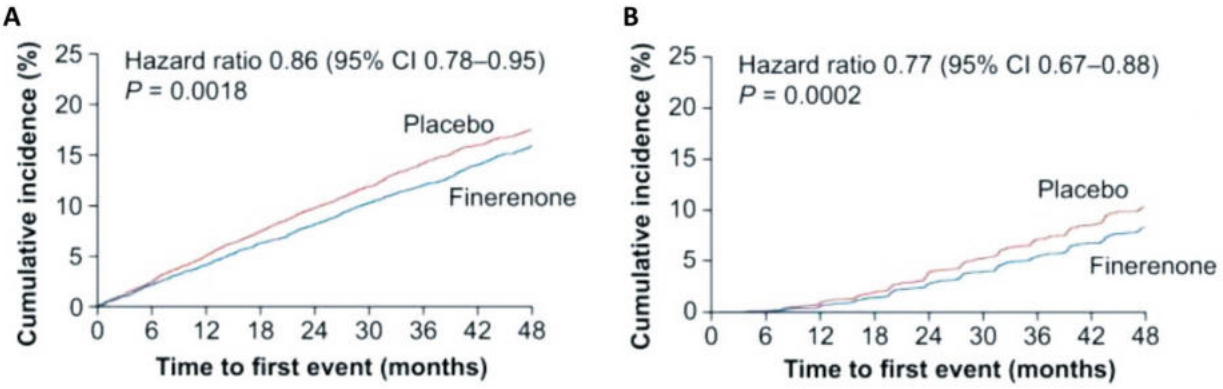


Figure 3: Time to efficacy outcomes, A) composite CV outcomes, B) composite kidney outcomes[16]

is >5.5 mmol/L. Interestingly, the recent CONFIDENCE trial by Agarwal *et al.* (2025), which included patients with CKD and DM, reported that initial therapy with finerenone plus empagliflozin led to a greater reduction in the urinary ACR than either treatment alone[17].

Remarkably, obesity is one of the parameters included in the PREVENT™ risk calculator[6]. GLP-1RAs stimulate insulin release in response to glucose load through incretin release. By delaying gastric emptying and effects on the satiety center in the brain, GLP-1RAs provoke weight loss[18]. In the FLOW trial, which involved 3,533 CKD patients with DM, semaglutide, a GLP-1 RA, significantly reduced the risk of clinically important kidney outcomes and death from CV causes[19]. Thus, GLP-1 RAs can be considered for obese CKD patients. Furthermore, recent pooled analysis suggested that semaglutide reduced the risk of the combined endpoint of CV death or worsening heart failure events in patients with heart failure with mildly reduced or preserved ejection fraction (HFpEF)[20]. The results supported the use of semaglutide to reduce the risk of clinical heart failure events in patients with HFpEF.

The 5 Pillars and Foundation in Countering CKM Syndrome

In summary, Dr. Chow outlined the 5 pillars in CKM management. In addition to the 4 pillars of pharmacotherapies above, statins are the important 5th pillar controlling dyslipidemia. In addition to these 5 pillars, Dr. Chow emphasized the importance of lifestyle modifications, including a low-salt diet, exercise, weight control, and smoking cessation, as the foundation for preventing CKM syndrome. As the final remark, Dr. Chow reminded us to be mindful of clinical inertia in managing CKM syndrome since Stage 0 (no risk factors observed) of the disease.

References

1. Sebastian SA, Padda I, Johal G. Cardiovascular-Kidney-Metabolic (CKM) syndrome: A state-of-the-art review. *Curr Probl Cardiol* 2024; 49. DOI:10.1016/j.cpcardiol.2023.102344. **2.** Vijay K, Neuen BL, Lerma E V. Heart Failure in Patients with Diabetes and Chronic Kidney Disease: Challenges and Opportunities. *Cardiorenal Med* 2022; 12: 1–10. **3.** Lewinski AA, Jazowski SA, Goldstein KM, Whitney C, Bosworth HB, Zullig LL. Intensifying Approaches to Address Clinical Inertia Among Cardiovascular Disease Risk Factors: A Narrative Review. *Patient Educ Couns* 2022; 105: 3381. **4.** Lee CH, Tan G, Tang SCW, *et al.* Incorporating the cardiovascular-kidney-metabolic health framework into the local healthcare system: a position statement from the Hong Kong College of Physicians. *Hong Kong Med J = Xianggang yi xue za zhi* 2025; 31: 58–64. **5.** Tang SCW, Ho KKL, Ko WWK, *et al.* Management of chronic kidney disease: a Hong Kong consensus recommendation. *Hong Kong Med J = Xianggang yi xue za zhi* 2024; 30: 478–87. **6.** Khan SS, Matsushita K, Sang Y, *et al.* Development and Validation of the American Heart Association's PREVENT Equations. *Circulation* 2024; 149: 430–49. **7.** Afkarian M, Sachs MC, Kestenbaum B, *et al.* Kidney disease and increased mortality risk in type 2 diabetes. *J Am Soc Nephrol* 2013; 24: 302–8. **8.** Stevens PE, Ahmed SB, Carrero JJ, *et al.* KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int* 2024; 105: S117–314. **9.** Luyckx VA, Tuttle KR, Abdellatif D, *et al.* Mind the gap in kidney care: translating what we know into what we do. *Kidney Int* 2024; 105: 406–17. **10.** Shin JI, Chang AR, Grams ME, *et al.* Albuminuria Testing in Hypertension and Diabetes: An Individual-Participant Data Meta-Analysis in a Global Consortium. *Hypertens (Dallas, Tex 1979)* 2021; 78: 1042–52. **11.** Wright JT, Williamson JD, Whelton PK, *et al.* A Randomized Trial of Intensive versus Standard Blood-Pressure Control. *N Engl J Med* 2015; 373: 2103–16. **12.** Williamson JD, Supiano MA, Applegate WB, *et al.* Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged ≥75 Years: A Randomized Clinical Trial. *JAMA* 2016; 315: 2673–82. **13.** Guo X, Sun G, Xu Y, *et al.* Benefit-harm trade-offs of intensive blood pressure control versus standard blood pressure control on cardiovascular and renal outcomes: an individual participant data analysis of randomised controlled trials. *Lancet* 2025; 406: 1009–19. **14.** KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int 2022; 102: S1–127. **15.** Bhandari S, Mehta S, Khwaja A, *et al.* Renin–Angiotensin System Inhibition in Advanced Chronic Kidney Disease. *N Engl J Med* 2022; 387: 2021–32. **16.** Agarwal R, Filippatos G, Pitt B, *et al.* Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis. *Eur Heart J* 2022; 43: 474-484A. **17.** Agarwal R, Green JB, Heerspink HJL, *et al.* Finerenone with Empagliflozin in Chronic Kidney Disease and Type 2 Diabetes. *N Engl J Med* 2025; 393: 533–43. **18.** Agarwal R, Fouque D. The foundation and the four pillars of treatment for cardiorenal protection in people with chronic kidney disease and type 2 diabetes. Nephrol Dial Transplant 2023; 38: 253–7. **19.** Perkovic V, Tuttle KR, Rossing P, et al. Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes. *N Engl J Med* 2024; 391: 109–21. **20.** Kosiborod MN, Deanfield J, Pratley R, et al. Semaglutide versus placebo in patients with heart failure and mildly reduced or preserved ejection fraction: a pooled analysis of the SELECT, FLOW, STEP-HFpEF, and STEP-HFpEF DM randomised trials. Lancet *(London, England)* 2024; 404: 949–61.

by Dr. Feng Xue

Speaking More Languages Could Help You Age Better

Population aging is a global health challenge, with accelerated aging linked to cognitive decline and neurodegenerative disorders.[1,2] Recent research published in Nature Aging (November 2025) provides compelling evidence that multilingualism—defined as the regular use of more than one language—acts as a protective factor against accelerated aging.[3] Using biobehavioral age gaps (BAGs) as a direct marker of healthy versus unhealthy aging[2], the study analyzed data from 86,149 participants across 27 European countries. Findings reveal that multilingual individuals exhibit delayed aging trajectories compared to monolinguals, with protective effects increasing alongside the number of languages spoken. These associations remained robust after adjusting for linguistic, physical, social, and sociopolitical confounders, underscoring the potential of multilingualism as a population-wide intervention for healthy aging.[3]

Introduction

The demographic shift toward older populations worldwide has intensified the urgency to identify modifiable factors that promote healthy aging. Aging is associated with structural and functional brain changes, leading to cognitive decline and increased vulnerability to dementia.[1] While lifestyle factors such as physical activity and education are well-established contributors to healthy aging, emerging evidence suggests that multilingualism may offer unique cognitive and functional benefits.[4,5]

Previous studies have linked bilingualism to delayed onset of dementia and enhanced cognitive reserve.[4,6] However, these findings were often limited to clinical cohorts, small sample sizes, and indirect proxies of aging, resulting in mixed conclusions.[4,5,7,8] The recent study by Amoruso et al. addresses these gaps by leveraging large-scale, multi-country data and introducing biobehavioral age gaps (BAGs) as a direct measure of aging trajectories.[3]

Study Design

The analysis included 86,149 participants aged 51–90 years from the Survey of Health, Ageing and Retirement in Europe (SHARE).[9] Individuals with dementia diagnoses were excluded to ensure generalizability to healthy populations. Data harmonization protocols ensured consistency across countries.[2]

BAGs were computed as the difference between predicted age—based on positive and adverse biobehavioral factors—and chronological age.[10] Negative BAG values indicate delayed aging, while positive values reflect accelerated aging. Predictors included:[3]

- **Protective factors:** functional ability, education, preserved cognition, physical activity, and well-being.
- **Risk factors:** cardiometabolic conditions, sensory impairments, unhealthy weight, sleep problems, alcohol consumption and female sex.

A gradient-boosting regression model predicted chronological age using these factors, validated through nested cross-validation and leave-one-country-out strategies to ensure robustness.[3,11]

Multilingualism was assessed at the country level using Eurostat data, categorizing individuals as monolingual or speaking one, two, or three or more additional languages.[3] Cross-sectional analyses estimated odds ratios (ORs) for accelerated aging, while longitudinal analyses calculated relative risks (RRs) over time.[3]

Research Findings

Biobehavioral Predictors of Aging

The model explained 24% of age variance ($R^2 = 0.24$), with functional ability emerging as the strongest predictor. Positive factors correlated with delayed aging, while adverse factors were linked to accelerated aging.[3]

Protective Role of Multilingualism

In cross-sectional analyses, monolinguals were **2.11 times more likely** to experience accelerated aging (OR = 2.11, 95% CI: 1.98–2.24). Conversely, speaking at least one additional language reduced this risk by more than half (OR = 0.46, 95% CI: 0.43–0.49). Protective effects scaled with the number of languages (**Figure 1**):[3]

- One language: OR = 0.77
- Two languages: OR = 0.51
- Three or more languages: OR = 0.64

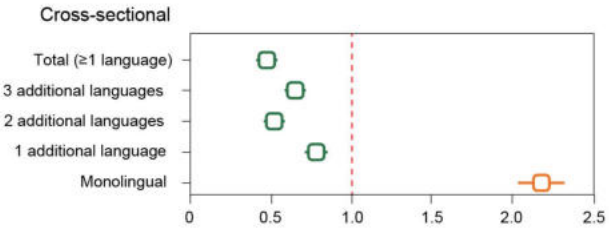


Figure 1: ORs from the cross-sectional analysis[3]

Longitudinal findings mirrored these results. Monolinguals had a **43% higher risk** of accelerated aging over time (RR = 1.43), while multilinguals exhibited progressively lower risks:

- One language: RR = 0.90
- Two languages: RR = 0.80
- Three or more languages: RR = 0.71

Robustness Across Confounders

Adjusting for linguistic, physical, social, and sociopolitical exposomes—including migration, gender equality, air quality, and institutional language policies—did not substantially alter the protective effect of multilingualism. Exceptions included diminished significance for speaking three additional languages after controlling for migration and for one additional language after adjusting for gender inequality.[3]

Age-Stratified Analysis

Protective effects persisted across age cohorts (51–64, 65–77, 78–90 years). However, benefits of speaking only one additional language weakened in older groups, while speaking two or more languages conferred stronger protection with advancing age.[3]

Implications

This study provides robust, population-level evidence that multilingualism delays aging trajectories, as reflected by lower BAGs and reduced risk of accelerated aging. The dose-dependent nature of the effect suggests cumulative cognitive benefits from managing multiple languages, consistent with theories of experience-dependent neuroplasticity.[12] Continuous engagement in multilingual contexts likely strengthens executive and attentional networks, which are critical for cognitive resilience.[13]

Importantly, these findings remained significant after accounting for macro-level factors, reinforcing the domain-independent protective role of multilingualism. Nonetheless, certain conditions—such as migration-related stress or structural inequalities—may attenuate benefits, highlighting the interplay between individual and societal factors.

The strengths of this study include the large, diverse sample, multi-country design, and use of BAGs as direct aging markers. The limitations involve reliance on country-level multilingualism estimates rather than individual metrics, potential cohort effects, and geographic restriction to Europe. Future research should incorporate individual-level language profiles, explore causal mechanisms through experimental designs, and extend analyses to non-European populations.

Conclusion

Multilingualism emerges as a powerful, scalable protective factor against accelerated aging, comparable to other lifestyle interventions emphasized in public health guidelines. By promoting functional ability and cognitive reserve, multilingualism offers a promising avenue for global healthy aging strategies. Integrating language learning into educational and public health frameworks could enhance resilience against age-related decline, reduce health disparities, and improve quality of life across the lifespan.

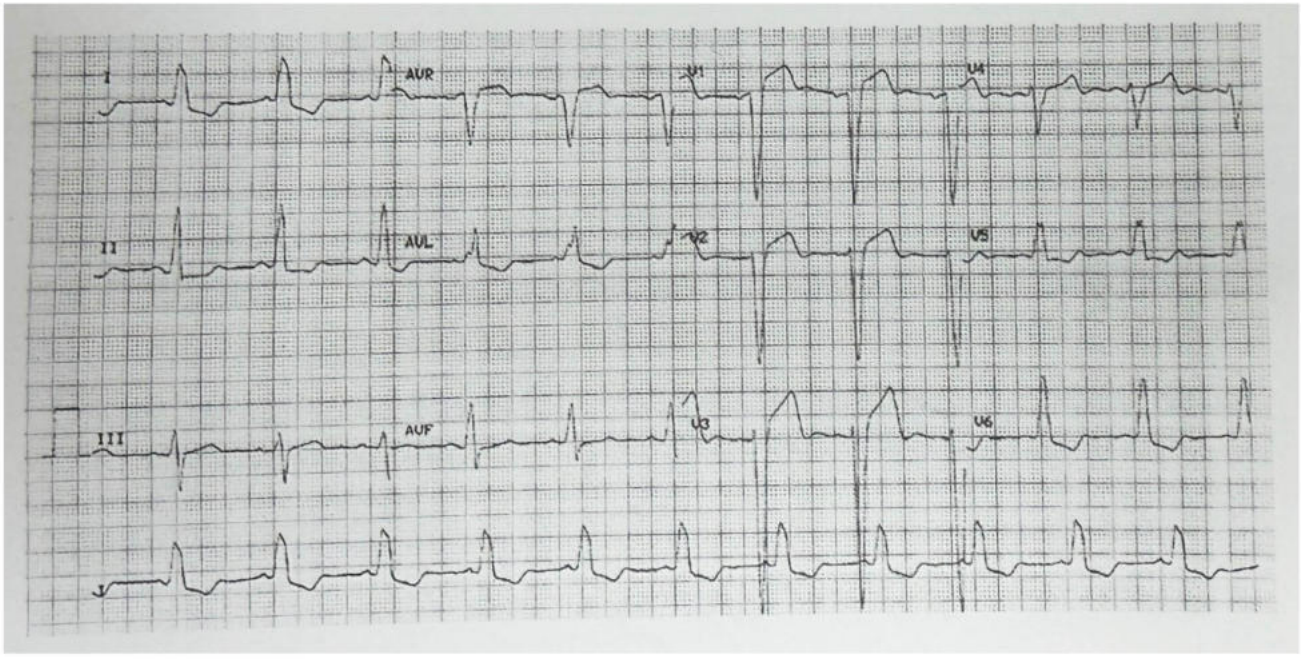
References

1. Fang M, et al. Nat Med. 2025;31: 772–6. **2.** Hernández H, et al. Nat Med. 2025; 31, 3089–100. **3.** Amoruso L, et al. Nat Aging. 2025; 5: 2340–54. **4.** Bialystok E. Trends Cogn Sci. 2021;25, 355–64. **5.** Venugopal A, et al. Alzheimers Dement. 2024;20: 2620–31. **6.** Alladi S, et al. Neurology. 2013;81:1938–44. **7.** Mukadam N, et al. J Alzheimer's Dis. 2017;58: 45–54. **8.** Brini S, et al. Neuropsychol Rev. 2020; 30: 1–24. **9.** Bergmann M, et al. Survey participation in the Survey of Health, Ageing and Retirement in Europe (SHARE), Wave 1–7. Based on Release 7.0.0. SHARE Working Paper Series 41–2019 (MEA, Max Planck Institute for Social Law and Social Policy. 2019). **10.** Ibanez A, et al. Nat Aging. 2024;4:1153–65. **11.** Jeong CU, et al. JMIR Aging. 2025;8:e64473. **12.** Pliatsikas C. Biling Lang Cogn. 2020;23: 459–71. **13.** Rothman J. Biling Lang Cogn. 2024;28: 793–801.

ECG CME DECEMBER 2025 (0.5 CME POINTS)

Dr. Pun Chiu On, Specialist in Cardiology

History: This 35 years old man complained of progressive exertional dyspnoea in past few months. This was his ECG.



Questions:

What is the ECG diagnosis?

A) Normal ECG

B) Complete right bundle branch block

C) Complete left bundle branch block

D) Acute myocardial infarction

E) Wolff-Parkinson-White syndrome

This ECG CME was prepared by Dr. Pun Chiu On, Specialist in Cardiology.

Please complete the Self-Study by visiting our website: https://cmevideo.hkdu.org/ or scan the QR code to submit your answers on or before ***28-January-2026***

SCAN ME

Answer to October Issue's CME

ECG diagnosis: First degree A-V block.

Reason for the ECG diagnosis:

First degree A-V block is diagnosed when PR interval (onset of P wave to onset of QRS complex) is greater than 0.2 seconds (i.e. more than 5 small squares, or more than 1 big square).
In this ECG, the PR interval is 0.24 seconds (i.e. 6 small squares). Therefore, first degree A-V block is diagnosed.
The other abnormalities in this ECG are:
(1) Supraventricular ectopic beats, which occasionally showed aberration as in V2.
(2) Old inferior myocardial infarction with pathological Q waves in leads III and aVF.

Possible aetiology:

- Normal variation.
- Increased in vagal tone and vagal stimulation.
- Drugs: digoxin, β -blockers, calcium antagonist such as verapamil and diltiazem.
- All sorts of cardiac diseases including ischaemia, rheumatic, cardiomyopathy, myocarditis, etc.

Significance:

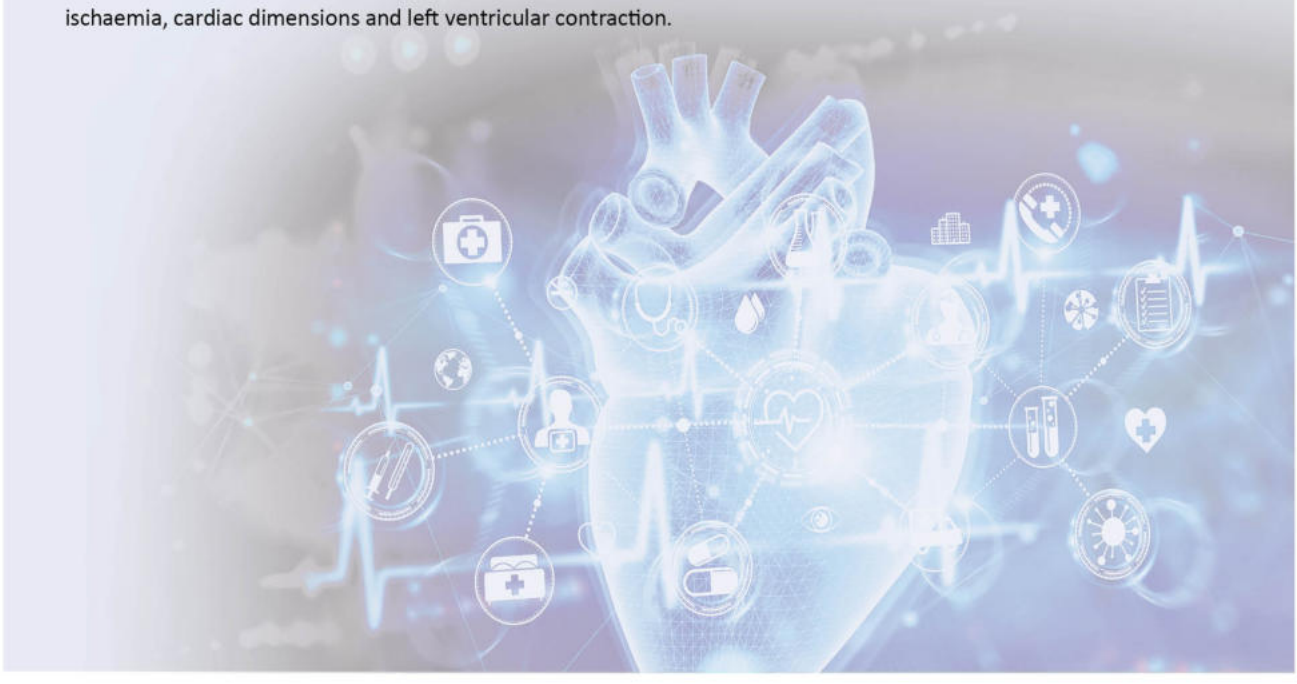
First degree A-V block by itself will not cause any adverse effect and requires no treatment.

Principle of management:

- Ask for history of heart disease and drug history.
- Physical examination to look for any cardiac disease.
- Manage the underlying cardiac disease, if any.
- If no cardiac disease is found and patient is not on any of the above drugs, no treatment is required.

Management of this patient:

- Although this patient has no heart disease from history and physical examination, and he is not on any of the above medication, further cardiac investigation would be advisable because of these ECG abnormalities. Diabetes mellitus could lead to ischaemic heart disease and diabetic cardiomyopathy. Also, diabetic patients could have silent ischaemia or silent infarction.
- Cardiac MRI would, in addition for diagnosis of old myocardial ischaemia, also enable assessment of any residual ischaemia, cardiac dimensions and left ventricular contraction.



by Dr. Feng Xue

Hong Kong Doctors Union Celebrates 59th Anniversary with Grand Gala Dinner

1966 2002 2025

The Hong Kong Doctors Union marked its 59th anniversary with a vibrant gala dinner celebration on the evening of 25 November, bringing together medical professionals and distinguished guests to honor nearly six decades of service and solidarity within the healthcare community. The event, themed "*59 Years of Caring Together,*" featured lively activities including a lucky draw and karaoke sessions, creating an atmosphere of camaraderie and joy.

The evening was hosted by **Dr. Luk Wai Leung Sunny**, President of the Hong Kong Doctors Union; and **Dr. She Siu Yam Dominic** and **Dr. Yam Chun Yin Abraham**, Vice-Presidents of the Union. In a special video address, **Professor Lo Chung-mau**, Hong Kong's Secretary for Health, and **Dr. Ronald Lam Man-kin**, Director of Health, extended their congratulations and praised the Union's longstanding contributions to the medical profession.

Among the notable attendees were:

- **Mr. Chen Zetao**, Deputy Director-General of the Coordination Department of the Liaison Office of the Central People's Government in the HKSAR
- **Dr. Leung Chi-hung**, respected medical leader
- **Professor Wu Yilong**, President of the Guangdong Medical Association, China
- **Dr. Pang Fei-chau**, Commissioner for Primary Healthcare, Health Bureau, the Government of Hong Kong

Founded as the Estate Doctors Association Ltd. in 1966, the organization initially focused on supervising the allocation of public housing estate clinics. Over time, it evolved into a robust advocate for doctors' welfare and rights. In 2000, the association transitioned into the Hong Kong Doctors Union Ltd., and by 2002, it had fully embraced its mission to serve all doctors in Hong Kong—be they employed or self-employed—by promoting their legitimate rights, welfare, recreation, and continuous professional development.

As the only trade union in Hong Kong dedicated exclusively to doctors, the Hong Kong Doctors Union continues to play a pivotal role in fostering unity within the profession and advancing healthcare standards for the community.

President Luk Wai Leung Sunny kick-starts the celebration together with the distinguished guests (from left to right: Professor Wu Yilong, Dr. Pang Fei-chau, President Luk Wai Leung Sunny, Mr. Chen Zetao, and Dr. Leung Chi-hung)

by Migee Tang

On-the-Pulse

Reproductive Medicine

Herbal Boost for Fertility[1]

New preclinical research suggests that the traditional Chinese herbal formula, Jinfeng Pills, may help restore endometrial receptivity in cases of thin endometrium, a challenging cause of infertility. In a rat model of endometrial injury, treatment with Jinfeng Pills significantly increased endometrial thickness, improved glandular and vascular density, and restored normal uterine architecture. The effects were accompanied by increased expression of key molecular markers involved in angiogenesis and implantation. Thin endometrium, typically defined as an endometrial thickness of <7 mm, is associated with reduced implantation rates and limited therapeutic options. These findings provide early mechanistic insight into how traditional herbal formulations may support endometrial repair and uterine receptivity, highlighting a potential avenue for integrative approaches in reproductive medicine.

Dentistry

From Kitchen to Clinic: Garlic for Oral Health?[2]

A recent systematic review suggests that garlic-based mouthwashes may match the antimicrobial effectiveness of chlorhexidine, the current gold standard in oral antiseptics. Higher concentrations of garlic extract were found to be comparable to chlorhexidine in reducing harmful oral bacteria, with some studies indicating longer-lasting antimicrobial activity. While garlic mouthwashes were associated with increased discomfort and an unpleasant odor, reported side effects were generally less severe than those linked to synthetic agents. Key antimicrobial effects are thought to be driven by allicin, a bioactive compound in garlic. Although promising, the authors emphasize the need for larger, standardized clinical studies to confirm efficacy and define garlic's role as a practical natural alternative in routine oral care.

Nutrition

Social Meals Linked to Better Nutrition in Older Adults[3]

A major international review suggests that who older adults eat with may be just as important as what they eat. Older adults who regularly eat alone are more likely to experience poorer diet quality, lower intake of fruits, vegetables and protein-rich foods, and a higher risk of weight loss and frailty. Data from over 80,000 independently living adults aged 65 and above across 12 countries were analysed and findings highlight shared meals as a potentially modifiable factor in healthy ageing, with social engagement shown to influence appetite, food variety and overall wellbeing. Experts suggest that simple interventions like community dining programs or social screening in primary care could help identify at-risk individuals and support better nutrition. The study underscores the growing recognition that mealtimes are not just biological, but social and emotional experiences with direct health implications.

Ophthalmology

Innovative Retinal Implant Restores Functional Vision[4]

A tiny wireless retinal implant has help patients with advanced age-related macular degeneration (AMD) regain usable vision in a recent trial. 81% of participants showed clinically meaningful improvements in visual acuity, with most able to read letters, numbers, and short words after one year. Patients gained 25 letters on a standard eye chart on average, which equates to about five lines of vision. The implant works by replacing damaged photoreceptors with a 2×2 mm wireless chip that converts light into electrical signals. Images captured by camera-equipped glasses are projected onto the implant, stimulating remaining retinal cells and sending visual information to the brain. While it doesn't restore perfect vision, the device could help many patients move above the threshold for legal blindness.

Cardiology

Unstiffening Ageing Hearts – RBM20-ASO[5]

Researchers have identified a promising experimental drug that could treat heart failure with preserved ejection fraction (HFpEF), the most common type of heart failure for which no therapy currently reduces mortality. In animal studies, the drug RBM20-ASO improved the heart's ability to relax and fill with blood by increasing heart muscle flexibility. The treatment works by modulating RBM20, a key regulator of titin, a spring-like protein that controls heart muscle stiffness. The drug restored heart compliance and reduced abnormal heart thickening in mouse models of HFpEF. Importantly, researchers found that only moderate doses were needed, limiting side effects. Further safety testing in larger animal models is underway. If successful, this approach could become the first disease-modifying therapy for HFpEF, targeting the root cause of heart stiffness rather than just symptoms.

Psychiatry

Voices in the Mind: Schizophrenia Hallucinations and Misidentified Inner Speech[6]

New research suggests that auditory hallucinations in schizophrenia may occur when the brain fails to recognize its own "inner speech", the silent voice most people use to think. Researchers compared EEG recordings between schizophrenic patients who do and do not regularly hear voices with healthy participants. In healthy individuals, the brain dampens its response to self-generated speech because it predicts the sound. In people actively experiencing hallucinations, the brain responded more strongly as if the voice came from an external source. This finding provides the strongest evidence to date that hallucinated voices may in fact be misidentified self-talk. This brain response could potentially become a biomarker to identify people at risk of psychosis earlier, opening the door to faster diagnosis and more targeted treatments.

"Fostering Innovation Through Continuous Medical Education with On the Pulse"

References

1. Gao H, et al. Reproductive and Developmental Medicine 2025;9(3):149-156. DOI: 10.1097/RD9.0000000000000140. **2.** Abdelaal YA, et al. Journal of Herbal Medicine 2025;54:101053. DOI: 10.1016/j.hermed.2025.101053. **3.** Wyman C, et al. Appetite. Published online September 26, 2025. DOI:10.1016/j.appet.2025.108327. **4.** Holz FG, et al. N Engl J Med. Published online October 20, 2025. DOI:10.1056/NEJMoa2501396. **5.** Methawasin M, et al. Cardiovasc Res 2025;121(13):2027-2041. DOI:10.1093/cvr/cvaf171. **6.** Whitford TJ, et al. Schizophr Bull. Published online October 21, 2025. DOI:10.1093/schbul/sbaf167.

Oncology:

EVEROLIMUS TEVA® TABLETS 10 MG

(everolimus)

TEVA

HK Reg. No. HK-68853 (17 Sep, 2025)

Composition[1]:

- Each tablet contains 10 mg everolimus

Indication[1]:

- Hormone receptor-positive advanced breast cancer
  - Everolimus is indicated for the treatment of hormone receptor-positive, human epidermal growth factor receptor 2 (HER2/neu) negative advanced breast cancer, in combination with exemestane, in postmenopausal women without symptomatic visceral disease after recurrence or progression following a non-steroidal aromatase inhibitor
- Neuroendocrine tumors of pancreatic origin
  - Everolimus is indicated for the treatment of unresectable or metastatic, well- or moderately-differentiated neuroendocrine tumors of pancreatic origin in adults with progressive disease
- Neuroendocrine tumors of gastrointestinal or lung origin
  - Everolimus is indicated for the treatment of unresectable or metastatic, well-differentiated (Grade 1 or Grade 2) non-functional neuroendocrine tumors of gastrointestinal or lung origin in adults with progressive disease
- Renal cell carcinoma
  - Everolimus is indicated for the treatment of patients with advanced renal cell carcinoma, whose disease has progressed on or after treatment with vascular endothelial growth factor (VEGF)-targeted therapy

Infectious Disease:

VAXIGRIP®

(influenza virus)

SANOFI

HK Reg. No. HK-68857 (24 Sep, 2025)

Composition[2]:

- VAXIGRIP® is a trivalent influenza vaccine available as a 0.5 ml suspension for injection in a pre-filled syringe. It contains inactivated, split influenza virus strains (H1N1, H3N2-like, and b/brisbane/60/2008-like)

Indication[2]:

VAXIGRIP® is indicated for the prevention of influenza disease caused by the two influenza A virus subtypes and the influenza B virus type contained in the vaccine for:

- active immunization of adults, including pregnant women, and children from 6 months of age and older
- passive protection of infant(s) from birth to less than 6 months of age following vaccination of pregnant women

The use of VAXIGRIP® should be based on official recommendations on vaccination against influenza

THE FIRST AND ONLY BTKi APPROVED IN FOLLICULAR LYMPHOMA

BRUKINSA® + Obinutuzumab reduced the relative risk of progression or death by 50% vs obinutuzumab alone[1]

Approx. 70% of patients had sustained responses at 18 months with BRUKINSA® + Obinutuzumab[1]

Reference

1. Zinzani PL, Mayer J, Flowers CR, et al. ROSEWOOD: A Phase II Randomized Study of Zanubrutinib Plus Obinutuzumab Versus Obinutuzumab Monotherapy in Patients With Relapsed or Refractory Follicular Lymphoma. J Clin Oncol. 2023; 41(33):5107-5117

Abbreviated Prescribing Information

Presentation: BRUKINSA® (zanubrutinib) capsules 80mg. **Indication:** BRUKINSA® as monotherapy is indicated for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy. BRUKINSA® as monotherapy is indicated for the treatment of adult patients with marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based therapy. BRUKINSA® as monotherapy is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL). BRUKINSA® in combination with obinutuzumab is indicated for the treatment of adult patients with refractory or relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies. **Dosage & Administration:** The recommended total daily dose of BRUKINSA® is 320 mg. The daily dose may be taken either once daily (four 80 mg capsules) or divided into two doses of 160 mg twice daily (two 80 mg capsules). **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Special Warnings & Precautions:** (1) Haemorrhage: Warfarin or other vitamin K antagonists should not be administered concomitantly with BRUKINSA®. Patients should be monitored for signs and symptoms of bleeding and monitor complete blood counts. Consider the risks and benefits of anticoagulant or antiplatelet therapy when co-administered with BRUKINSA®, (2) Infections: Consultation with a liver disease expert physician is recommended for patients who test positive for HBV or have positive hepatitis B serology, before initiating treatment. Patients should be monitored and managed according to the medical standards to prevent hepatitis B reactivation. Consider prophylaxis according to standard of care in patients who are at increased risk for infections. Patients should be monitored for signs and symptoms of infection and treat appropriately, (3) Cytopenia: Monitor complete blood counts monthly during treatment, (4) Second primary malignancies including skin cancer: Advise patients to use sun protection, (5) Atrial fibrillation and flutter: Monitor signs and symptoms for atrial fibrillation and atrial flutter and manage as appropriate, (6) Women of childbearing potential: Women of childbearing potential must use a highly effective method of contraception while taking BRUKINSA®, (7) BRUKINSA® contains sodium: This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'. **Undesirable effects:** The most commonly occurring adverse reactions (≥20%) were neutropenia, thrombocytopenia, upper respiratory tract infection, haemorrhage/haematoma, rash, bruising, anaemia, musculoskeletal pain, diarrhoea, pneumonia and cough. Refer to the full prescribing information for other undesirable effects. **Interactions:** If a strong and moderate CYP3A inhibitor must be used, reduce the BRUKINSA® dose for the duration of the inhibitor use. Concomitant use with strong and moderate CYP3A inducers should be avoided. No clinically significant differences in BRUKINSA® pharmacokinetics were observed when co administered with gastric acid reducing agents. **Pregnancy & Lactation:** BRUKINSA® should not be used during pregnancy. Breast-feeding should be discontinued during treatment with BRUKINSA®. **Full prescribing information should be consulted prior to prescribing.**

Brukinsa® zanubrutinib 80mg capsules

BeiGene

BeiGene (Hong Kong) Co., Ltd.
Room 2701, Level 27, One Chinachem Central,
22 Des Voeux Road Central, Central, Hong Kong

VV-QDOC-229771 Approved on 28 Jan 2025

Hematology:

JAYPIRCA®

(pirtobrutinib)

ELI LILLY

HK Reg. No. HK-68865, HK-68866 (08 Oct, 2025)

Composition[3]:

- Each film-coated tablet contains 50/100 mg of pirtobrutinib

Indication[3]:

- JAYPIRCA® as monotherapy is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) who have been previously treated with a Bruton tyrosine kinase (BTK) inhibitor
- JAYPIRCA® as monotherapy is indicated for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) who have been previously treated with a BTK inhibitor

Hepatology:

HEPWIN®

(entecavir)

VIATRIS

HK Reg. No. HK-68889 (28 Oct, 2025)

Composition[4]:

- Each film-coated tablet contains entecavir monohydrate equivalent to 0.5 mg entecavir

Indication[4]:

- Indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults with:
  - compensated liver disease and evidence of active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active inflammation and/or fibrosis
  - decompensated liver disease
- For both compensated and decompensated liver disease, this indication is based on clinical trial data in nucleoside naive patients with HBeAg positive and HBeAg negative HBV infection
- Also indicated for the treatment of chronic HBV infection in nucleoside naive pediatric patients from 2 to <18 years of age with compensated liver disease who have evidence of active viral replication and persistently elevated serum ALT levels, or histological evidence of moderate to severe inflammation and/or fibrosis

References

1. EMC. Everolimus 10 mg Tablets.4 April 2024. Available from: https://www.medicines.org.uk/emc/product/12240/smpc#gref. [Accessed 18 November 2025]. **2.** EMC. Vaxigrip suspension for injection in pre-filled syringe. 9 July 2025. Available from: https://www.medicines.org.uk/emc/product/100673/smpc#gref. [Accessed 18 November 2025]. **3.** EMA. Jaypirca Summary of Product Characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/jaypirca-epar-product-information_en.pdf. [Accessed 18 November 2025]. **4.** EMA. Summary of Product Characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/entecavir-viatris-epar-product-information_en.pdf. [Accessed 18 November 2025].

Keep Up With the Pace of Drug Development Evolution and Discover the Newly Launched Treatment in Hong Kong

ONCE-WEEKLY
wegovy® 一週一次 維秀美®
semaglutide injection 2.4 mg

Wegovy®: the ONLY weight management medication recommended by cardiology guidelines[6]*

Your Trustworthy Choice for Transformative Weight Loss and Heart Protection[1-4]

≥20%
WEIGHT LOSS

Achieved by ~1 in 3 patients treated over 68 weeks[2,3*]

20%
REDUCTION IN MACE

vs placebo on top of CV standard of care in adults with established CVD[4†]

(HR=0.80; 95% CI=0.72-0.90; p<0.001)

>20
MILLION

patients treated with semaglutide worldwide since launch[5]

NOW AVAILABLE

*__STEP 1__ was a double-blind trial that enrolled 1961 adults with BMI ≥ 30 kg/m² (≥ 27 kg/m² in persons with ≥ 1 weight-related coexisting condition) who did not have diabetes. Participants were randomly assigned in 2:1 ratio to 68 weeks of treatment with once-weekly subcutaneous semaglutide (2.4 mg) or placebo, plus lifestyle intervention. On-treatment data at week 68 showed that 34.8% of the participants on semaglutide had weight loss of ≥ 20%.[2] __STEP 4__ was a randomized clinical trial that evaluated the effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity.[3] †__SELECT__ was a multicenter, double-blind, randomized, placebo-controlled, event-driven superiority trial that enrolled patients aged ≥ 45 who had preexisting CVD and BMI ≥ 27 kg/m² but no history of diabetes. Patients were randomly assigned in a 1:1 ratio to receive once-weekly subcutaneous semaglutide (2.4 mg) or placebo. The primary CV end point was a composite of death from CV causes, non-fatal myocardial infarction, or non-fatal stroke in a time-to-first-event analysis.[4] ‡__2024 ESC Guidelines for the management of chronic coronary syndromes:__ semaglutide should be considered in chronic coronary syndrome patients without diabetes, but with overweight or obesity (BMI ≥ 27 kg/m²) to reduce CV mortality, myocardial infarction, or stroke (class of recommendation=IIa; level of evidence=B).[6]
BMI=body mass index; CI=confidence interval; CV=cardiovascular; CVD=cardiovascular disease; ESC=European Society of Cardiology; HR=hazard ratio; MACE=major adverse cardiovascular events.

References: 1. Wegovy® Hong Kong Prescribing Information. 2025. **2.** Wilding JPH, et al. N Engl J Med. 2021; 384:989-1002. **3.** Rubino D, et al. JAMA. 2021;325:1414-25. **4.** Lincoff AM, et al. N Engl J Med. 2023;389:2221-32. **5.** Data on File. REF-73669 **6.** Vrints C, et al. Eur Heart J. 2024;45:3415-537.

novo nordisk® 諾和諾德

Novo Nordisk Hong Kong Ltd
Unit 2901-02 & 17, 29/F, Tower A, 83 King Lam Street, Cheung Sha Wan, Kowloon, Hong Kong
Tel: +852 3725 1388 | Fax: +852 2386 0800 | www.novonordisk.com

Scan for Wegovy® Prescribing Information

HK25SEM000025

Hope of life beyond CD30+ lymphoma[1*]

Takeda ONCOLOGY
Takeda Pharmaceuticals (HK) Ltd
P.O. Box 47256
Morrison Hill Post Office Hong Kong
Tel : 2133 9800 Fax : 2856 2728

Abbreviated Prescribing Information (EU-OCT2023 - HK-JAN2024)
ADCETRIS 50 mg powder for concentrate for solution for infusion

Active Ingredient: Brentuximab vedotin **Indication:** Treatment of adult patients with previously untreated CD30+ Stage III or IV Hodgkin lymphoma (HL) in combination with doxorubicin, vinblastine and dacarbazine (AVD). Treatment of adult patients with CD30+ HL at increased risk of relapse or progression following ASCT. Treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma (HL) following autologous stem cell transplant (ASCT) or at least 2 ptior therapies when ASCT or multi-agent chemotherapy is not a treatment option. In combination with cyclophosphamide, doxorubicin and prednisone (CHP) for the treatment of adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL). Treatment of adult patients with relapsed or refractory sALCL. Treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) after at least 1 prior systemic therapy. **Dose & Administration:** Previously untreated HL: in combination with chemotherapy [doxorubicin [A], vinblastine [V] and dacarbazine [D] [AVD]], 1.2mg/kg IV infusion over 30 min on days 1 and 15 of each 28-day cycle for 6 cycles. HL at increased risk of relapse or progression following ASCT & CTCL after at least 1 prior systemic therapy: 1.8 mg/kg IV infusion over 30 min every 3 wk up to max of 16 cycles. Previously untreated sALCL: in combination with chemotherapy (cyclophosphamide [C], doxorubicin [H] and prednisone [P] [CHP]), 1.8 mg/kg IV infusion over 30 minutes every 3 weeks for 6 to 8 cycles. Relapsed or refractory HL & relapsed or refractory sALCL: 1.8 mg/kg IV infusion over 30 min every 3 wk, patients who achieve stable disease or better should receive a minimum of 8 cycles and up to a max of 16 cycles. **Contraindications:** Hypersensitivity to brentuximab vedotin or the excipients. Combined use of brentuximab & bleomycin. **Special Population:** Closely monitor for new or worsening neurological, cognitive or behavioural signs or symptoms suggestive of progressive multifocal leukoencephalopathy (PML); new or worsening abdominal pain suggestive of acute pancreatitis; new or worsening pulmonary symptoms; emergence of serious & opportunistic infections; immediate & delayed infusion-related reactions. Discontinue use if anaphylaxis & Stevens-Johnson syndrome occurs. Patient w/rapidly proliferating tumour & high tumour burden at risk of tumour lysis syndrome. Monitor for symptoms of neuropathy. Patient experiencing new or worsening peripheral neuropathy may require delay & dose reduction or discontinuation of treatment. Monitor CBC prior to therapy; serum glucose. Patient w/ an elevated BMI w/ or w/o history of DM; renal & hepatic impairment; on controlled Na-diet. Women of childbearing potential should use 2 methods of contraception during & until 6 months after therapy. Men should not father a child during therapy & for up to 6 mth after last dose. May affect ability to drive or operate machinery. Childn & elderly. **Adverse Reactions:** Infection, sepsis/septic shock, upper resp tract infection, herpes zoster, pneumonia, herpes simplex, oral candidiasis; neutropenia, anaemia, febrile neutropenia, thrombocytopenia; Decreased appetite, hyperglycaemia, peripheral sensory neuropathy, peripheral motor neuropathy, dizziness; cough, dyspnoea; diarrhoea, nausea, vomiting, constipation, abdominal pain, stomatitis; elevation of ALT/AST, alopecia, pruritus, rash; myalgia, arthralgia, back pain, bone pain; fatigue, pyrexia, infusion-related reactions, chills.

For detailed information, please consult full prescribing information.
For reporting suspected side effects for Takeda products at AE.HongKong@takeda.com
For asking medical information and other inquiries for Takeda products at medinfohk@takeda.com

Reference: 1* Adcetris Package Insert, EU-OCT2023 - HK-JAN2024

C-APROM/HK/ ADCE/0054 (10/2025)